NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Overview

HealOzone for the treatment of tooth decay

(occlusal pit/fissure caries and root caries)

The overview is written by members of the Institute's team of technical analysts. It forms part of the information received by the Appraisal Committee members prior to the first committee meeting. The overview summarises the evidence and views that have been submitted by consultees and evaluated by the Assessment Group, and highlights key issues and uncertainties. In order to allow sufficient time for the overview to be circulated to Appraisal Committee members prior to the first Appraisal Committee meeting, it is prepared before the Institute receives Consultees' comments on the Assessment Report. These comments are therefore not addressed in the Overview.

A list of the sources of evidence used in the preparation of this document is given in Appendix A.

1 Background

1.1 The condition

Dental caries (tooth decay) is a chronic disease caused by the localised and progressive demineralisation (loss of mineral content) of the hard surfaces of the tooth. Both deciduous (milk/primary) and permanent teeth are susceptible to caries, although the progression may be more rapid in deciduous teeth as they are less well mineralised.

Tooth decay is a multi-stage process initiated by the local accumulation of cariogenic bacteria (those which cause dental caries) on the hard surfaces of the tooth. Cariogenic bacteria metabolise dietary carbohydrates to produce plaque acids, which cause erosion of the tooth enamel (non-cavitated dental caries). Without successful treatment the demineralisation and erosion will extend into the dentine and eventually into the pulp (cavitated dental caries) and cause pain. The progression of dental caries is a slow in most individuals, with enamel lesions taking over 2 years to cavitate.

The presence and number of cariogenic bacteria and the pH of the mouth determine whether dental caries occurs, reverses or progresses. In the absence of cariogenic bacteria the pH of the mouth is neutral, enabling remineralisation (the replacement of the mineral content) of the tooth. This is facilitated by good oral hygiene and the use of fluoride-containing toothpaste and mouthwashes. However, as the number of cariogenic bacteria increases, the pH of the mouth becomes more acidic, preventing

remineralisation, and increasing the likelihood of tooth demineralisation and dental caries.

The type of dental caries is classified by its origin: pit and fissure caries (PFC) occurs in the pits (small depressions) and fissures (small grooves) of the occlusal (biting) surface of teeth, and root caries (RC) occurs in the area between the tooth and receding gum. Caries can also occur between adjacent teeth. Primary dental caries are caries that occur on a previously sound natural tooth. Secondary dental caries refers to tooth decay at the margin of a restoration (filling) and will often necessitate replacement of the filling (re-restoration).

Significant pain and discomfort, which can lead to disturbances in eating and loss of sleep, are common symptoms of untreated dental caries. Invasive restorative dental treatments (such as anaesthetic injections and drilling) are associated with pain and anxiety, which can lead to treatment avoidance.

Diagnosis of dental caries

The presence of occlusal (pit and fissure) caries is identified by visual examination. The Ekstrand method of ranking the activity and severity of lesions is often used in clinical research, although it is not clear whether this is widely used in clinical practice. Radiological (X-rays and digital radiography) diagnosis is also widely used as an adjunct to visual examination, either to estimate the depth of occlusal lesions or to identify lesions that are 'hidden' on visual examination.

The severity of RC lesions is commonly assessed by probing the lesion and classifying it as 'soft, leathery or hard'; this method is used in clinical practice and dental research. Other diagnostic methods (for example, the use of visible light such as quantitative light-induced fluorescence, laser fluorescence, electrical current and ultrasound) are not widely used in clinical practice and, although they are used in dental research, some of these techniques are less well validated.

The Adult Dental Survey of 1998 reported that 55% of adults in the UK had one or more decayed or unsound teeth, with an average of 1.5 teeth affected. The 2003 Dental Health Survey of Children reported obvious tooth decay in deciduous teeth in 43% (5 year olds) and 57% of children (8 year olds), and obvious tooth decay in permanent teeth of 52% (8 year olds), 70% (12 year olds) and 77% (15 year olds). The incidence of RC begins at the age of 30–40 and is most prevalent in the elderly; nearly 90% of people over the age of 65 show signs of gum disease and RC, compared with 14% of people aged16 to 24 years.

1.2 Current management

All dental patients routinely receive instructions on good oral hygiene and dietary advice to reduce the consumption of fermentable carbohydrates.

Topical fluoride therapy reduces the progression of dental caries by promoting the remineralisation of early (non-cavitated) caries lesions, thereby reducing the

demineralisation of sound tooth enamel. Fluoride-containing toothpastes are routinely used. Patients at high risk of developing caries may additionally receive fluoride-containing mouth rinse and gel, and have fluoride varnish applied to specific tooth surfaces at intervals of 3 or 6 months.

A recent Cochrane review (August 2003) evaluated the overall effect of topical fluoride (toothpastes, mouth rinses, gels and varnishes) on the prevention of dental caries in children and adults, and conducted a subgroup analysis for the effectiveness of each topical fluoride treatment. The effectiveness of fluoride treatment was reported as the prevented fraction of decayed, missing or filled tooth surfaces (D(M)FS). D(M)FS is the difference in the mean caries increment between the fluoride treatment and the control group expressed as a percentage of the caries increment in the control group.

Overall, topical fluoride was found to be associated with a prevented fraction of D(M)FS of 0.26 (95% confidence interval [CI] 0.23 to 0.29, $p < 0.00001$) in permanent teeth (Table 1), which corresponds to a number needed to treat (NNT) of 20 in a population of children with a caries increment of 2.5 D(M)FS per year, or a NNT of 20 with a population caries increment of 0.2 D(M)FS per year.

Table 1 Effectiveness of topical fluoride treatment on the prevention of dental caries in children and adults (Cochrane review)

Intervention	Number of trials	Prevented fraction of D(M)FS[a]
Permanent teeth		
Any fluoride treatment	133	0.26 (95% CI, 0.23 to 0.29, $p < 0.00001$)
Fluoride varnish	3	0.40 (95% CI, 0.09 to 0.72, $p < 0.01$)
Fluoride gel	13	0.21 (95% CI, 0.14 to 0.28, $p < 0.00001$)
Fluoride mouth rinse	30	0.26 (95% CI, 0.22 to 0.29, $p < 0.00001$)
Fluoride toothpaste	70	0.24 (95% CI. 0.21 to 0.28, $p < 0.00001$)
Deciduous teeth		
Any fluoride treatment	5	0.33 D(M)FS (95% CI, 0.22 to 0.44, $p < 0.0001$)
[a]D(M)FS = decayed, missing or filled tooth surfaces		

The treatment of dental caries depends on the stage or severity of the lesion at presentation (whether a lesion is cavitated or non-cavitated) and location of the lesion.

- Non-cavitated PFC is currently managed by the removal of plaque and treatment with topical fluorides (for example, toothpaste and mouth rinse), antimicrobial agents (for example, chlorhexidine) and pit and fissure sealants where appropriate.

- Cavitated PFC is currently managed by the removal of plaque and tooth decay (using drills or air abrasion) and restorative treatment with a composite resin, glass-ionomer cement or amalgam. Amalgam is commonly used for filling permanent teeth. The lifetime of a restoration is thought to be approximately 8 years.

- Non-cavitated RC is currently managed by the removal of plaque and tooth decay and treatment with topical fluorides (for example, toothpaste and mouth rinse), which may be sufficient to prevent the progression of RC where the tooth is accessible to cleaning.

- The management of cavitated RC involves the removal of plaque and restorative treatment with fluoride varnish, chlorhexidine, glass ionomer cements or resin-based fillings.

Pit and fissure sealants (composite resin and glass-ionomer cements) are thought to prevent caries development as long as they remain intact. A Cochrane review demonstrated that the majority of resin sealants remain intact at 36 months. Most recent resin sealants contain fluoride.

Following treatment, the 'activity' status of dental caries lesions is assessed at follow-up visits to determine whether further preventative treatment is necessary. Progressive dental caries lesions ('active' caries) require preventative treatment, whereas 'inactive/arrested' lesions that fail to progress do not require further preventative treatment.

2 The technology

The HealOzone (HZ) system is CE marked for the treatment of PFC and RC. The system comprises an ozone delivery device, a pH balancer (mineral reductant) and a patient kit (fluoride-containing toothpaste, mouthwash and mouth spray) for home use.

The procedure for using HZ involves the application of ozone to the surface of the tooth for between 10 and 120 seconds, and the application of a mineral reductant to neutralise residual bacterial acid and ozone. Patients self-administer topical fluoride treatment at home using the 'patient kit'. Treatment with HZ may be repeated at intervals of 3 and 6 months if dental caries has not reversed.

The manufacturer's submission states that direct application of ozone to the site of dental caries on the tooth surface destroys the micro-organisms responsible for tooth decay (pages 17 and 18 of the manufacturer's submission). HealOzone treatment in conjunction with the fluoride-containing patient kit enable remineralisation of the tooth and the reversal or arrest of tooth decay in non-cavitated dental caries. Sterilisation of the tooth surface with ozone prior to sealant placement is hypothesised to improve sealant retention, and HZ treatment prior to filling placement in cavitated lesions is hypothesised to improve the longevity of restorations.

Currently, 294 HZ devices are in use in dental practices in the UK and over one million patients in the UK are estimated to have received HZ treatment to date. HZ is not available on the NHS and therefore the devices are thought to be restricted to practices that treat only private patients, or a mix of NHS and private patients.

The capital cost of the HZ device is £11950 (excluding VAT), with annual maintenance costs of between £220 and £450 depending on the service contract.

The manufacturer estimated the additional cost per HZ treatment on the basis of the cost of consumables, staff costs and the proportion of teeth requiring an initial restoration (that is, capital and maintenance costs excluded). The average estimated cost of adding HZ to conventional treatment ranged from £18 to £21 per tooth depending on the type of dental caries.

3 The evidence

The Assessment Group identified ten randomised controlled trials (RCTs) of HZ treatment. Three RCTs (one published, one unpublished and one published in abstract only) evaluated the effect of HZ treatment on RC, and seven RCTs (two PhD theses, one pilot study and four abstracts) evaluated the effect of HZ treatment on PFC.

Only one unpublished RCT evaluated the effect of HZ treatment on deciduous teeth. Two studies investigated the effect of HZ treatment on sealant retention − one in the treatment of RC, and another in the treatment of PFC. All the clinical evidence relates to the effectiveness of HZ treatment of primary dental caries. There is no clinical evidence in the Assessment Report or the submission on the effectiveness of HZ treatment for secondary dental caries.

The clinical effectiveness of HZ treatment was assessed by comparing the number of patients showing either progression, or conversely reversal, of dental caries in the HZ treatment group compared with the control group. Sealant retention was the key outcome measure in studies of HZ treatment prior to sealant placement.

The Assessment Group reported several confounding factors that make it difficult to draw conclusions about the effectiveness of HZ.

- The reporting of methodology used in the RCTs was incomplete (for example, randomisation and blinding).
- The studies used various doses of HZ (10 and 40 seconds) and number of repeat HZ treatments before the final follow-up.
- As HZ was always used in combination with oral hygiene/dietary advice, and other active interventions (reductant and the ‘patient kit’), the contribution of the HZ device to the effectiveness of treatment is difficult to ascertain.
- Data analysis was conducted at the lesion level and did not take into account patient factors (for example, that two lesions within the same patient are not entirely independent).

3.1 Clinical effectiveness

The effectiveness of HZ treatment was evaluated separately for the treatment of cavitated and non-cavitated PFC, and cavitated and non-cavitated RC (see Table 2).

Non-cavitated root caries

Three RCTs evaluated the effectiveness of HZ treatment for non-cavitated RC. The published study (Holmes) reported a caries reversal rate of 98% at 12 months with HZ treatment compared with 1% in the control arm. At 21 months follow-up caries reversal was 100% in the HZ treatment group; in the control group 8% of caries reversed, 80% of lesions remained stable and 12% of lesions progressed. The small proportion of caries reversal occurring with fluoride treatment in the control arm is not consistent with the results of Cochrane reviews.

The abstract by Lynch et al. reported 80% (clinical severity 4 to 3) and 94% (clinical severity 1 to 0) reversal of caries with HZ treatment compared with no change in lesion severity in the control arm at 6 months follow-up ($p < 0.01$). Again, the failure of fluoride to reverse dental caries in the control arm is not consistent with the results of Cochrane reviews.

The Baysan et al. study investigated the effectiveness of HZ treatment in a mixed population of cavitated and non-cavitated RC at 12 months follow-up. The combined results of this study could not be disaggregated to provide separate results for the cavitated and non-cavitated populations. Overall (in the mixed population), HZ treatment was associated with 99% reversal of dental caries compared with 11.6% reversal in the control arm ($p < 0.001$), and sealant retention was 61% with HZ treatment compared with 26.1% ($p < 0.05$) in the control arm.

Cavitated root caries

Only one RCT (Baysan et al.) included patients with cavitated RC. This study also included non-cavitated RC, and very few of the results were disaggregated. It reported that following HZ treatment 9.1% and 1.4% of cavitated lesions had reversed and become hard at 1 month and 9 months follow-up, respectively. No results were reported for the control arm.

Non-cavitated pit and fissure caries

Five RCTs (one PhD thesis and four abstracts) that evaluated the effect of HZ treatment in adults with PFC reported conflicting results.

Abu-Naba'a (PhD thesis) reported no significant difference in the reversal of dental caries with HZ treatment (7.4% reversed, 56.6% remained stable and 36.1% progressed) compared with the control group (5.6% reversed, 48.6% remained stable and 45.8% progressed). There was no significant difference in sealant retention with HZ (32.7%) compared with the control group (29.8%, $p > 0.05$).

All abstracts reported a significant improvement with HZ treatment compared with the control group. The reversal of dental caries in three abstracts ranged from 86.6% to 100% compared with no change in the clinical severity of dental caries in the control group. Another abstract reported that all caries lesions were hard in the HZ treatment group compared with 17% in the control group.

Cavitated pit and fissure caries

A small pilot study (reported in the PhD thesis of Abu-Naba'a) which evaluated the effect of HZ treatment on cavitated RC reported a significant reversal of dental caries with HZ treatment compared with the control group ($p < 0.05$).

Deciduous dentition

Abu-Salem (PhD thesis) evaluated the effectiveness of HZ treatment in non-cavitated PFC in deciduous teeth. No change in the severity of dental caries was reported with HZ treatment but a significant progression of dental caries in the control arm ($p < 0.01$).

Table 2 Summary of clinical effectiveness of HealOzone

Study	Patients (lesions)	Treatment (seconds)	Control	Results			Comments
				Outcome	HZ	Control	
Non-cavitated root caries							
Holmes (2003) (published) Follow-up 3,6,12,18, 21 months	89 (178)	HZ 40 s	Air	Clinical severity − become hard − remain leathery − become soft	(12 m) 98% 2% 0%	(12 m) 1% 75% 24%	Adults (60–82 years) Non-cavitated RC All received oral hygiene advice and the 'HZ patient kit'
Lynch, Johnson et al. (2004) **Abstract** Follow-up 6 months	260 (520)	HZ (? s) (n=260)	No HZ (n=260)	Clinical severity (CS) − reversed (CS 4−3) − reversed (CS 1−0)	 48/60 189/200	 0/60 ($p < 0.01$) 0/200 ($p < 0.01$)	Non–cavitated RC
Cavitated and non-cavitated root caries				**Outcome**	**HZ**	**Control**	**Comments**
Baysan and Lynch (2004) (unpub) Follow-up 12 months	79 (220)	HZ (10 s) + reductant	Reductant only	Clinical severity − reversed (CS 1−0) − reversed (CS 2−1)	(12 m) 47% 52%	(12 m) 0% ($p < 0.001$) 11.6% ($p < 0.001$)	Adults (30–72 years) **Cavitated + non-cavitated lesions** (not disaggregated) All received oral hygiene advice
		HZ (10 s) + sealant	Sealant alone	Sealant intact	61%	26.1% ($p < 0.05$)	Overall improvement with HZ treatment, deterioration with non-cavitated lesions
Non-cavitated pit and fissure caries				**Outcome**	**HZ**	**Control**	**Comments**
Abu-Naba'a (2003) (main study) PhD thesis (unpublished) Follow-up 1, 3, 6, 9, 12 months	90 (258)	HZ (10 s)	No HZ	Reversal (12 m) Stable (12 m) Progression (12 m)	7.4% 56.6% 36.1%	5.6% 48.6% 45.8%	People aged 12 to >41 years Non-cavitated PFC All received oral hygiene advice, fluoride toothpaste (1100 ppm), and reductant
		HZ (10 s) + sealant	Sealant alone	Sealant retention	32.7%	29.8%, $p > 0.05$	
Holmes and Lynch (2004) **Abstract** Follow-up 6 months	38 (76)	HZ (40 s) + glass ionomer sealant	Drill and fill	Post op sensitivity Reversal	None All lesions were hard	6/35	Non-cavitated occlusal caries
Holmes (2003) **Abstract** Follow-up 6 months	376 (2364)	HZ (10–40 s)	No HZ	Reversal	99%	No change	Non-cavitated occlusal caries
Hamid (2003) **Abstract** Follow-up 6 months	184 (184)	HZ (40 s)	No HZ	Reversal	86.6%	No change ($p < 0.05$)	Non-cavitated PFC (extending 1 mm into dentine) HZ treatment repeated at 3 months
Meigighian et al. (2004) **Abstract** Follow-up 6 months	80 (300)	HZ (20−40 s)	No HZ	Reversal	100% reversal with HZ , none in controls ($p < 0.05$)		
Cavitated pit and fissure caries				**Outcome**	**HZ**	**Control**	**Comments**
Abu-Naba'a (2003) (pilot study) PhD thesis (unpublished) Follow-up 1, 3, 6 months	8 (38)	HZ (40 s) + reductant	Reductant alone	Clinical severity (6 m) − hardness index − improvement in visual index	11/13 harder 8/13	4/12 harder ($p < 0.05$) 1/12 ($p < 0.05$)	**Cavitated PFC** All received oral hygiene advice and fluoride toothpaste (1100 ppm)
				ECM/DIAGNOdent	No difference in scores between HZ and control ($p > 0.05$)		
Deciduous teeth				**Outcome**	**HZ**	**Control**	**Comments**
Abu-Salem (2004) PhD thesis (unpub) Follow-up 3, 6, 9, 12 months	21 (74)	HZ (10 s) + reductant	Reductant alone	Clinical severity ECM/ DIAGNOdent	Little reduction in clinical severity with HZ and deterioration in CS with control		**Children** age 7–9 with non-cavitated PFC All received oral hygiene advice/fluoride toothpaste (1100 ppm)

Holmes (2003) – visual assessment of clinical severity in terms of hardness (soft, leathery and hard). No information was provided on how these categorise were defined.

Baysan and Lynch (2004), and Lynch and Johnson 2004 – 5-point visual assessment of clinical severity (all hard lesions [0], small leathery lesion approaching hard [1], shallow leathery lesion in an easy to reach surface [2], leathery lesion in difficult-to-reach surface [3], all soft lesions [4]. No information was provided on the validity/ reproducibility of the severity index.

Abu-Naba'a pilot and main study (2003) – Change in clinical severity using the Ekstrand method (0 = least severe, 4 = most severe)

Abstracts of HZ treatment in PFC – no significant change was observed in the control arm, although numerical values were not given.

3.2 Cost effectiveness

No published economic evaluations were identified on the use of HZ treatment. The manufacturer submission modelled the cost effectiveness of HZ for the treatment of RC, non-cavitated PFC and cavitated PFC (Table 3). The Assessment Group modelled the cost effectiveness of HZ treatment for non-cavitated RC and non-cavitated PFC. Separate modelling of the cost effectiveness of HZ in deciduous teeth was not undertaken.

Table 3 Cost effectiveness of HealOzone: comparison of industry and Assessment Group models

Model	KaVo		Assessment Group	
Type	Markov		Markov	
Comparison	HealOzone (HZ) + conventional treatment vs. conventional treatment		HealOzone (HZ) + conventional treatment vs. conventional treatment	
Population	• Root caries (RC), non-cavitated pit and fissure caries (NC-PFC) and cavitated PFC (C-PFC)		non-cavitated RC and non-cavitated PFC	
Conventional treatment	• RC – fillings (glass ionomer, composite resins and amalgam) • NC-PFC – sealants • C-PFC – fillings (glass ionomer, composite resins)		• NC-RC – preventative (root debridement, remineralising fluorides, chlorhexidine, sealant). Filling if no reversal of dental caries • NC-PFC – preventative (watchful waiting, oral hygiene/removal of plaque, fluoride applications and sealant). Filling if no reversal of dental caries	
Time horizon	5 years		5 years	
Effectiveness inputs	Reversal with HZ • RC • NC-PFC • C-PFC	Average 84.5% (range 69 to 100%) – Holmes RCT/Hamid abstract 93.3% (range 86.6 to 100%) – all RCTs 79% (range 59 to 99%) – 4 further RCTs	Reversal with HZ • NC-RC • NC-PFC	98% (Holmes 12 months) 7.4% (Abu Naba'a 12 months)
	Control progression • RC • NC-PFC • C-PFC	Average (RCTs of sealants/fillings) 3.9% (2.2 to 5.6%) 0% 4.9% (2.2 to 7.6%)	Control reversal • NC-RC • NC-PFC	1% (Holmes 12 months) 5.6% (Abu Naba'a 12 months)
Costs inputs	Additional cost of HZ treatment (excluding HZ device)		Additional cost of HZ treatment (excluding HZ device)	
	Cost of administering HZ	£20.20	Cost of administering HZ	£20
	Additional weighted NHS cost of HZ treatment • RC • NC-PFC • C-PFC	£15.93 £14.70 £11.37	Additional weighted NHS cost of HZ treatment • NC-RC • NC-PFC • Filling	£11.01 £11.01 £12.75
	NHS perspective = 100% of patients <18 years and 20% cost for patients >18 years		NHS perspective - 100% cost of patients <18 years and 40% cost for patients >18 years.	
Discounting	Cost and benefits were discounted by 3.5%		Cost and benefits were discounted by 3.5%	
CEA incremental cost of HZ	Incremental cost per tooth treated with HZ	£6.24	Cost per filling avoided (at 5 years) • NC-PFC – HZ treatment is associated with an additional cost of £15.71 and a 2.6% reduction in fillings • NC-RC – Conventional treatment is dominated by the HZ + conventional treatment	
	Cost per filling avoided (at 5 years) • NC-PFC • C-PFC • RC	£9.58 £11.63 £5.18		

Effectiveness data in the Assessment Group and manufacturer's model was based on RCTs, although different estimates were used. Costs were based on an NHS perspective and only considered the costs to the NHS (excluding co-payment by eligible patients). This represented 100% of the cost of patients under the age of 18, and 20% (manufacturer model) or 40% (Assessment Group model) of the total cost of treatment for patients over the age of 18. However, the methods guide stipulates that where co-payments for treatment are made, appraisals should consider the total cost of treatment. Unit costs were based on SDR (Statement of Dental Remuneration) codes for the different types of caries (cavitated PFC or RC, and non-cavitated PFC or RC). The manufacturer presented the incremental cost of HZ treatment per caries reversal, progression avoided and filling avoided, and a threshold analysis of the utility required for cost-effectiveness ratios of HZ treatment of between £10,000 to £40,000 per quality adjusted life year. The Assessment Group presented the cost of adding HZ to conventional treatment and the number of fillings avoided.

Manufacturer's model

The manufacturer model compared the cost effectiveness of adding HZ to conventional treatment, which did not include preventative treatment (for example, topical fluoride or dietary advice) (Table 4).

Capital and running costs of the HZ device were assumed to be funded by the dental practice.

Effectiveness data for the addition of HZ treatment to conventional management for non-cavitated PFC and RC was based on the average reversal rate of dental caries reported in the RCTs. As one small study evaluated the effectiveness of HZ treatment for cavitated lesions (PFC), effectiveness data for cavitated PFC was based on four abstracts of HZ treatment in PFC where teeth required drilling and filling – these studies were subsequently excluded from the Assessment Group's systematic review.

Effectiveness data for conventional treatment was based on the average annual progression rate of dental caries for sealants and fillings reported in clinical studies. Annual progression rates of 0% for sealant treatment of non-cavitated PFC, 4.9% for restorative treatment (glass ionomer, composite resin and amalgam) of non-cavitated PFC and 3.9% for restorative treatment (glass ionomer and composite resin) of RC were used in the control arm of the model.

Table 4 Manufacturer's model: incremental NHS cost of HealOzone (HZ) treatment per 1000 teeth treated

Population	Additional cost of HZ treatment	Number of fillings avoided	Cost per filling avoided
Non-cavitated pit and fissure caries (PFC)	£1410	147	£9.58
Cavitated PFC	£2187	188	£11.63
Root caries	£2642	511	£5.18

The most clinically important outcome is the number of fillings avoided with HZ treatment. The cost per filling avoided was presented over a 10-year time horizon. The addition of HZ per filling avoided was £9.58 in non-cavitated PFC, £11.63 in cavitated PFC and £5.18 in RC. The manufacturer presented a threshold analysis which demonstrated, for example, that a utility gain of 0.003 (approximately equivalent to 1 week of perfect health) for the treatment of all types of caries produced an ICER (incremental cost-effectiveness ratio) of £30,000 per QALY (page 48 of the manufacturer's submission).

Assessment Group model

The Assessment Group developed a deterministic Markov model that separately compared the cost effectiveness of adding HZ to conventional management for the treatment of non-cavitated PFC and non-cavitated RC. A diagram and description of the model is found on pages 69−70 of the Assessment Report. Conventional management of non-cavitated PFC caries included watchful waiting, removal of plaque, oral hygiene/dietary advice, fluoride application and sealants. Conventional management of non-cavitated RC included root debridement, remineralising fluorides, chlorhexidine and sealants.

Patients in the HZ arm received HZ treatment in addition to conventional management and progress through the model in 1-year cycles according to the transition probabilities in Table 15 (page 71) of the Assessment Report. At the end of each cycle patients either move to the 'cure' (no filling) health state where they stay for the remainder of the model, or 'progression'. The effectiveness of treatment is based on the reversal of dental caries − that is, the percentage of teeth that do not require filling. Data on the effectiveness (reversal) of adding HZ to conventional treatment, and conventional treatment alone is based on the largest full text RCTs included in the systematic review.

The Assessment Group model assumed that 50% of patients who exhibit progression of dental caries following HZ treatment receive re-treatment with HZ in the subsequent cycle; the remaining 50% receive a filling (where they stay for the remainder of the model). Therefore, patients receive a maximum of two annual treatments with HZ. This is not consistent with clinical studies or the manufacturer submission, which indicate that patients receive re-treatment with HZ at intervals of 3 or 6 months. The assumption of 50% re-treatment with HZ would have little effect on the RC model, where 98% of non-cavitated caries are cured by HZ treatment in each cycle. However, this assumption in the non-cavitated PFC subgroup, where the cure

rates associated with HZ treatment are lower, reduces the likelihood of cure (reversal of caries) in subsequent cycles, introducing bias against the effectiveness of HZ treatment.

The costs of adding HZ to conventional treatment, and conventional treatment alone, were presented as the unit cost to the NHS for the treatment of non-cavitated PFC and RC. The incremental cost of adding HZ to conventional treatment was £9.02 for non-cavitated PFC, £6.09 for non-cavitated RC and £12.75 per filling required.

Capital and running costs of the HZ devices were not included in the Assessment Group model.

The outcome of the cost effectiveness for each model is presented as the incremental cost of adding HZ treatment per filling avoided (tooth cured) (Table 5). Health benefits were not estimated in quality adjusted life years (QALYs) because the adverse events (pain and anxiety) were considered to be transient. Sensitivity analysis varied the reversal rate of dental caries with HZ between 0% and 100% compared with base case conventional treatment, and conventional treatment between 0% and 100% compared with base case HZ treatment to assess the effect of uncertainty in the effectiveness data (pages 76–79 of the Assessment Report).

Table 5 Assessment Group model: incremental cost effectiveness of adding HealOzone (HZ) treatment

	Conventional treatment		HZ + conventional treatment		ICER
	Cost (£)	Fillings (%)	Cost (£)	Fillings (%)	
Non-cavitated pit and fissure caries	£ 24.78	91.8	£40.49	89.2	+ £15.71 for the avoidance of 2.6% fillings
Non-cavitated root caries	£21.45	98.5	£14.63	0.01	Conventional treatment is dominated by the addition of HZ

The addition of HZ to the conventional treatment of non-cavitated PFC is associated with an incremental cost of £15.71 and incremental benefits of the avoidance of 2.6% fillings over 5 years. Varying the caries reversal rate with conventional treatment alone compared with the base case HZ demonstrated that the addition of HZ to conventional treatment was more costly at all conventional 'cure rates'. When the reversal rate of adding HZ treatment was varied compared with base case conventional treatment, the cost of adding HZ treatment breaks even with conventional treatment when the reversal rate associated with HZ treatment reached 70%.

The addition of HZ to the conventional treatment was shown to dominate current management for the treatment of non-cavitated RC as it was less costly and was associated with a 98.4% reduction in the proportion of teeth filled over 5 years. Sensitivity analysis demonstrated that the addition of HZ treatment remained less costly than conventional treatment at caries reversal rates of below 40% (and base

case caries reversal rates with HZ treatment), and a HZ cure rate of 80% or above (and base case caries reversal rates with conventional treatment).

4 Issues for consideration

- The Assessment Group considers that the evidence base for the effectiveness of HZ treatment is weak.
- Given the statistically significant effectiveness of fluoride treatment reported in the Cochrane review, and the design of HZ studies that administered fluoride treatment in both arms, the lack of reversal of dental caries in the control arm of these studies would not be anticipated.
- The RCTs identified suggest that HZ is effective for the treatment of RC but not PFC. It would be worthwhile exploring whether this is consistent with clinical expectations.
- Given the weak evidence base for the effectiveness of cavitated caries, can it be assumed that the effectiveness of HZ treatment of cavitated lesions will be the same as for the treatment of non-cavitated lesions?
- The cost of HZ treatment in all models may be underestimated as it represents costs to the NHS alone and does not include any contributions from the patient.
- Both economic models do not include the capital and maintenance costs of the HZ device.
- It is thought that the HZ device is only used in private practice. If this is to be provided on the NHS will the cost of equipment be met by the dental practices or provided by the NHS?

5 Ongoing research

None

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December 2004

7 Appendix A. Sources of evidence considered in the preparation of the overview

A Brazzelli M, McKenzie L, Fielding S, Fraser C, Clarkson J, Kilonzo M and Waugh N (Aberdeen Health Technology Assessment Group). *Systematic review of the effectiveness and cost-effectiveness of 'HealOzone' for the treatment of occlusal pit/fissure caries and root caries.* November 2004

B Submissions from the following organisations:

I Manufacturer/sponsors:

- KaVo

II Professional/specialist and patient/carer groups:

- Organisation A
- Organisation B

III Commentator organisations (without the right of appeal):

- Organisation A
- Organisation B

C Marinho VCC, Higgins JPT, Logan S and Sheiham A (2003) Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries ion children and adolescents. *The Cochrane Database of Systematic Reviews* 2003, Issue 4. Art No: CD002782.