

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

Tooth Decay - HealOzone

Response to consultee and commentator comments on the draft scope

Consultee	Comments	Response
Welsh Assembly Government	No comments	None required
Tor-faen (Local Health Board)	<u>Para 1</u> –suggested change from and may create a ‘cavity’, to read and may, if it progresses, create a ‘cavity’.	Clarification made as per comments from consultees.
Tor-faen (Local Health Board)	<u>Para 1</u> last sentence suggested change - if untreated, tooth decay progresses... to read if untreated, tooth decay further progresses.	Clarification made as per comments from consultees.
Tor-faen (Local Health Board)	<u>Para 2</u> It may be worthwhile to add a statement about the difference between permanent teeth and deciduous teeth. The deciduous or milk teeth have less well mineralised enamel and dentine, and their enamel is thinner. As a result these teeth are more susceptible to decay than permanent teeth.	Added to first paragraph: Deciduous (milk) teeth are more susceptible to decay than permanent teeth because the enamel and dentine is less well mineralised and the enamel is thinner. Added to first paragraph rather than second because second paragraph relates to where the cavities occur and therefore what the CE marking relates to. The comment also relates to comments from other consultees about differentiating adults from children.
Tor-faen (Local Health Board)	<u>Para 3</u> -suggested change <i>caries can be stopped or reversed...</i> to read <i>It is possible to stop or reverse caries with fluoride use and change of diet.</i>	Amended to: “If it is caught at an early stage, it is possible to stop or reverse caries with use of fluoride to remineralise the tooth, and a change of diet.”

Tor-faen (Local Health Board)	<p><u>Technology</u></p> <p>- reference is made to remineralisation kits yet the intervention is described as HealOzone alone. Is it intended to investigate the impact of HealOzone above and beyond use of mineralisation and normal practice? Or is it intended to compare HealOzone and remineralisation kit use with normal practice? A study investigating the former would identify benefits of ozone above and beyond use remineralisation media.</p>	The Institute recognised the need to include an assessment of the contribution of remineralisation to the outcomes achieved. The scope has therefore been clarified.
Tor-faen (Local Health Board)	<p><u>Population</u> Given that there could be different impacts on deciduous and permanent teeth there are two potential populations:</p> <ul style="list-style-type: none"> • <i>children and adults with permanent teeth with occlusal pit caries, fissure caries and/or root caries and</i> • <i>children with deciduous teeth with occlusal pit caries, fissure caries and/or root caries....</i> 	The Institute agrees that clarification would improve the scope and it has therefore been amended
Tor-faen (Local Health Board)	<p><u>Comparator</u></p> <p>The current standard treatments are identified as the comparators. As previously mentioned the use of HealOzone plus the remineralisation kit is referenced in the section headed 'Technology'. Ideally the current standard treatment plus remineralisation kit should be an option for comparison.</p>	The Institute recognised the need to include an assessment of the contribution of remineralisation to the outcomes achieved. The scope has therefore been clarified.
Tor-faen (Local Health Board)	<p><u>Other considerations</u></p> <p>- the separation of the effectiveness of non-cavitated and cavitated caries would seem appropriate.</p>	No action required.
Tor-faen (Local Health Board)	As indicated previously Torfaen Local Health Board would suggest that deciduous and permanent teeth are looked at as there are differences between them, which affects the disease process.	The Institute recognised that there were differences, but agrees that clarification would improve the scope and it has therefore been amended
Tor-faen (Local Health Board)	The criteria for cavitated caries are well developed and covers the addition of HealOzone to current management strategies and highlights outcomes.	No action required.
Tor-faen (Local Health Board)	<p>However it is not clear what is understood by progression of dental caries. I would not recommend removal of teeth for sectioning nor over-frequent use of radiographs.</p> <p>Some consideration should be given to the measure of progression to be used and whether it includes visual examination of teeth, dental pain history which suggests caries is affecting the pulp of the tooth, and any additional assessment criteria such as radiographic assessment.</p>	<p>Specific outcome measures will be defined at the protocol stage.</p> <p>For clarification amended to: Incidence of symptoms associated with pulpal pathology (cavitated caries only)</p>
Tor-faen (Local Health Board)	It is not clear whether dental pain history is part of the criteria for caries	Dental pain would be captured in a number of these

Health Board)	progression or one of the adverse events.	outcome measures, including 'health-related quality of life'. The text has been amended to: -Progression of dental caries -Incidence of symptoms associated with pulpal pathology (cavitated caries only) Dental pain has also been included in 'patient-centred outcome measures'.
Tor-faen (Local Health Board)	criteria for un-cavitated caries are not similarly separated out. I would suggest that these should be further developed. They should include clinical assessment of progression or regression of the carious lesions, e.g.: <ul style="list-style-type: none"> • progression of enamel only lesions into dentine, • progression to cavitation (i.e. breakdown of enamel), • dental pain. 	Specific outcome measures will be defined at the protocol stage. These suggested outcome measures are all encompassed in 'progression of dental caries'. (Cavitated caries) in brackets has been added after re-restoration and pulpal damage to imply that the other outcomes are for both cavitated and non-cavitated. Dental pain has also been included in 'patient-centred outcome measures'.
Tor-faen (Local Health Board)	the evaluation ideally should separate non-cavitated lesions into enamel only from non-cavitated lesions into enamel and dentine if any ability of ozone to reverse dentine caries is to be investigated. The effects of HealOzone on non cavitation lesions could potentially be its greatest impact if it proves effective. Currently 3 million children across the UK are seen each year for a school dental screening which involves visual screening of the teeth for dental disease. Currently the criteria normally used is visual evidence of caries into dentine as this relates to the intervention of restoration of the tooth. Using normal interventions this is too late to reverse the disease using conventional interventions even if cavitation is not present (i.e. enamel has not yet collapsed). For non-cavitated lesions in enamel current guidance would be that dietary advice should be given and regular application of fluoride to the affected teeth. Dietary intervention of this type is known to be of very limited effectiveness and fluoride application needs to be regular which is potentially costly or likely to be intermittently applied. If a painless alternative could be found which requires less frequent application than fluoride it might be possible to outreach an effective intervention to reverse caries in the socially deprived groups who are least likely to see a dentist and simultaneously most likely to have the dental disease.	The Institute agrees that clarification would improve the scope and it has therefore been amended to state "Where the evidence is available, separate consideration will be given to the clinical and cost-effectiveness of HealOzone for different severities of lesions." The considerations section has also been amended to reflect the intention of this appraisal to look at each component of the appraisal.
National Public	The appraisal document as currently drafted, lacks enough detail to ensure that	The purpose of a NICE appraisal is to evaluate the

Health Service for Wales	confounding factors are sufficiently controlled for, to enable the true clinical and cost effectiveness of this device to be determined:	clinical and cost-effectiveness from available data. The scoping document is not a specification for a prospective study.
National Public Health Service for Wales	The draft indicates that the objective of the appraisal is to “appraise the clinical and cost effectiveness of the HealOzone procedure in comparison with conventional treatment for the treatment and management of occlusal pit caries, fissure caries and root caries”. This can only be satisfactorily achieved by evidence derived from randomised controlled trials of the HealOzone and existing prevention / management regimes. The appraisal document as currently drafted, lacks enough detail to ensure that confounding factors are sufficiently controlled for, to enable the true clinical and cost effectiveness of this device to be determined.	The scoping document is not intended to specify all the parameters of the appraisal. These will be further defined in the protocol. During the appraisal consideration will be given to the strength of the evidence base.
National Public Health Service for Wales	<i>Coronal caries or root caries?</i> The draft proposes investigating the HealOzone in the management of both coronal caries and root caries. These are very different conditions affecting vastly different age groups and should be the subject of separate appraisals.	The Institute recognised that there were differences but agrees that clarification would improve the scope and it has therefore been amended
National Public Health Service for Wales	<i>Cavitated or non-cavitated lesions?</i> Cavitated and non-cavitated coronal caries represent very different clinical entities in terms of disease management. Conventional treatments would advocate procedures to encourage remineralisation of non-cavitated lesions, but restoration of cavitated lesions. These conditions should be treated separately in appraising effectiveness of the new technology.	The Institute recognised that there were differences but agrees that clarification would improve the scope and it has therefore been amended
National Public Health Service for Wales	Diagnosis of non-cavitated carious lesions in pits and fissures is notoriously difficult and the methods for diagnosis would need to be controlled – will for example radiographs be utilised?	This is beyond the remit of the appraisal. Consideration will be given to current relevant guidelines.
National Public Health Service for Wales	<i>The additional benefits of the HealOzone, above the application of the remineralising solution</i> The procedure described in paragraph 1, page 2 of the scoping document describes the application of a solution which contains amongst other constituents fluoride and xylitol. The conventional treatment for non-cavitated lesions would be to apply fluoride varnish or solution. In appraising the effectiveness of the HealOzone, it will be necessary to design the trial in such a way as to identify the contribution of the application of the ozone, the remineralising solution and the control (presumably application of conventional fluoride varnish or solution). In other words, what additional advantages does the application of the ozone offer over the remineralising solution?	It was the intention of the Institute to examine the components of the package of care. The Institute however agrees that the scope would benefit from clarification. Amendments have therefore been made to the considerations section.
National Public Health Service for	<i>Single and multiple surface lesions – cost effectiveness</i> The appraisal is limited to single surface (occlusal) and presumably root surfaces.	The scope of the appraisal is restricted to the CE marked indications, which are indicated in the

Wales	It is my understanding that the HealOzone is restricted to use on single surface lesions (due to the need to maintain a seal and prevent the escape of Ozone). This needs to be born in mind in the appraisal. The cost effectiveness of a device restricted to managing single surface lesions needs to be taken into consideration.	population. The Institute acknowledges the comment.
National Public Health Service for Wales	<i>Outcome measures</i> The outcome measures stated in “Other considerations” are very general. As examples: - More consideration needs to be given to how progression of dental caries will be measured, will this involve radiographs for example?	The scope of the appraisal is not intended to specify outcome measures in detail. The outcome measures will be more explicitly defined in the protocol.
National Public Health Service for Wales	The time to filling replacement suggests a long term study. Precise guidelines on the criteria for a failed restoration would need to be defined.	The appraisal is not intended to produce guidelines on management of caries and therefore this is beyond the remit of the appraisal. The data would be required to substantiate any claim that HealOzone has an impact on time to filling replacement i.e. longer-term outcomes. Recommendations on this aspect will only be made if such data were available. The scope has been amended to state “The time horizon for the economic evaluation should reflect the necessity for longer-term follow up to evaluate the impact of HealOzone on both progression of caries and need for re-restoration.”
National Public Health Service for Wales	Quality of life and oral health related quality of life measures are an increasingly complex area and careful consideration would need to be give to the measure chosen.	The limitations of specific measures are acknowledged by the Institute and taken into consideration for all appraisals.
National Public Health Service for Wales	<i>Patient Education</i> It is stated that education about improved dental hygiene and diet will be assumed. This is potentially a significant confounding factor and <u>must</u> be controlled for in testing the HealOzone against conventional treatments.	The Institute agrees that clarification would improve the scope and it has therefore been amended
National Public Health Service for Wales	<i>Timescale</i> No details of the timescale over which the effectiveness of the treatment to be tested have been given. Trial of caries preventive / management agents require at least two and preferably three years.	The Institute recognised that longer-term follow up would be appropriate. The consideration section of the scope has been amended to clarify this. “The time horizon for the economic evaluation should reflect the necessity for longer-term follow up to evaluate the impact of HealOzone on both progression of caries and need for re-restoration.”
National Public Health Service for Wales	<i>Number of participants</i> No details have been given of the number of patients to be recruited to the appraisal etc. It will be necessary to ensure that any trial of effectiveness is	Recruiting patients to studies is not within the Institute’s remit. The Institute will examine the currently available evidence base. Consideration to

	sufficiently powered to demonstrate effectiveness.	the power of the individual studies will be given during the assessment phase. No amendment made to scope.
National Public Health Service for Wales	<i>Blinding</i> It would obviously be important that the clinician assessing the outcome of the treatment was blind to the treatment status of the patients.	As per standard appraisal methods consideration will be given to the potential for bias to be introduced into study results by lack of appropriate blinding. No amendment made to scope.
National Public Health Service for Wales	<i>Stratification</i> In order to ensure comparability, the subjects who will receive the test and control treatment will require stratification in order that they have disease of similar severity at baseline and are comparable in other demographic variables such as age, sex and socioeconomic status.	No amendment made to scope. The degree to which studies have been appropriately designed will be considered during the assessment phase.
National Public Health Service for Wales	<i>Safety issues</i> As stated, the device carries a CE mark, but it would be judicious to check for any adverse outcomes as a result of using the device	Wording clarified to 'adverse effects of treatment'.
National Public Health Service for Wales	<i>Mechanism of action</i> In conducting the appraisal it would be beneficial to determine the mechanism of action of the ozone delivery device as a caries preventive/management agent. Is it antimicrobial, is it an effect on de / remineralisation? What for example is the purpose and contribution of the "pH balancer" described at the bottom of page one in the draft scope?	The Institute recognised that this is an important aspect of this appraisal and will be taken into consideration. Scope has been amended to clarify the Institute's intentions.
Lay Advisory Group	We are aware that there has been publicity and some controversy about ozone treatment for tooth decay and welcome the appraisal by NICE.	No action required.
Lay Advisory Group	<u>Patient compliance</u> The Draft Scope makes it clear that the success of the technology depends on a high degree of patient concordance/ compliance. It states that "To remineralise the tooth, patients apply products for several weeks. The patient then returns to the dentist for assessment....". <u>However, the role of the patient as a very active participant in the treatment is not adequately reflected in the Draft Scope.</u> The regular application of a product to the teeth is far more demanding of patients than other treatment, such as regularly taking medication.	The Institute recognises that this is an important consideration. The scope has been amended to state: "Where the evidence permits, the appraisal will attempt to determine the incremental cost-effectiveness associated with each component of the procedure."
Lay Advisory Group	<u>Other Considerations</u> , the first sentence should perhaps include a reference to the importance of patient input to the "the package of care".	The Institute recognises that this is an important consideration. The scope has been amended to include that where the evidence permits, consideration will be given to the suitability of treatment for different groups of individuals.

Lay Advisory Group	<u>The degree of concordance/ compliance</u> is an important variable in measuring the clinical and cost-effectiveness of the procedure. It is probable that the procedure is unsuitable for certain groups of patients : for example, some with special needs. This should be reflected in the Scope, which at present only refers to children as a group for which the suitability of the technology is questioned.	The Institute recognises that this is an important consideration. The scope has been amended to include that where the evidence permits, consideration will be given to the suitability of treatment for different groups of individuals.
Lay Advisory Group	<u>Patient education</u> : the Scope states that "It is assumed that patients will be given education about improved dental hygiene and diet". It is not clear if this assumption relates to current standard practice as well the HealOzone procedure, a point which should be made explicit.	The Institute recognised that HealOzone is used as part of a package of care. The scoping document has been clarified to reflect this.
British Dental Association	<u>Evidence base</u> ; it would be extremely difficult for NICE to conduct a systematic review of published literature pertaining to the outcomes listed. There is very little published information to date and the outcome measures listed have largely not been considered in the studies available (they concentrate more on bacterial counts and short term patient satisfaction). Many unrefereed abstracts about HealOzone have been presented at conferences, but very few, if any, full papers in substantive refereed Journals have been published.	It is acknowledged by NICE that this appraisal will be challenging. The strength of the evidence base always forms part of the assessment exercise and is taken into account.
British Dental Association	The Cochrane collaboration has undertaken a systematic review on this subject and it would seem logical for this work to be utilised by NICE.	The Cochrane Oral Health Group is also one of the consultees for this appraisal. The Institute recognises that the Cochrane Review is an important part of the evidence base and if the systematic review is available, it will be incorporated into the assessment. It is however only one part of the evidence base of the appraisal.
British Dental Association	<u>Cost effectiveness analysis</u> Cost effectiveness analysis requires a definition of what is meant by "effective". Thus, it is essential to decide at the outset what is meant by "effective" dental care. Patient-centred measurement of effectiveness might centre around relief and prevention of pain, retention of functional dentition into middle/old age or an aesthetically pleasing result. In contrast, the dentist-centred view of "effective" treatment might be removal of potentially pathogenic bacteria, patient short term satisfaction with treatment or reversal of incipient caries (patients would not be aware of incipient caries until it were pointed out by a dentist). Thus, before any review of effectiveness or cost effectiveness of any type of dental treatment can be undertaken, decisions must be made as to the "objective" of dental care itself.	This is implicit within every appraisal. The outcome measures will be considered further at the protocol stage. The Institute recognises the importance of patient-centred outcomes measures in each appraisal but appreciates that the scope would benefit from clarification: Outcome measures therefore amended to state "Patient-centred outcome measures (i.e. relief and prevention of pain, retention of functional dentition and patient satisfaction).
British Dental Association	<u>Outcome measures</u> Measurement of both caries progression and pulpal pathology in anything other than extracted teeth is extremely difficult (for example, a tooth might have a dead	The Institute acknowledges this difficulty. The scope has been amended to state, "symptoms associated with pulpal pathology."

	pulp and therefore be "unhealthy" in a dentists view, but might not cause any symptoms). Without symptoms pulpal pathology cannot be assessed. Perhaps pain as a proxy for pulpal health might be a more sensible outcome to assess.	
British Dental Association	The outcome of "time to re-restoration" would require longitudinal studies of considerable length. Such longitudinal studies of HealOzone cannot possibly be available as it is a new product.	The Institute acknowledges that such data may not be currently available. This is however is perhaps one of the most relevant outcomes for assessment in terms of cost-effectiveness. The data would be required to substantiate any claim that HealOzone has an impact on time to filling replacement i.e. longer-term outcomes. Recommendations on this aspect will only be made if such data were available.
Faculty of General Dental Practitioners	Comments are provided by the Lay Advisory Group (above)	No action needed
Cochrane Oral Health Group	Would like the HTA report suspended until the Cochrane review is published.	The Cochrane Oral Health Group is one of the consultees for this appraisal. As per the established process, the Institute will seek input from the group during all phases of this Appraisal. The Institute considers the Cochrane Review to be an important aspect of this appraisal and will ensure that if it is made available it will be taken into consideration with the rest of the evidence base.
Cochrane Oral Health Group	Occlusal Pit and fissure caries should be distinguished from root caries. Different management etc	The Institute recognised that there were differences but agrees that clarification would improve the scope and it has therefore been amended
Cochrane Oral Health Group	Evidence base likely to be extremely biased and most evidence is on root caries	Any biases in the evidence available will be taken into consideration during the appraisal.
Cochrane Oral Health Group	Root caries predominates in an aged population. Prevention is most ideally and cost-effective when applied to the young	Background section amended to state: "Root caries is more common in older people and generally occurs " HealOzone is not CE marked for prevention and therefore this is outside the scope of the appraisal.
Cochrane Oral Health Group	It is important to mention the relationship of the formation of cavitated dental caries to time. Cavitations may occur rapidly over several months under the right conditions or circumstance or take years. This is also relevant to the outcome measures	Background section amended to state" Under the right conditions, the development of a cavity may occur rapidly over a period of months and without effective treatment, cavitated dental caries commonly leads to the loss of the tooth."

Cochrane Oral Health Group	It is important that it is also noted untreated (or ineffectively treated) cavitated dental caries commonly leads to tooth loss without conventional treatment	Background section amended to state” Under the right conditions, the development of a cavity may occur rapidly over a period of months and without effective treatment, cavitated dental caries commonly leads to the loss of the tooth.”
Cochrane Oral Health Group	“ Carious lesions tend to occur in areas that are difficult to clean” suggests or implies that cleaning is an effective method for the prevention of dental decay. It is not.	Background section amended.
Cochrane Oral Health Group	What is the relevance to CE marking and the effectiveness of HealOzone. The CE mark relates to manufacture of electrical appliances and their safety emission standards	The Institute can only appraise the device in accordance with its CE marking.
Cochrane Oral Health Group	I am not aware of any research that shows ozone permeates the dental cavity. It is applied to the surface for decayed teeth (non cavitated?) I believe. This is misleading and should be rephrased	The sentence has been rephrased; please see comments from Kavo.
Cochrane Oral Health Group	The dentist should not be making the assessment of whether the treatment has been successful that is the purpose of this technology assessment which should be based on the quality of the body of the evidence	Dentist’s clinical judgement is necessary to assess whether an individuals patients treatment has been successful in repairing tooth decay. It is the role of the Institute to assess the totality of evidence for the effectiveness of HealOzone therapy compared to current standard treatment.
Cochrane Oral Health Group	HealOzone is not available on the NHS in solely NHS dental practices (the machine may reside there be used on attending private patients) it is not included as a treatment in Amendment 92 of the statement of dental remuneration for NHS dental services and is not an approved or accepted mode of treatment by the dental reference service of the Dental Practice Board. As such use of the HealOzone procedure on NHS patients would require the signature of form FP171D by the patient or equivalent for the provision of private treatment on and NHS patient. This sentence is misleading and should be rephrased or removed.	Reference to NHS and private deleted. NICE have raised this issue with the DoH/WAG. NICE understand that the Chief Dental Officer is considering what further action to take pending the outcome of the appraisal.
Cochrane Oral Health Group	Need to distinguish between the ozone and the remineralisation stages [paraphrased].	The Institute recognised this need but agrees that clarification would improve the scope and it has therefore been amended
Cochrane Oral Health Group	Costing data is wrong	Amended cost data have now been received from the manufacturer and incorporated into the scope.
Cochrane Oral Health Group	Intervention: HealOzone is not an intervention- the application of ozone gas to decayed tooth structure is	This is standard terminology for the scope however the Institute’s intentions have been further clarified.

Cochrane Oral Health Group	Intervention: The remineralisation kit is a stand-alone intervention and should be investigated separately; there is a considerable volume and body of evidence that fluoride rinses are able to initiate remineralisation process without the application of ozone gas.	The Institute recognised that there are a number of aspects to the procedure but agrees that clarification would improve the scope and it has therefore been amended.
Cochrane Oral Health Group	Populations: Please look carefully at the sample sizes and data available and do not extrapolate from older patients to children or vice versa, from root caries to occlusal pit and fissure caries or vice versa as the conventional treatment options for these groups are very different	The Institute agrees that clarification would improve the scope and it has therefore been amended
Cochrane Oral Health Group	Current Standard Treatments (comparators): When looking at cost-effectiveness of the HealOzone procedure please bear in mind whether you are dealing with non-cavitated lesions. The comparators for conventional management of the 2 different caries sites (pit and fissure, and root caries) would be different in the general practice setting	The Institute recognised that there were differences but agrees that clarification would improve the scope and it has therefore been amended.
Cochrane Oral Health Group	A reasonable comparator for early root caries would be a strategy involving root debridement in conjunction with the application of fluorides, glass ionomers, Chlorhexidine, sealants and patient education with early diagnosis and review. As you say in Para 4 of the background the treatment strategy is dependent on the stage at which the caries is detected	This has been added to the background section and the comparators section of the scope has been amended.
Cochrane Oral Health Group	A reasonable comparator for early pit and fissure caries would be the placement without local anaesthetic of a preventative resin restoration	The term 'restoration' is intended to encompass this. No amendment made.
Cochrane Oral Health Group	Filling and drilling is not a good comparator for either early root or pit and fissure caries as it is the current contemporary management for cavitated lesions or lesions well into dentine. There is little if any good study design available recommending HealOzone for the management of well established, cavitated, occlusal pit and fissure lesions or class V cavities.	The Institute understood this distinction therefore did not add restoration to the non-cavitated lesions in the comparator section. 'Where appropriate' has however been added to the comparator definition for cavitated lesions. The appraisal will identify any limitations to the evidence base.
Cochrane Oral Health Group	Other considerations: As mentioned earlier the HealOzone procedure contains the application of strong fluoride solution in the remineralisation product. How therefore can an intervention and comparator be the same medicament. To appraise the cost-effectiveness of HealOzone and comparator procedures within the NHS it will be essential to utilise the data sets available at the dental practice board or utilised by the dental rates study group	The Institute recognised that HealOzone is part of a package of care. The scope has therefore been further clarified to reflect this.
Cochrane Oral Health Group	Outcomes to be assessed should include: Time to conventional therapy- tooth decay is a slowly progressing disease assessing the effectiveness of HealOzone is a very difficult measure in the short-	Time to re-restoration was included in the scope. Progression of dental caries would also potentially cover this outcome. The outcomes will be more fully

	term.	specified in the protocol. The Institute acknowledges that such data may not be currently available. This is however is perhaps one of the most relevant outcomes for assessment in terms of cost-effectiveness. The data would be required to substantiate any claim that HealOzone has an impact on time to filling replacement i.e. longer-term outcomes. Recommendations on this aspect will only be made if such data were available.
Cochrane Oral Health Group	Time to pulpal symptoms or the symptoms of acute pulpitis, surely the incidence of pulpal pathology can only be assessed/measured by histology or cytology in vitro	The Institute recognised this limitation but agrees that clarification would improve the scope and it has therefore been amended. The scope has therefore been amended to symptoms associated with pulpal pathology (cavitated caries only).
Cochrane Oral Health Group	Suitability of the treatment of children, does this not abrogate the requirement to confirm the HealOzone procedure is effective first?	The scope has been clarified. It is also an important consideration, which would potentially have an impact on the cost-effectiveness in this patient group.
Cochrane Oral Health Group	It should not be assumed patients are given education about improved dental hygiene and diet it must be confirmed that controlled, identical advice or no advice is given to both control and treatment groups for data to be comparable.	The Institute recognised this, but agrees that clarification would improve the scope and it has therefore been amended.
Cochrane Oral Health Group	The reductant is a highly concentrated fluoride containing suspension.	The background section has been amended following clarification from the manufacturer.
Cochrane Oral Health Group	The lower limit costing mentioned for the procedure is not realistic in time nor capital expenditure.	Amended cost data have now been received from the manufacturer.
Cochrane Oral Health Group	There is no mention of device calibration on a daily basis which is mandatory under medical devices legislation. The "green light goes on" is neither calibration nor testing.	For the purposes of this appraisal it will be assumed that the device would be being used correctly.
Assessment Group	Intervention and Title: HealOzone <i>for primary carious lesions</i>	The information received from the manufacturer does not specify whether HealOzone is CE marked for primary or secondary dental caries. The scope cannot therefore be restricted to primary carious lesions.
Assessment Group	Other considerations: Reword to :The HealOzone procedure encompasses a 'package of care' <i>including the use of ozone, mineral-permeable sealant, and remineralising products.</i>	Ambiguity noted, wording clarified.

Assessment Group	Other considerations- Include: For non-cavitated caries the use of HealOzone to arrest primary carious caries and reduce the need of further treatment will be compared with current management strategies (i.e. removal of the plaque and application of sealants and remineralising products) excluding the use of HealOzone.	The scope has been clarified by amendments to the considerations and comparators section.
Assessment Group	Other considerations- Include: For cavitated but not deep caries the use of Heal Ozone procedure will be compared with current management strategies (i.e. removal of the plaque and decayed tissue by restorative treatment) excluding the use of HealOzone.	The Institute recognised that there were differences in the management strategies for deep and non-deep cavitated caries. This is already explicitly stated in the considerations section: Where the evidence is available, separate consideration will be given to the clinical and cost-effectiveness of HealOzone for different severities of cavitated lesions
Assessment Group	For deep cavitated caries the addition of the HealOzone procedure to conventional dental care (i.e. removal of the plaque and decayed tissue by restorative treatment or replacement of 'failed' restorations) will be compared with strategies excluding the HealOzone procedure.	The Institute recognised that there were differences in the management strategies for deep and non-deep cavitated caries. This is already explicitly stated in the considerations section: Where the evidence is available, separate consideration will be given to the clinical and cost-effectiveness of HealOzone for different severities of cavitated lesions
Assessment Group	OUTCOMES: add <ul style="list-style-type: none"> • Number of fillings • Patient satisfaction 	Outcome section amended to include patient-centred outcome measures. Number of fillings is related to progression of dental caries; these outcomes will be further specified at the protocol stage.
Assessment Group	If evidence is available suitability of treatment for children will be assessed.	Amended to: "Where the evidence is available, separate consideration will be given to the clinical and cost-effectiveness of HealOzone for different severities of lesions."
Assessment Group	It is assumed that patients will be given education about improved dental hygiene and diet.	The considerations section of the scope has been amended.
KaVo Dental Limited UK	Background: Dental caries (tooth decay) is the localised destruction of the tissues of the tooth by bacteria, which produce a "niche environment" within the lesion, favouring their own development. It is a multifactorial, multistage process that extends from	A number of amendments have been made to the background section to reflect the comments from all of the consultees.

	infection to demineralisation and cavitation. Commensal bacteria (adhere to - delete) invade the hard outer layer of a tooth (the enamel) and metabolise carbohydrates to produce acids that demineralise the tooth enamel (non-cavitated dental caries) and may eventually create a “cavity” (cavitated dental caries). If untreated, tooth decay progresses through the enamel to the dentine and then the pulp. Progression involves the sequential colonisation and recolonisation of the lesion by several hundred differing bacterial species, each more acidogenic (acid-producing) and acidoduric (acid-loving) than their predecessors. The process may take anything from a minimum of 14 weeks to over 2 years, depending upon a diverse range of patient-specific risk factors.	
KaVo Dental Limited UK	The treatment strategy is dependent upon the stage at which the caries is identified, the type of caries, and the assessment of risk and prognosis. Caries can be stopped or reversed if it is caught at an early stage. Early detection is crucial to obtaining the most impressive results; retaining tooth tissue and ensuring true patient health. It is generally accepted that the sole use of mechanical probing or radiographical evidence (X-Rays), are not suitable methods to detect these changes at an early enough stage. If dentists have already invested in commercially available equipment, specifically designed to both disclose and quantify demineralised enamel (Quantative LASER fluorescence – QLF), then these objectives may easily be met. Treatment strategies include application of fluorides, chlorhexidine, sealants, antimicrobials, salivary enhancers and patient education. Current management of cavitated dental caries consists of (removing – delete) amputation of decayed tooth tissue and then filling the resultant man-made cavity with man-made materials, which are destined to fail over time. Each subsequent restorative filling procedure unnecessarily removes a quantity of healthy tissue and further weakens the entire tooth. This means that once drilled, patient’s teeth are condemned to a lifetime of ever increasing sized fillings, with all the financial implications to both individual patients and the NHS.	The Institute appreciates the comments made and recognises that they are pertinent. However, this level of detail is not required in the background of the scoping document. The background section has however been amended to reflect comments from all of the consultees.
KaVo Dental Limited UK	HealOzone is a fully certified Medical Device which is CE marked for the treatment and management of occlusal pit caries, fissure caries and root caries.	No amendment made; if it is CE marked then it is ‘fully certified’.
KaVo Dental Limited UK	The HealOzone device includes an ozone generator, hose and handpiece (which – delete) that delivers ozone at a concentration of 2,100 ppm (to – delete) into the surface of the tooth. Ozone is a powerful antimicrobial agent that permeates the dental (cavity – delete) lesion, killing all the acid-producing micro-organisms responsible for tooth decay. Ozone also renders bacterial by-products, toxins/acids/bio-molecules etc., inactive. Once this “niche environment” has thus been eradicated, buccal pH levels automatically rise through neutral to slightly alkaline. At this stage, Nature is then able to remineralise the lesion with minerals found within the patient’s saliva, which is a natural healing response. Whilst the	The background section has been amended to reflect the comments from all of the consultees. However some of the detail suggested by KaVo has not been incorporated as the background section is intended to give an overview rather than to be comprehensive.

	<p>patient is still in the dental operating chair, the tooth is then additionally (washed – delete) flushed with a “pH balancer” (and a mineral permeable seal is applied. – delete) to ensure that when Nature “calls” for minerals, only the best quality are available for absorption. The patient is then sent home with an “at home kit” of toothpaste and mouth rinse, (To remineralise the tooth, patients apply products – delete) containing fluoride, calcium, zinc, phosphate and xylitol for several weeks. The “pH balancer” and “at home kit” ensure that even with a deficient diet, the patient can maintain a high level of good quality minerals, throughout the natural re-mineralisation process period. Taking-up good quality “pharmaceutical grade” minerals, strengthens the tooth and makes it more resistant to further caries attack</p>	
KaVo Dental Limited UK	<p>In pre-cavitated dental caries, the lesion will arrest and reverse in approximately 6 to 8 weeks, with no further intervention. Well within the 14 week “window of opportunity” available.</p>	<p>Background section amended: In pre-cavitated dental caries no further intervention is generally required as, with correct after-care, the lesion should arrest and reverse in approximately 6 to 8 weeks. In cavitated dental lesions that would be prone to food impaction, any necrotic carious tissue is removed, and the lesion is sealed with a fluoride-releasing glass ionomers. The patient then returns to the dentist for assessment of the success of the treatment and the need to undertake repetition of treatment or restorative repair.</p>
KaVo Dental Limited UK	<p>In cavitated dental lesions that would be prone to food impaction, temporisation with a glass ionomers sealing material, having fluoride-releasing properties is employed. Depending upon severity of lesion, it may be necessary to remove the necrotic, “texture less” carious tissue first, leaving carious enamel/dentine that is soft or leathery, in situ.</p>	<p>Background section amended: In pre-cavitated dental caries no further intervention is generally required as, with correct after-care, the lesion should arrest and reverse in approximately 6 to 8 weeks. In cavitated dental lesions that would be prone to food impaction, any necrotic carious tissue is removed, and the lesion is sealed with a fluoride-releasing glass ionomer. The patient then returns to the dentist for assessment of the success of the treatment and the need to undertake repetition of treatment or restorative repair.</p>
KaVo Dental Limited UK	<p>The patient then returns to the dentist for assessment of the success of the treatment and need for repetition or to undertake definitive, restorative repair.</p>	<p>Amended to: The patient then returns to the dentist for assessment of the success of the treatment and the need to undertake repetition of treatment or restorative repair.</p>
KaVo Dental Limited UK	<p>HealOzone is currently available in (a limited number of – delete) x 236 (May 2004) UK NHS and private dental practices, with a further x 1,200 approx., being used throughout Europe, Singapore, New Zealand, Australia, Russia and Canada. FDA approval for the American Market is currently being sought. The initial cost of</p>	<p>Scope amended to reflect current pricing as per information from KaVo.</p>

	the device is (£11,000 – delete) £12,000 (excluding VAT) with annual maintenance costs in the region of £160 (and – delete) or £630 per annum (excluding VAT), depending upon level of Maintenance Contract purchased. The current cost of the HealOzone treatment to the patient, is between (£5 – delete) £10 and (£70 – delete) £90 per (treatment – delete) lesion including the cost of the remineralisation kit (which lasts for approximately one month). However many (trial – delete) HealOzone practices are charging the same price as a composite filling, approximately (£13 – delete) £35 to £45 for the first tooth and £25 to £30 for subsequent teeth.	
KaVo Dental Limited UK	Current standard treatments (comparators) – “management strategies (removal of plaque and all decayed tissue and	The comparators section has been amended to reflect the comments received from a number of consultees.
KaVo Dental Limited UK	Other Considerations – (a) “the HealOzone procedure to augment current management strategies (removal of plaque and some decayed tissue and restorative treatment or ...”	The considerations section has been amended to reflect the comments received from a number of consultees.
KaVo Dental Limited UK	Other Considerations – (b) Please add to “Outcomes include:” Reduction in postoperative trauma Reduction in patient anxiety Reduction in anaesthetic use Reduction in use of burs Reduction in overall treatment delivery time Reduction in tooth tissue amputation Improved patient motivation Acceptance by dental phobic patients Natural healing response Proactive, not reactive preventative dentistry Micro-invasive not minimally invasive dentistry	The outcome measures specified in the scoping document are a broad indication of the more specific ones that will be further defined at the protocol stage.

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