Evidence Brief: Impact of Mental Health Conditions on Peri-implantitis and Dental Implant Failure

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AUTHORS

Author roles, affiliations, and contributions to the present report (using the CRediT taxonomy) are summarized in the table below.

Author	Role and Affiliation	Report Contribution
Nicholas J. Parr, PhD, MPH	Associate Director, ESP Coordinating Center, Portland VA Health Care System Portland, OR	Conceptualization, Methodology, Investigation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing, Project administration, Supervision
Erin H. Beech, MA	Senior Research Associate, ESP Coordinating Center, Portland VA Health Care System Portland, OR	Investigation, Methodology, Data curation, Project administration, Writing – original draft, Writing – review & editing

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted health care topics of importance to clinicians, managers, and policymakers as they work to improve the health and health care of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program comprises four ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, interface with stakeholders, and address urgent evidence needs. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee composed of health system leadership and researchers. The program solicits nominations for review topics several times a year via the program website.

The present report was developed in response to a request from the VHA Office of Dentistry, Oral Health Quality Group. The scope was further developed with input from Operational Partners (below) and the ESP Coordinating Center review team.

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Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

Gretchen Gibson, DDS, MPH
Director
Oral Health Quality Group, VHA Office of Dentistry

Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence (see Appendix D in Supplemental Materials for disposition of comments). Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center works to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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EXECUTIVE SUMMARY

Key Findings

- Antidepressant use at the time of implant placement likely increases risk of implant failure based on moderate-strength evidence from 9 studies (N = 25,364 implants).
- Evidence from only the most rigorous available studies indicates that antidepressant use at the time of implant placement is associated with an approximately 20% increase in risk of early implant failure.
- Available evidence is insufficient to draw conclusions about the effect of mental health conditions on risk of implant failure, and no studies included peri-implantitis as an outcome of interest.
- Veteran implant candidates may benefit from approaches to screen for known and likely risk factors for implant failure, and from research on the effectiveness and feasibility of tailored peri-implant maintenance programs.

Background

The Evidence Synthesis Program Coordinating Center is responding to a request from the VHA Office of Dentistry, Oral Health Quality Group, for an Evidence Brief on the impact of mental health conditions on development of peri-implantitis and dental implant failure. Findings from this Evidence Brief will be used to inform development and use of an implant risk assessment tool.

Methods

To identify studies, we searched MEDLINE, Cochrane Database of Systematic Reviews, CINAHL, PsycINFO, and other sources up to March 2022. We used prespecified criteria for study selection, data abstraction, and rating internal validity and strength of the evidence. See the Methods section and our PROSPERO protocol for full details of our methodology.

Dental implants are an increasingly common intervention to address missing or damaged teeth, particularly among older adults and individuals without sufficient natural teeth roots to support dentures or fixed dental prosthesis. Implants are surgically placed in the bone, and over several months heal into the bone in a process known as osseointegration. Complications can occur during or after osseointegration and may ultimately result in loss of the implant.

Because placement requires incisions to the gums and extended periods of healing in a bacteria-rich environment, soft and hard tissues surrounding the implant site may become infected and inflamed. In advanced disease, known as peri-implantitis, chronic inflammation of the tissues around the implant results in loss of bone that can lead to implant failure. In addition to bacterial infection, inflammation, and bone loss at the implant site, other factors associated with increased risk of implant failure include prior gum disease (periodontitis), mechanical overloading of the implant (*eg*, bruxism, hyperocclusion), diabetes and hyperglycemia, and tobacco smoking.

Research in recent decades has also suggested a link between dental implant failure and use of medications commonly prescribed to treat depression, especially selective serotonin reuptake inhibitors (SSRIs). Additionally, depression or other mental health conditions may compromise immune function and lead to poorer dietary and oral hygiene practices. Conceivably, these systematic and behavioral changes could lead to oral inflammation and infections that, in turn, increase an implant recipient's risk of peri-implantitis and implant failure. The present review aimed to synthesize evidence from studies examining the role of mental health conditions and SSRI use in peri-implantitis and dental implant failure risk.

EVIDENCE BRIEF

INTRODUCTION

PURPOSE

The Evidence Synthesis Program (ESP) Coordinating Center is responding to a request from the VHA Office of Dentistry, Oral Health Quality Group, for an Evidence Brief on the impact of mental health conditions on development of peri-implantitis and dental implant failure. Findings from this Evidence Brief will be used to inform development and use of an assessment tool to assess the aggregate risk of complications in VA patients requiring dental implants.

BACKGROUND

Dental implants are an increasingly common intervention to address missing or damaged teeth, particularly among older adults and individuals without sufficient natural teeth roots to support dentures or fixed dental prosthesis.[1-3] Implants are surgically placed in the bone, and over several months heal into the bone in a process known as osseointegration.[1,4,5] At the time the implant is placed or after osseointegration, an abutment that extends beyond the gumline is connected to the implant to serve as the attachment point for one or more prosthetic teeth.[1,6] Later placement of the abutment may be preferred by patients because the abutment is visible for a shorter period,[1] but doing so requires a second gum incision[1,6] that may increase complication risk. The prosthetic tooth, multiple bridged teeth, or a denture are loaded onto the abutment immediately, after a brief healing period (*eg*, 1–8 weeks), or after healing is completed.[7] Single or bridged teeth are often fixed to the abutment and are cleaned alongside the patient's natural teeth.[1]

Complications can occur after implant placement and may ultimately result in loss of the implant.[1,8] Because placement requires incisions to the gums and extended periods of healing in a bacteria-rich environment, soft and hard tissues surrounding the implant site may become infected and inflamed.[5,9] In advanced disease, known as peri-implantitis, chronic inflammation of the tissues around the implant results in loss of bone.[9] Even minor bone loss associated with peri-implantitis can lead to osseointegration failure and loss of newly placed implants.[8] Implants may also fail after the initial healing process; in these cases, bone loss continues to the point of implant loss.[8] In addition to bacterial infection and inflammation leading to bone loss at the implant site, other factors associated with increased risk of implant failure include prior gum disease (periodontitis), mechanical overloading of the implant (*eg*, bruxism), diabetes and hyperglycemia, and tobacco smoking.[1,10,11]

Research in recent decades has also suggested a link between dental implant failure and use of medications commonly prescribed to treat depression, especially selective serotonin reuptake inhibitors (SSRIs).[2,12,13] It is known that SSRIs and other classes of antidepressant medications influence bone metabolism, potentially slowing implant osseointegration and elevating risk of implant failure.[2,12] Additionally, depression or other mental health conditions may compromise immune function and lead to poorer dietary and oral hygiene practices.[14-16] Conceivably, these systematic and behavioral changes could lead to oral inflammation and infections that, in turn, increase an implant recipient's risk of peri-implantitis and implant failure. The present review aimed to synthesize evidence from studies examining the role of mental health conditions and SSRI use in peri-implantitis and dental implant failure risk.

DATA ABSTRACTION AND ASSESSMENT

Effect information and population, intervention, and comparator characteristics were abstracted from all included studies. The internal validity (risk of bias) of each included study was rated using the Quality In Prognostic Studies (QUIPS)[17] tool. The QUIPS tool includes 6 domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. Domains are rated as low, moderate, or high risk of bias. As all our included studies obtained data via record review, we did not rate studies on the study attrition domain. Instead, missing data concerns were captured in other domains. Any study which was rated high in 2 or more domains was considered high overall risk of bias. Any study which was rated low risk of bias in all 6 domains was considered low overall risk of bias. Studies which did not meet either of those conditions were considered moderate overall risk of bias. All data abstraction and internal validity ratings were first completed by 1 reviewer and then checked by another; disagreements were resolved by consensus or discussion with a third reviewer.

We graded the strength of available evidence using an approach based on the AHRQ Methods Guide for Comparative Effectiveness Reviews,[18] which provides a rating of confidence in reported findings based on study methodology (design, quality, and risk of bias), consistency (whether effects are in the same direction and have a consistent magnitude), and directness (whether assessed outcomes are clinically important to patients and providers). When information on precision of findings (*eg*, confidence intervals) is available, certainty of evidence is also evaluated. We used the following general algorithm: *high strength* evidence consisted of multiple, large studies with low risk of bias, consistent and precise findings, and clinically relevant outcomes; *moderate strength* evidence consisted of multiple studies with low to moderate risk of bias, consistent and precise findings, and clinically relevant outcomes; *low strength* evidence consisted of a single study, or multiple small studies, with moderate to high risk of bias, inconsistent or imprecise findings, and/or outcomes with limited clinical relevance; and *insufficient* evidence consisted of a single study with moderate or high risk of bias, or no available studies.

SYNTHESIS

Few studies investigating the association of mental health conditions with dental implant failure were identified, and these studies were synthesized narratively. For studies of the association between antidepressant/SSRI use and implant failure, we synthesized available outcome data using random-effects meta-analyses. Studies included in meta-analyses reported outcomes as counts, proportions, or ratios, generally at the implant unit of analysis (1 study[13] reported results at the person level, and while we included these findings in analyses, it is possible that results of this study underestimate the relation of antidepressant use with implant failure). When studies reported counts or proportions but did not provide an adjusted ratio, risk ratios (RRs) were calculated directly from cell counts (no cell contained zero events). Reported adjusted odds ratios were converted to RRs using the square-root transformation.[19] Two studies[20,21] included in meta-analyses reported adjusted hazard ratios (HRs), and because implant failure was rare in these studies (occurring in approximately 10% of the intervention group), we considered these HRs to be approximately equivalent to RRs.

LITERATURE OVERVIEW

Our search identified 704 potentially relevant articles. Of these, 12 observational studies of retrospective[4,13,20,21,26-32] or prospective[33] cohorts met eligibility criteria and were included in the present review (see Table 1 for key study characteristics and Appendix C in the Supplemental Materials for additional study details). All included studies used clinical record data. The median sample size of studies was 561 participants (range: 54–5,456) or 1,376 implants (range: 224–10,096). Studies were conducted in the US or Canada ($N = 5$),[13,20,21,27,31] Sweden ($N = 3$),[28-30] Belgium ($N = 2$),[26,33] India ($N = 1$),[32] or Turkey ($N = 1$).[4]

Nine studies[4,13,20,21,26,28,29,32,33] examined the occurrence of implant failures among patients prescribed antidepressants compared with patients not prescribed antidepressants (studies varied in whether they limited eligible antidepressants to SSRIs). Three additional studies compared implant failures among patients with and without mental health conditions (depression,[31] depression or anxiety,[27] or provider judgment of "psychological illness" as cause of failure[30]). The majority of studies counted implants that failed at any time point relative to implant, abutment, or tooth placement, or did not specify a time period for eligible failures. Three studies[26,28,33] reported implant failures occurring before and up to abutment placement, and 1 study[4] included cases of osseointegration failure leading to implant removal (rather than implant failure per se) that occurred before tooth loading. No studies included peri-implantitis as an outcome of interest.

All studies were rated as moderate risk of bias (see Appendix C in the Supplemental Materials for full risk of bias ratings). The most severe risk of bias, present in 3 studies,[4,30,33] was failure to control for potential confounding in reported analyses. Other studies controlled for some, but not all, likely confounders (*eg*, patient age, sex, smoking status, bone quality, systemic diseases such as diabetes and osteoporosis, *etc*), typically by including potential confounders as covariates in statistical models. These studies were considered at moderate risk of bias from confounding.

Several studies were at risk of selection biases because eligibility was limited only to observations with complete data, or because participants who lost fewer than half of their implants, or any implants lost after an initial failure, were excluded. Some studies also did not clearly describe how antidepressant use or implant failure was determined or defined. Studies of mental health conditions[27,30,31] did not adequately describe the diagnostic status, severity, or duration of conditions, or relied on diagnostic data collected through methods subject to bias (*eg*, provider judgment of a mental health condition as the reason for implant failure).

Finally, some studies prescribed prophylactic antibiotics to implant recipients, and recipients in at least 1 study[13] were also participating in a post-implant support program. Both factors could have attenuated observed associations between antidepressant use and implant failure risk in those studies, and inconsistency in the delivery and uptake of these preventive approaches across studies may be a source of heterogeneity in implant failure risk.

Table 1. Characteristics of Included Primary Studies

Study	Country	Sample Size *# Implants*	Population	Exposures	Outcomes Assessed
Alsaadi 2007[26]	Belgium	N=2004 *(6946 implants)*	Consecutive patients treated with endosseous implants	Antidepressant, no antidepressant	Early implant failure (before and up to abutment connection)
Alsaadi 2008[33]	Belgium	N=283 *(720 implants)*	Consecutive patients treated with endosseous implants	Antidepressant, no antidepressant	Early implant failure (before and up to abutment connection)
Altay 2018[4]	Turkey	N=631 *(2055 implants)*	All patients rehabilitated with dental implants presenting with no systemic conditions and not taking any medications other than SSRIs for psychiatric disorders	SSRI, no SSRI	Early osseointegration failure (before tooth loading)
Block 2021[31]	US	N=224 *(224 implants)*	All patients with 1 or more implants removed by senior author. Failed sample included 1 implant per patient case and was the first implant placed or failed. Control group was a consecutive series of patients with implant placement in 2012 who did not have implant failure	Depression, no depression	Implant failure within 1 year, 1-4 years,* and more than 4 years
Carr 2019[20]	US	N=5456 *(5456 implants)*	All patients who received their first dental implant	SSRI, no SSRI, other SSRI type (history of use, active SSRI use, follow-up SSRI use)	Implant failure
Chatzopoulos 2018[27]	US	N=4519 *(4519 implants)*	Patients at least 18 years of age with a complete demographic and medical history who received root canal treatment or implant treatment	Depression or anxiety, no depression or anxiety	Implant failure
Chrcanovic 2016[28]	Sweden	N=2670 *(10096 implants)*	Patients consecutively treated with implant-supported prostheses	Antidepressant, no antidepressant	Implant failure (up to* and after the abutment connection)

DISCUSSION

Evidence on the association between antidepressant use and implant failure risk is moderate strength and relies on observational studies of varying sizes and rigor. As a whole, available evidence suggests that implant failures are more likely in patients using antidepressants at the time of implant placement than in patients not using antidepressants. The degree to which implant failure risk is elevated varies across studies, but findings from the most rigorous studies indicate that antidepressant use at the time of implant placement is associated with an approximately 20% increase in risk of early implant failure. A limited number of studies investigated whether the presence of mental health conditions increases implant failure risk; although studies reported associations between depression or anxiety and implant failure, evidence from these studies is insufficient to make conclusions. Moreover, the mechanism by which mental health conditions influence implant failure risk remains unclear. No studies examined the impact of antidepressant use or mental health conditions on peri-implantitis risk.

Our estimate of mean implant failure risk associated with antidepressant use is smaller than that reported in a recently published meta-analysis[2] of 5 included studies[4,21,29,32,33] (RR_{Mean} = 3.73, 95% CI [1.85, 7.52]). An analysis of the same studies using our data and methodology, not reported above, results in a smaller risk estimate (RR_{Mean} = 2.44, 95% CI [2.10, 2.84]). This discrepancy may be attributable, at least in part, to the use of raw counts of implant failures for all studies in the published meta-analysis, compared with our use of ratios adjusted for potential confounders reported by 2 studies.[21,29] Additionally, although both analyses used random-effects models, the authors of the published review appear to have used a different method to estimate heterogeneity than we employed, and did not report use of statistical adjustments to account for the small number of pooled studies and uncertainty in estimates of heterogeneity. Differences in these aspects of the analytic approaches could impact the width of reported confidence intervals.

LIMITATIONS

Limitations of our review methods include use of a second reviewer check during study selection, data abstraction, and quality assessment rather than dual independent review. Additionally, both statistical precision and heterogeneity can be poorly estimated in small meta-analyses. We took steps to ameliorate these concerns, namely use of corrections to better account for uncertainty in the estimation of heterogeneity as well as cluster-robust methods to calculate confidence intervals, but some caution should be used in interpreting reported meta-analytic confidence intervals and prediction intervals.

FUTURE RESEARCH

Loss of implants in the early period between implant placement and abutment connection is consistent with the purported mechanism by which antidepressant use elevates failure risk. SSRIs and other antidepressants influence the formation of bone,[2,12] and consequently would hamper the initial osseointegration process (leading to earlier failure) rather than compromise a fully integrated implant. It is possible that other processes, including mechanical overloading of an implant through bruxism, could increase failure risk at later stages.[8] Conceivably, mental health conditions such as anxiety could be linked to bruxism[34] (which may, in turn, elevate implant failure risk), but we found no research that explicitly examined this pathway, nor

comparable pathways for other mental health conditions (*eg*, a link between depression, neglect of oral health, and implant failure).

Research is needed that would clarify relationships between mental health conditions, behavioral responses, and implant outcomes across a wide range of mental health conditions. In the nearer term, Veterans may benefit from research on, and implementation of, screening methods that would facilitate earlier detection of known and likely implant failure risk factors in implant candidates, as well as osseointegration issues in implant recipients. Particularly in older adults like those routinely served by the VA, there have been calls to more aggressively screen implant candidates for prior medical and social risk factors and to better account for these factors in individual treatment plans.[3] A screening tool for peri-implant disease risk factors[35] has been recently published, and although this tool lacks an antidepressant use or mental health condition domain, one could potentially be added and evaluated within VA clinical settings.

Additionally, systematic reviews[36,37] of evidence on tailored peri-implant maintenance therapy (PIMT; comprising regular prophylaxis, evaluation of implant healing, and/or instruction on oral hygiene) have identified benefits of these programs in addressing oral health-related risk factors for implant failure (*eg*, inflammation and bone loss). Because PIMT may be helpful in limiting the impacts of these risk factors regardless of their etiology, it may constitute a promising innovation to be investigated for implementation in the VA. In the context of VA integrated care, it is conceivable that benefits of screening and maintenance programs might be enhanced with linkages to other available supports such as smoking cessation assistance, nutrition support therapy, and mental health and substance use treatment services.

CONCLUSIONS

Moderate-strength evidence indicates that antidepressant use is likely associated with elevated risk of implant failure. Available studies provide suggestive evidence that implants may be at greater risk of failing before abutment placement, which is consistent with the purported mechanism by which antidepressants influence the osseointegration process and the likelihood of implant failure. Although antidepressant use alone may increase the risk of implant failure, many failures could be the result of a complex array of risk factors. Veteran implant candidates may benefit from approaches to screen for known and likely risk factors for implant failure, and from research on the effectiveness and feasibility of tailored peri-implant maintenance programs.

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