

A cost-effectiveness evaluation of enamel matrix derivatives alone or in conjunction with regenerative devices in the treatment of periodontal intra-osseous defects

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Abstract

Purpose: To identify the most cost-effective approach to treatment of infrabony lesions with enamel matrix derivatives (EMD).

Methods: We incorporated costs and clinical outcomes of 12 different treatment techniques (including flap operation, EMD alone, and EMD in association with other reconstructive devices) within a decision tree model in which costs were based on insurance regulations in Germany and health outcomes followed a recent meta-analysis. The most cost-effective treatment option was identified on the basis of the maximum net benefit criterion.

Results: Treatment techniques using EMD were cost-efficient if the decision maker's willingness-to-pay (WTP) was at least €150–175 per incremental mm of pocket probing depth reduction and clinical attachment level gain, respectively (1-year perspective). When EMD was affordable, the maximum net benefit was achieved by treatment with EMD in conjunction with bioactive glass or bovine bone substitutes. Additional application of platelet-rich plasma (PRP) or a resorbable membrane came at relatively high costs.

Conclusions: If EMD use is indicated, EMD in conjunction with either bioactive glass or bovine bone substitutes is more cost-effective than EMD alone. The additional use of PRP or a resorbable membrane may only be justifiable when monetary resources for treatment are very generous.

Key words: decision analytic modelling; economic evaluation; enamel matrix derivatives; maximum net benefit; probabilistic sensitivity analysis

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Conflict of interest and source of funding statement

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In recent years, the use of enamel matrix derivatives (EMD) has frequently been discussed as a clinically effective treatment for infrabony lesions (Zucchelli et al. 2003, Gurinsky et al. 2004, Venezia et al. 2004, Sculean et al. 2005, Bokan et al. 2006, Kuru et al. 2006, Esposito et al. 2009). Nevertheless, health care decision makers often have to compromise between an attainable level of treatment effectiveness and available monetary resources (Drummond et al. 2005). This specifically applies to EMD, which can be used either alone, in combination with various bone grafting materials (autologous bone or bone substitutes), or with different types of membranes (resorbable or non-resorbable) for guided tissue regeneration. Hence, there exist substantial differences in cost when comparing therapeutic alternatives for infrabony lesions. Therefore, it remains uncertain which of the options can be regarded as optimum when monetary resources for dental health services are limited.

A recent paper (Tu et al. 2010) has systematically explored the currently available clinical evidence for the treatment of infrabony lesions with EMD and various combinations. Despite providing a comprehensive summary of the existent evidence, the authors have concluded that a cost-effectiveness perspective has never been incorporated but would provide essential information for making clinical decisions. The purpose of this study is, therefore, to identify the most cost-effective approach for EMD treatment of infrabony lesions on the basis of currently available evidence.

Methods

The perspective considered in this study is that of a decision maker who seeks to optimize the use of available resources from a societal perspective (Claxton et al. 2000), i.e. by comparing the benefits to and costs for a society resulting from the treatment of infrabony lesions with EMD alone or combinations of EMD with other therapeutics. We assume the decision-making process is occurring in Germany and model the data within a decision tree (Buxton et al. 1997).

Health outcomes

Identification of clinical outcome data

Tu et al. (2010) report changes in clinical outcomes [pocket probing depth

(PPD) and clinical attachment level (CAL), see Table 1] as well as radiographic defect fill size 6 and 12 months after alternative EMD treatment techniques for infrabony lesions. Because this can be considered the most comprehensive source of evidence to date, we use their results for our economic analysis. We parameterize health outcomes in our decision tree model as per treatment effectiveness 12 months after treatment.

Some particularities of our evidence source (Tu et al. 2010) should be noted. First, all clinical endpoints in this study can only be considered surrogate outcomes of infrabony lesion therapy. Ideally, cost-effectiveness analysis would rely on tooth survival as the true outcome of dental treatment (Prentice 1989, Fleming & DeMets 1996). But in the absence of such evidence, treatment decisions based on surrogate endpoints can still be considered appropriate as they represent the best evidence currently available.

Second, Tu et al. (2010) compared radiographic defect fill for seven different treatment strategies, whereas for PPD reduction and CAL gain, there is evidence available for 12 treatment options. Thus, because of considerable non-comparability with the clinical outcomes (PPD and CAL), we did not incorporate radiographic-defect fill in our decision tree model.

Finally, one membrane (see Table S1) in the meta-analysis is currently not licensed for application in Europe. As per the perspective of our study (decision making in Germany), we did not consider the outcomes of treatment involving this membrane in our decision tree model.

Costs

The costs that arise from treatment of an infrabony lesion include cost of materials (anaesthesia, surgical instruments, bone grafts, membranes, EMD, and suturing materials) and reimbursement of dentist and staff. Except for EMD, substitutive bone grafts, and membranes (which are charged according to the manufacturers' prices), accounting of material costs as well as reimbursement of dental professionals correspond to fees per item as listed in the Gebührenordnung für Zahnärzte (GOZ, see Bundesgesetzblatt 2001). The GOZ is uniformly valid throughout Germany and usually constitutes the medical fee schedule for privately insured patients. In the case of therapies for infrabony lesions, however, it also applies to publicly insured patients because the according surgical procedures are not covered by the German Public Health System. Specifically, the constituent costs of infrabony lesion treatment according to the GOZ are calculated on the basis of the following formula (Bundesgesetzblatt 2001):

$$\text{Cost}_{\text{GOZ}} = p_{\text{GOZ}} \times \mu \times \tau$$

where p_{GOZ} is the chargeable item points according to the GOZ, μ the monetary conversion factor (5.62421 euro cents per GOZ item point), and τ the treatment time factor, dependent on the complexity of the individual case.

In order to account for different complexity in the treatment of an infrabony lesion, we relied on two frequently applied treatment time factors. Specifi-

Table 1. PPD reduction and CAL gain 12 months after treatment of an infrabony lesion

	PPD reduction (mm) [95% HPD interval]	CAL gain (mm) [95% HPD interval]
EMD alone (intercept)	4.49 [−2.57; 11.57]	3.26 [−2.03; 9.37]
EMD & ePTFE	−0.04 [−1.88; 1.58]	0.03 [−2.37; 0.70]
EMD & synthetic resorbable membrane	−0.10 [−2.34; 1.77]	0.17 [−1.53; 1.26]
EMD & autogenous bone	−0.05 [−1.50; 1.94]	0.33 [−0.67; 2.32]
EMD & bioactive glass	0.43 [−0.45; 1.96]	0.54 [−0.03; 2.13]
EMD & HA	−1.49 [−3.59; 0.02]	−0.91 [−2.98; −0.08]
EMD & DFDBA	−0.53 [−1.20; 0.21]	−0.23 [−0.85; 0.34]
EMD & TCP	0.04 [−1.21; 1.03]	0.56 [−0.39; 1.27]
EMD & bovine bone	0.78 [0.15; 1.37]	0.93 [−0.48; 1.54]
EMD & bovine bone & PRP	1.01 [−1.58; 3.73]	0.82 [−0.65; 2.57]
EMD & bovine bone & porcine membrane	1.28 [−0.71; 3.21]	1.18 [−0.04; 2.51]
Flap OP	−0.87 [−1.44; −0.56]	−1.19 [−1.54; −0.82]

Values extracted from Tu et al. (2010); baseline-unadjusted coefficients.

PPD, pocket probing depth; CAL, clinical attachment level; HPD, high probability density; EMD, enamel matrix derivative.

cally, we modelled clinical cases associated with an average ($\tau = 2.3$) and an increased ($\tau = 3.5$) expenditure of treatment time (Bundesgesetzblatt 2001). In summary, Table 2a lists treatment costs for infrabony lesions as per the GOZ and dependent on time needed for treatment.

In addition, we made the following assumptions to enable precise accounting of costs:

- the amount of EMD that is applied during treatment equals 0.7 ml (see Table 2b),
- the costs of TCP, DFDBA, and HA substitutive bone grafts as well as the costs of an ePTFE membrane correspond to averages as derived from four different manufacturers each. These and all other material costs follow current market prices in Germany (see Table 2b; a detailed list of products included for the calculation of costs can be found in the Table S1).

Deciding on cost-effectiveness

These clinical and monetary considerations were incorporated in a decision tree as shown in Fig. 1. Then, for any of the 12 treatment options considered, we calculated the net benefit (Stinnett & Mullahy 1998) as follows:

$$NB = (\lambda \times B) - C$$

where λ is the threshold value for willingness-to-pay (WTP) for an additional mm of PPD reduction or CAL gain B: PPD reduction or CAL gain (mm), and

C the costs for providing treatment of infrabony lesion.

Accordingly, the optimum treatment strategy is the one that yields the maximum net benefit in comparison with all the other options under consideration (Stinnett & Mullahy 1998). Note that WTP is a general concept in health economic evaluation for characterizing the maximum amount of money that an individual is willing to sacrifice to receive one incremental unit of a health benefit (Drummond et al. 2005).

To incorporate uncertainties regarding PPD reduction and CAL gain, a probabilistic sensitivity analysis (Weinstein et al. 2003) was implemented that assigns a triangular distribution function to each health outcome. The upper and lower bounds equate to the 95% high probability density intervals and the most likely point within each distribution is defined by the point estimate for PPD reduction or CAL gain, respectively. A Monte-Carlo simulation (Doubilet et al. 1985) with 50,000 repetitions was then conducted in order to identify the probabilities with which different treatment strategies yield the maximum net benefit criterion.

All data modelling and probabilistic sensitivity analysis were conducted with the software package TreeAge (TreeAge Software Inc., Williamstown, MA, USA). Finally, it should be noted that we followed the guidelines of the German Institute for Quality and Efficiency in Health Care (IQWiG 2009) and applied an annual discount rate of 3% for both costs and health outcomes.

Table 2a. Costs of treatment procedures in the treatment of infrabony lesions according to the GOZ

Procedures	Cost for average treatment time ($\tau = 2.3$) (€)	Cost for increased treatment time ($\tau = 3.5$) (€)
Local anaesthesia	9.06	13.79
Flap OP (osteoplasty included)	35.58	54.15
Extraction of autologous particulate bone	86.73	131.99
Implantation of autologous/alloplastic material	23.28	35.42
Placement of a membrane for bone regeneration	58.21	88.59
Removal of a membrane for bone regeneration	50.81	77.32
Taking of a blood sample	5.36	8.16
Administration of platelet-rich plasma (PRP)	99.06	150.74

Costs for average treatment times are calculated on the basis of a 2.3 treatment time factor; costs for increased treatment times are calculated on the basis of a 3.5 treatment time factor; costs for treatment of infrabony lesions according to the GOZ are VAT exempt.

EMD, enamel matrix derivative.

Table 2b. Prices for bone grafts, membranes, and EMD

Materials	Cost (€)
Average cost for TCP	55.16
Average cost for DFDBA	57.22
Average cost for HA	46.11
Bovine bone graft (0.5 g)	83.30
Bioactive glass (0.5 cc)	39.91
Average cost for ePTFE membrane	65.75
Synthetic resorbable membrane	166.29
Porcine resorbable membrane	124.95
EMD 0.7 ml and EDTA conditioner	207.30

VAT included for all monetary values; details about products included for calculation of prices can be found in the Table S1.

EMD, enamel matrix derivative.

Results

Cost-effectiveness according to PPD

Figure 2 shows the cost-effectiveness plane according to PPD and average expenditure of treatment time. The graph assigns each available treatment option an effectiveness value on the x-axis and a cost value on the y-axis. In general, the more to the right and the more to the bottom of the plane a strategy is positioned the higher its cost-effectiveness is. Note that in health economics, a treatment alternative that is more expensive but does not render a greater health gain than the alternative strategy is dominated (Drummond et al. 2005).

Further, Fig. 2a thus shows that, according to PPD, flap operation (flap OP) is on average more effective and less costly than treatment of an infrabony lesion by means of EMD combined with HA. Therefore, the latter therapeutic approach is dominated by flap OP as a treatment strategy. The graph also indicates that infrabony lesion treatment by means of EMD and bioactive glass dominates the treatment strategies ‘‘EMD & autogenous bone’’, ‘‘EMD & ePTFE membrane’’, ‘‘EMD & synthetic resorbable membrane’’, ‘‘EMD & TCP’’, and ‘‘EMD & DFDBA’’. Further, Fig. 2a shows that the strategies ‘‘EMD alone’’, ‘‘EMD & bioactive glass’’, ‘‘EMD & bovine bone’’, ‘‘EMD & bovine bone & PRP’’, and ‘‘EMD & bovine bone & porcine membrane’’ are – in an increasing order of magnitude – not only more effective but also more costly than ‘‘flap OP’’.

It is yet unclear to which extent cost-effectiveness considerations will be influenced by uncertainties regarding clinical effectiveness values. The decision uncertainty can be depicted by

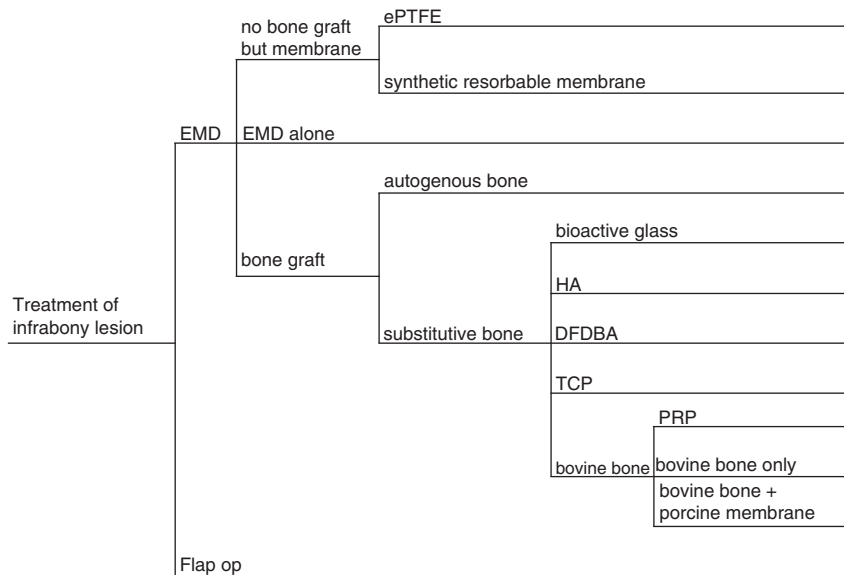


Fig. 1. Stylized decision tree for treatment of an infrabony lesion.

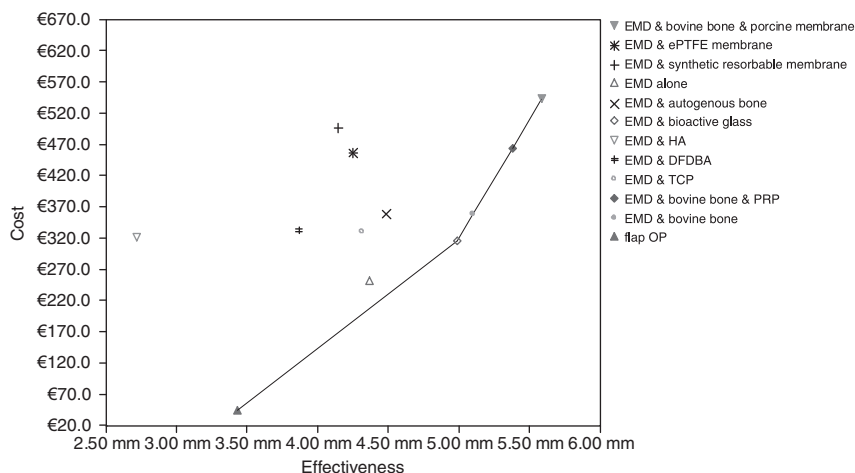


Fig. 2. The cost-effectiveness plane for pocket probing depth reduction (average treatment time).

means of cost-effectiveness acceptability frontiers, which identify the treatment strategies along the WTP axis, which fulfil the maximum net benefit criterion. In addition, they assign the probability with which each of these options is cost-effective.

Figure 3a shows the cost-effectiveness acceptability frontier according to PPD and average treatment time. It shows that:

- flap OP is the most cost-effective therapeutic alternative for WTP values below €175 per additional mm of PPD reduction,
- EMD & bioactive glass is the most cost-effective therapeutic alternative for WTP values between €175 and

€375 per additional mm of PPD reduction,

- EMD & bovine bone & PRP is the most cost-effective therapeutic alternative for WTP,
- values between €375 and €400 per additional mm of PPD reduction, and
- EMD & bovine bone & porcine membrane is the most cost-effective therapeutic alternative for WTP values above €400 per additional mm of PPD reduction.

Figure 3b shows the cost-effectiveness acceptability frontier according to PPD and increased treatment time. As for the PPD scenario with average treatment costs, the graph identifies relatively low probabilities for treatment strategies to be cost-effective. The

cost-efficient treatment strategies and WTP thresholds are now identified as follows:

- flap OP is the most cost-effective therapeutic alternative for WTP values below €200 per additional mm of PPD reduction,
- EMD & bioactive glass is the most cost-effective therapeutic alternative for WTP values between €200 and €400 per additional mm of PPD reduction,
- EMD & bovine bone is the most cost-effective therapeutic alternative for WTP values between €400 and €450 per additional mm of PPD reduction, and
- EMD & bovine bone & porcine membrane is the most cost-effective therapeutic alternative for WTP values above €450 per additional mm of PPD reduction.

A summary of all cost-efficient treatment strategies according to PPD reduction is provided in Table 3a.

Cost-effectiveness according to CAL

Figure 4 shows the cost-effectiveness plane according to CAL and average expenditure of treatment time. Similar to Fig. 2 (PPD), it shows that, according to CAL, the therapeutic alternative “flap OP” dominates the treatment of an infrabony lesion by means of EMD combined with HA. Furthermore, the graph indicates that “EMD & bioactive glass” dominates the therapeutic options “EMD & autogenous bone”, “EMD & ePTFE membrane”, “EMD & synthetic resorbable membrane”, “EMD & TCP”, and “EMD & DFDBA”. The strategy “EMD & bovine bone & PRP” is dominated by “EMD & bovine bone”. Figure 2b also shows that the strategies “EMD alone”, “EMD & bioactive glass”, “EMD & bovine bone”, and “EMD & bovine bone & porcine membrane” are – in an increasing order of magnitude – not only more effective but also more costly than “flap OP”.

Figure 5a depicts the cost-effectiveness acceptability frontier according to the CAL and average treatment time. It shows that:

- flap OP is the most cost-effective therapeutic alternative for WTP values below €150 per additional mm of CAL gain,

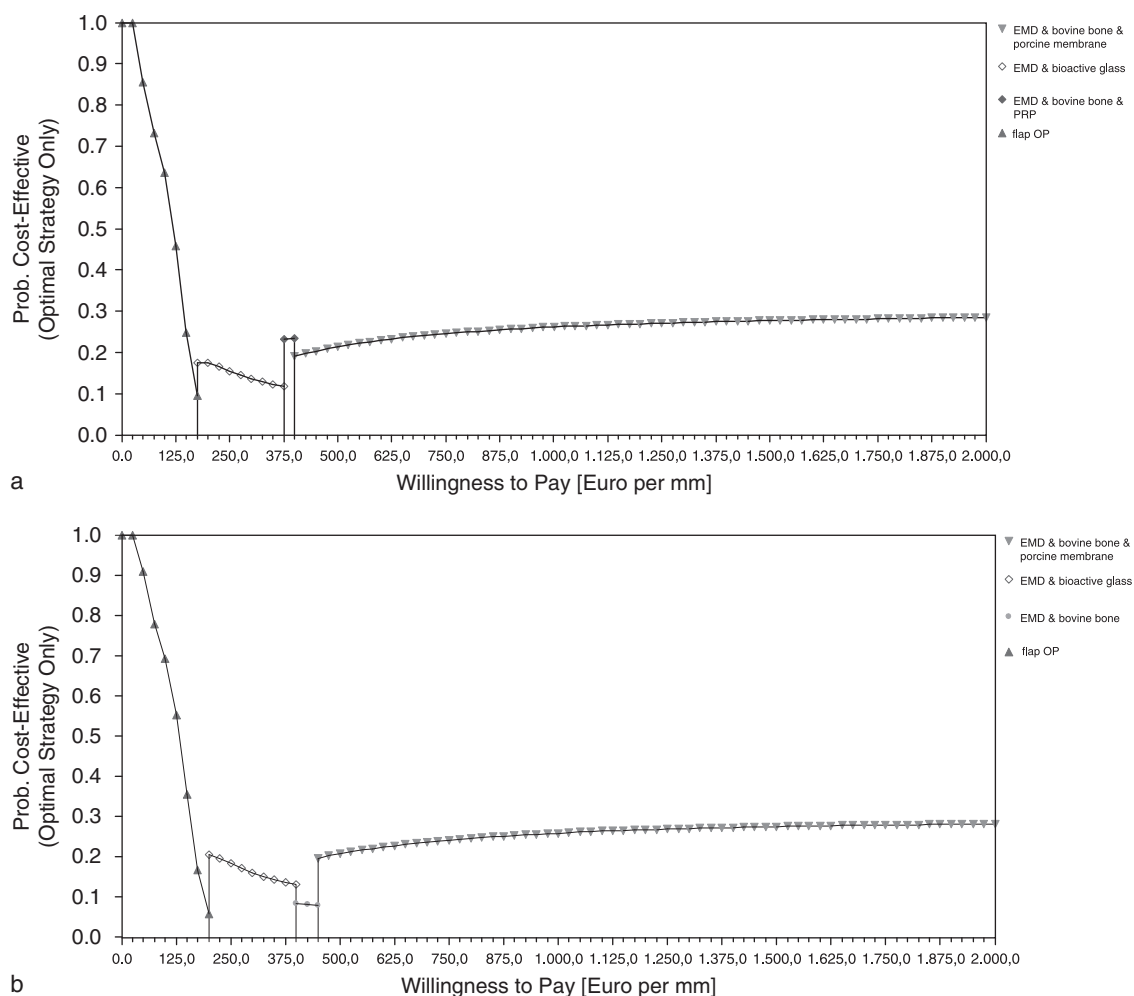


Fig. 3. (a) Cost-effectiveness acceptability frontier for pocket probing depth (PPD) (average treatment time). (b) Cost-effectiveness acceptability frontier for PPD (increased treatment time).

- EMD & bioactive glass is the most cost-effective therapeutic alternative for WTP values between €150 and €450 per additional mm of CAL gain,
- EMD & bovine bone is the most cost-effective therapeutic alternative for WTP values between €450 and €825 per additional mm of CAL gain, and
- EMD & bovine bone & porcine membrane is the most cost-effective therapeutic alternative for WTP values above €825 per additional mm of CAL gain.

Figure 5b shows the cost-effectiveness acceptability frontier according to CAL and increased treatment time. As for the CAL scenario with average treatment costs, the graph identifies the same cost-efficient treatment options along the WTP axis as for average treatment time (“flap OP”, “EMD & bioactive

glass”, “EMD & bovine bone”, and “EMD & bovine bone & porcine membrane”). The WTP thresholds of €150 per additional mm of CAL gain (which compares “flap OP” *versus* “EMD & bioactive glass”) and of €450 per additional mm of CAL gain (which compares “EMD & bioactive glass” *versus* “EMD & bovine bone”) hold for both an average and an increased expenditure of treatment time. However, the WTP threshold that distinguishes between “EMD & bovine bone” and “EMD & bovine bone & porcine membrane” alters between the two cost scenarios. An according summary of all cost-efficient treatment strategies according to CAL gain is provided in Table 3b.

Discussion

On the basis of currently available evidence and current market prices, this

paper identifies the most cost-effective approach for the treatment of infrabony lesions. Application of therapeutic techniques, which involve EMD, is advisable when a decision maker is willing to pay at least €175–200 per additional mm of PPD reduction. Similarly, treatment options with EMD are advisable when the resources that can be spent for treatment of an infrabony lesion amount to at least €150 per additional mm of CAL gain. For lower levels of WTP, however, EMD techniques cannot be considered cost-efficient in comparison with flap operation. In cases where the available monetary resources facilitate treatment techniques with EMD, a combination of EMD and bone grafts may be more cost-effective (as compared with EMD alone). When considering CAL gain, treatment with EMD & bioactive glass is cost-efficient when WTP is up to €450 per additional mm of CAL gain. The use of bovine bone

Table 3a. Cost-efficient treatment strategies according to PPD reduction

	Average treatment time ($\tau = 2.3$)	Increased treatment time ($\tau = 3.5$)
WTP < threshold 1	Flap OP	Flap OP
Threshold WTP 1	175 (€ per mm)	200 (€ per mm)
Threshold 1 < WTP < threshold 2	EMD & bioactive glass	EMD & bioactive glass
Threshold WTP 2	375 (€ per mm)	400 (€ per mm)
Threshold 2 < WTP < threshold 3	EMD & bovine bone & PRP	EMD & bovine bone
Threshold WTP 3	400 (€ per mm)	450 (€ per mm)
WTP > threshold 3	EMD & bovine bone & porcine membrane	EMD & bovine bone & porcine membrane

The average (increased) treatment time corresponds to a 2.3 (3.5) treatment time factor for calculation of costs according to the GOZ.

PPD, pocket probing depth; WTP = decision maker's willingness to pay.

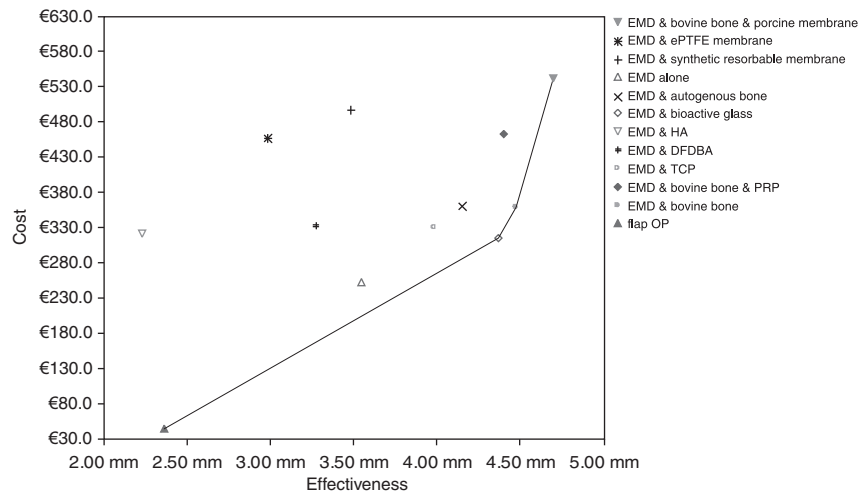


Fig. 4. The cost-effectiveness plane for clinical attachment level gain (average treatment time).

Table 3b. Cost-efficient treatment strategies according to CAL gain

	Average treatment time ($\tau = 2.3$)	Increased treatment time ($\tau = 3.5$)
WTP < threshold 1	Flap OP	Flap OP
Threshold WTP 1	150 (€ per mm)	150 (€ per mm)
Threshold 1 < WTP < threshold 2	EMD & bioactive glass	EMD & bioactive glass
Threshold WTP 2	450 (€ per mm)	450 (€ per mm)
Threshold 2 < WTP < threshold 3	EMD & bovine bone	EMD & bovine bone
Threshold WTP 3	825 (€ per mm)	950 (€ per mm)
WTP > threshold 3	EMD & bovine bone & porcine membrane	EMD & bovine bone & porcine membrane

An average (increased) treatment time corresponds to a 2.3 (3.5) treatment time factor for calculation of costs according to the GOZ.

CAL, clinical attachment level; WTP, decision maker's willingness-to-pay.

grafts with/without membrane fulfils the maximum net benefit criterion only for higher WTP values. On the other hand, when considering PPD reduction, treat-

ment with EMD & bioactive glass is cost-efficient when WTP is up to €375–400 per additional mm of PPD reduction. Treatment techniques that use

bovine bone grafts fulfil the maximum net benefit criterion only for further increased WTP values.

The above findings represent a typical example of decision making under uncertainty (Claxton 1999); it is important to note that a tooth with an intra-osseous defect is likely to have a better long-term prognosis when receiving treatment in a timely manner as compared with delaying treatment until more evidence is available; in the worst scenario, a tooth with an intra-osseous lesion but receiving no treatment may already have been lost by the time the evidence can be considered fully reliable. For such a case, it is suggested that treatment decisions should be based on the expected cost-effectiveness given the currently available evidence (Claxton 1999) and that uncertainties regarding treatment outcomes should rather be used for determining the extent to which further research is needed (Claxton et al. 2006). To the latter effect, the present paper points at the following.

First, the evidence, which this paper relies on, is based on a limited number of clinical studies such as in the case of using bioactive glasses as a bone graft material. Second, the sample sizes of the underlying clinical studies may be regarded as comparably small and this is why our results indicate considerable uncertainty in identifying cost-efficient treatment strategies for infrabony lesions. For example, we could identify a probability of around only 10% (according to CAL) for the combined use of EMD and bovine bone being a cost-efficient treatment strategy. Third, the reliable time period of health outcomes is restricted to 12 months only; a longer follow-up period after infrabony lesion treatment would provide better information and ideally consider tooth survival as the true outcome of treatment. Our findings should thus be interpreted with caution. Nevertheless, the present paper provides valuable guidance for priority setting in future clinical studies (Claxton & Posnett 1996). Further research that seeks to identify more robust information on long-term treatment effectiveness of infrabony lesions is therefore encouraged. Specifically, more studies on the treatment with EMD combined with either bioactive glass or bovine bone grafts appear desirable.

In terms of generalizability of our findings, some concern may be that the results of this paper would only be valid

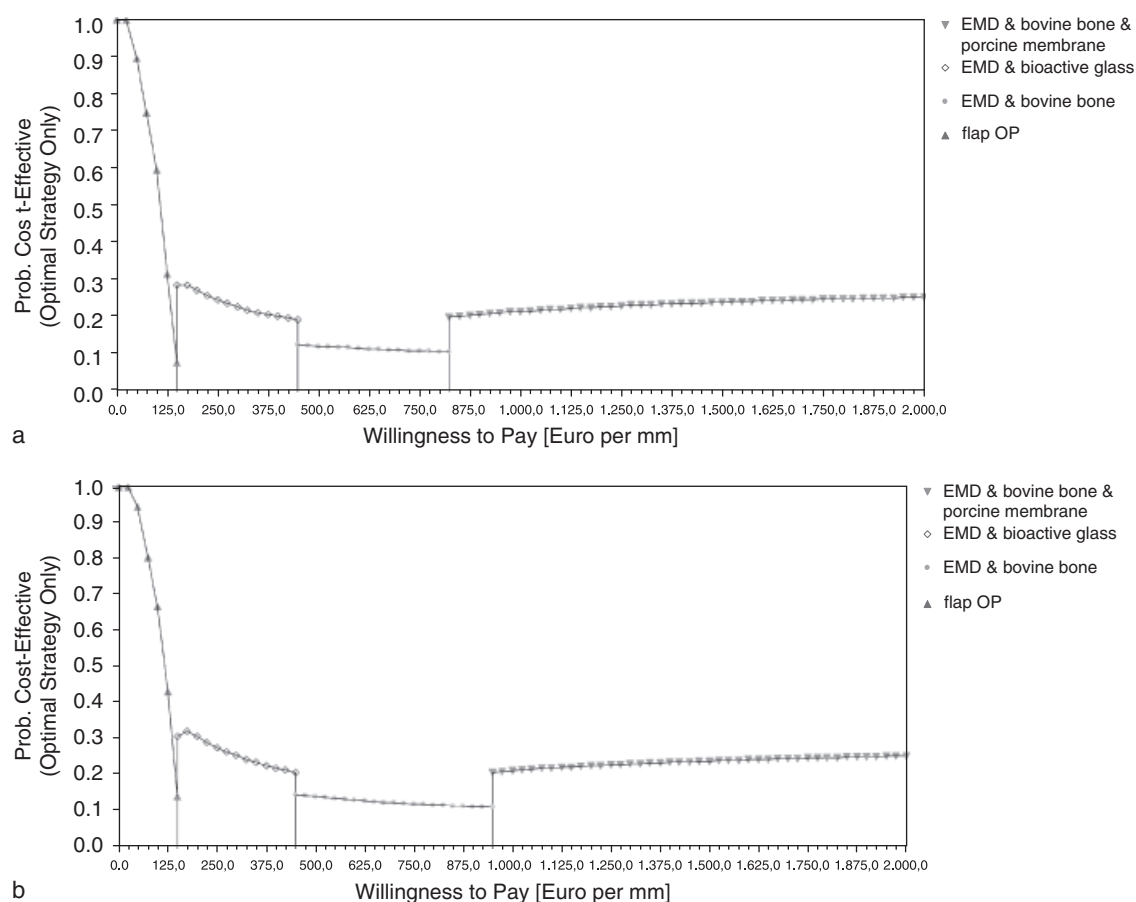


Fig. 5. (a) Cost-effectiveness acceptability frontier for clinical attachment level (CAL) (average treatment time). (b) Cost-effectiveness acceptability frontier for CAL (increased treatment time).

for Germany. Note, however, that the clinical evidence we rely on is not restricted to any single geographic setting. Furthermore, the precise costs we incorporate in our decision analytic model can, of course, only be considered fully reliable for the specific scenario we assume. However, the cost differential between the treatment strategies in our model is mainly caused by the prices of bone substitutes and/or the application of a membrane for guided tissue regeneration. Even though the according market prices may vary across countries, their relative price ranking can be expected to be in line with the cost scheme we use in our model. Therefore, we expect quite broad generalizability of our findings regarding the relative dominance of using EMD alone or in combination with other reconstructive devices.

On the whole, this study adds a new perspective to the current literature in the field. Recently, cost-effectiveness considerations have been increasingly estab-

lished as an important aspect of decision making in dentistry (Braegger 2005, Guyatt et al. 2008, Pennington et al. 2009a). For example, the previous literature has investigated economic aspects of supportive periodontal treatment (Gaunt et al. 2008, Pretzl et al. 2009), the lifetime cost-effectiveness of endodontic and implant approaches for treatment of an irreversibly pulpitic maxillary incisor (Pennington et al. 2009b), and the cost-effectiveness of different sinus lift techniques (Listl & Faggion 2010). Recently, the Consensus Report of the Sixth European Workshop on Periodontology has emphasized that the cost of bioactive agents for periodontal tissue engineering and regeneration should be compared with the expected clinical benefits (Palmer & Cortellini 2008).

Although our model indicates some uncertainty in identifying cost-efficient treatment strategies, yet our findings have significant implications for rating the strength of recommendations of proposed therapies (Guyatt et al. 2008).

This is specifically vital in a shared decision-making process in which patients should be well informed about the suggested interventions (Faggion 2010). Viewed in this light, the particular contribution of the present study is to increase the transparency in the decision-making process for the treatment of intra-osseous lesions.

To conclude, the results of the present analysis lead to the following recommendations for clinicians: (1) when monetary resources are high (>€150–200 per additional mm of PPD reduction or CAL gain, respectively), application of EMD (either alone or in combination with other devices) has a more advantageous cost-effectiveness ratio with respect to flap operation; (2) in cases where EMD application is indicated, the association of EMD with either bioactive glass or bovine bone substitutes shows a more advantageous cost-effectiveness ratio than EMD alone; (3) the use of PRP or a resorbable membrane in addition to EMD and bovine bone grafts may

only be justifiable when monetary resources for treatment are very generous.

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Supporting Information

Additional supporting information may be found in the online version of this article:

Table S1. Current market prices for bone grafts, membranes, and EMD.

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Clinical Relevance

Scientific rationale for the study: Previous clinical evidence suggests that treatment of infrabony lesions with EMD is effective. However, monetary resources for treatment can be limited and may restrict therapeutic possibilities. The purpose of

this study was to identify the most cost-effective technique for the treatment of infrabony lesions with EMD. *Principal findings:* Decision analytical modelling revealed that EMD in conjunction with bioactive glass or bovine bone substitutes is the most cost-effective treatment option as long

as EMD use is generally affordable. The additional use of platelet-rich plasma or a resorbable membrane comes at a relatively high cost. *Practical implications:* EMD in conjunction with specific types of bone graft may be cost-efficient for the treatment of infrabony lesions.

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