

SYSTEMATIC REVIEW

Comparison of technical, biological, and esthetic parameters of ceramic and metal-ceramic implant-supported fixed dental prostheses: A systematic review and meta-analysis



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The rapid development of implant materials and surface modification techniques has increased success rates in implant prosthodontics, which has made implant treatment a popular choice for patients with missing or unrestorable teeth.¹ The material used for conventional tooth-supported crowns influences periodontal health.² Similarly, the material used for implant-supported crowns may also affect peri-implant health and esthetics, both are important outcome measures.^{3,4}

Ceramic and metal-ceramic restorations are the most common implant-supported fixed dental prostheses (FDPs). Ceramic restorations have good color⁵ and are biocompatible, but they are susceptible to bulk fracture or chipping, which restricts their

ABSTRACT

Statement of problem. Differences between ceramic and metal-ceramic implant-supported fixed dental prostheses are unclear.

Purpose. The purpose of this systematic review and meta-analysis was to compare the technical, biological, and esthetic complication rates of implant-supported ceramic and metal-ceramic restorations.

Material and methods. Six databases were searched to identify randomized controlled clinical trials (RCTs) and prospective and retrospective cohort studies of implant-supported fixed dental prostheses. The survival rate, marginal adaptation, marginal bone loss, pocket probing depth, crown color match, and mucosal discoloration of ceramic and metal-ceramic single crowns were assessed. For implant-supported fixed partial dental prostheses (FPDPs), only the survival rate was assessed. The risk of bias was assessed for individual studies and across studies by using the Cochrane guidelines, Newcastle-Ottawa scale, and funnel plots.

Results. Twenty studies were included in this meta-analysis. Ceramic and metal-ceramic implant-supported single crowns were compared in terms of the survival rate (OR=0.84 [0.32, 2.23], $P=.730$), marginal adaptation (mean difference [MD]=0.33 [0.19, 0.47], $P<.001$), marginal bone loss (MD=-0.03 [-0.07, 0.02], $P=.260$), pocket probing depth (MD=-0.07 [-0.14, 0.00], $P=.060$), crown color match (MD=-0.15 [-0.29, 0.00], $P=.040$), and mucosal discoloration (standardized mean difference [SMD]=-0.14 [-0.86, 0.58], $P=.710$). The survival rate of ceramic and metal-ceramic implant-supported FPDPs was also compared (odds ratio [OR]=1.92 [1.26, 2.94], $P=.003$).

Conclusions. No significant difference was observed between ceramic and metal-ceramic implant-supported single crowns in terms of the survival rate, marginal bone loss, pocket probing depth, or mucosal discoloration. However, metal-ceramic single crowns had better marginal adaptation and poorer crown color match than did ceramic single crowns. In addition, current evidence indicates that metal-ceramic implant-supported FPDPs might have a higher survival rate than ceramic FPDPs. (*J Prosthet Dent* 2020;124:26-35)

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Clinical implications

Based on the results of this meta-analysis, metal-ceramic crowns might be recommended considering the clinical efficacy of implant-supported single crowns and implant-supported FPDs.

application.⁶ Metal-ceramic restorations have excellent mechanical properties, but the metal framework can affect periodontal tissue and cause image artifacts.⁷ They may also cause allergic reactions and discoloration to the marginal gingiva.⁵ For these reasons, metal-ceramic restorations are gradually being replaced by ceramic restorations.⁷ However, metal-ceramic crowns are still the gold standard.⁸ Therefore, the choice of ceramic or metal-ceramic implant-supported restoration is important and controversial.

In addition to the survival rate of implant-supported FPDs, various complications have important effects on the long-term success of implant-supported FPDs.⁹⁻¹² Meta-analyses have been conducted to compare survival and complication rates between ceramic and metal-ceramic tooth-supported FPDs.¹³⁻¹⁶ These studies reported that ceramic and metal-ceramic single crowns have similar survival rates and that ceramic fixed partial dental prostheses (FPDPs) have a higher failure rate than do their metal-ceramic counterparts. In addition, systematic reviews have analyzed the survival and complication rates of implant-supported single crowns and FPDs, but a comparison of ceramic and metal-ceramic restorations was not included.^{15,17,18} Two recently published systematic reviews involved the comparison of survival and complication rates between ceramic and metal-ceramic implant-supported single crowns and FPDs.^{19,20} However, the studies included in those reviews were not conducted to compare ceramic and metal-ceramic implant-supported restorations, and only zirconia ceramic was analyzed.

Studies have compared complications between implant-supported ceramic and metal-ceramic restorations, but differences in the quality of these studies and the evaluation indices used hampered interpretation of their findings.²¹⁻²⁵ To support clinical decision-making, the survival and complication rates of the 2 restoration types need to be established by using an evidence-based approach and clinical data. Therefore, the purpose of this meta-analysis was to compare the technical, biological, and esthetic complication rates of ceramic and metal-ceramic implant-supported FPDs and to provide clinical recommendations for appropriate material selection to enhance the long-term success of implant-supported FPDs.

Table 1. PICOS elements

Element	Contents
Patient	Patients treated with fixed dental prosthesis to treat partial edentulism; other forms of restoration, edentulous patients, animal experiments, and in vitro studies excluded.
Intervention	Ceramic single crowns and fixed partial dental prosthesis (FPDPs).
Comparator	Metal-ceramic single crowns and FPDs.
Outcomes	Survival rate, marginal adaptation, marginal bone loss, pocket probing depth, crown color match, and mucosal discoloration; results quantitatively assessed.
Studies	Randomized controlled trials or prospective or retrospective cohort studies; case studies, unpublished materials, and review articles excluded.

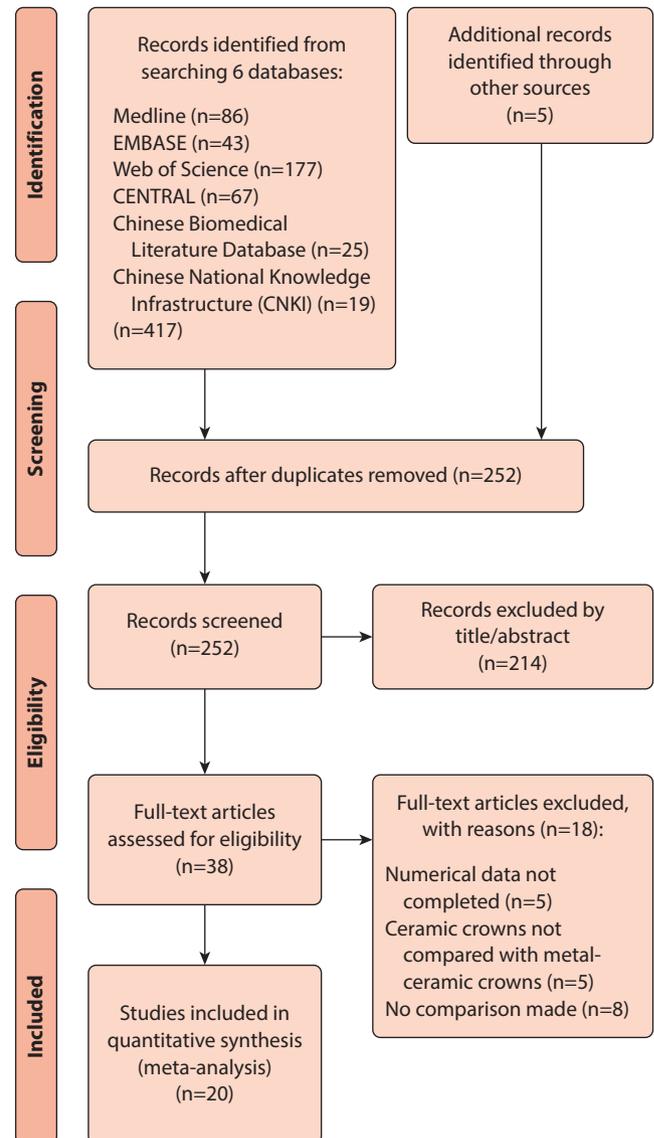


Figure 1. PRISMA flow of study selection for systematic review and meta-analysis.

MATERIAL AND METHODS

The present systematic review and meta-analysis was performed based on the recommendations and principles

Table 2. Characteristics of studies included in final analysis (N=20)

First Author of the Study	Year	Country	Study Design	Restoration Form	Final Follow-up Time	Number of All-Ceramic	Number of Metal-Ceramic	Complications
Holderegger	2008	Switzerland	RCT	Single crowns	2 weeks	15	15	⑥
Jemt	2008	Sweden	Retrospective	Single crowns	10 years	17	11	③
Zembic	2009	Switzerland	RCT	Single crowns	3 years	18	10	①③④⑥
Hosseini	2011	Denmark	RCT	Single crowns	1 year	38	37	①②③⑤⑥
Gallucci (a)	2011	USA	RCT	Single crowns	2 years	10	10	③
Gallucci (b)	2011	USA	RCT	Single crowns	2 years	10	10	①③⑤⑥
Schwarz	2011	Germany	Retrospective	Single crowns	5.8 years	53	179	①
Feng	2012	China	Retrospective	Single crowns	5 years	120	859	①
Feng	2013	China	Retrospective	Single crowns	1 year	60	60	③④
Hosseini	2013	Denmark	Prospective	Single crowns	3 years	52	46	①②⑤
Lops	2013	Italy	Retrospective	Single crowns	5 years	37	44	①③④
Zembic	2013	Switzerland	RCT	Single crowns	5 years	17	11	①
Lee	2014	Korea	Prospective	Single crowns	4 years	7	13	①③④
Peng	2014	China	Prospective	Single crowns	Immediately	11	18	⑤
Fenner	2016	Switzerland	Prospective	Single crowns	7 years	13	15	①②③④⑤
Cheng	2018	China	RCT	Single crowns	1 year	35	34	①
Sailer	2009	Switzerland	RCT	FPDPs	3 years	36	31	①
Esquivel-Upshaw(a)	2014	USA	RCT	FPDPs	3 years	41	48	①
Esquivel-Upshaw(b)	2014	USA	RCT	FPDPs	2 years	36	36	①
Shi	2016	China	Retrospective	FPDPs	8 years	127	152	①

RCT, randomized controlled trial; FPDPs, fixed partial dental prostheses. ①, Survival rate; ②, Marginal adaptation; ③, Marginal bone loss; ④, Pocket probing depth; ⑤, Crown color match; ⑥, Mucosal discoloration.

of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement²⁶ and was registered at PROSPERO (CRD42018111459).

The authors searched for relevant studies in Medline, EMBASE, Web of Science, The Cochrane Central Register of Controlled Trials (CENTRAL), China National Knowledge Infrastructure (CNKI), and Chinese Biomedical Literature Database without restriction from inception to September 10, 2018. All articles published in English and Chinese that described comparisons of ceramic and metal-ceramic implant-supported FDPs were searched. The authors used the following combined text and MeSH terms: “implant-supported,” “ceramic,” and “metal-ceramic.” A complete Medline search strategy is provided in [Supplemental Table 1](#). The authors also manually searched the reference lists of identified articles to find additional related papers and review articles.

Randomized controlled trials (RCTs) and prospective and retrospective cohort studies involving the comparison of ceramic and metal-ceramic implant-supported FDPs were included. The inclusion and exclusion criteria were set according to the patient, intervention, comparator, outcome, studies (PICOS) model ([Table 1](#)).²⁷ Two (M.-L.H., Y.-D.Z.) authors independently screened the titles and abstracts of the articles. Articles that fit the PICOS model were retrieved for full-text assessment to identify studies for the meta-analysis. Two (M.-L.H., Y.-D.Z.) investigators extracted and analyzed data from the included studies and reached a consensus. The

following data were tabulated: first author, publication year, country, study design, restoration form, final follow-up time, numbers of ceramic and metal-ceramic restorations, and complications. For studies with more than one follow-up period, data for the final follow-up period were extracted.

Two independent (M.-L.H., Y.-D.Z.) authors assessed the quality of the included RCTs by using the Cochrane collaboration tool for the assessment of risk of bias.²⁸ The quality and risk of bias of the selected nonrandomized studies were evaluated by using the Newcastle-Ottawa scale.²⁹ The authors surmised that an RCT had a low risk of bias when all areas showed low risk and that it had a moderate risk of bias when one or more areas had an uncertain risk of bias or no bias; other situations were considered to be at high risk.³⁰ The risk of bias of nonrandomized studies was evaluated by a star scoring scale, with higher scores denoting better quality.²⁹ The possibility of publication bias across included studies was evaluated by using funnel plots.³¹ In all these steps, any disagreement between the authors was resolved by consulting a third (H.L.) author to reach consensus through discussion.

Meta-analyses can be conducted only when sufficient similarities are found among the final included studies. The authors used odds ratios (ORs), mean differences (MDs), and standardized mean differences (SMDs) with 95% confidence intervals (CIs) to assess differences in the effects of ceramic and metal-ceramic implant-supported FDPs.³² The degree of heterogeneity among studies was

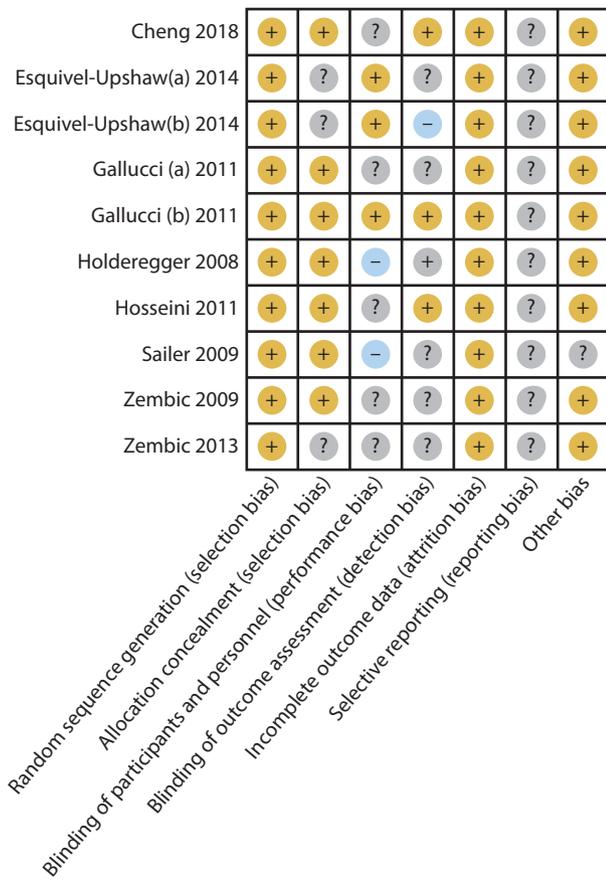


Figure 2. Risk of bias summary for each included RCT.

assessed using the I^2 statistic, with moderate to high degrees of heterogeneity indicated by $I^2 > 50\%$.³³ All data were analyzed by using a software program (RevMan 5.3; Nordic Cochrane Center, Cochrane Collaboration) ($\alpha = .05$).

RESULTS

The search of 6 databases and the reference sections of relevant articles identified 417 records. Manual searching resulted in the identification of 5 additional records. In total, 170 duplicate articles were removed, and 214 additional articles that did not meet the inclusion criteria were excluded during filtering based on article titles and abstracts. The full texts of the remaining 38 articles were read, and 20 articles were selected for inclusion in this systematic review and meta-analysis (Fig. 1).

The characteristics of the 20 selected studies are shown in Table 2.^{6,21-25,34-47} Ten (50%) were RCTs and 10 (50%) were prospective or retrospective cohort studies. They were published between 2008 and 2018, and 16 (80%) involved restoration with single crowns and 4 (20%) involved restoration with FPDs. The survival rate, marginal adaptation, marginal bone loss, pocket probing depth, crown color match, and mucosal

discoloration of implant-supported single crowns were evaluated. However, for the FPDP restorations, only the survival rate was evaluated.

Seven of the RCTs had a moderate risk of bias and 3 had a high risk of bias. The most common type of bias of these RCTs was selective reporting (Figs. 2 and 3). The mean risk of bias of the nonrandomized studies was 6.4 stars, according to the Newcastle-Ottawa scale.⁴⁸ Details of the assessment of nonrandomized studies are provided in Supplemental Table 2. Potential publication bias with respect to the survival rate and marginal bone loss for implant-supported single crowns was assessed by using funnel plots (Figs. 4 and 5). The plots revealed no significant asymmetry or evidence of bias among the studies selected for the 2 meta-analyses. Because the other 5 meta-analyses each included fewer than 9 studies, they were not subjected to funnel plot analysis.

The results showed that metal-ceramic implant-supported single crowns had better marginal adaptation (MD=0.33 [0.19, 0.47], $P < .001$) and poorer crown color match (MD=-0.15 [-0.29, 0.00], $P = .040$) than did ceramic single crowns. However, no significant difference was observed between them in terms of the survival rate (OR=0.84 [0.32, 2.23], $P = .730$), marginal bone loss (MD=-0.03 [-0.07, 0.02], $P = .260$), pocket probing depth (MD=-0.07 [-0.14, 0.00], $P = .060$), or mucosal discoloration (SMD=-0.14 [-0.86, 0.58], $P = .710$) (Figs. 6-11). Metal-ceramic implant-supported FPDPs had a higher rate of survival than ceramic FPDPs (OR=1.92 [1.26, 2.94], $P = .003$) (Fig. 12).

DISCUSSION

In this systematic review and meta-analysis, the technical, biological, and esthetic complications of ceramic and metal-ceramic implant-supported FDPs were compared. The purpose of the study was to provide information to support clinicians' treatment decision-making. The systematic review and meta-analysis was performed to evaluate and summarize the results of RCTs.⁴⁹ Because an insufficient number of RCTs comparing the complications of ceramic and metal-ceramic of implant-supported FDPs were available, prospective and retrospective cohort studies were also included.

Restoration survival was defined as the absence of ceramic chipping or fracture. No significant difference in the survival rate was observed between ceramic and metal-ceramic implant-supported single crowns ($P = .730$), consistent with the findings of a previous systematic review.¹⁹ The similar performance may be because many ceramic crowns are now made of zirconia, which has better fracture resistance than lithium disilicate glass-ceramic or alumina ceramic restorations.⁵⁰ Another possibility is that some of the studies had short follow-up

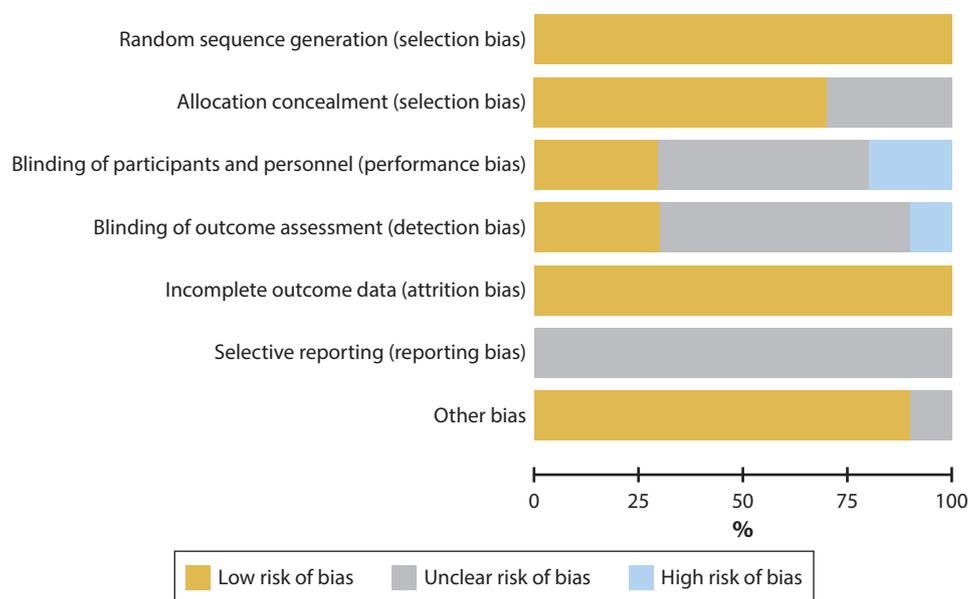


Figure 3. Risk of bias graph for included randomized clinical trials.

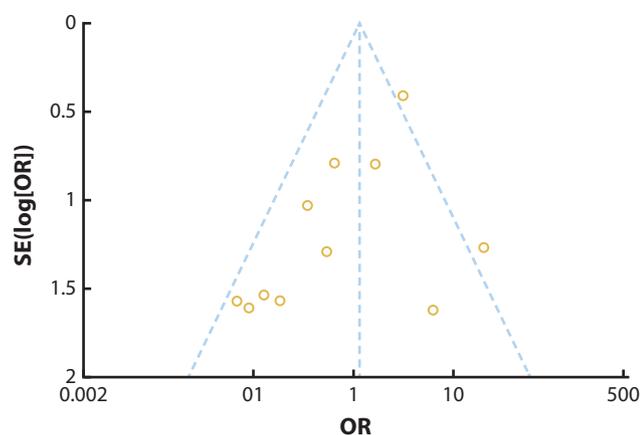


Figure 4. Funnel plots for comparison of survival rate between ceramic and metal-ceramic implant-supported single crowns. OR, odds ratio; SE, standard error.

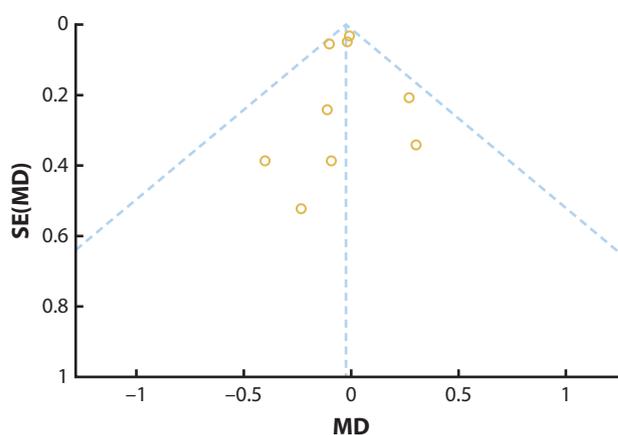


Figure 5. Funnel plots for comparison of marginal bone loss between ceramic and metal-ceramic implant-supported single crowns. MD, mean difference; SE, standard error.

periods, which may have masked differences. A review of implant-supported single crowns found that the 5-year survival rate of ceramic crowns was lower than that of metal-ceramic crowns.¹⁸ In addition, a systematic review and meta-analysis showed no significant difference in the rate of ceramic chipping between ceramic and metal-ceramic tooth-supported single crowns.¹³

Marginal adaptation is a key factor for the long-term success of single crowns.⁹ Marginal defects can damage soft tissue around the implant and endanger the success of the restoration.¹⁰ The results of the meta-analysis of marginal adaptation of implant-supported single crowns indicated that metal-ceramic restorations were better than ceramic restorations ($P < .001$). This result was presumably due to the more accurate processing of metal relative to ceramic. However, considering that only a few

studies were included in this meta-analysis, this conclusion needs to be verified further with a larger number of studies. Tooth-supported metal-ceramic single crowns have been reported to have better marginal adaptation than ceramic single crowns.¹⁶

Good osseointegration is a precondition for the success of implant restoration, and marginal bone loss is used to evaluate this success of implant restorations.¹¹ The meta-analysis of marginal bone loss revealed no significant difference between ceramic and metal-ceramic implant-supported single crowns ($P = .260$). Of note, the I^2 value was 0 in this meta-analysis, indicating little heterogeneity among the included studies. These results suggest that marginal bone loss is not affected by the crown material used, which agrees with the findings of a previous clinical study.⁴³ However, in practical

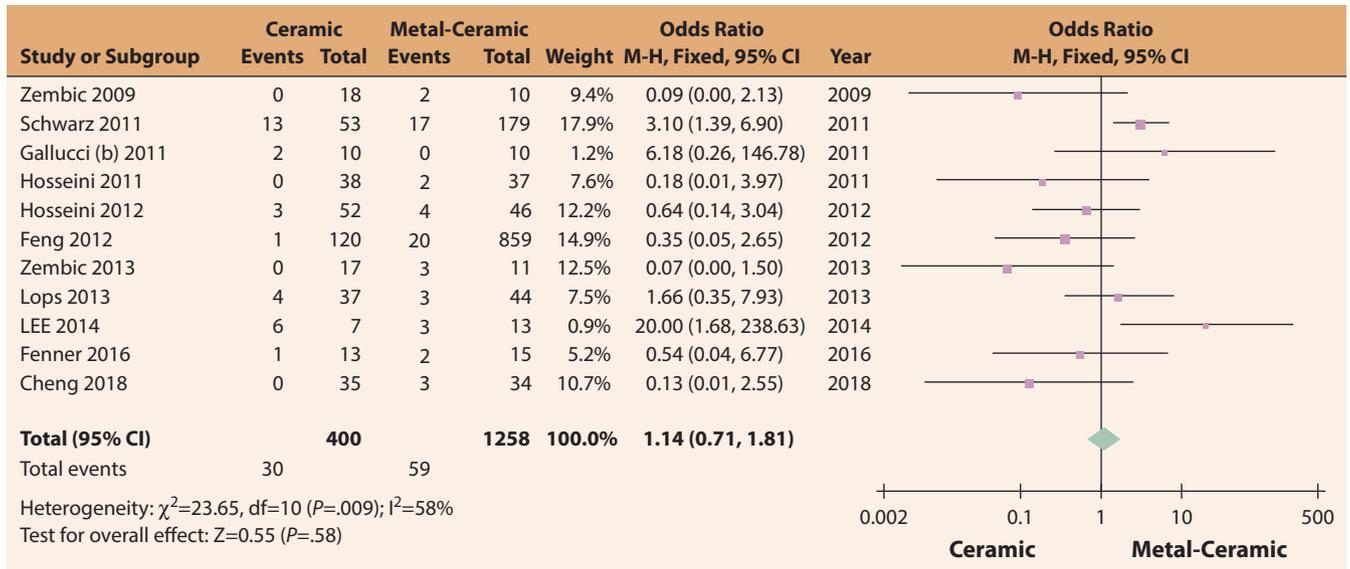


Figure 6. Forest plot of survival rate of implant-supported single crowns with comparison between ceramic and metal-ceramic single crowns. SD, standard deviation.

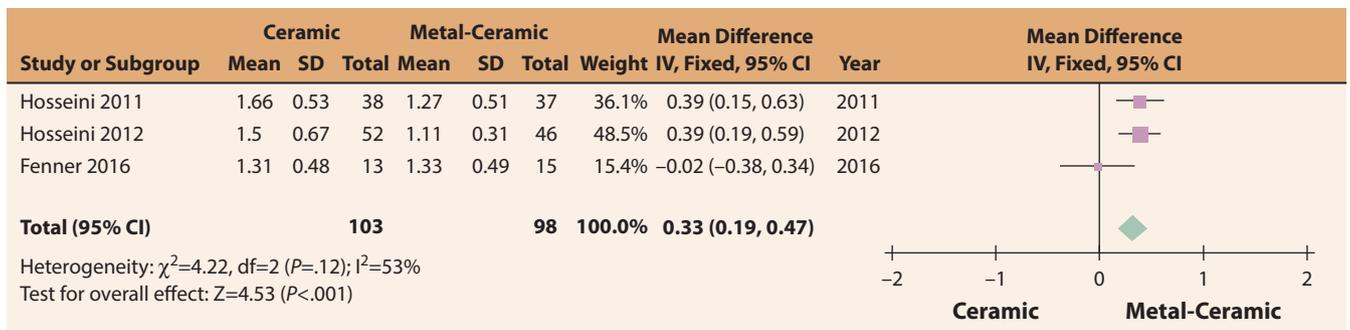


Figure 7. Forest plot of marginal adaptation of implant-supported single crowns with comparison between ceramic and metal-ceramic single crowns. SD, standard deviation.

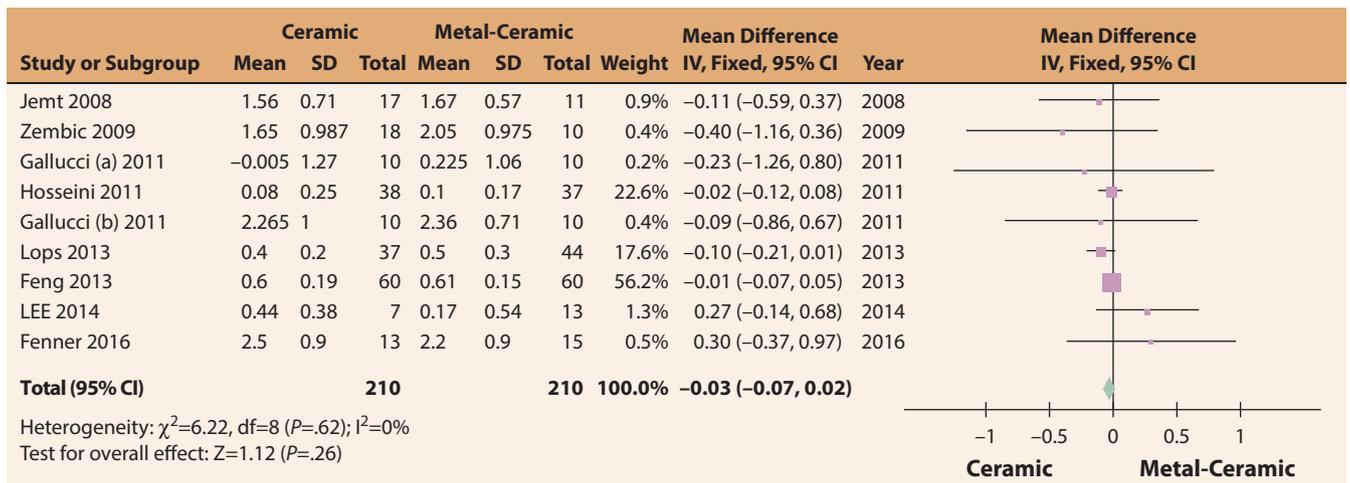


Figure 8. Forest plot of marginal bone loss of implant-supported single crowns with comparison between ceramic and metal-ceramic single crowns. SD, standard deviation.

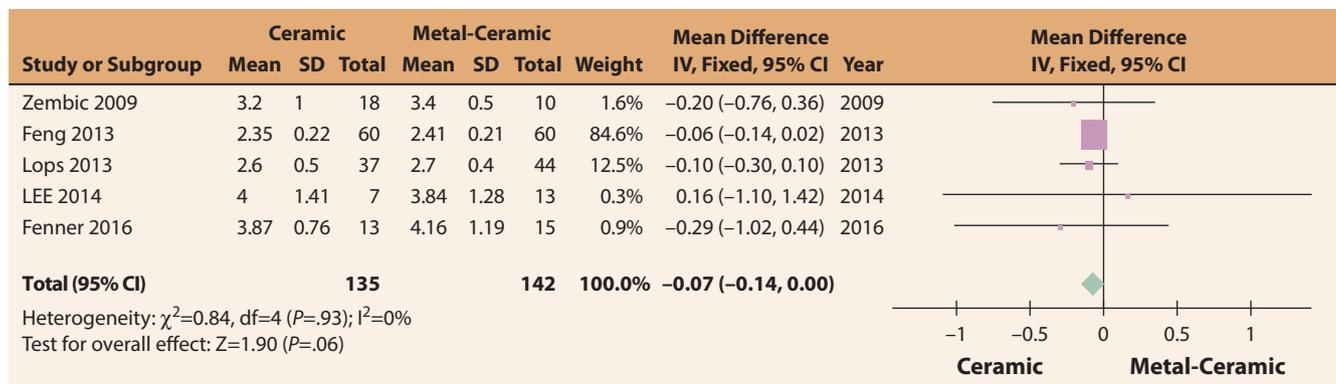


Figure 9. Forest plot of pocket probing depth of implant-supported single crowns with comparison between ceramic and metal-ceramic single crowns. SD, standard deviation.

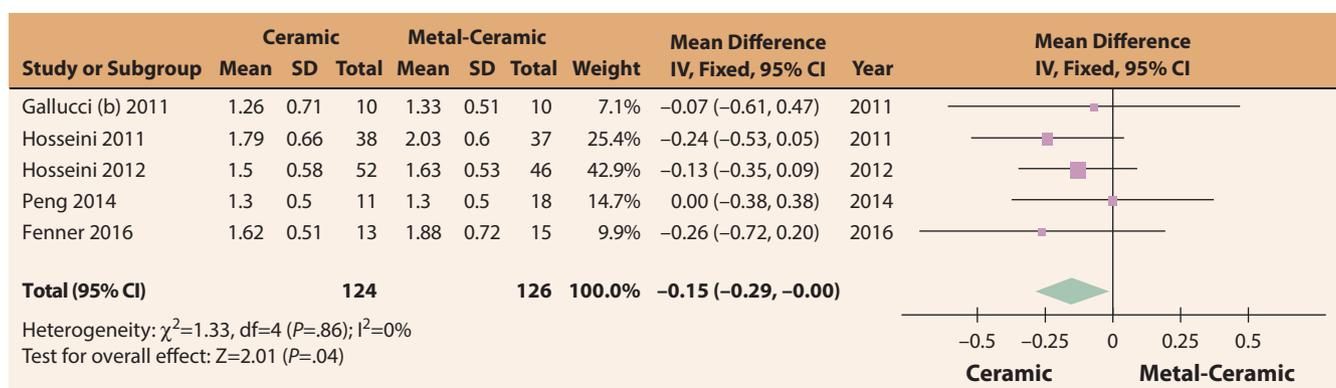


Figure 10. Forest plot of crown color match of implant-supported single crowns with comparison between ceramic and metal-ceramic single crowns. SD, standard deviation.

application, distortion and elongation of the radiograph from radiation exposure and use of different X-ray angles may hamper accurate assessment of marginal bone loss around an implant.³⁹ In addition, the follow-up periods varied among these studies, which may also have affected the results.

The health of soft tissues around an implant influences its long-term stability.⁵¹ Adhesion to peri-implant tissue is also essential to maintain gingival height and achieve a good esthetics for the implant-supported restoration.¹² Periodontal probing involves examination of the soft tissue around the implant and does not disrupt the implant's attachment with surrounding soft and hard tissues.⁵² The meta-analysis of pocket probing depth showed no significant difference between ceramic and metal-ceramic implant-supported single crowns ($P=.060$). This result is consistent with that of a previous clinical study.³⁷ Little heterogeneity was present among the included studies ($I^2=0$). These findings suggest that the implant superstructure material used has no significant influence on pocket probing depth.

The increasing popularity and success rate of implant restorations has resulted in a greater focus on esthetic

outcomes, with crown color match and mucosal discoloration being indicators of the esthetic success of a restoration.³⁵ The meta-analysis of crown color match of implant-supported single crowns suggested that ceramic restorations had better esthetics than metal-ceramic restorations ($P=.040$). This result is consistent with the findings of a previous review¹⁹ and likely reflects the similarity of ceramic crowns' light transmission to that of natural teeth.⁵ However, another study reported no significant difference in color or translucency between ceramic and metal-ceramic crowns,³⁶ possibly because of the limited number of crowns evaluated. Little heterogeneity was present among the studies included in this meta-analysis ($I^2=0$), perhaps because few studies were included. Further research is needed to confirm this result.

The meta-analysis of mucosal discoloration indicated no significant difference between ceramic and metal-ceramic implant-supported single crowns ($P=.710$). This result is consistent with those of previous clinical studies.^{34,36} The effect of the implant-supported crown material on the soft tissue around the implant is influenced by the thickness of the mucosa, which may explain

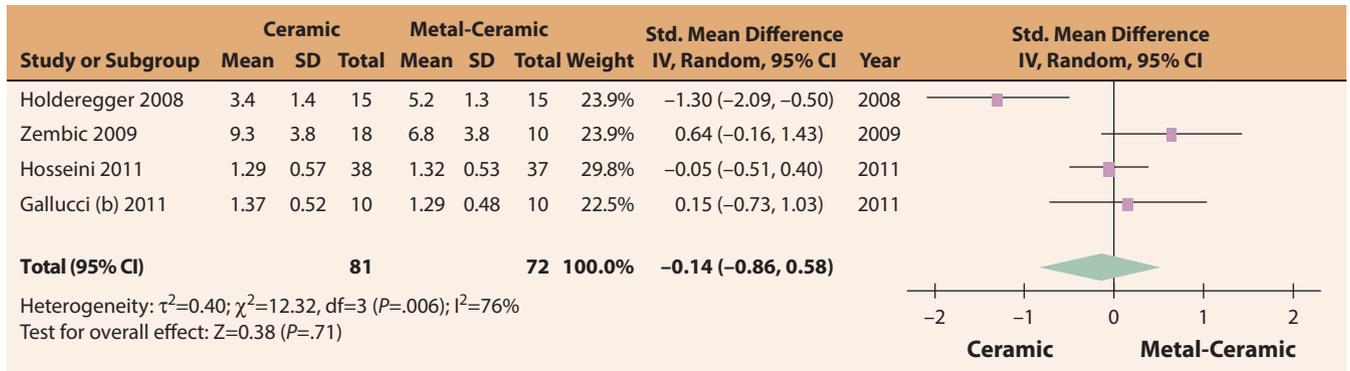


Figure 11. Forest plot of mucosal discoloration of implant-supported single crowns with comparison between ceramic and metal-ceramic single crowns. SD, standard deviation.

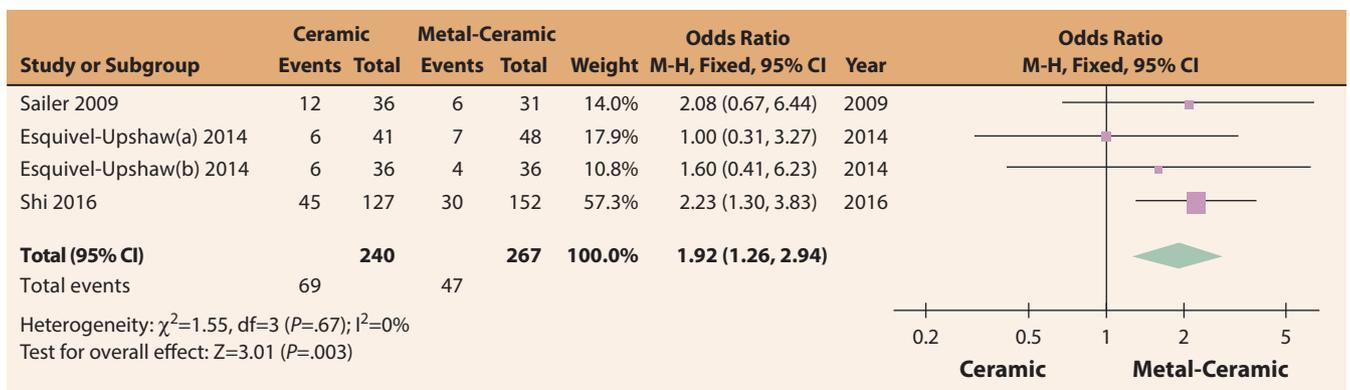


Figure 12. Forest plot of survival rate of implant-supported FPDPs with comparison between ceramic and metal-ceramic FPDPs. FPDPs, fixed partial dental prostheses.

the lack of a significant difference in mucosal discoloration between ceramic and metal-ceramic restorations.³⁶ To combine data on different scales from the studies of mucosal discoloration for comparison, the SMDs were calculated by using the standard deviation from each study. This type of data processing may affect results. The final esthetic outcome of a prosthesis may also be influenced by the color of the adhesive and the thickness and transparency of the porcelain material.⁵³ Clinicians and patients likely differ in their assessments of esthetic outcomes, which should be considered during treatment planning.

According to the results of the meta-analysis of the survival rates of implant-supported FPDPs, ceramic FPDPs had a lower rate of survival than did metal-ceramic FPDPs ($P=.003$). This result is consistent with those of previous systematic reviews and meta-analyses of implant- and tooth-supported FPDPs.^{14,20} Longer span FPDPs produce greater stress, which could influence the results. Of note, the $I^2=0$ in this meta-analysis, indicating that there is little heterogeneity among the included studies. Only the survival rate was analyzed because of the small number of studies and amount of

data on other complications of ceramic and metal-ceramic implant-supported FPDPs.

An additional result of the present study was that the studies showed little heterogeneity in terms of marginal bone loss, pocket probing depth, crown color match of implant-supported single crowns, and the survival rate of implant-supported FPDPs. Less heterogeneity means greater comparability among studies and greater credibility of the results.

This meta-analysis had several limitations, including the low number of RCTs; therefore, prospective and retrospective cohort studies were also included, which may have influenced the findings. The number of studies included in the examination of each outcome was small, except for the assessments of survival rate and marginal bone loss. Some of the included studies had short follow-up periods, and the maintenance of a good repair effect requires long-term oral health maintenance and regular review, but the influence of patient compliance on the repair effect was not described in most of the included studies. The search scope of this study was limited to articles published in English and Chinese in 6 major literature databases, which may have resulted in selection

bias. Therefore, to overcome these problems, further high-quality, well-designed RCTs with larger sample sizes are required.

CONCLUSIONS

Based on the findings of this systematic review and meta-analysis, the following conclusions were drawn:

1. Ceramic implant-supported single crowns had better crown color match than metal-ceramic single crowns but vice versa for marginal adaptation.
2. No significant difference was observed between them in terms of the survival rate, marginal bone loss, pocket probing depth, or mucosal discoloration.
3. Current evidence indicates that metal-ceramic implant-supported FPDPs might have a higher rate of survival than ceramic implant-supported FPDPs.

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Noteworthy Abstracts of the Current Literature

Effect of screw channel angulation on reverse torque values of dental implant abutment screws

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Purpose. To compare the reverse torque values (RTVs) of abutment screws tightened from three different angles.

Material and methods. Implant abutment screws (n=48), abutments (3), and regular platform implant analogs (3) were divided into three angulation groups (n=16/group). Custom guides of 0°, 10°, and 20° were fabricated to verify driver angulation. The implant components for each group were assembled and all screws torqued to 35 Ncm using a universal screwdriver in a manual torque wrench at the appropriate angle. Torque was reapplied 10 minutes after initial torque. A digital gauge was then used to measure reverse torque at a position parallel (0°) to the implant analog. RTVs were recorded and compared using one-way ANOVA and Tukey HSD post-hoc comparisons ($\alpha=0.05$).

Results. All mean RTVs fell below the targeted torque value of 35Ncm, with some values in each angulation group 10% below of the target value. Mean RTVs in descending order from targeted torque value were: 10° group=32.07 ± 0.97 Ncm, 0° group=31.16 ± 1.12 Ncm, and 20° group=30.08 ± 0.88 Ncm. One-way ANOVA revealed significant differences between angulation groups (F=15.954, P<0.001). Tukey HSD post hoc comparisons revealed that the mean RTVs of the three angulation groups were significantly different from each other (0° vs. 10°: P=0.033; 0° vs. 20°: P=0.011; 10° vs. 20°: P< 0.001).

Conclusions. All RTVs did not reach the targeted torque value of 35 Ncm. Mean screw RTVs were significantly influenced by screwdriver insertion angulation.

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Supplemental Table 1. Search strategy in MEDLINE

((implant-supported[All Fields] AND ((porcelain-fused-to-metal[Title/Abstract] OR PFM[Title/Abstract] OR ("Metal Ceramic Alloys"[Mesh] OR "Dental Porcelain"[Mesh]))) AND (((all-ceramic[Title/Abstract] OR all-ceramics[Title/Abstract] OR ceramic[Title/Abstract] OR zirconium oxide[Title/Abstract] OR zirconia[Title/Abstract] OR alumina[Title/Abstract] OR aluminum oxide[Title/Abstract])) AND (((randomized controlled trial[Publication Type] OR randomized [Title/Abstract] OR controlled clinical trials[Title/Abstract] OR prospective[Title/Abstract] OR retrospective[Title/Abstract]))

Supplemental Table 2. Quality assessment and risk of bias of included nonrandomized studies

Study	Coding Manual for Cohort Studies	Newcastle-Ottawa Scale
Jemt et al ⁴⁴	Selection	
	1) Representativeness of the exposed cohort	d
	2) Selection of nonexposed cohort	c
	3) Ascertainment of exposure	a☆
	4) Demonstration that outcome of interest was not present at the start of study	a☆
	Comparability	
	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	a☆
Schwarz et al ⁶	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	a☆
	3) Ascertainment of exposure	a☆
	4) Demonstration that outcome of interest was not present at the start of study	a☆
	Comparability	
	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	a☆
Hosseini et al ²¹	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	a☆
	3) Ascertainment of exposure	a☆
	4) Demonstration that outcome of interest was not present at the start of study	a☆
	Comparability	
	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	a☆

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Supplemental Table 2. (Continued) Quality assessment and risk of bias of included nonrandomized studies

Study	Coding Manual for Cohort Studies	Newcastle-Ottawa Scale
Feng et al ⁴⁷	3) Adequacy of follow-up of cohorts	a☆
	Total scale	☆☆☆☆☆☆
	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	a☆
	3) Ascertainment of exposure	a☆
	4) Demonstration that outcome of interest was not present at the start of study	a☆
	Comparability	
	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
Feng et al ⁴⁶	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	a☆
	3) Adequacy of follow-up of cohorts	b☆
	Total scale	☆☆☆☆☆☆
	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	a☆
	3) Ascertainment of exposure	a☆
	4) Demonstration that outcome of interest was not present at the start of study	a☆
	Comparability	
Lops et al ⁴³	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	b
	3) Adequacy of follow-up of cohorts	a☆
	Total scale	☆☆☆☆☆☆
	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	a☆
	3) Ascertainment of exposure	a☆
4) Demonstration that outcome of interest was not present at the start of study	a☆	
Comparability		
Lee et al ³⁹	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	a☆
	3) Adequacy of follow-up of cohorts	b☆
	Total scale	☆☆☆☆☆☆
	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	c
	3) Ascertainment of exposure	a☆
4) Demonstration that outcome of interest was not present at the start of study	a☆	

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Supplemental Table 2. (Continued) Quality assessment and risk of bias of included nonrandomized studies

Study	Coding Manual for Cohort Studies	Newcastle-Ottawa Scale
	Comparability	
	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	a☆
	3) Adequacy of follow-up of cohorts	a☆
	Total scale	☆☆☆☆☆
Peng et al ⁴⁵	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	a☆
	3) Ascertainment of exposure	a☆
	4) Demonstration that outcome of interest was not present at the start of study	a☆
	Comparability	
	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	b
	3) Adequacy of follow-up of cohorts	d
	Total scale	☆☆☆☆☆
Fenner et al 2016 ⁴¹	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	a☆
	3) Ascertainment of exposure	a☆
	4) Demonstration that outcome of interest was not present at the start of study	a☆
	Comparability	
	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	a☆
	3) Adequacy of follow-up of cohorts	c
	Total scale	☆☆☆☆☆
Shi et al 2016 ²⁴	Selection	
	1) Representativeness of exposed cohort	d
	2) Selection of nonexposed cohort	a☆
	3) Ascertainment of exposure	a☆
	4) Demonstration that outcome of interest was not present at the start of study	a☆
	Comparability	
	1) Comparability of cohorts based on design or analysis	a☆
	Outcome	

(continued on next column)

Supplemental Table 2. (Continued) Quality assessment and risk of bias of included nonrandomized studies

Study	Coding Manual for Cohort Studies	Newcastle-Ottawa Scale
	1) Assessment of outcome	a☆
	2) Was follow-up long enough for outcomes to occur?	a☆
	3) Adequacy of follow-up of cohorts	b☆
	Total scale	☆☆☆☆☆

Selection: 1) d: no description of derivation of cohort; 2) a: drawn from same community as exposed cohort ☆, c: no description of derivation of nonexposed cohort; 3) a: secure record (such as, surgical records) ☆; 4) a: yes ☆, b: no. Compatibility: 1) a: study controls for ___ (select most important factor) ☆. Outcome: 1) a: independent blind assessment ☆, b: record linkage ☆; 2) a: yes (select adequate follow-up period for outcome of interest) ☆; 3) a: complete follow-up—all participants accounted for ☆.