



**Prosthodontic complications of complete arch fixed implant metal-ceramic and all-ceramic prostheses with minimum 5 years mean follow-up period. A systematic review and meta-analysis**

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**Title:** Prosthodontic complications of metal-ceramic and all-ceramic complete arch fixed implant prostheses with minimum 5 years mean follow-up period. A systematic review and meta-analysis.

**Review article**

**Running title:** Complete fixed implant prostheses complications

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**Abstract**

**Purpose:** The purpose of this systematic review and meta-analysis was to review and analyze the prosthodontic complications, survival and success of metal-ceramic (MC) and all-ceramic (AC) complete arch fixed implant dental prostheses (CFIDPs) with a minimum mean follow-up period of 5 years.

**Materials and Methods:** A structured literature search was conducted using 3 electronic databases (MEDLINE, the Cochrane Library, Web of Science) for clinical studies reporting on prosthodontic complications of metal-ceramic and/or all-ceramic CFIDPs published between 2000 and 2016. This was complemented with hand searching in relevant journals, references, as well as searching in grey literature. Risk of bias analysis for randomized controlled trials was done following the recommendations from Cochrane collaboration. Quality appraisal for studies that were non-randomised was executed according to the Newcastle-Ottawa scale (NOS). The final selection included only studies with a minimum mean follow-up time of 5 years.

**Results:** The electronic databases search yielded 1804 relevant titles and abstracts; 11 studies were finally selected (9 for metal-ceramic and 2 for all-ceramic CFIDPs). Risk of bias in most selected studies was low. Heterogeneity across studies of MC CFIDPs was within acceptable range but not among AC CFIDPs studies, so no meta-analysis was performed for the latter.

Regarding MC CFIDPs, most studies recorded 100% survival rate (survival range: 92.4-100%, success range: 47-96.7%), with veneer fracture being the commonest complication. 5- and 10-year cumulative complication rates for MC CFIDPs veneer fractures were 22.1% and 39.3% respectively but with variable confidence intervals. The 2 studies included for AC CFIDPs reported 100% survival rates but differed in success rates, with the one utilizing predominantly monolithic zirconia restorations reporting 90.9% whereas the one using bi-layered zirconia reporting 60.4%, with complications attributed to veneer fracture.

**Conclusions:** Metal-ceramic and all-ceramic CFIDPs presented with veneer fractures as primary complication which may require significant maintenance; other complications were negligible after a mean follow-up period of at least 5 years. More long-term studies, especially on all-ceramic CFIDPs are needed.

**Keywords:** Systematic review, Meta-analysis, complete implant prostheses, metal-ceramic, all-ceramic

## 1. Introduction

Complete arch fixed implant-supported dental prostheses (CFIDPs) [1] were originally made of noble alloy frameworks and acrylic resin and denture teeth as veneering materials [2]. Technological advancements allowed different materials, such as titanium and zirconia, to be used for the framework, whilst the veneering material could be made of dental ceramics or dental composites [2-4]. Furthermore, monolithic restorations made of zirconia are now clinically available [4-6]. CFIDPs have allowed for easier insertion and splinting of implants, without the need for interproximal contact adjustments [7] and are the only design choice for fixed rehabilitation of edentulous jaws when the number of implants is limited to 4-6. However, as with all prostheses, various prosthodontic complications do occur during aftercare and maintenance, which may pose a significant clinical, laboratory, and financial burden to both the clinician and patient [8-10].

Acrylic resin has been used as veneering material of CFIDPs for longer compared to ceramics but it has a high incidence of veneering fracture as well as material wear [8, 9]. However, repairs are relatively easy and cost-effective compared to ceramic chipping and fracture [11]. Metal-ceramic CFIDPs have also been used extensively during the past decade. Studies [12, 13] have shown that metal-ceramic partial FIDPs present with ceramic fractures as frequent complications, however there is limited information when it comes to CFIDPs [8, 9]. Recent years have also witnessed the introduction of zirconia frameworks for CFIDPs, either bi-layered or monolithic [6, 14, 15]. A number of studies [16-19] have demonstrated that ceramic chipping is the predominant issue with bi-layered zirconia tooth- or implant-supported fixed partial dentures, but very little evidence is available for the use of zirconia in CFIDPs.

A number of systematic reviews [8, 9, 20] have been conducted during the last years looking at the prosthodontic complications, success and survival of CFIDPs, however, the included articles in these systematic reviews were based on metal-acrylic CFIDPs. This was due to the fact that none of the studies investigating metal-ceramic or zirconia-based CFIDPs satisfied the mean follow-up period of at least 5 years. This finding was very significant as 5 years is considered a medium follow-up time,

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3 whereas the classic metal acrylic CFIDPs, despite their maintenance issues, have follow-up times up  
4 to 20 years [8, 9, 20].  
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8 More recent systematic reviews focusing on zirconia-based fixed prosthesis [16] and CAD-CAM  
9 implant-supported restorations [21] either failed to identify studies with more than 3-5 years follow-up,  
10 or did not proceed to any meta-analysis as there were problems with the quality of included studies  
11 and the sufficiency of data.  
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16 The aim of this systematic review was to investigate the updated literature focusing on the  
17 prosthodontic complications of metal-ceramic and all-ceramic CFIDPs with a mean follow-up time of  
18 at least 5 years.  
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## 22 23 **2. Materials and Methods**

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26 This article reported in a manner following the Preferred Reporting Items for Systematic reviews and  
27 Meta-analyses (PRISMA) Statement guidelines [22].  
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### 30 31 **2.1 Search strategy**

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34 A structured literature search was conducted independently by two individuals (CKKW and UN) using  
35 different electronic databases (MEDLINE, the Cochrane Library, Web of Science) for clinical studies  
36 reporting on prosthodontic complications of metal-ceramic and/or all-ceramic CFIDPs. The OpenGrey  
37 database was used for identification of grey literature.  
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42 The search terms that were used, alone or in combination, were 'Dental Prosthesis, Implant-  
43 Supported (MeSH Term)', 'Dental Implants (MeSH Term)', 'Dental Prosthesis Design (MeSH Term)',  
44 fixed prostheses', 'fixed restoration', 'implant prostheses', 'implant superstructure', 'implant  
45 suprastructure', 'implant rehabilitation', 'implant reconstruction', 'dental restoration failure (MeSH  
46 Term)', 'Jaw,Edentulous (MeSH Term)', 'full arch', 'complete' 'treatment outcome (MeSH Term)',  
47 treatment failure (MeSH Term)', 'prosthodontic or technical or mechanical or screw complication or  
48 outcome or failure', 'veneer fracture', 'framework fracture', 'ceramics or dental porcelain (MeSH Term)'  
49 'Metal Ceramic Alloys (MeSH Term)', 'ceramic' 'chromium alloys (MeSH Term)', 'cobalt chromium'  
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3 'gold alloys (MeSH Term)', 'gold alloys'. A representation of the search strategy is depicted in Table 1  
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5 (Supplemental table).  
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13 The search covered a time span between January 2000 and May 2016 as previous years had been  
14 extensively covered through previous systematic reviews [8,9,20] on the subject. The option of  
15 'related articles' was also used. Review articles, as well as references from different studies, were  
16 also used to identify relevant articles. E-publications, ahead of print were also included. Hand  
17 searching was done for the time span between January 2006 and May 2016 on the following journals:  
18 *Journal of Prosthetic Dentistry, International Journal of Prosthodontics, Journal of Oral Rehabilitation,*  
19 *International Journal of Oral and Maxillofacial Implants, Clinical Oral Implants Research, Clinical*  
20 *Implant Dentistry and Related Research, European Journal of Oral Implantology, Journal of*  
21 *Prosthodontics, and Implant Dentistry.*  
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## 31 **2.2 Study selection**

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34 During the first screening phase, the titles, abstracts and/or full texts were reviewed by the two  
35 reviewers together based on the following inclusion and exclusion criteria: 1. More than 1 year of  
36 mean follow up period 2. More than 10 prostheses followed up 3. Metal-ceramic and all-ceramic  
37 CFIDPs studied. Any laboratory studies, animal studies, and expert opinion articles were excluded.  
38 Review articles were used to further augment the search. Any disagreement was resolved by  
39 discussion and, in case of doubt, the full text of the article was obtained. Hand searching of selected  
40 journals was also implemented at this point. The full texts of all the articles, which passed the first  
41 screening phase were obtained for further eligibility analysis, as well as for further searching of the  
42 references.  
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52 During the eligibility analysis, the selected full texts were further screened independently according to  
53 the following inclusion criteria:  
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3 1. Clinical studies with a mean follow-up period of at least 1 year, with the ultimate goal  
4 to look at studies with minimum of 5- year mean follow-up, if numbers permitted. The mean  
5 follow-up time should clearly be stated in the article. If only a range was mentioned, then the  
6 smallest time value was noted.  
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9 2. Clinical examination of patients during the follow-up visit.
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11 3. Details of the materials used for the prostheses.
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13 4. Number of patients and prostheses stated. Minimum number for a study should be  
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15 10 prostheses.
- 16  
17 5. Study outcome stated as prosthodontic complications.  
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21 The list of selected articles by two reviewers was then compared and a Kappa score was calculated  
22 to determine the reviewers' agreement.  
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25 Articles that were laboratory studies, expert opinions, narrative reviews, technical articles, or animal  
26 studies were excluded. No language criterion was implemented. All types of clinical studies i.e.  
27 randomized and non-randomized controlled clinical trials, case control studies, cohort studies and  
28 case series studies were included.  
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### 33 34 **2.3 Risk of bias assessment** 35

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37 The quality of the final included articles was assessed with various tools according to the types of  
38 study design [23]. Risk of bias analysis for randomized controlled trials was done following the  
39 recommendations from Cochrane collaboration [24]. Quality appraisal for studies that were non-  
40 randomized was executed according to the Newcastle-Ottawa scale (NOS) [25]. The NOS calculates  
41 the study quality based on three major components: 1. Selection 2. Comparability 3. Outcome for  
42 cohort studies. It assigns a maximum of 4 stars for Selection, a maximum of 3 stars for Outcome and  
43 a maximum of 2 stars for Comparability. According to that quality scale, a maximum of 9 stars/points  
44 can be given to a study, and this score represents the highest quality, where six or more points were  
45 considered high quality. For case series studies, an 18-item quality appraisal tool developed by  
46 Institute of Health Economics, Alberta, Canada was used [26]. The 18 items were assessed by  
47 marking whether the particular item was or was not reported or partially reported/unclear. Score of 1  
48 would be given when the item was reported and clear, score of 0 would be given otherwise. If the  
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3 study scored above 9, then the risk of bias was considered low; if the score was 9 or below, then the  
4 risk of bias was considered as potentially high.  
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#### 7 8 **2.4 Data extraction and statistical analysis** 9

10 Data of the final studies were tabulated for the following prosthodontic complications: veneer fracture,  
11 abutment fracture, abutment screw loosening and fracture, prosthetic screw loosening and fracture,  
12 framework fracture, loss of retention (for cement-retained prostheses), material wear and phonetics  
13 complications. In cases of multiple publications following the same cohort of patients, the study with  
14 the longest follow-up was included. In the case of studies with incomplete information, the  
15 corresponding authors were contacted.  
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18 The number and type of complications during the observation period of the study were recorded in  
19 order to calculate the survival and success rates. Success was defined as the prosthesis remaining in  
20 situ without any modifications or changes. On the other hand, survival was defined as the prosthesis  
21 remaining in situ with or without modification during the entire observation period [27]. Complication  
22 rates of CFIDPs were calculated by dividing the total number of complications by the total exposure  
23 time. The total exposure time was calculated by multiplying the mean follow-up time by the number of  
24 CFIDPs stated in included studies. The mean follow-up time was extracted directly from articles.  
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26 Poisson regression analyses was performed to calculate the 5-, 10-, 15-year survival proportions by  
27 the relationship between event rate and the survival function  $S(t) = \exp(-t \times \text{event rate})$ , assuming a  
28 constant rate of occurring events. The result referred to the proportion of a population at risk that  
29 would develop a complication in a given period of time and it took into the account all of the patients in  
30 all the selected studies.  
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33 Study heterogeneity was assessed with the  $I^2$  statistic in order to express the percentage of the total  
34 variation across studies, with <25% corresponding to low heterogeneity, 26-75% moderate and over  
35 75% corresponding to very high. The inverse variance method was used for random-effects or fixed-  
36 effects model. Where statistically significant ( $P < 0.10$ ) heterogeneity was detected, a random-effects  
37 model was used to assess the significance of treatment effects, and vice versa[28]. If there was high  
38 heterogeneity across studies, then no cumulative complication rates would be calculated.  
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### 3. Results

#### 3.1 Study selection

Figure 1 shows the process in selecting the final articles from the initial yield of 1804 titles and Abstracts (Medline via Ovid yielded 1446, Cochrane database yielded 211 and Web of Science yielded 340 articles). After de-duplications from 3 different databases, i.e. Medline, Cochrane and Web of Science, 1434 potential titles and abstracts were extracted. Two non-English articles (1 Chinese and 1 Slovenian) were yielded, titles and abstracts in English were available and with the translation through online translation software, they were excluded during the screening phase. Hand searching yielded 78 studies. Grey literature search was executed using the Opengray database, in this way, some not yet published articles could be found. However, no extra articles were yielded identified.

Following the first screening phase 127 articles were selected for full text eligibility screening, where 2 assessors independently screened through the articles according to the 5 inclusion/exclusion criteria. A total of 104 studies were excluded during the eligibility phase, with the main reason for exclusion being insufficient details on the prostheses or materials other than metal-ceramic and all-ceramic (Figure 1). The screening for eligibility phase led to the inclusion of 23 articles with a mean follow-up time of at least 1 year [29-51]. Inter-assessor agreement during the eligibility screening II was 'Good' (Kappa value: 0.87).

The 23 selected articles were read as full texts and data extraction was done. Studies were broadly classified in terms of mean follow up period, i.e. 1, 3 or 5 years of mean follow up. 11 articles [35-45] had a mean period of at least 5 years. Further information was requested by sending e-mails to the corresponding authors; about half of the corresponding authors replied and the answers provided made the information more complete and clarified. At this point, it was decided to proceed with the 11 studies providing at least 5 years of mean follow-up time, as their number was deemed adequate for meaningful conclusions to be drawn.

All the final selected studies were published after 2011. Nine studies [35-39, 41-43, 45] were based on metal-ceramic prostheses, while 2 studies [40, 44] on all-ceramic prostheses. No study directly

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3 compared metal-ceramic prostheses with all-ceramic CFIDP. Most of the articles were retrospective in  
4 nature. The demographics are shown in Table 2. A total of 235 metal-ceramic CFIDPs and 70 all-  
5 ceramic prostheses were observed over a minimum mean follow-up period of 5 years up to a  
6 maximum 14.7 years.  
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### 10 11 **3.2 CFIDPs in included studies**

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14 Different studies had different prostheses design, namely screw- and cement-retained. For screw-  
15 retained ones, some prostheses were screwed directly onto the fixtures, some screwed onto  
16 abutments, while cement-retained CFIDPs were cemented onto abutments. Table 3 contains details  
17 of the prostheses. The included prostheses were supported by various implant systems, number of  
18 implants, and had variable opposing dentition but none of these factors could be analyzed  
19 meaningfully.  
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### 26 27 **3.3 Prosthodontic complications, success and survival rates**

#### 28 29 30 **3.3.1 Prosthodontic complications**

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32 In terms of prosthodontic complications, information for the following was extracted: porcelain veneer  
33 fracture, abutment fracture, abutment screw loosening & fracture, prosthetic screw loosening &  
34 fracture, framework fracture, loss of retention (which only applied to cement-retained prostheses),  
35 material wear and phonetics problems. Tables 4 and 5 show the complication incidences for metal-  
36 ceramic and all-ceramic CFIDPs respectively, along with each study's reported survival and success  
37 rate. For metal-ceramic CFIDPs, the most commonly reported complication was veneer fracture, while  
38 other complications had little or no occurrence across studies. The included studies had no  
39 incidences of abutment fracture, abutment screw fracture and prosthetic screw fracture. For all-  
40 ceramic CFIDPs, the most commonly reported complication was veneer fracture as well, followed by 1  
41 incident of prosthetic screw loosening. Due to the low incidence of various complications, apart from  
42 veneer fracture, only the latter was further considered for statistical meta-analysis.  
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#### 53 54 **3.3.2 Survival and Success rates**

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3 In terms of survival and success rate for metal-ceramic CFIDPs, all the studies, apart from Romanos  
4 et al. [43] and Malo et al. [37] had 100% prostheses survival rate. However, reported success rates of  
5 metal-ceramic CFIDPs ranged from 47.0% to 96.7% (Table 4). During the assessment of the  
6 descriptive statistics of the metal-ceramic CFIDPs, it was noted that one study [37] reported an  
7 unusually high number of veneer fracture complications (50%). This study described a very different  
8 prosthesis design compared to all other studies with possible technical issues and was therefore,  
9 considered as an outlier and was not considered during the subsequent meta-analyses. In terms of  
10 survival and success rates for all-ceramic CFIDPs, both studies had 100% reported survival rate,  
11 however, the success rate ranged from 60.4% to 90.9% (Table 5).

### 20 21 **3.4 Results of Risk of bias assessment**

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23 Different tools of risk of bias assessment were used for different study designs, the tools were used to  
24 ensure the data for meta-analyses came from properly designed studies. Table 6 shows the result of  
25 the risk of bias assessment. The Newcastle-Ottawa Scale (NOS) was used for the 1 cohort study [35]  
26 and the 3 case-control studies [36, 42, 44]. These studies scored 6 or more points therefore, the risk  
27 of bias was considered low. For the case series studies, 3 studies [38, 39, 41] were assigned with  
28 scores >9 which refers to low risk of bias. However, there were 2 studies [40, 43] which were scored  
29 as potentially subjected to a higher risk of bias.

### 30 31 32 33 34 35 36 37 38 **3.5 Heterogeneity of and estimated complication rate**

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40 When considering veneer fracture complications specifically, the heterogeneity overall was 'high' ( $I^2=$   
41 79.1%,  $p< 0.001$ ) (Figure 2). However, when analyzed further the heterogeneity of studies on metal-  
42 ceramic CFIDPs was 'moderate to high' ( $I^2= 52.7%$ ,  $p= 0.039$ ), whereas, the heterogeneity of studies  
43 on all-ceramic CFIDPs, was very high, ( $I^2= 94.3%$ ,  $p< 0.001$ ). Therefore the cumulative 5-, 10-, 15-  
44 year complication rates of veneer fractures were calculated for metal-ceramic CFIDPs only, taking into  
45 consideration the  $I^2$  score mentioned. Table 7 and 8 show the incidences of veneer fractures of metal-  
46 ceramic and all-ceramic CFIDPs respectively. The estimated rate (per 100 prostheses years) of  
47 veneer fracture ranged from 0% to 5.33% in metal-ceramic prostheses; and ranged from 0.91% to  
48 7.92% in all-ceramic prostheses. The complication rates per year based on random effect of veneer  
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3 fractures on metal-ceramic CFIDPs was 5% (95% CI: 1%- 8%). The cumulative 5-, 10-, 15-year  
4 complication rates for veneer fractures were 22.1%, 39.3% and 52.8% for metal-ceramic CFIDPs.  
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#### 7 8 **4. Discussion**

##### 9 10 **4.1 Selection process**

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12 Systematic reviews and meta-analyses are designed to search for articles in a systematic way and  
13 pool the data for analysis in order to generate more robust results. Randomized controlled clinical  
14 trials (RCT) are at the top portion of the hierarchy of study design, but it is not always possible to carry  
15 out RCTs due to ethical reasons, time and costs etc. In the present systematic review, most of the  
16 final selected articles were case series studies and case-control studies and, hence, the results  
17 should be viewed with some caution. The electronic search covered a time span between January  
18 2000 and May 2016. The search did not extend to previous years as these had been extensively  
19 searched through other systematic reviews [8,9,20] using similar inclusion and exclusion criteria and  
20 search strategies, and no relevant studies were identified; one of the authors (HP) was a co-author in  
21 one of those previous reviews [8].  
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33 During the electronic search process, around 1400 potential titles and abstracts were yielded, and 6  
34 of the final selected studies originated from the main electronic database search, whereas 5 were  
35 identified during hand searching. This result may reflect the possibility that the search strategy had  
36 been too narrow. In the selection of potential articles from the main electronic databases, both  
37 assessors chose the articles together at the same time. Any discrepancies in opinion were solved  
38 immediately through discussion, this saved the time of revisiting the titles and abstracts when there  
39 were discrepancies. In the full text screening process, which was performed independently, the inter-  
40 assessor agreement was 'Good'. This implied that the inclusion and exclusion criteria were clear and  
41 unambiguous to both the assessors.  
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51 One of the inclusion criteria in this study was a minimum mean follow-up period of 5 years. Even  
52 though this represented a measurable mid-term clinical service time, it did not ensure that all  
53 prostheses were functioning for at least 5 years. Many of the studies did not provide a range of  
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3 follow-up years and therefore the absolute follow-up time for each prosthesis should be interpreted  
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5 with caution.  
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#### 7 8 **4.2 Risk of bias assessment of the included studies** 9

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11 In the current study, most of the included studies showed a low risk of bias, except for 2 studies [40,  
12 43]. Upon review, the lower rating in the assessment of these two studies was due to insufficient  
13 description in the materials and methods section. However, the results of these two studies were  
14 similar to the others. Therefore, the data extracted from these articles was still included in the meta-  
15 analysis. None of the selected studies had declared a specific conflict of interest or financial  
16 sponsorship. Regarding the risk of bias assessment tool for the case series studies [26], a clear cut-  
17 off point was not provided by the authors and so a score of 9 was used in this study. Therefore, the  
18 absolute score may not necessary reflect the absolute risk of bias, and thus, caution in interpreting  
19 the data should be taken.  
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#### 28 **4.3 Results of the current study** 29

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31 In terms of the results yielded from the final selected studies looking at CFIDPs, the most important  
32 new finding compared to previous reviews[8, 9] was the existence of 9 metal-ceramic and 2 all-  
33 ceramic CFIDP studies which satisfied the inclusion criterion of at least 5 years of follow-up time. In  
34 all of the included studies the reported prosthodontic complications were mainly limited to veneer  
35 fractures in both kind of prostheses. The very low incidence of all the other related prosthodontic  
36 complications compared favorably with the respective incidences reported in metal-acrylic CFIDPs[8,  
37 9], and may reflect the improvement on dental technology and implant components with time, taking  
38 into account that all the studies in the current publication were published after 2011. Since veneer  
39 fractures were the primary prosthodontic complication the cumulative rates of other complications  
40 were not analyzed further.  
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51 An important point that needs to be clarified is the fact that during the complication analysis, the  
52 incidence of complications reported were assumed to happen on different prostheses, the assumption  
53 being that no complications occurred repeatedly on the same prostheses. Therefore, the results of  
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3 current study may have over-estimated the complications on a prosthesis level. This assumption was  
4 held because it was not possible to extract this kind of information from the included studies.  
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8 In terms of heterogeneity of studies, the 2 studies of all-ceramic CFIDPs presented with very high  
9 heterogeneity considering veneer fractures ( $I^2= 94.3\%$ ) and therefore, no calculation of cumulative  
10 complication rates was performed. This was due to the fact that one study[44] used predominantly  
11 monolithic zirconia frameworks, while the other study[40] used bi-layered zirconia restorations. For  
12 the studies of metal-ceramic CFIDPs, the heterogeneity was high overall, but within acceptable limits  
13 ( $I^2= 52.7\%$ ) for veneer fractures. Therefore, veneer fracture rates based on random effects and  
14 cumulative 5-, 10- and 15-year rates were calculated.  
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18 Most of the MC CFIDP studies reported 100% survival rates; 2 studies [37, 43] reported some more  
19 serious technical complications which necessitated remakes. One of these studies [37] used  
20 individual all-ceramic crowns cemented over the superstructure and experienced a high complication  
21 rate, and was therefore excluded from further analysis as an outlier. It is noteworthy that overall  
22 success rates of MC CFIDPs ranged from 47%-96.7% and this reflects the need for prosthodontic  
23 aftercare and maintenance involved in these prostheses, as well as the heterogeneity regarding  
24 clinical techniques. Many other factors, such as method of fixation, number of implants, and opposing  
25 dentition could play an important role in the frequency of complications but that level of analysis was  
26 not possible in this study.  
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40 The cumulative 5- and 10-year complication rates of veneer fractures on metal-ceramic CFIDPs were  
41 22.1% and 39.3% respectively. The 5- and 10-year rates represent the actual performance, based on  
42 the mean clinical follow-up period of the included studies. The cumulative 15-year complication rates  
43 only represented an estimation based on time projection, so they have to be interpreted with caution.  
44 It is important to note however, that all these rates were accompanied by a wide range of confidence  
45 intervals which highlights the variation in veneer fracture events based on a number of factors that  
46 could not be analyzed in this study. All this information is very important to both clinicians and  
47 patients as it affects expectations and maintenance costs.  
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55 Although a direct comparison of complications between various materials used for CFIDPs was not  
56 possible, previous meta-analyses permitted some indirect comparisons with the current study results.  
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3 Metal-acrylic CFIDPs experienced a reported cumulative 5-year complication rate of 30.6% to 33.3%  
4 in resin veneer fractures [8, 9]. In current study, metal-ceramic CFIDPs experienced a cumulative 5-  
5 year complication rate of 22.1%. Therefore, metal-ceramic CFIDPs seemed to be experiencing a  
6 lower incidence of veneer fractures. It is noteworthy to add that some authors may have disregarded  
7 minor chipping of ceramic, while only reporting on major fractures of ceramic. If that was the case, this  
8 study may have under-estimated the incidence of ceramic veneer fracture complications. Another  
9 suggestion for the higher complications in metal acrylic prostheses, would be the inclusion of studies  
10 of metal acrylic which was done in the early times when the technology and knowledge was still  
11 lacking. This is a very important finding, reported for the first time, which can aid in treatment  
12 planning, consent and expectations of treatment and maintenance costs. Another factor to consider  
13 is that, usually, a veneer fracture is much easier to repair in a metal-acrylic compared to a metal-  
14 ceramic CFIDP [11]. Comparing the incidence of screw loosening between the current review and  
15 previous systematic reviews of metal-acrylic CFIDPs, the current study presented a lower incidence.  
16 For prosthetic screw loosening, the cumulative 5-year complication rate for metal-acrylic CFIDPs was  
17 reported as 5.3% [8], whereas there was only 1 incidence in 139 (0.72%) metal-ceramic CFIDPs and  
18 1 in 70 (1.43%) all-ceramic CFIDPs after a mean follow-up period of 5 years in the current study. A  
19 similar pattern emerges for abutment screw loosening, where the cumulative 5-year complication rate  
20 for metal-acrylic CFIDPs was 4.7% to 9.3% [8, 9], whereas there were 2 incidences in 220 (0.91%)  
21 metal-ceramic and no incidence in all-ceramic CFIDPs. The incidence of screw fractures, prosthetic  
22 screw fractures and abutment screw fractures reported for metal-acrylic CFIDPs in previous studies  
23 [8, 9] showed a cumulative 5-year complication rate of 4.1% and 2.1-10.4% respectively. This  
24 contrasted with this study, where there was no prosthetic screw fracture nor abutment screw fractures  
25 in metal-ceramic and all-ceramic CFIDPs. Regarding framework fractures, metal-acrylic CFIDPs  
26 experienced a cumulative 5-year complication rate of 3.0% to 4.9%. Whereas for metal-ceramic  
27 CFIDPs, there was only 1 in 235 (0.43%) prostheses after a mean follow up period of 5 years and all-  
28 ceramic CFIDPs experienced no framework fracture at all. A possible explanation for the minimum  
29 incidence of all these mechanical complications in the included studies of this review, compared to  
30 previous studies on MA CFIDPs, could be the advances in materials, screw mechanics and  
31 interfaces, as well as dental technology, as most of the metal-acrylic CFIDPs studies were older  
32 compared to the ones looking into metal-ceramic or all-ceramic prostheses.  
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3 A recent systematic review [16] looking at the clinical success of both tooth- and implant-supported  
4 zirconia fixed dental prostheses identified 4 studies of CFIDPs. Three of these studies [33, 52, 53]  
5 were not included in the current review as they did not satisfy the inclusion criteria, one study[40] was  
6 included and one[44] more was identified. However, that review [16] showed a cumulative 5-year  
7 complication rate of 30.5%, with the predominant complication being fracturing of the veneering  
8 material on bi-layered prostheses which is consistent with the findings of the current study. An  
9 important finding that stands out from both reviews is the fact that the study with the least problems  
10 [40] utilized predominantly monolithic zirconia CFIDP with only the labial side of the prostheses  
11 veneered. However, it seems that this is the only study on monolithic zirconia CFIDPs with a mean  
12 follow-up of 5 years. The same inconclusive results regarding complications of zirconia CFIDPs were  
13 also reported in a very recent systematic review[54]. This observation may provide some preliminary  
14 evidence to support a better clinical performance of monolithic over bi-layered all-ceramic CFIDPs.  
15 Another recent systematic review by Berthold et al.[21], examining CAD/CAM fabricated implant-  
16 supported restorations, identified some studies on metal-ceramic or all ceramic CFIDPs and also  
17 reported that the most commonly reported technical complication was veneer fractures, in line with  
18 the results of the present study. Therefore, the results of this study showed that the mid-term clinical  
19 documentation of AC CFIDPs is still minimal and more studies are needed before it can be proposed  
20 as mainstream treatment choice material.

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The data extraction and subsequent analyses highlighted, once more, the heterogeneity and lack of standardized reporting of most studies, which makes any meta-analysis very challenging [55]. A standardized method of reporting should be implemented in future studies for better clarification of complications that will allow readers to reach more meaningful conclusions relevant to their practice [56]. This heterogeneity also did not allow any meaningful analysis of the effects of other potentially significant factors, such as method of fixation, opposing dentition, and parafunctional habits.

## 5. Conclusions

Within the limitations of this study, the following conclusions could be drawn: Metal-ceramic and all-ceramic CFIDPs presented with veneer fractures as the main complication while other complications were negligible after a mean follow up period of at least 5 years. The cumulative 5- and 10-year complication rates for veneer fractures were 22.1%, 39.3% respectively for metal-ceramic CFIDPs,



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3 but with variable confidence intervals. Only 2 studies of all-ceramic CFIDPs were identified, having a  
4 mean follow-up time of at least 5 eyars, with predominantly monolithic restorations performing better  
5 compared to veneered ones. More long-term studies are needed to document the use of all-ceramic  
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8 CFIDPs.  
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### 10 11 **Acknowledgments**

12  
13  
14 The authors would like to acknowledge the statistical support provided by Mr. Bob Blizard,  
15 Biostatistics Teaching Fellow at the UCL Eastman CPD and Biostatistics Unit.  
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### 18 19 20 **Conflict of interest declaration:**

21 The authors declare no conflict of interest.  
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For Review JOPR

Table 1. Representative search strategy (Supplementary Table)

No.	Search Strategy
1.	Dental Prosthesis, Implant-Supported/
2.	Dental Implants/
3.	Dental Prosthesis Design/
4.	2 and 3
5.	(fixed adj3 (prothes* or superstructure* or suprastructure* or restoration* or rehabilitation* or reconstruction*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
6.	(implant* adj5 (prothes* or superstructure* or suprastructure* or restoration* or rehabilitation* or reconstruction*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
7.	1 or 4 or 5 or 6
8.	Dental Restoration Failure/
9.	dental restoration* failure*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
10.	Treatment Outcome/
11.	Treatment Failure/
12.	Dental Prosthesis, Implant-Supported/ae [Adverse Effects]
13.	Dental Prosthesis Design/ae [Adverse Effects]
14.	((prosthodontic or technical or mechanical or screw* or veneer* or framework* or abutment*) adj3 (complication* or outcome* or failure*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
15.	(veneer* adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
16.	(framework* adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
17.	(screw* adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
18.	(abutment* adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
19.	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20.	ceramics/ or dental porcelain/
21.	ceramic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
22.	dental porcelain*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
23.	Metal Ceramic Alloys/
24.	metal ceramic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
25.	Chromium Alloys/
26.	cobalt chromium*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
27.	Titanium/
28.	titanium*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
29.	Gold Alloys/



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31.	Zirconium/
32.	zirconia*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
33.	20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31

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**Table 2.** Demographics of final selected articles

Study	Gender		No. of patient		Age (years)		Type of center	Mean follow up (years)	Range of follow up (years)
	M	F	Planned	Actual	Range	Mean			
(Ayna et al 2015) [35]	4	9	13	13	64-77	73	NR	5	NR
(Crespi et al., 2014) [45]	13	15	28	28	46-77	59.3 +/- 16.2	University	8	NR
(Hjalmarsson et al., 2011) [36]	6	9	15	15	46-85	67	Private	5	NR
(Maloet al.2012) [37]	29	23	52	43	38-81	59.5	Private	6.5	0.75-10.6
(Mangano et al., 2014) [39]	NR	NR	NR	NR	NR	NR	Private	10	NR
(Mangano et al, 2015) [38]	NR	NR	NR	NR	NR	NR	Private	14.7	10-20
(Oliva et al., 2012) [40]	11	6	17	17	NR	52.88	Private	5	NR

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(Penarrocha-Oltra et al., 2013) [41]	12	21	33	33	29-64	50.8 +/- 7.6	University	5	NR
(Ravald et al., 2013) [42]	19	27	63	46	51-88	74	University	12	12-15
(Romanoset al., 2014) [43]	15	12	27	27	NR	59.13 +/- 10.56	University	6.6	NR
(Tartaglia et al., 2016) [44]	NR	NR	32	32	65	42-90	Private	5	NR

\*NR= Not reported  
[ ] = Reference number

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**Table 3.** Information of CFIDPs of included articles

Study	Implant system	Materials of prostheses	Type of retention	Implants per CFIDP	Total no. of prostheses	No. of maxillary CFIDPs	No. of mandibular CFIDPs	Opposing dentition
(Ayna et al., 2015) [35]	Nobel Speedy	MC	Screw retained, with multiunit abutment	4	13	NA	13	NR
(Crespi et al., 2014) [45]	Outlink, Sweden & Martina	MC	17 screw retained (directly to fixture), 17 cement retained	8	34	24	10	Cement retained group: 8 ND, 9 mixed (ND with IP), Screw retained group: 5 ND, 12 mixed
(Hjalmarsson et al, 2011) [36]	13 Astratech, 1 Struamann, 1 Biomet 3i	MC (Co-Cr)	Implant level screw retained	5-8 implants, mean 6.3	15	15	0	9 ND, 1 ND with IP, 4 IP, 1 CD
(Malo et al., 2012) [37]	Nobel Speedy	MC	Screw retained	mean 5, range 4-11	66	28	38	33 IP Others: NR
(Mangano et al., 2014) [39]	Sistema Leone	MC	Cement retained	NR	19	NR	NR	NR
(Mangano et al., 2015) [38]	Mac System	MC	Cement retained	6 in 10 restorations, 8 in 4 restorations	14	NR	NR	NR

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(Oliva et al., 2012) [40]	Straumann and Osstem	AC	Screw retained	3	22	11	11	19 IP, 3 ND, 2 mixed
(Penarrocha-Oltra et al., 2013) [41]	TSA Avantblast	MC	Cement retained	6 to 8	15	15	0	6% ND or TP, 72.8% IP, 3% OD, 18.2% CD
(Ravald et al., 2013) [42]	Astra Tech AB and Branemark Mark II	MC	Screw retained	6 in upper, 5 in lower	26 gold alloy with ceramics, 2 titanium with ceramic	NR	NR	NR
(Romanoset al., 2014) [43]	Ankylos,	MC	Cement retained	6 or 8	31	NR	NR	NR
(Tartaglia et al, 2016) [44]	Milde Implants, Titanmed	AC	Screw retained	4 to 6	48	40	8	NR

\*MC= Metal-ceramic AC= All-ceramic ND= Natural Dentition CD= Complete Denture OD= Overdenture IP= Implant supported prostheses  
 TP= Teeth supported prostheses NR= not reported  
 [ ] = Reference

**Table 4.** Complication incidences of metal-ceramic CFIDPs

Study	Complications										Survival rate	Success rate
	Veneer fracture	Abutment fracture	Abutment screw loosening	Abutment screw fracture	Prosthetic screw loosening	Prosthetic screw fracture	Framework fracture	Loss of retention (cement retained)	Material wear	Phonetics problem		
(Ayna et al., 2015) [35]	(0/13)	(0/13)	(0/13)	(0/13)	(1/13)	(0/13)	(0/13)	NA	NR	NR	100%	92.3%
(Crespit et al., 2014) [45]	(4/34)	(0/34)	(0/34)	(0/34)	(0/17)	(0/17)	(0/34)	(0/17)	NR	NR	100%	88.2%
(Hjalmarsson et al., 2011) [36]	(4/15)	NA	NA	NA	(0/15)	(0/15)	(0/15)	NA	(1/15)	(2/15)	100%	53.3%
(Malo et al., 2012) [37]	(33/66)	(0/66)	(2/66)	(0/66)	(0/66)	(0/66)	(0/66)	NR	NR	NR	92.4%	47.0%
(Mangano et al., 2014) [39]	(2/19)	(0/19)	(0/19)	(0/19)	NA	NA	(0/19)	(1/19)	NR	NR	100%	84.2%
(Mangano et al., 2015) [38]	(2/14)	(0/14)	(0/14)	(0/14)	NA	NA	(0/14)	(0/14)	NR	NR	100%	85.7%
(Penarrocha-Oltra et al., 2013) [41]	(1/15)	(0/15)	(0/15)	(0/15)	NA	NA	(0/15)	(1/15)	NR	NR	100%	86.7%
(Ravald et al., 2013) [42]	(7/28)	(0/28)	(0/28)	(0/28)	(0/28)	(0/28)	(0/28)	NA	NR	NR	100%	75.0%

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(Romanos et al., 2014) [43]	(0/31)	(0/31)	(0/31)	(0/31)	NA	NA	(1/31)	(0/31)	NR	NR	96.70%	96.7%
Sum of complication incidence	(53/235)	(0/220)	(2/220)	(0/220)	(1/139)	(0/139)	(1/235)	(2/96)	(1/15)	(2/15)		

NA= Not applicable, NR= Not reported  
 [ ] = Reference

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**Table 5.** Complication incidences of all-ceramic CFIDPs

Study	Complications										Survival rate	Success rate
	Veneer fracture	Abutment fracture	Abutment screw loosening	Abutment screw fracture	Prosthetic screw loosening	Prosthetic screw fracture	Framework fracture	Loss of retention (cement retained)	Material wear	Phonetic problems		
(Olivan et al., 2012) [40]	(1/22)	(0/22)	(0/22)	(0/22)	(1/22)	(0/22)	(0/22)	NA	NR	NR	100%	90.9%
(Tartaglia et al., 2016) [44]	(19/48)	(0/48)	(0/48)	(0/48)	(0/48)	(0/48)	(0/48)	NA	NR	NR	100%	60.4%
Sum of complication rates	(20/70)	(0/70)	(0/70)	(0/70)	(1/70)	(0/70)	(0/70)	NA	NR	NR		

NA= Not applicable, NR= Not reported

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**Table 6. Risk of bias assessment**

Type of Studies/ Risk of Bias assessment tools used	Article/ Year /Reference	Results
Randomized Controlled Trials	(Crespi et al., 2014) [45]	Selection bias: unclear risks Performance bias and detection bias: not applicable Attrition bias and reporting bias: low risks Other bias: none were detected
Cohort Studies/ Newcastle-Ottawa Scale	(Ayna et al., 2015) [35]	Selection: Score= 4* a)Representation of the exposed cohort= 1* b)Selection of the exposed non cohort=1* c)Ascertainment of exposure=1* d)Demonstration of outcome of interest=1*  Comparability: Score =1* a)Comparability of cohorts on the basis of design or analysis =1* (based on design)  Outcome: Score=3* a)Assessment of outcome= 1* b) Follow-up long enough for the outcome to occur=1* c)Adequacy of follow up cohort=1*
Case Control Studies/ Newcastle-Ottawa Scale	(Hjalmarsson et al., 2011) [36]	* Selection: Score=4* a)Case definition adequate=1*

b)Representative of cases=1\*  
 c)Selection of controls=1\*  
 d)Definition of controls=1\*

Comparability: Score=1\*

a)Comparability on the basis of cases and controls on the basis of design and analysis= 1\*( based on study design)

Exposure: Score=2\*

a)Ascertainment of exposure=1\*

b)Same method of ascertainment for cases and controls=1\*

c)Non-response rate=0\*

(Ravald et al., 2013)

[42]

Selection: Score=4\*

a)Case definition adequate=1\*

b)Representative of cases=1\*

c)Selection of controls=1\*

d)Definition of controls=1\*

Comparability: Score=1\*

a)Comparability on the basis of cases and controls on the basis of design and analysis= 1\*( based on study design)

Exposure: Score=1\*

a)Ascertainment of exposure=0\*

b)Same method of ascertainment for cases and controls=1\*

c)Non-response rate=0\*

(Tartaglia et al., 2016)

[44]

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 Selection: Score=4\*

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- a)Case definition adequate=1\*
- b)Representative of cases=1\*
- c)Selection of controls=1\*
- d)Definition of controls=1\*
  
- Comparability: Score=1\*
- a)Comparability on the basis of cases and controls on the basis of design and analysis= 1\*( based on study design)
  
- Outcome: Score=2\*
- a)Ascertainment of exposure=1\*
- b)Same method of ascertainment for cases and controls=1\*
- c)Non-response rate=0\*

Case Series Studies/ 18-item assessment tool developed by IHE, Alberta, Canada	(Mangano et al., 2014) [39]	12/18
	(Mangano et al., 2015) [38]	11/18
	(Oliva et al., 2012) [40]	9/18
	(Penarrocha-Oltra et al., 2014) [41]	12/18
	(Romanoset al., 2014) [43]	8/18

**Table 7.** Veneer fractures of metal-ceramic CFIDPs

	Study	No. of prostheses	Mean follow-up (y)	Total exposure time (y)	No. of veneer fracture events	Estimated rate*
1	(Ayna et al., 2015) [35]	13	5	65	0	0.0
2	(Crespi et al., 2012) [45]	34	8	272	4	1.5
3	(Hjalmarsson et al., 2011) [36]	15	5	75	4	5.3
4	(Mangano et al., 2014) [39]	19	10	190	2	1.1
5	(Mangano et al., 2015) [38]	14	14.7	205.8	2	1.0
6	(Penarrocha-Oltra et al., 2013) [4]	15	5	75	1	1.3
7	(Ravald et al., 2013) [42]	28	12	336	7	2.1
8	(Romanos et al., 2014) [43]	31	6.6	204.6	0	0.0

\*per 100 prostheses-years

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Summary estimates	Rate (%)	95% CI
Based on random effects	5.00	1.0-8.0
Cumulative 5-y complication rates	22.1	4.9-33.0
Cumulative 10-y complication rates	39.3	9.5-55.1
Cumulative 15-y complication rates	52.8	13.9-69.9

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**Table 8.** Veneer fractures of all-ceramic CFIDPs

Study	No. of prostheses	Mean follow-up (y)	Total exposure time (y)	No. of veneer fracture events	Estimated rate*
1 (Oliva et al., 2012) [40]	22	5	110	1	0.9
2 (Tartaglia et al., 2016) [44]	48	5	240	19	7.9

\*per 100 prostheses-years

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**FIGURE LEGENDS:**

**Figure 1.** Search results

**Figure 2.** Forest plot of veneer fracture complications

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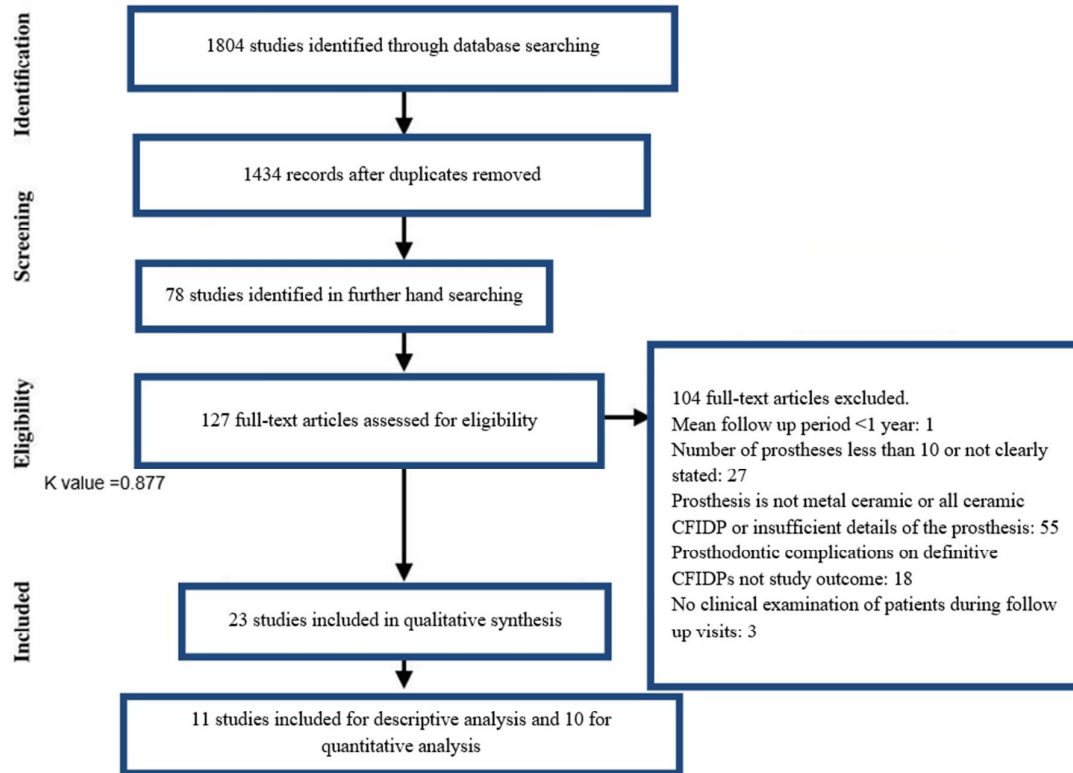


Figure 1. Search results

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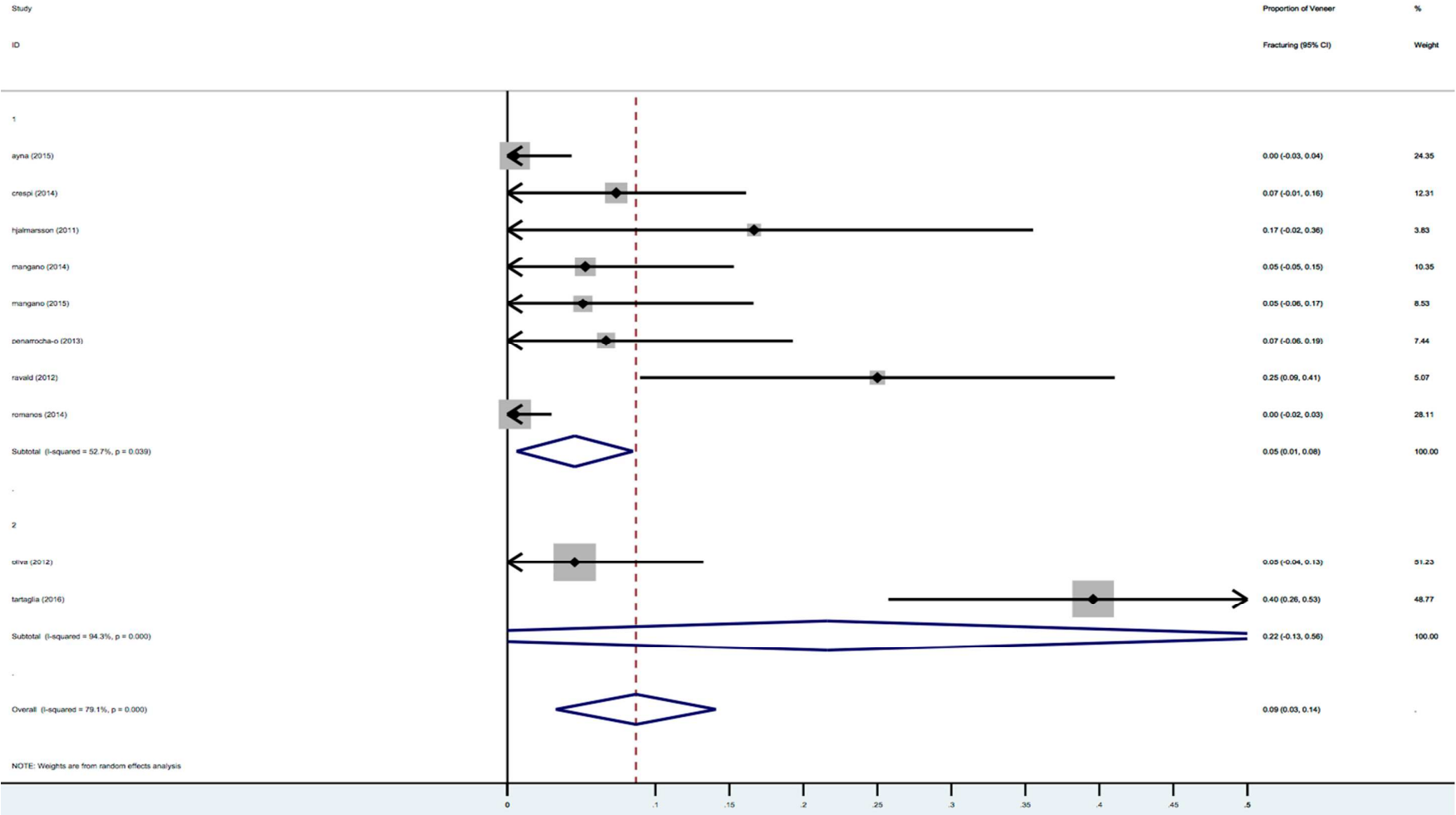


Figure 2. Forest plot of veneer fracture complications

Table 1. Representative search strategy

No.	Search Strategy
1.	Dental Prosthesis, Implant-Supported/
2.	Dental Implants/
3.	Dental Prosthesis Design/
4.	2 and 3
5.	(fixed adj3 (prothes* or superstructure* or suprastructure* or restoration* or rehabilitation* or reconstruction*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
6.	(implant* adj5 (prothes* or superstructure* or suprastructure* or restoration* or rehabilitation* or reconstruction*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
7.	1 or 4 or 5 or 6
8.	Dental Restoration Failure/
9.	dental restoration* failure*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
10.	Treatment Outcome/
11.	Treatment Failure/
12.	Dental Prosthesis, Implant-Supported/ae [Adverse Effects]
13.	Dental Prosthesis Design/ae [Adverse Effects]
14.	((prosthodontic or technical or mechanical or screw* or veneer* or framework* or abutment*) adj3 (complication* or outcome* or failure*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
15.	(veneer* adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
16.	(framework* adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
17.	(screw* adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
18.	(abutment* adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
19.	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20.	ceramics/ or dental porcelain/
21.	ceramic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
22.	dental porcelain*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
23.	Metal Ceramic Alloys/
24.	metal ceramic*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
25.	Chromium Alloys/
26.	cobalt chromium*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
27.	Titanium/
28.	titanium*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

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29.	Gold Alloys/ gold alloy*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
30.	Zirconium/ zirconia*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
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