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Evidence-based Research in Alternative Protocols to Dental Implantology: A Closer Look at Publication Bias

David R. Moradi; Peter K. Moy, DMD; and Francesco Chiappelli, PhD

Abstract

Several techniques exist for the surgical placement of dental implants. The aim of this study was to assess systematically, the efficacy of these protocols by the evidence-based perspective. Five best-case studies involving 607 early/immediately loaded implants and 300 conventionally loaded implants were identified by examining the available literature and rigorous inclusion/exclusion criteria. Overall analyses demonstrated a 98.4 percent success rate for the early/immediate procedure and a 95.3 percent for the conventional protocol. Success rates in the articles reviewed were based on implant survival over a follow-up period of between one to two years. A meta-analysis was generated to evaluate the presented evidence and to aid in decision-making.

Despite its common implementation, this technique presents many caveats, among which publication bias is one of the most common. To investigate the possible presence of publication bias, a funnel plot analysis complemented several statistical tests. By means of the systematic investigation of dental implants, the authors' results confirm the presence of publication bias in implant dentistry literature, which strongly suggests that clinicians ought not base their decisions solely on the results presented by a few published studies. Rather, it is recommended that clinicians cautiously draw conclusions and seek studies that present accountable and clinically relevant results. Furthermore, it is suggested that clinicians attend seminars to learn of the effective advances in evidence-based dentistry, so as to develop the ability to easily detect inadequate literature due to attempted correlation with the most current research. It is also recommended that additional research is necessary to analyze which fields of research are more prone to bias, thus forewarning clinicians before formulating clinical conclusions.

As an alternative to fixed and removable bridges, partials, and dentures, dental implants have become very popular throughout the field of dentistry.

Providing a foundation for the replacement of missing dentition, once covered with artificial teeth, implants look, feel, and function just like natural teeth.[1] Due to implant popularity, much research has recently been conducted aiming to improve the surgical procedures implemented. The conventional placement of an implant requires two procedures.

- First (stage 1), a titanium implant is placed within the jawbone and covered by the gingival tissue.
- Second (stage 2), a small post known as an abutment is attached to the implant, protruding through gingival tissue and thus providing an anchorage for the artificial tooth.[1] The second surgical procedure begins only after the titanium implant has integrated with the jawbone.



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1a. Implants after healing period.

1b. Stage II conventional procedure.

1c. Implants ready for prosthesis.

Figures 1a-c. Conventional implant preparation.

The time period required for osseointegration, formerly known as the "healing period," takes about three to six months of time. During this time interval, the patient wears a temporary denture and should stay on soft diets.

Recent advances in implant dentistry demonstrate that the healing period can greatly be reduced or even eradicated, despite the necessity for osseointegration.[2] In a process known as "early loading," the prosthesis is placed in six weeks or less after the first stage procedure. In the "immediate load" technique, the implant, abutment, and prosthesis are all placed in one visit or within two to three days.[1] Not only do these techniques simplify the surgical process, but they also eliminate the problematic and irritable usage of postoperative partial dentures. In addition to comfort, patient satisfaction greatly increases because patients enjoy sooner the functional and esthetically pleasing look of the implant.[3] Through these surgical advancements, dentists are able to provide patients with the most convenient and advanced dental treatments.

However, despite the great expediency of the early/immediate load procedures, practitioners must inquire about the overall success of the implant, defined as an implant that sustains a loading force for a minimum of one year. Can the implant withstand the masticatory forces and succeed by loading the prosthesis in such a minimal time period? To minimize the risk of implant failure, it is best that implants are kept load-free during the healing period until osseointegration occurs.[4] Despite this, current literature explains that the early/immediate load treatments are both predictable and reliable. Furthermore, the research community affirms that these forms of treatment, compared to the conventional procedure, neither increase the number of implant failures nor bone loss.[3]

Presented with these conflicting ideas, dentists are left unaware of the most efficient technique, which promises implant success. To clear up ambiguities, the most effective method to investigate implant success can be achieved through the evidence-based perspective. As the most receptive form of research, evidence-based research provides systematic research on research and seeks to discover the best available evidence regarding a specific treatment.[5] Thus, in a patient population in need of dental implants, is the immediate load technique more effective than the conventional implant procedure in increasing implant success?

Methods

Part I: Conventional Protocol

Due to the rising demand of dental implants, several modes of surgical procedures exist. In general, the standard protocol for implant placement includes the conventional procedure, which emphasizes the load-free healing period as one of the most important requirements for implant/bone integration[6] (**Figures 1a-c**).

1. Search Strategy

A best-case study was designed to evaluate the current published literature on the conventional implant protocol. The PICO question was formulated as follows: In a patient population in need of dental implants, is the conventional implant procedure more effective than the early/immediate load technique in increasing implant success?

The search was restricted to articles relevant to the PICO question within the PubMed database. Only articles written in English were considered, excluding contact with any relevant authors regarding original data. Review articles, abstracts, unpublished reports, and publications in press were not considered. The search used two search titles including "conventional

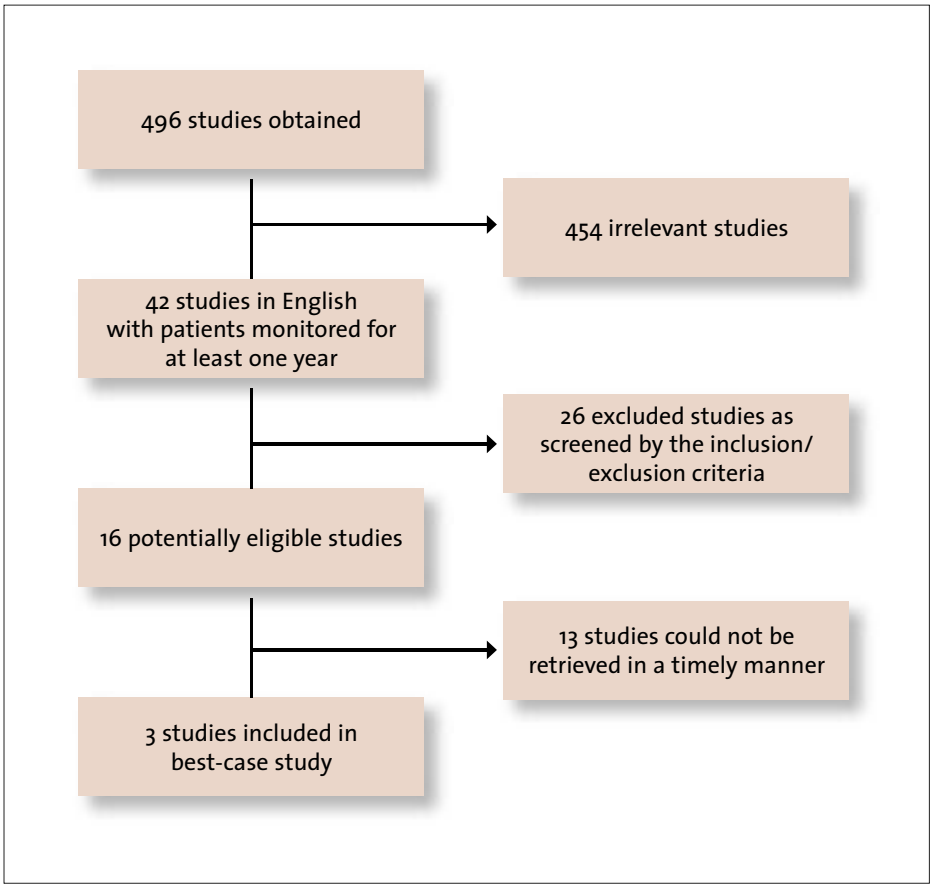

Figure 2. Conventional protocol: Search results.

load dental implants" and "conventional dental implants." The search was limited to studies that prospectively monitored a patient's implant(s) for several years following surgery. Only studies that considered both protocols — conventional and early/immediate — were included in our search. The titles and abstracts of all published articles obtained from this search were examined to determine the applicability of the articles to the study's purpose/PICO question.

2. Inclusion/Exclusion Criteria

A screening was carried out based on the following inclusion criteria:

1. Execution of at least a one-year minimal prospective follow-up,
2. Implant success was assessed based on survival after at least one year,
3. Patients had adequate bone (no need for bone grafting),
4. Usage of any type of dental implant (i.e., ITI, Nobel Biocare, Astra, 3i, etc.),
5. Usage of any type of prosthesis (i.e., single dentition, partials, dentures …),
6. Patients had adequate oral hygiene (absence of any oral disease),
7. Subjects were humans, and
8. English articles.

Studies with men and women of all ages, as well as patients of any race and/or ethnicity, were included in the study. Furthermore, it was essential that the papers provided statistics on implant survival/failure needed for the production of a meta-analysis.

Using the PubMed database, the search conducted generated an initial lot of 478 papers using the phrase "conventional dental implants," and a total of 18 papers using the phrase "conventional load dental implants" as keyword search item entries. Of these papers, 42 articles included patients who were monitored for at least one year and were written in the English language. Another screening was executed to filter out papers that only included one protocol. A final screening was executed to filter out trials failing to meet the inclusion and exclusion criteria of the search strategy. These irrelevant studies were thus omitted from the best-case study (**Figure 2**).

3. Quality Assessment

Three trials provided data on 220 conventionally loaded dental implants and 321 early/immediately loaded dental implants in patients with adequate bone quality and oral hygiene. Reports were evaluated for quality of methodology, design, and data analysis based on the Wong Scale-Revised.[7] This scale is based on reviewer responses of nine questions concerning the research quality of each individual paper. Each of the nine questions was scored from 1 to 3 (with 3 equaling the best). An overall comprehensive score ranging from 9 to 27 was generated from the summation of the individual scores of each individual question.[7]

The literature regarding the conventional implant protocol was reliable in that all of the papers in the best-case study obtained a total Wong

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WHAT

- What is the research question/purpose/outcome sought? Is the stated purpose tested and measured correctly?
- What are the findings; how are they presented? Do the findings respond to the stated purpose/outcome sought?
- What is the clinical significance of the findings, and what is their statistical significance? Do the findings mean anything anyway ... research-wise or clinic-wise?

WHO

- What was the sample tested, is the sample representative of the population under study, of your patients?
- Are numbers presented in the paper that you can trust, and would that permit you to compute the Number Needed to Treat (NNT)? List experimental group event rate (EER) and control group event rate (CER), and compute NNT. Is there any information about Intention to Treat (ITT)
- Can the information provided in the paper be of any use directly to any patient or the group of patients in your practice now?

HOW

- How was the question addressed from the perspective of design, and were the appropriate caveats discussed?
- How was the outcome measured; were issues of reliability and validity presented?
- How were the data presented and analyzed (SESTA)?

Figure 3. Wong Scale—Revised.

Scale score of 18 or greater. The scores imply that the quality of the methodology, design, and data analysis of these papers met the minimum cut-off requirement of acceptability. Analysis of the scores led to the establishment of criterion of acceptability for each of the individual domains of research assessed by the Wong Scale-Revised (**Figure 3**).

Part II: Early/Immediate Protocol

1. Search Strategy

By the same approach, the authors formulated a PICO question with respect to the early/immediate loading of implants, which greatly expedites the implant process. In brief, it stated that: In a patient population in need of dental implants, is the immediate load technique more effective than the conventional implant procedure in increasing implant success? As described, the outcome of interest (implant success) was based on implant survival for at least one year.

As above, the search was restricted to articles relevant to the PICO question within the PubMed database. Only articles in English were considered, excluding contact with any relevant authors regarding original data. Review articles,

4a. Extraction of tooth.

4b. Immediate implant placement.

4c. Final abutment ready for prosthesis

Figures 4a-c. Early/immediate implant preparation.

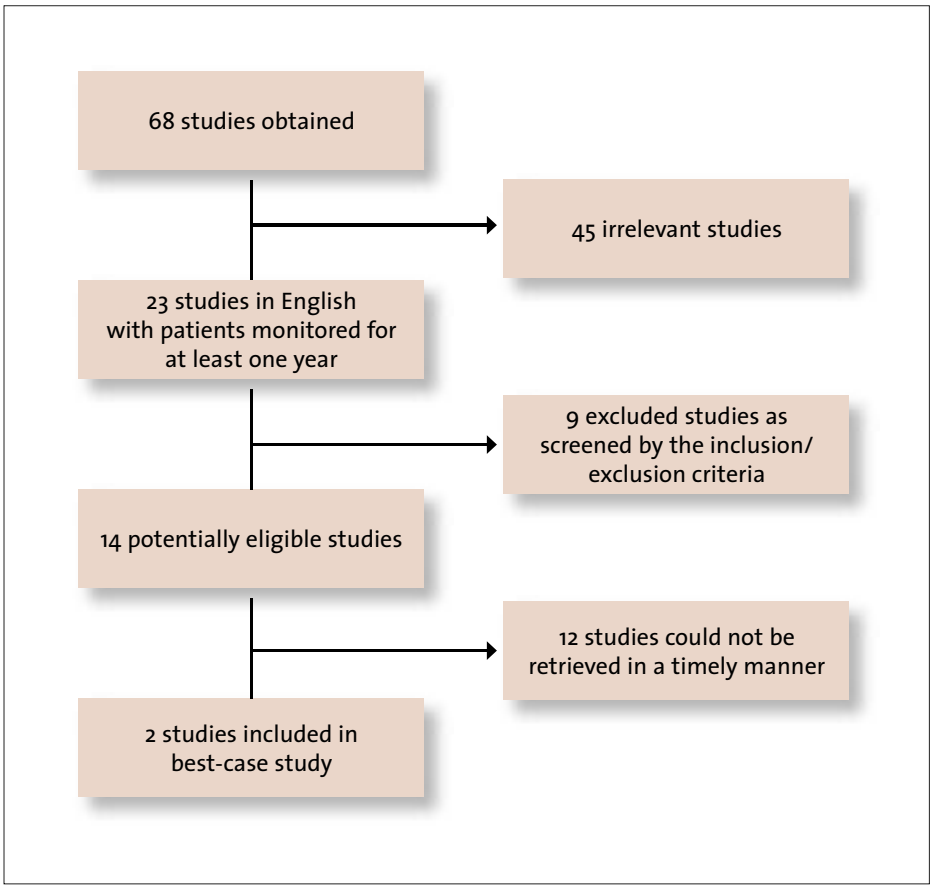

Figure 5. Early/immediate search results.

abstracts, unpublished reports, and publications in press were not considered. The search used two search titles including "early load dental implants" and "immediate load dental implants." The search was limited to studies that monitored a patient's implant(s) for a minimum of one year following surgery and studies that considered both protocols. The titles and abstracts of all published articles obtained from this search were examined to determine the applicability of the articles to the study's purpose/ PICO question (**Figures 4a-c**).

2. Inclusion/Exclusion Criteria

A screening was carried out based on the same inclusion criteria utilized for the conventional protocol. Using the PubMed database, the search conducted generated an initial lot of 28 papers using the phrase "early load dental implants," and a total of 40 papers using the phrase "immediate load dental implants" as keyword search item entries. Of these papers, 23 articles included patients who were monitored for at least one year and were written in the English language.

Another screening was executed to filter out papers that only included one protocol. A final screening was executed to filter out trials failing to meet the inclusion and exclusion criteria of the search strategy. These irrelevant studies were thus omitted from the best-case study (**Figure 5**).

3. Quality Assessment

Two trials provided data on 286 early/immediately load dental implants and 80 conventional load dental implants in patients with adequate bone quality and oral hygiene. As mentioned previously, the quality of methodology, design, and data analysis of each individual paper met the minimum cut-off requirement of acceptability according to the Wong Scale-Revised. Analysis of the scores led to the establishment of criterion of acceptability for each of the individual domains of research assessed by the Wong Scale-Revised.

Results

Following the acceptable sampling analysis, a meta-analysis was generated using the data collected from the two searches. Data from the five studies resulted in a total of 607 early/ immediately loaded implants and 300 conventionally loaded implants. The meta-analysis compared the success rates (survivability of dental implants after at least one year) of implants placed via these two procedures. The overwhelming finding of this analysis indicated that the early/immediate procedure, compared to the conventional protocol, yielded a *greater* success rate in terms of implant survival for at least one year.

The data show that the best available evidence derived from this best-case study suggested that the procedure of choice for individuals in need of

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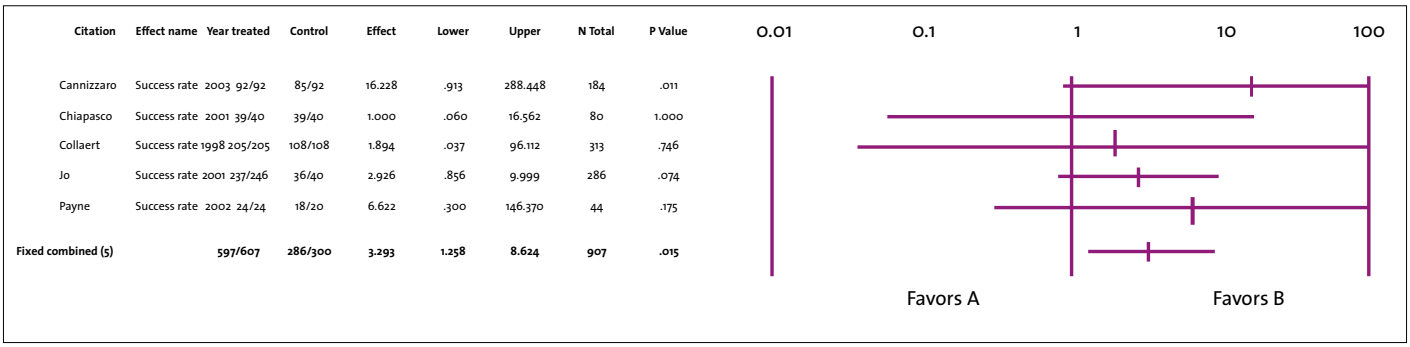

Figure 6. Meta-analysis (A=Conventional protocol; B=Early/immediate protocol).

Table 1

Success/Failure Rates of Early/Immediate vs. Conventional Protocols

Authors of best case studies	Success and (failure) of early/immediate protocol	Success and (failure) of conventional protocol
Cannizzaro et al., 2003	100% (0%)	92.4% (7.6%)
Chiapasco et al., 2001	97.5% (2.5%)	97.5% (2.5%)
Collaert et al., 1998	100% (0%)	100% (0%)
Jo et al., 2001	96.3% (3.7%)	90% (10%)
Payne et al., 2002	100% (0%)	98% (10%)

dental implants is the early/immediate procedure, in terms of success rate, as defined by the PICO question. As each individual study confirmed, the early/immediate protocol either yielded a greater or equivalent success rate when compared to the conventional procedure. Overall, the combined results of the five best-case papers show a success rate of 98.4 percent for the early/immediate procedure and a 95.3 percent for the conventional protocol. Thus, clinicians should be confident in choosing the early/immediate protocol as the best procedure, promising patients lasting and effective implants (**Figure 6 and Table 1**).

Discussion

Dental implants are significantly altering the standard of care and quality of life. Providing one of the most beneficial solutions to the replacement of missing dentition, dental implants improve a patient's way of life by promising a lasting and confident smile. Furthermore, implants open the door to a lifetime of renewed comfort in that patients no longer deal with the frustration, inconvenience, and frequent embarrassment that traditional removable restorations offer.[1] Implants are unquestionably enhancing the way of life of mankind in the 21st century.

Evidence-based research is the finest form of research in the health sciences because it provides a systematic method of performing research on research to reach an ultimate conclusion. This form of research yields the best source of evidence regarding the effectiveness of a treatment for each patient. Especially significant in the case of dental implants, evidence-based research examines clinical data and amalgamates the outcomes of several procedures, thus generating a final and assertive conclusion. The generation of a meta-analysis graphically represents this conclusion by summarizing the results of several applicable papers. In turn, the presented evidence can aid clinicians in making clinical decisions. Due to the high demand of dental implants, the most effective procedure must be implemented to provide patients with the finest and most superb dental care.

1. Publication Bias in Evidence-based Research Through Implant Dentistry

Before clinicians base their decisions on results generated by the evidence-based method, they must first question the validity of the published dental implant literature. Despite the substantial literature of clinically relevant information regarding implants, clinical decisions cannot be made solely based

on reported results because implant literature is significantly biased.[8] Not only does this apply to implant literature, but publication bias is also a major problem in social and other biomedical sciences as well.[9] Because it is easier to publish studies with significant results, studies that show results with no difference between the controls and treated groups and/or studies with poor results are seldom published.[10] This problem jeopardizes the validity of a meta-analysis because accumulated data is solely extracted from published literature.[11] With this awareness, it is quite evident that publication bias is a major flaw in evidence-base research due to its dependency on meta-analyses.

Publication bias can be noticed through the results generated in this study. As observed through the meta-

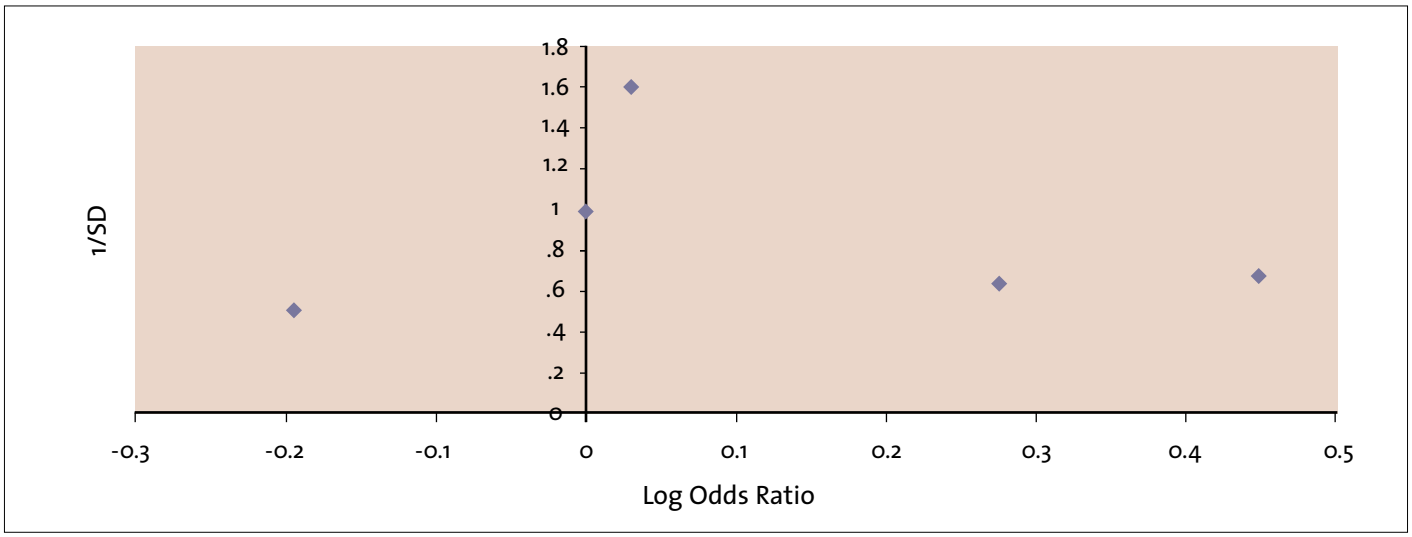

Figure 7. Funnel plot analysis of the publication bias.

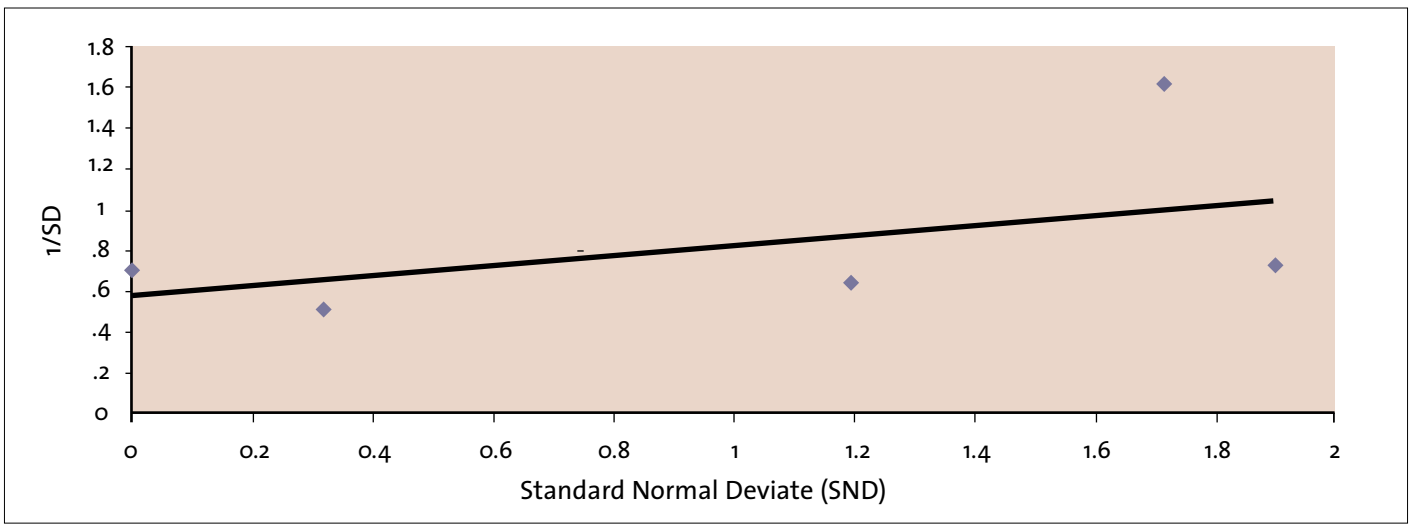

Figure 8. Egger's regression analysis of the publication bias.

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9a. Site ready for implants.

9b. Early load prosthesis.

9c. Temporary prosthesis.

Figures 9a-c. Implant process.

analysis produced from the five best-case papers, all five papers confidently confirmed the success of the early/immediate protocol. Not only do they exhibit success, but three papers enthusiastically explained that the early/immediate protocol yielded even more successful results than the conventional procedure.[2,12,13] The other two papers validated both procedures as equally successful by presenting success rates of 100 percent and 97.5 percent for both procedures.[14,15] It is interesting to note that all five papers failed to explicate, if any, failure rates, especially for the early/immediate protocol (**Table 1**). If exposed, the authors did not justify why the implants failed but rather presented certain "complications" that occurred during the surgical procedure.[2] For example, one paper presented mobility as the cause of early/immediate implant failure. However, instead of justifying failure as a lack of osseointegration, the authors provided secondary explanations such as bacterial infestation.[2]

Analysis of the generated results demonstrated that studies with extremely successful results — although possibly dubious — are most commonly published, while studies with adverse, yet meaningful results are generally disregarded.

Detection of publication bias can best be shown through the generation of a funnel plot.[11] A funnel plot is a type of scatterplot that estimates the effects of each study used in a meta-analysis against a measure of its precision.[16] In the absence of bias, the plot is symmetrical, and is thus in the shape of an "inverted funnel." This shape is expected because in studies with smaller sizes, a large variation exists in the effective size of these studies. Thus, random variations become increasingly influential.[17] However, in the presence of publication bias, the plot becomes asymmetrical due to the omission of nonsignificant, left-handed studies that are less likely to become published.[9] It can be observed that data points in the authors' funnel plot are greatly skewed to the right, thus confirming the presence of publication bias (**Figure 7**).

In addition to graphically assessing publication bias, various statistical methods also exist. One of the most common tests detecting publication bias is the Egger's regression test.[18] This test assesses asymmetry (bias) using precision to predict the standardized effect.[18] The slope of the generated regression line indicates the effect size and direction, while the y-intercept indicates the presence of bias.

If there is no bias present, the intercept will be zero. However, in the presence of bias, the intercept is significantly different from zero.[9] Implementation of Egger's test confirms the possibility of publication bias as exhibited through the funnel plot. As observed in Figure 8, the y-intercept greatly deviates from the origin, reinforcing the presence of publication bias (**Figures 7 and 8**).

2. Prevention of Publication Bias

Due to the presence of publication bias, a clinician cannot confidently reach conclusions regarding specific protocols based on published literature. If a clinician were to adhere to the authors' systematic review regarding the efficacy of early/immediate load dental implants, he or she would select this protocol over the conventional procedure. This is because the authors' systematic review displays this convenient procedure with remarkable success and effectiveness, as demonstrated through the convincing meta-analysis (**Figure 6**). Furthermore, clinicians can sooner satisfy patients with yearning esthetic results (**Figures 9a-b**) as opposed to inconvenient temporary prosthetics (**Figure 9c**). Thus, due to publication bias, the authors' results — although skewed — portray the early/immedi-

ate protocol as the most convenient and successful procedure, although this most definitely may not be the case.

At this point, it is best to ask what clinicians must do regarding the erroneous results presented in systematic reviews. As explained, regardless of a paper's relevancy, clinicians cannot base their decisions on systematic reviews and/or meta-analyses unless they thoroughly assess the methods used in executing the study.[10] There are many steps clinicians can take to determine the validity of a study, or better yet, exclude adverse studies. Firstly, clinicians can conduct an unbiased search for studies. This can be achieved through the execution of both electronic and manual searches. While conducting this search, it is best to include "grey literature."[9] In the health and social sciences, there are systematic differences between the results presented in both studies. Furthermore, by meticulously documenting what has been searched and how the search was implemented, the prevalence of publication bias greatly decreases.

In addition to this systematic approach of investigating the literature, clinicians can perform several analyses to analyze the sensitivity of a paper's results based on the characteristics of the study.[10] Because systematic reviews and meta-analyses are most commonly used to assess evidence regarding certain procedures, one step to directly investigate the possible presence of publication bias — as was conducted in this study — would be to produce a funnel plot.[16] Although the construction of an asymmetrical plot does not decisively confirm publication bias, clinicians become conscious of a paper's atypical results.[11] To further investigate irregularities, clinicians can conduct various statistical tests such as the Egger's regression test.[10] Other tests include a modified version of Macaskill's test and/or the permutation test.[16] Another alternative lies in the "trim and fill" model.[9] This model develops a method that determines where missing data fall, adds them to the analysis, and subsequently re-computes the combined effect. By conducting these analyses, clinicians become aware of the possible presence of publication bias and can therefore eliminate misleading systematic papers, which would otherwise lead to inaccurate conclusions.

By conducting these analyses, clinicians become aware of the possible presence of publication bias and can therefore eliminate misleading systematic papers.

In addition to graphically and statistically testing published literature, another approach can be taken to prevent making decisions based on biased results: searching for unpublished data.[10] This option would result in accurate conclusions because it completely eliminates any form of bias in that the clinician collects all the necessary data. If access is limited, however, clinicians can contact authors of published literature and request additional data. If available, the accumulation of raw data can be used to reach final conclusions regarding specific protocols (**Figure 9**).

3. Probability of Literature Assessment

Clinicians can systematically detect the presence of publication bias. In this study, the authors addressed whether clinicians would actually undertake these steps before reaching their final conclusions. It is quite evident that determining the validity of a study requires much time investment and patience. Based on this fact, would a clinician actually spend quality time on assessing the validity of a paper by conducting tedious statistical tests, seeking grey literature, and/or contacting authors? Considering a clinician's limited time, it is highly unlikely a typical clinician would alter his or her priorities to accomplish these tasks.[17]

It is understandable that a clinician will not conduct time-consuming statistical tests that require complicated calculations. Furthermore, it is improbable that clinicians would search for grey literature and contact authors to seek unpublished data. However, contrary to the inconveniences these two options present, the generation of a funnel plot is theoretically simple and quite easy, and relatively quick to implement.[17] Thus, this option seems to be the most appropriate and convenient method to evaluate systematic reviews and meta-analyses.

4. Alternative Method of Assessment

In order to provide the best form of treatment, clinicians must stay current with new advances and clinical breakthroughs.[8] Therefore, in addition to solely investigating the literature, clinicians should attend lectures to analyze the literature and discuss clinical advances as a group. In this way, new advances would be carefully investigated as a group of clinicians seeking the finest and most effective procedure, rather than by authors wanting to glorify their

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impressive, yet trivial results. By attending seminars, clinicians can promptly detect inadequate literature due to their acquaintance with the most current research. Not only does this method beneficially impact patients, but it also aids clinicians in implementing the best procedures with the confidence of attaining successful results. This trend reaffirms the need for lifelong learning in that clinicians must continuously be aware of the newest and most successful advances in the dental field.[8]

Further research investigating the success rates of both protocols several years following implant surgery is needed. This will allow clinicians to choose a protocol resulting in lasting implants with more confidence.

In summary, the analysis of the effects of publication bias through evidence-based research in alternative protocols to dental implantology indicates that the results of several studies cannot be confidently used to reach a final, assertive conclusion. Despite its efficacy, evidence-based research is flawed in terms of data collection. Despite the many methods of dealing with publication bias, clinicians do not have the power or authority to restrain authors from publishing their significant results. With the awareness that publication bias can never be completely eradicated, it is recommended that clinicians seek studies that present reasonable results. By executing various analyses, clinicians can attempt to eliminate publication bias, thus basing their decisions on the remaining high quality evidence. Furthermore, clinicians should attend seminars to learn of the effective advances in dentistry. Due to the dental innovations, including implants, constant research is required to keep dentistry up-to-date and paramount. However, despite its significance, research must be carefully executed to eliminate publication bias. Through clinicians who are conscious of the valid research, patients will benefit from clinical advances, consequently demonstrating the excellence of dental clinicians. ■■■■

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