Dental Implants in Edentulism

AMS-MOH Clinical Practice Guidelines
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### Levels of evidence and grades of recommendation

#### Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
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<tr>
<td>1++</td>
<td>High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias</td>
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<tr>
<td>1+</td>
<td>Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias</td>
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<tr>
<td>1-</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
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<td>2++</td>
<td>High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</td>
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#### Grades of recommendation

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<td>B</td>
<td>A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+</td>
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<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+</td>
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<tr>
<td>GPP</td>
<td>Recommended best practice based on the clinical experience of the guideline development group</td>
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Dental Implants in Edentulism
Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
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Foreword

Edentulism continues to be a major oral health problem as periodontal disease emerges as the primary cause of tooth loss. Coupled with a graying population and an increasingly sophisticated patient profile, the demand for dental implant supported prostheses has increased significantly in recent years.

However, dentists need to be conscious of maintaining competency standards as well as continue to ensure a high level of vigilance against new techniques and treatment with dental implants just as we do in many other fields of Dentistry.

An evidence-based approach is needed to ensure that only techniques that have withstood the rigors of scientific scrutiny are offered to our patients.

This Clinical Practice Guideline is a timely resource to help identify the state of evidence available in the various aspects of Implant Dentistry.

I hope that dental practitioners will find this set of guidelines useful in the management of their patients.

A/PROF PATRICK TSENG
Chief Dental Officer
Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

**Dental implants in irradiated bone**

*C* The implant team must work closely with the cancer team members such as the radiation oncologist, oral and maxillofacial surgeon, prosthodontist, otolaryngologists/head and neck surgeons, plastic surgeon, speech therapists, dietician and physiotherapist. Such a combined consultation will lead to optimal planning as addressing questions such as:

(a) Can bone from tumour resection be saved and reused in the same surgery?
(b) Can implants be placed prior or during the resection surgery?
(c) Expected healing outcome from multidisciplinary treatment plan (pg 11).

**Grade C, Level 2+**

**D** Patients who receive implants and who were treated with radiation more than 5 years ago should be treated with utmost care (pg 12).

**Grade D, Level 2+**

**D** The use of hyperbaric oxygen though controversial may be considered as an adjunct to promote healing in these patients (pg 12).

**Grade D, Level 2+**

*C* Placement of endosseous implants in patients with a history of head and neck radiation therapy may be performed by clinicians with experience and training in head and neck radiation therapy (pg 12).

**Grade C, Level 2+**

**Dental implants in patients receiving oral bisphosphonates**

*C* Patients who have received or are receiving oral bisphosphonates may undergo dental implant therapy with caution (pg 13).

**Grade C, Level 2+**
Patients on oral bisphosphonate therapy have to be counselled about the potential risks and complications before proceeding with dental implant treatment (pg 13).

**Grade C, Level 2+**

A minimum pre-surgical serum CTX (beta-crosslaps) value of 150pg/ml is recommended before extractions and/or implant surgery in patients on oral bisphophonate therapy (pg 14).

**Grade C, Level 2+**

Other non invasive treatment alternatives must also be discussed with patients (pg 14).

**Grade C, Level 2+**

**Dental implants in patients with controlled periodontal disease**

In patients who have been successfully treated for periodontal diseases and have lost teeth, dental implants can be used for tooth/teeth replacements. However, even well-maintained periodontal patients need to be informed of the higher than normal risks and potential for complications in dental implant therapy in the long-term (pg 16).

**Grade C, Level 2+**

Patients with periodontal diseases should have their condition treated and well maintained before dental implants can be considered. Annual follow up visits to their dentist are necessary to better maintain implants in patients with a history of treated periodontitis (pg 16).

**GPP**

**Dental implants in smokers**

Smokers who undergo dental implant therapy are at higher risk of early implant failures and should be closely followed-up during the early healing phase of osseous integration (pg 17).

**Grade C, Level 2+**
For smokers who undergo dental implant therapy, particular attention should be paid to complications such as peri-implantitis, marginal bone loss and bone graft healing as part of post-surgical implant care. Where possible, alternative prosthodontic treatment methods should be explored with such patients (pg 17).

Grade C, Level 2+

Patients who are smokers can proceed with dental implant therapy provided they are warned about the higher risks of failures, especially early failures (pg 18).

GPP

Smokers should be advised to stop smoking during the healing period and where possible prior to dental implant therapy and they should seek counselling help to stop the habit altogether (pg 18).

GPP

Narrow diameter implants

Implants of diameters between 2.5mm to 3.3mm can be used predictably for mandibular overdenture retention (pg 19).

Grade B, Level 2++

Due to lack of clinical data regarding implants of less than 2.5mm in diameter (micro-implants), these implants are not recommended for routine treatment of edentulism (pg 19).

GPP

Extraction and replacement with an implant-supported prosthesis versus endodontic treatment and restoration of teeth with pulpal pathosis

Patients with pulpal and/or periapical pathosis may be treated with either root canal therapy or extraction and replacement with an endosseous implant-supported dental prosthesis with similar survival rates (pg 20).

Grade A, Level 1+
Both non-surgical root canal therapy followed by an appropriate restoration and single-tooth implant are acceptable treatment modalities for the treatment of abscessed teeth. The decision to treat a tooth endodontically or to replace it with an implant must be based on factors other than the treatment outcomes of the procedures themselves, such as medical history, caries, patients’ preference and other socio-economic factors (pg 21).

Grade D, Level 3

**Implant-supported versus tooth-supported fixed dental prosthesis**

For the fixed replacement of a single missing tooth, based on 5-year survival outcomes, an implant-supported single crown or a tooth-supported fixed dental prosthesis are viable options. Other factors apart from survival rates should be taken into consideration when deciding on the choice of replacement (pg 23).

Grade B, Level 2++

**GPP** Patients should receive information that tooth replacements with fixed dental prosthesis or implants are associated with incidences of biological and technical complications (pg 23).

**Dental implants in posterior maxilla with sinus bone grafting**

Implants may be placed in posterior maxillary grafted sinuses via the lateral approach (pg 25).

Grade B, Level 2++

Implants may be placed in posterior maxillary grafted sinuses via the transalveolar approach (pg 25).

Grade B, Level 2++

Rough surface/textured implants may be placed in grafted posterior maxillary sinuses with non-autogenous bone graft (pg 25).

Grade C, Level 2+
Implants in augmented ridges

**C** Implants may be placed in peri-implant defects (dehiscence and fenestration) treated with guided bone regeneration techniques (pg 27).

*Grade C, Level 2+

**GPP** Localised defects in edentulous ridges should be carefully evaluated and grafting can be considered to optimise the outcome of implant treatment (pg 27).

*GPP

**C** Implants may be placed in sites covered with resorbable membranes (pg 27).

*Grade C, Level 2+

**GPP** Both resorbable and non-resorbable membranes can be considered when augmenting localised defects. Special attention however should be given to the manipulation and follow-up of patients who have undergone non-resorbable membrane application in the light of its higher complication rates (pg 27).

*GPP

**C** Implants may be placed in atrophied ridges augmented by various techniques (other than onlay grafting) (pg 28).

*Grade C, Level 2+

**GPP** Atrophic ridges should be carefully evaluated and different grafting options must be considered as we plan for implant rehabilitation in these situations. Implant positions must be carefully planned out in grafted atrophic ridges to ensure better, long-term implant survival rate. An optimal balance of load distribution, satisfactory esthetics and functionality must be taken into consideration (pg 28).

*GPP

**C** The efficacy of different grafting techniques in severely atrophic edentulous sites seem to be comparable. Apart from onlay grafting in severely resorbed maxillary areas which shows higher potential for failure and complications, the other techniques proved to be equally effective (pg 28).

*Grade C, Level 2+*
Connection of dental implants to natural teeth

**D** As the treatment of choice, a fixed dental prosthesis supported by osseointegrated implants should be connected to other osseointegrated implants, independent of natural teeth. Connection of osseointegrated implants to natural teeth via a fixed dental prosthesis may be done with adequate warning of a higher complication and failure rates (pg 29).

Grade D, Level 2+

**D** When implants are connected to natural teeth, rigid connection should be used, and only on teeth which are periodontally sound. Regular checks are necessary as mechanical complications and increased marginal bone loss may be expected around either implant or tooth. Modified connections retaining the rigid characteristics that have been proposed without long term results should not be used until more results are available (pg 29).

Grade D, Level 3

Placement protocol/timing

**C** Dental implants should be placed in healed sockets as the treatment of choice (pg 31).

Grade C, Level 2+

**C** Implants may be placed into fresh extraction sockets with the patient’s understanding that the survival rate is lower than that placed into healed sockets. Immediate loading of implants placed into fresh extraction sockets should not be done routinely (pg 31).

Grade C, Level 2++

Loading protocol/timing

*Edentulous mandible*

**A** Root-form endosseous implants (two or four units) inserted for the purpose of retaining or supporting a removable dental prosthesis that are rigidly splinted together may be loaded immediately (pg 33).

Grade A, Level 1++
B Root-form endosseous implants (four or more units) inserted for the purpose of supporting a fixed one-piece full arch dental prosthesis may be loaded immediately (pg 33).

Grade B, Level 2++

**Edentulous maxilla**

B Root-form endosseous implants (two or four units) inserted for the purpose of retaining or supporting a removable dental prosthesis should not be loaded immediately (pg 34).

Grade B, Level 2++

C Root-form endosseous implants (six or more units) inserted for the purpose of supporting a fixed one-piece full arch dental prosthesis may be loaded immediately (pg 34).

Grade C, Level 2+

**Single tooth replacement**

A Conventional loading of a single root-form endosseous implant inserted for the purpose of supporting a single crown is the loading protocol of choice. Immediate loading of a single root-form endosseous implant inserted for the purpose of supporting a single crown may be done with caution (pg 34).

Grade A, Level 1++

**Multiple-tooth edentulous maxilla/mandible**

B Conventional loading of multiple root-form endosseous implants inserted for the purpose of supporting a multiple-unit fixed prosthesis in the anterior or posterior maxilla/mandible is the loading protocol of choice. Immediate loading of multiple root-form endosseous implants inserted for the purpose of supporting multiple-unit fixed prosthesis in the anterior or posterior maxilla/mandible may be done with caution (pg 34).

Grade B, Level 2++
1.1 Objectives and scope of guideline

Dental implants are fast becoming an integral part of dental practice in Singapore. Until recently, implant dentistry was not taught in the proper milieu of most dental schools. On the academic front there has been much research and publications on this subject with varying levels of rigor. As such, a set of evidence-based guidelines covering some areas of controversies was deemed beneficial to practicing dentists in Singapore. The guidelines are not to be viewed as a protocol, but provide a framework to:

- guide dental healthcare professionals in their quest to give evidence-based care to their patients
- appraise the various implant treatment options available today based on published evidence in the literature.

1.2 Target group

These guidelines are intended for use by general dental practitioners, oral and maxillofacial surgeons, prosthodontists, periodontists and endodontists.

1.3 Guideline development

These guidelines have been produced by a committee comprising general dental practitioners, endodontists, oral and maxillofacial surgeons, orthodontists, periodontists and prosthodontists appointed by the Academy of Medicine Singapore and Ministry of Health. They were developed using the best available current evidence and expert opinion. The workgroup formulated this clinical practice guideline by reviewing published international guidelines and current evidence available in the research and clinical practice literature. The grading system used in the guidelines is described on the inside front cover of this booklet.
1.4 Assessing the evidence

In assessing the evidence, different study designs were considered including randomised controlled trials, cohort studies, case control studies, uncontrolled clinical trials and expert opinions. Best practice guidelines important in implant dentistry were also included.

1.5 Scope of guideline

The workgroup identified certain areas in the practice of implant dentistry in Singapore where variation exists among dentists. This guideline covers these identified areas. These guidelines are not meant to be exhaustive in coverage of other aspects of implant dentistry or the management of edentulism with other treatment modalities. This guideline provides recommendations for the use of dental implants for management of edentulism in patients with compromised healing abilities and patients with deficient bone stock. It also provides recommendations for the choice of loading and placement protocols as well implant geometry and dimensions. It is hoped that this guideline will help dentists in making evidence based clinical decisions in their management of edentulism with dental implants.

1.6 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review 5 years after publication, or if new evidence appears that requires substantive changes to the recommendations.
2 Dental implants in irradiated bone

2.1 Would head and neck radiation affect the success rate of Endosseous dental implants?

Radiation therapy was originally considered a contraindication for installation of dental implants. Nevertheless, the need to optimally rehabilitate cancer patients has challenged this position. The fact that modern cancer therapy has significantly prolonged the life of these patients means that implant therapy will play a significant role in the enhancement of their quality of life, sometimes more than 20 years after radiation and chemotherapy. Reasons for implants in irradiated patients will include:

1. Better masticatory ability from an implant prosthesis.
2. Less damage to the oral mucosa from a denture especially if xerostomia is present.
3. Facilitation of swallowing and speech.
4. Some patients suffer combined defects from surgery in adjacent tissues such as cheeks, maxillary sinuses, nose and orbits. These defects usually require cosmetic and functional coverage, so that the patient can speak and be a fully social person. In most situations, retention and function of prosthesis would require dental and oral facial implants. Thus generally, a rehabilitated patient will have a better quality of life.

However, dental implant rehabilitation of irradiated patients should be performed at healthcare establishments with expertise in the management of cancer patients. It should not be done as part of routine general dental practice.

2.2 Drawbacks from rehabilitating cancer patients

1. Waiting time for the onset of tumour recurrence and distant metastases is controversial. There is no fixed guideline on the time interval between radiation ablative surgery and the placement of the dental implants.
The implant team must work closely with the cancer team members such as the radiation oncologist, oral and maxillofacial surgeon, prosthodontist, otolaryngologists/head and neck surgeons, plastic surgeon, speech therapists, dietician and physiotherapist. Such a combined consultation will lead to optimal planning as addressing questions such as:\textsuperscript{2,3}

(a) Can bone from tumour resection be saved and reused in the same surgery?
(b) Can implants be placed prior or during the resection surgery?
(c) Expected healing outcome from multidisciplinary treatment plan.

\textbf{Factors from radiotherapy that might affect osseointegration of dental implants}

1. Radiotherapy before/after tumour surgery. From a healing point of view, it is better to have dental implant surgery before radiotherapy. Initial studies have shown that implants placed before radiotherapy have very low failure rate.\textsuperscript{4} But on long term follow-up, their failure rates increase with time when compared with implants placed in nonirradiated bone.

2. Radiation dosage. In an experiment by Grannstrom et al\textsuperscript{5}, radiation effects corresponding to 48-65 Gy as a standard fractionation therapy produced few failures in dental implants. At doses above cumulative radiation effect of 120 Gy of standard fractionation therapy, all implants failed.

3. Adjunctive chemotherapy has a negative effect on osseointegration.

4. Time from radiotherapy to implant placement surgery. This is a controversial topic but with modern statistical studies, more light has been shed. Contrary to what one may think, irradiation from decades ago seems to have a more negative effect on implant survival than recently administered radiotherapy. This may be attributed to earlier forms of radiation therapy being of lower energy (less focussed) resulting in more scatter and a longer exposure time,
whereas today, higher energy forms (more focussed) are delivered in a shorter time resulting in less scatter. Another cause may be due to the progressive endarteritis obliterans taking place in the irradiated bone, which is known to increase with time. Endarteritis obliterans will result in poorer healing due to lack of blood-flow in the soft and hard tissues.

D Patients who receive implants and who were treated with radiation more than 5 years ago should be treated with utmost care.2

Grade D, Level 2+

D The use of hyperbaric oxygen though controversial may be considered as an adjunct to promote healing in these patients.5-8

Grade D, Level 2+

5. Implant length. Very short implants (3-7mm) are particularly prone to failure. Short implants (7-8mm) have a much higher failure rates than longer implants (>8mm).

6. Types of prosthesis. A fixated prosthesis has a higher survival rate than an over denture. Facial prostheses have the highest failure rates.

7. Soft tissue complications must be considered together with osteoradionecrosis as they define whether an infection has set in or not.

C Placement of endosseous implants in patients with a history of head and neck radiation therapy may be performed by clinicians with experience and training in head and neck radiation therapy.1

Grade C, Level 2+
3 Dental implants in patients receiving oral bisphosphonates

3.1 What is the success rate of dental implants placed in patients who have received or are receiving oral bisphosphonates therapy as compared to those without?

Oral bisphosphonates are commonly prescribed for management of osteoporosis. They act by inhibiting the resorptive functions of osteoclasts. There is a preferential uptake in bones with high bone turnover, such as the maxilla and mandible. It has been observed that some patients who have received or are receiving oral bisphosphonates develop osteonecrosis of the jaws that is not related to a history of radiotherapy. This is usually related to a episode of trauma such as dentoalveolar surgery, including dental implants. Unlike intravenous bisphosphonates, the incidence of bisphosphonate-related osteonecrosis of the jaw (BRONJ) amongst patients on oral bisphosphonates is low. Nevertheless, due to the significant morbidity of the condition, elective surgery of the jaws in these patients need to be carefully considered. There is a lack of high quality studies on the management of this disease in the literature due to its relatively recent documentation as well as the variability in reports in the literature. These recommendations are based on the currently available evidence and it is expected to change in the near future as better evidence are available.

C Patients who have received or are receiving oral bisphosphonates may undergo dental implant therapy with caution.9,10

Grade C, Level 2+

C Patients on oral bisphosphonate therapy have to be counselled about the potential risks and complications before proceeding with dental implant treatment.9,10

Grade C, Level 2+
A minimum pre-surgical serum CTX (beta-crosslaps) value of 150pg/ml is recommended before extractions and/or implant surgery in patients on oral bisphophonate therapy.\textsuperscript{11} 
\textbf{Grade C, Level 2+}

Other non invasive treatment alternatives must also be discussed with patients.\textsuperscript{9,10} 
\textbf{Grade C, Level 2+}
4 Dental implants in patients with controlled periodontal disease

4.1 Dental implants for patients who have been treated for periodontal diseases

Plaque-induced periodontal diseases are mixed infections that are characterized by inflammation of the periodontium. It results in attachment loss and if left untreated, may result in loosening and eventual loss of teeth. It is thought that specific groups of indigenous oral bacteria are associated with these infections. Susceptibility and severity of periodontal disease are determined by the patient’s host immunity and local factors.12

Traditionally, plaque-induced periodontal diseases are treated using the following methods:13

(1) Excellent daily personal oral hygiene practices by the patient.
(2) Professional non-surgical periodontal mechanical debridement with or without local or systemic anti-microbial therapy to modify local factors.
(3) Resective periodontal surgery
(4) Regenerative periodontal surgery
(5) Extractions of unsalvageable teeth

In situations where extractions are warranted, dental implant therapy is an option for teeth replacement in these patients. It has been reported that in the short term, implant survival in patients with a history of treated periodontitis is high (>90%) and in some studies comparable to that of periodontally-healthy patients.14-25 Regular supportive periodontal therapies were often reported in these studies.

However, implant patients that have been treated for periodontitis were reported to have higher risk of peri-implantitis and biological complications (odds ratio about 3.1-4.7) compared to implant patients with no history of periodontitis.15,16,18,26-28
Over a longer term, it was noticed that implant success is lower in patients that have been treated for periodontal disease as compared to patients with healthy periodontium.14-25

C In patients who have been successfully treated for periodontal diseases and have lost teeth, dental implants can be used for tooth/teeth replacements. However, even well-maintained periodontal patients need to be informed of the higher than normal risks and potential for complications in dental implant therapy in the long-term.15,16,18,26-28

Grade C, Level 2+

GPP Patients with periodontal diseases should have their condition treated and well maintained before dental implants can be considered. Annual follow up visits to their dentist are necessary to better maintain implants in patients with a history of treated periodontitis.

GPP
5 Dental implants in smokers

5.1 Smokers and dental implant therapy

It is difficult to completely attribute the adverse effects on implant therapy to smoking alone as in most of the studies, the population who were smokers would also suffer from other medical conditions (e.g. diabetes, osteoporosis) that could have adverse influences on osseous integration.

There is however, a significantly enhanced risk for implant failure among smokers compared with non-smokers; with the risks being higher in the first year with a slight decrease of up to about 5 years post implant surgery. There is a higher early implant failure rate in such patients. There is also evidence that implant failures were enhanced even after 5 years. Most reports state an approximate failure rate as two times higher.

Light or moderate cigarette smoking has similar risks of implant failures and heavy smoking (>20 cigarettes per day) increases the risk.

Smokers who undergo dental implant therapy are at higher risk of early implant failures and should be closely followed-up during the early healing phase of osseous integration.

Smoking has a strong influence on the complication rates of implants: it causes significantly more marginal bone loss after implant placement, it increases the incidence of peri-implantitis and affects the success rates of bone grafts.

For smokers who undergo dental implant therapy, particular attention should be paid to complications such as peri-implantitis, marginal bone loss and bone graft healing as part of post-surgical implant care. Where possible, alternative prosthodontic treatment methods should be explored with such patients.
The failure rate of implants placed in the maxillary arch is higher though the mechanism is not understood. Studies indicated higher failures of implants in grafted maxillary sinuses, higher rate of infection and impaired wound healing after second stage surgery. Medical conditions such as diabetes and osteoporosis may compound the risks of implant failures in such patients.

GPP Patients who are smokers can proceed with dental implant therapy provided they are warned about the higher risks of failures, especially early failures.

GPP The higher failure risks of dental implants apply to all smokers whether heavy or light smokers.

GPP Smokers should be advised to stop smoking during the healing period and where possible prior to dental implant therapy and they should seek counselling help to stop the habit altogether.
6 Narrow diameter implants

6.1 What is the success rate and clinical longevity of narrow diameter implants placed in patients requiring dental implant as compared to regular diameter implants?

Endosseous dental implants have been gaining in popularity as the choice of tooth replacement. As the indications expanded from fully edentulous patients to partially edentulous patients, implant design evolved to accommodate the expanded indications. However, many of these new products have not undergone the necessary scientific validation. Small diameter implants have been developed to fit into narrow residual ridges, purportedly to circumvent the need for bone grafting or other augmentation procedures. A review of the literature was done to evaluate the evidence base of narrow diameter implants and recommendations made accordingly.

B Implants of diameters between 2.5mm to 3.3mm can be used predictably for mandibular overdenture retention.\textsuperscript{43-45}

\textbf{Grade B, Level 2++}

Patients with implants between 2.5mm to 3.3mm for mandibular overdenture retention had good survival rates of more than 98\% in two prospective studies

\textbf{GPP} Due to lack of clinical data regarding implants of less than 2.5mm in diameter (micro-implants), these implants are not recommended for routine treatment of edentulism.\textsuperscript{46}
7 Extraction and replacement with an implant-supported prosthesis versus endodontic treatment and restoration of teeth with pulpal pathosis

7.1 In medically healthy patients, with periodontically sound teeth, who have pulpal and/or periradicular pathosis, what is the comparative survival rates of root canal therapy versus extraction followed by replacement with an implant-supported prosthesis?

Prevention of oral disease and preservation of natural dentition for continued oral function, are everyday goals of dentistry. Root canal treatment has long been used to salvage abscessed teeth for continued function providing many years of use. Implants are increasingly being used to replace diseased or missing teeth in a variety of clinical situations including the missing single tooth.

Initial non-surgical root canal treatment and the replacement of a single tooth with an implant are both viable treatment options. Varying success rates have been reported for each treatment modality in multiple outcome studies. A reason for the variability of reported outcomes is the inconsistent definition of success. Endodontic studies have used well-defined criteria in determining “success rates” whereas implant studies use a definition of success-failure that is quite different and more consistent with the outcome category of “survival”.47-51

Dentists have to recommend optimal treatment plans for their patients. The objective of this guideline is to evaluate and summarize the current literature on the prognosis, preferences and economics of managing an abscessed tooth with either nonsurgical root canal treatment or extraction followed by implant replacement.

Patients with pulpal and/or periapical pathosis may be treated with either root canal therapy or extraction and replacement with an endosseous implant-supported dental prosthesis with similar survival rates.47,48,50,51

Grade A, Level I+
Both non-surgical root canal therapy followed by an appropriate restoration and single-tooth implant are acceptable treatment modalities for the treatment of abscessed teeth. The decision to treat a tooth endodontically or to replace it with an implant must be based on factors other than the treatment outcomes of the procedures themselves, such as medical history, caries, patients’ preference and other socio-economic factors.47,48

Grade D, Level 3
For the fixed replacement of missing teeth, what is the survival of a tooth-supported fixed dental prostheses compared to an implant-supported single crown?

Missing teeth can be replaced via several means. When a single tooth is missing, the missing tooth can be replaced by a fixed dental prostheses. The 5-year survival of conventional tooth-supported fixed dental prostheses is 94%\textsuperscript{52,53} and the 10-year survival ranges from 87-89%.\textsuperscript{52-55} These figures represent fixed dental prostheses that remain in function but may have encountered some complication that did not require its replacement. This should be distinguished from “complication-free” which refers to fixed dental prostheses that remain intact throughout the period reported.

Tooth-supported fixed partial dentures have a 5-year complication-free rate of 84.3%\textsuperscript{52} and the 10-year complication-free rate ranges from 71-81%.\textsuperscript{55} However, few publications report adequately on the biological and technical complications encountered.

A missing tooth can also be replaced using an implant-supported single crown. The 5-year survival rate of implant-supported single crowns ranged from 94-96%\textsuperscript{52,53,56}, longer term survival rates are however unavailable. There is almost no information on the complication-free rates for implant-supported single crowns.\textsuperscript{57,58}

Implant single crowns tend to exhibit early failures with the failure rates and complications tapering off over time.\textsuperscript{53} They also tend to have more technical complications such as screw loosening and ceramic veneer fractures.\textsuperscript{52} Technical complications for implant single crowns tended to show a decrease with the use of implants with internal connections.\textsuperscript{59} Biological complications occur either less often or as often as for fixed dental prostheses.\textsuperscript{52,56}
For the fixed replacement of a single missing tooth, based on 5-year survival outcomes, an implant-supported single crown or a tooth-supported fixed dental prosthesis are viable options. Other factors apart from survival rates should be taken into consideration when deciding on the choice of replacement.52-59

**Grade B, Level 2**

**GPP** Patients should receive information that tooth replacements with fixed dental prosthesis or implants are associated with incidences of biological and technical complications.52-59

GPP

Single implant supported crowns may experience screw loosening or fracture of the veneering ceramic while tooth-supported replacements can be affected by recurrent caries and loss of vitality. Other complications resulting in loss of the prosthesis such as framework, implant or tooth fracture, loss of supporting structures may also occur, although less commonly.52-59
9 Dental implants in posterior maxilla with sinus bone grafting

9.1 Sinus grafting for implant placement

Reduced vertical bone height (≥10mm length) in the posterior maxillary region limits placement of standard implants. Treatment options in the posterior maxilla with inadequate bone quantity include:

1) Insertion of short implants to avoid the need for sinus grafting but a minimum of 6mm residual bone height is required.
2) Placement of tilted implants mesial or distal to the sinus cavity if these areas have adequate bone quantity.
3) Sinus floor elevation (SFE) for augmentation
   • can be done by a two-stage approach via a lateral window followed by implant placement after a healing period.
   • can be done by a one-stage approach using either a lateral window or a transalveolar technique.

The decision to use the one- or the two-stage approach is based on the amount of residual bone available and the likelihood of achieving primary stability of the inserted implants at the time of surgery.

Autogenous bone grafts are considered the gold standard for bone grafting for reasons of cellular viability and osteogenic capacity.

4) Shortened dental arch

A review of the literature was done to address the following questions based on the current available evidence. It should be borne in mind that most studies in the systematic reviews were conducted in an institutional environment (i.e. universities or specialists’ clinics).
9.2 Do implants placed in posterior maxillary grafted sinuses via the lateral approach survive longer than those implants placed in pristine bone?

Implants placed in posterior maxillary grafted sinuses via the lateral approach have a similar estimated 3-year implant survival rate compared to implants placed in pristine bone.\textsuperscript{60}

\textcolor{blue}{B} Implants may be placed in posterior maxillary grafted sinuses via the lateral approach.\textsuperscript{60} 

\textbf{Grade B, Level 2++}

9.3 Do implants placed in posterior maxillary grafted sinuses via the transalveolar approach survive longer than those implants placed in pristine bone?

Implants placed in posterior maxillary grafted sinuses via the transalveolar approach have a similar estimated 3-year implant survival rate compared to implants placed in pristine bone.\textsuperscript{61}

\textcolor{blue}{B} Implants may be placed in posterior maxillary grafted sinuses via the transalveolar approach.\textsuperscript{61} 

\textbf{Grade B, Level 2++}

9.4 Do grafted sinus implants with non-autogenous bone grafts survive longer than those grafted sinus implants in autogenous bone grafts?

Rough surface/textured implants placed in grafted posterior maxillary sinuses with non-autogenous bone graft have similar survival rates compared to implants placed in grafted posterior maxillary sinuses with autogenous bone graft.\textsuperscript{60,62}

\textcolor{blue}{C} Rough surface/textured implants may be placed in grafted posterior maxillary sinuses with non-autogenous bone graft.\textsuperscript{60,62} 

\textbf{Grade C, Level 2+}
Inasmuch as we want to ensure our patients that their implants would last throughout their lifetime, many factors influence implant survival and each unique case can have varied results. The type of implant used, systemic conditions, oral hygiene and localized factors pertaining to bone and periodontal tissues may affect the outcome of one’s implant treatment in various ways.

Bone augmentation has long been studied as one of the factors that may influence implant survival especially in sites of severe resorption or atrophy. Various methods and materials have been developed, employed and indicated for different types of bony defects and each one has its pros and cons. While a number of studies have attempted to assess the benefits of grafting in terms of enhancing implant survival, varying success rates have been reported in multifarious studies. In many studies, it has been concluded that survival rates of implants are similar whether in grafted or pristine bone.63-65

Grafting is imperative in cases of atrophy to ensure adequate bone dimensions prior to implant placement. In cases where dehiscence or fenestration is noted, dentists must weigh the rationale for grafting and recommend augmentation to patients when implant survival is jeopardized due to lack of bone. The objective of this guideline is to evaluate, assess and summarize the outcome of pertinent studies that feature the cumulative success rate of implants in grafted bone as opposed to pristine sites.

10.1 What is the survival of dental implants placed in edentulous ridges with localised defects that require bone grafting compared to pristine sites?

Peri-implant defects (dehiscence and fenestration) treated with Guided Bone Regeneration (GBR) showed implant survival rates that are comparable to those placed in conventional sites where grafting is not required.63,65,66 Complications which do not affect survival may be seen more in grafted cases compared with non-grafted cases.
Implants may be placed in peri-implant defects (dehiscence and fenestration) treated with guided bone regeneration techniques.65

**Grade C, Level 2+**

Localised defects in edentulous ridges should be carefully evaluated and grafting can be considered to optimise the outcome of implant treatment.

**GPP**

### 10.2 What is the efficacy of different grafting techniques used for augmentation of edentulous ridges with localised defects?

Survival of implants placed in sites covered with resorbable membranes seem to be comparable with those placed in non-resorbable membranes.67-71 The rate of complications observed in sites with non-resorbable membranes, however, seem to be higher than those protected by resorbable ones. 71

**C** Implants may be placed in sites covered with resorbable membranes.

**Grade C, Level 2+**

**GPP** Both resorbable and non resorbable membranes can be considered when augmenting localised defects. Special attention however should be given to the manipulation and follow-up of patients who have undergone non-resorbable membrane application in the light of its higher complication rates.

### 10.3 What is the survival rate of dental implants placed in atrophic edentulous ridges that require bone grafting compared to pristine sites?

Implants placed in augmented atrophic ridges demonstrated similar survival rates compared to those placed in pristine bone. Apart from onlay grafting, augmentation procedures showed comparable implant survival rates and it is difficult to demonstrate which technique ensures better success based on the
Implants may be placed in augmented atrophied ridges with comparable survival rates as those placed in pristine bone.\textsuperscript{75}

\textbf{C} Implants may be placed in atrophied ridges augmented by various techniques (other than onlay grafting).\textsuperscript{77}

\textbf{GPP} Atrophic ridges should be carefully evaluated and different grafting options must be considered as we plan for implant rehabilitation in these situations. Implant positions must be carefully planned out in grafted atrophic ridges to ensure better, long-term implant survival rate. An optimal balance of load distribution, satisfactory esthetics and functionality must be taken into consideration.

\textbf{GPP} Other augmentation options should be considered before choosing onlay grafting for severely resorbed maxillary edentulous sites.

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10.4 \textbf{What is the efficacy of different grafting techniques used for augmentation of atrophic edentulous sites?}

Implants placed in sites of onlay grafting seem to have lower survival rates amongst the grafting techniques developed for atrophic ridges.\textsuperscript{76} Apart from onlay grafting, the other methods seem to be equally effective in augmenting sites of severe resorption.\textsuperscript{74}

\textbf{C} The efficacy of different grafting techniques in severely atrophic edentulous sites seem to be comparable. Apart from onlay grafting in severely resorbed maxillary areas which shows higher potential for failure and complications, the other techniques proved to be equally effective.

\textbf{GPP} Other augmentation options should be considered before choosing onlay grafting for severely resorbed maxillary edentulous sites.
11 Connection of dental implants to natural teeth

11.1 What is the success rate of implants connected to natural teeth versus those connected to implants?

The long term success of implants which are connected to natural teeth could not be determined from the small number of comparative cohort/case studies published. Through theoretical and experimental models, it is believed that the biological and mechanical differences between direct bone contact of an osseointegrated implant and transmission via periodontal ligaments of a natural tooth result in a reactive differential to the masticatory forces when they are joined. While the reported findings were inconclusive, more recent systematic reviews have suggested that higher rates of various complications and failure could occur when osseointegrated implants are joined to natural teeth. Short term (<10 years) clinical studies have found no significant difference between implant survival but more biological complications including tooth intrusion have been observed when compared to conventional fixed design. The clinician has to be reminded that more potential complications may eventually mean less cost-effectiveness. Therefore implant-implant supported fixed prosthesis is the first choice.

D As the treatment of choice, a fixed dental prosthesis supported by osseointegrated implants should be connected to other osseointegrated implants, independent of natural teeth. Connection of osseointegrated implants to natural teeth via a fixed dental prosthesis may be done with adequate warning of a higher complication and failure rates.

Grade D, Level 2+

D When implants are connected to natural teeth, rigid connection should be used, and only on teeth which are periodontally sound. Regular checks are necessary as mechanical complications and increased marginal bone loss may be expected around either implant or tooth. Modified connections retaining the rigid characteristics that have been proposed without long term results should not be used until more results are available.

Grade D, Level 3
12 Placement protocol/timing

12.1 What is the success rate of dental implants placed immediately following tooth extraction (Immediate Placement) or before complete socket healing (Early Placement) compared to implantation into healed sites?

The original protocols for implant therapy were to place implants in well healed alveolar ridges, submerge the implants for a period of 6-9 months, followed by surgically uncovering the implants to place transmucosal abutments, and wait another period before starting the prosthetic restoration.

Patients have to wait a long period prior to having the dental prosthesis to masticate with.

Newer protocols advised placing implants into fresh extraction sockets or extraction sockets that have partially healed over 1-3 months.

Studies varied from immediate insertion of an implant in an extraction socket and placing an immediate provisional prosthesis to immediate placement of implants but not loading it in the initial period and delayed placement of a dental implant to allow time for the socket to heal to varying degrees. Parameters looked at include, survival rates of implants, aesthetic outcome, gingival loss, chronic infection or not in sockets and anterior as opposed to posterior teeth.

Although implants placed into fresh extraction sockets do survive, there is a slightly lower survival rate as compared to implants placed into healed alveolus.

The survival rate of implants is also reduced when they are immediately loaded as compared to loading after a healing period. There is a lack of good long-term randomised controlled trials. The majority of studies are short-term, between 6 months to 2 years. The number of cases is also small.
C Dental implants should be placed in healed sockets as the treatment of choice.

*Grade C, Level 2+*

C Implants may be placed into fresh extraction sockets with the patient’s understanding that the survival rate is lower than that placed into healed sockets.\textsuperscript{90-94} Immediate loading of implants placed into fresh extraction sockets should not be done routinely.\textsuperscript{92,93}

*Grade C, Level 2++*
13 Loading protocol/timing

13.1 Immediate loading of dental implants

When dental implantology was first introduced to dentists at large, a two-stage protocol was recommended. This involved allowing a period of load-free submucosal healing of the implant of three to six months to enable osseointegration to take place. While this protocol has succeeded in producing a high success rate of more than 95%, it presented inconveniences to the patient and the dentist.

In the last ten years, there was a significant increase in the number of publications in the dental literature on shortening or eliminating this waiting period. This is a reflection of the growing demand from patients and dentists for a shorter treatment duration. A wide variety of shortened healing time has been studied and has been classified as early loading. As the time duration mentioned in the literature varies tremendously, the focus of this guideline is on immediate loading. The Cochrane Collaboration’s definition of immediate loading was adopted and this considers loading of the implants within 48 hours of placement as immediate loading. Conventional loading is defined as loading after a period of load-free healing of three to six months.96

There were many publications comparing immediate loading of implants with conventional loading. Some papers showed no significant difference96-105 in outcomes between the different loading protocols while others showed a higher complication rate101,106,107 with immediately loaded implants. These studies had specific inclusion and exclusion criteria97,108 such as the following:

1. No medical contraindication
2. No existing infection
3. Healed sites with no grafting
4. No parafunctional occlusal habits
5. Use of rough surface implants of a specified minimum dimension
6. High stability as measured by insertion torque or resonance frequency analysis
7. Non-functional loading (in partially edentulous cases)

It is also pertinent to note that the treatment in these studies were conducted by experienced clinicians.109

Outcomes96,98,106,109-112 measured consisted mainly of:

1. survival rates of implants and prostheses
2. marginal bone loss
3. probing depth
4. bleeding index
5. plaque index
6. perio test
7. resonance frequency analysis
8. soft tissue aesthetics
9. post-operative pain and oedema

The literature on immediate loading of dental implants is growing but the currently available evidence on this new loading protocol is equivocal. All studies acknowledged that more randomised controlled trials are needed.

This clinical practice guideline serves to provide evidence-based recommendations for the use of immediate loading protocols for the various indications for dental implants.

13.2 Edentulous mandible

A Root-form endosseous implants (two or four units) inserted for the purpose of retaining or supporting a removable dental prosthesis that are rigidly splinted together may be loaded immediately.96,98-104

Grade A, Level 1++

B Root-form endosseous implants (four or more units) inserted for the purpose of supporting a fixed one-piece full arch dental prosthesis may be loaded immediately.98,101,104,105

Grade B, Level 2++
13.3 Edentulous maxilla

B Root-form endosseous implants (two or four units) inserted for the purpose of retaining or supporting a removable dental prosthesis should not be loaded immediately.\textsuperscript{101} 

\textbf{Grade B, Level 2++}

C Root-form endosseous implants (six or more units) inserted for the purpose of supporting a fixed one-piece full arch dental prosthesis may be loaded immediately.\textsuperscript{98,101,105} 

\textbf{Grade C, Level 2+}

13.4 Single tooth replacement

A Conventional loading of a single root-form endosseous implant inserted for the purpose of supporting a single crown is the loading protocol of choice.\textsuperscript{113} Immediate loading of a single root-form endosseous implant inserted for the purpose of supporting a single crown may be done with caution.\textsuperscript{96-98,104,105,107,114,115} 

\textbf{Grade A, Level 1++}

13.5 Multiple-tooth partial edentulous maxilla/mandible

B Conventional loading of multiple root-form endosseous implants inserted for the purpose of supporting a multiple-unit fixed prosthesis in the anterior or posterior maxilla/mandible is the loading protocol of choice.\textsuperscript{104-106,109,110,116-118} Immediate loading of multiple root-form endosseous implants inserted for the purpose of supporting multiple-unit fixed prosthesis in the anterior or posterior maxilla/mandible may be done with caution.\textsuperscript{96-98,111,112} 

\textbf{Grade B, Level 2++}
The use of endosseous implant-supported/retained dental prostheses has increased tremendously in the last ten years on a world-wide scale. The Millenium Research Group reported in 2008 that sales of dental implant components globally will grow by 14.5% per year. In Singapore, Medisave withdrawal for dental implant and related surgeries in 2009 exceeded that in 2008 by 12%. In 2010, the amount withdrew from Medisave increased by another 15% over the amount in 2009. In 2011, the amount withdrew exceeded that in 2010 by 5%.

The workgroup researched the success/survival rates of alternative treatment modality such as teeth-supported fixed dental prostheses and found that they were comparable to that of endosseous implant-supported dental prostheses. As such, the advantage of not requiring the preparation of sound adjacent teeth renders implant-supported prostheses the teeth replacement option of choice. In general, the cost of an implant-supported prosthesis is higher than a tooth-supported or mucosa-supported one. The justification for the use of a more expensive option lies in its conservation of natural dentition, superior function (compared with removable prostheses) and indications that preclude the use of tooth-supported fixed prosthesis (e.g. limited residual dentition).

In patients with certain co-morbidities such as a history of head and neck radiation therapy and bisphosphonate therapy, any use of dental implants should be done with great caution. From the cost-effectiveness point of view, the potential for serious complications requiring extensive and expensive remedies may ultimately outweigh all the advantages.

Design of implants has also evolved with time but not all new designs have been scientifically validated. The use of narrow diameter implants to retain mandibular overdentures in severely atrophied ridges was found to be very cost effective as the additional cost yielded a significant improvement in function.
However, there is a lack of high-level evidence in the literature to support the routine use of narrow-diameter implants for support of fixed dental prostheses replacing multiple teeth. Extending the use of a proven treatment modality beyond its evidence-based indications may negate its clinical efficacy and cost-effectiveness.

Dentists should continue to offer patients all available options for replacement of lost or unsalvageable teeth with the proper financial counselling.
However, there is a lack of high-level evidence in the literature to support the routine use of narrow-diameter implants for support of fixed dental prostheses replacing multiple teeth. Extending the use of a proven treatment modality beyond its evidence-based indications may negate its clinical efficacy and cost-effectiveness. Dentists should continue to offer patients all available options for replacement of lost or unsalvageable teeth with the proper financial counselling.

15 **Clinical quality improvement**

The following clinical quality improvement parameters to help dental healthcare professionals improve their practice, based on the recommendations in this guideline, are proposed:

1) Percentage of dental implant patients with head and neck radiation therapy developing osteoradionecrosis.

2) Percentage of dental implant patients receiving oral bisphosphonates developing bisphosphonates-related osteonecrosis of the jaws.

3) Failure rate of dental implants in patients with controlled periodontal disease.

4) Complication rates of dental implants in smokers.

5) Complication rates of narrow diameter implants.

6) Complication rates when a fixed dental prosthesis joins an implant to a natural tooth.

7) Failure rates in implants placed in fresh extraction sockets.

8) Percentage of implants with osseointegration failure when loaded immediately for support of single tooth prostheses in the maxilla or mandible.
References


50. Iqbal MK, Kim S. For teeth requiring endodontic treatment, what are the difference in outcomes of restored endodontically treated teeth compared to implant supported restorations? J Oral Maxillofac Implants. 2007;Suppl:96-116.


119. Competitor insights for dental implants, Sep 2008, Millennium Research Group, Inc. 175 Bloor St. East, South Tower, Suite 701, Toronto, ON M4W 3R8, Canada.


Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CPE point under Category 3A (Self-Study) of the SDC Online CPE programme. Before you login to claim the CPE point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to “judge” your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

*Instruction: Please choose the best answer.*

1. The estimated 3-year implant survival rate of rough surface/textured implants placed in
   A) grafted posterior maxillary sinuses with non-autogenous bone graft compared to implants placed in grafted posterior maxillary sinuses with autogenous bone graft are higher  
   B) grafted posterior maxillary sinuses with non-autogenous bone graft compared to implants placed in grafted posterior maxillary sinuses with autogenous bone graft are lower  
   C) grafted posterior maxillary sinuses with non-autogenous bone graft compared to implants placed in grafted posterior maxillary sinuses with autogenous bone graft are similar  
   D) none of the above are true

2. Select the statement that is true.
   A) An implant supported single crown and tooth supported fixed dental prostheses show similar 5-year survival outcomes.  
   B) The survival of implant supported single crowns exceeds that of tooth supported fixed dental prostheses.  
   C) Implant supported single crowns have fewer complications than tooth supported fixed dental prostheses.  
   D) Tooth supported fixed dental prostheses and implant supported single crowns have well documented incidences of complications.
3. The failure rate for dental implant therapy in smokers is
   A) 2x higher than non smokers
   B) still marginally higher than non smokers after 5 years
   C) 5x higher than non smokers
   D) the same for heavy smokers and light smokers

4. Root-formed endosseous implants inserted in the maxilla may be loaded immediately, by default,
   A) for retention of a removable prosthesis
   B) for support of a fixed one-piece full arch prosthesis
   C) for all single tooth replacement in the anterior region
   D) for none of the above

5. In the long term, the cost-effectiveness of an implant and tooth supported prosthesis (implants connected to natural teeth) is likely to be lower because:
   A) short term clinical studies have found a lower chance of implant survival
   B) published studies have conclusively shown a lower rate of long term survival
   C) more recent systematic reviews have suggested higher rates of various complications and failures
   D) none of the above
The failure rate for dental implant therapy in smokers is

A) 2x higher than non-smokers
B) still marginally higher than non-smokers after 5 years
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C) for all single tooth replacement in the anterior region
D) for none of the above ()

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Answer Sheet

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### Workgroup members

The members of the workgroup, who were appointed in their personal professional capacity, are:

**Chairman**  
Dr Chan Siew Luen  
Aesthetic Reconstructive Jaw Surgery  
Mt Elizabeth Medical Centre

**Members** (in alphabetical order of surname)

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- **A)** 2x higher than non-smokers
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- **A)** for retention of a removable prosthesis
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- **C)** for all single tooth replacement in the anterior region
- **D)** for none of the above

### In the long term, the cost-effectiveness of an implant and tooth supported prosthesis (implants connected to natural teeth) is likely to be lower because:

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    Oral & Maxillofacial Surgeon  
    Private Practice  
    The Oral Maxillofacial Practice
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    Private Practice  
    Poon and Phay Dental Surgeons
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    Singapore
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    Private Practice  
    Apollonia Dental Surgery
  - **Dr Tan Kwong Shen Winston**  
    Oral & Maxillofacial Surgeon  
    Private Practice  
    The Oral Maxillofacial Practice
  - **Dr Wong Keng Mun**  
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    Private Practice  
    T32 Dental Centre
  - **Dr Yeo Boon Keng Alvin**  
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## Levels of evidence and grades of recommendation

### Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
<th>1++</th>
<th>High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>1+</td>
<td>Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1−</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias</td>
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<tr>
<td>2++</td>
<td>High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</td>
<td></td>
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<tr>
<td>2+</td>
<td>Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</td>
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<tr>
<td>2−</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal</td>
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<tr>
<td>3</td>
<td>Non-analytic studies, e.g. case reports, case series</td>
<td></td>
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<tr>
<td>4</td>
<td>Expert opinion</td>
<td></td>
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</tr>
</tbody>
</table>

### Grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Recommendation</th>
<th>A</th>
<th>At least one meta-analysis, systematic review of RCTs, or RCT rated as 1++ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+</td>
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</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++</td>
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<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+</td>
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<tr>
<td>GPP</td>
<td>(good practice points) Recommended best practice based on the clinical experience of the guideline development group</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>