Health Technology Assessment 2010; Vol. 14: No. 28

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June 2010
10.3310/hta14280

Health Technology Assessment
NIHR HTA programme
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Declared competing interests of authors: none

Published June 2010
DOI: 10.3310/hta14280

This report should be referenced as follows:

Clegg AJ, Loveman E, Gospodarevskaya E, Harris P, Bird A, Bryant J, *et al.* The safety and effectiveness of different methods of earwax removal: a systematic review and economic evaluation. *Health Technol Assess* 2010;**14**(28).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE, *Science Citation Index Expanded* (*SciSearch*®) and *Current Contents*®/Clinical Medicine.

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 06/77/04. The contractual start date was in April 2008. The draft report began editorial review in April 2009 and was accepted for publication in October 2009. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

ISSN 1366-5278

Published by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk), on behalf of NETSCC, HTA.

Printed on acid-free paper in the UK by the Charlesworth Group

Abstract

The safety and effectiveness of different methods of earwax removal: a systematic review and economic evaluation

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Background: Build-up of earwax is a common reason for attendance in primary care. Current practice for earwax removal generally involves the use of a softening agent, followed by irrigation of the ear if required. However, the safety and benefits of the different methods of removal are not known for certain.

Objectives: To conduct evidence synthesis of the clinical effectiveness and cost-effectiveness of the interventions currently available for softening and/or removing earwax and any adverse events (AEs) associated with the interventions.

Data sources: Eleven electronic resources were searched from inception to November 2008, including: The Cochrane Library; MEDLINE (OVID), PREMEDLINE In-Process & Other Non-Indexed Citations (OVID), EMBASE (OVID); and CINAHL.

Methods: Two reviewers screened titles and abstracts for eligibility. Inclusion criteria were applied to the full text or retrieved papers and data were extracted by two reviewers using data extraction forms developed a priori. Any differences were resolved by discussion or by a third reviewer. Study criteria included: interventions – all methods of earwax removal available and combinations of these methods; participants – adults/children presenting requiring earwax removal; outcomes – measures of hearing, adequacy of clearance of wax, quality of life, time to recurrence or further treatment, AEs and measures of cost-effectiveness; design – randomised controlled trials (RCTs) and controlled clinical trials (CCTs) for clinical effectiveness, cohort studies for AEs and cost-effectiveness, and costing studies for cost-effectiveness. For the economic evaluation, a deterministic decision tree model was developed to evaluate three options: (1) the use of softeners followed by irrigation in primary care; (2) softeners followed by self-irrigation; and (3) a 'no treatment' option. Outcomes were assessed in terms of benefits to patients and costs incurred, with costs presented by exploratory cost–utility analysis.

Results: Twenty-six clinical trials conducted in primary care (14 studies), secondary care (8 studies) or other care settings (4 studies), met the inclusion criteria for the review – 22 RCTs and 4 CCTs. The range of interventions included 16 different softeners, with or without irrigation, and in various different comparisons. Participants, outcomes, timing of intervention, follow-up and methodological quality varied between studies. On measures of wax clearance Cerumol, sodium bicarbonate, olive oil and water are all more effective than no treatment; triethanolamine polypeptide (TP) is better than olive oil; wet irrigation is better than dry irrigation; sodium bicarbonate drops followed by irrigation by nurse is more effective than sodium bicarbonate drops followed by self-irrigation; softening with TP and self-irrigation is more effective than self-irrigation only; and endoscopic de-waxing is better than microscopic de-waxing. AEs appeared to be minor and of limited extent. Resuts of the exploratory economic model found that softeners followed by self-irrigation were more likely to be cost-effective [£24,433 per quality-adjusted life-year (QALY)] than softeners followed by irrigation at primary care (£32,130 per QALY) when compared with no treatment. Comparison of the two active treatments showed that the additional gain associated with softeners followed by irrigation at primary care over softeners followed by self-irrigation was at a cost of £340,000 per QALY. When compared over a lifetime horizon to the 'no treatment' option, the ICERs for softeners followed by self-irrigation and

of softeners followed by irrigation at primary care were £24,450 per QALY and £32,136 per QALY, respectively.

Limitations: The systematic review found limited good-quality evidence of the safety, benefits and costs of the different strategies, making it difficult to differentiate between the various methods for removing earwax and rendering the economic evaluation as speculative.

Conclusions: Although softeners are effective, which specific softeners are most effective remains uncertain. Evidence on the effectiveness of methods of irrigation or mechanical removal was equivocal. Further research is required to improve the evidence base, such as a RCT incorporating an economic evaluation to assess the different ways of providing the service, the effectiveness of the different methods of removal and the acceptability of the different approaches to patients and practitioners.

Contents

List of abbreviations

AE	adverse event
BNF	*British National Formulary*
CCT	controlled clinical trial
CDSR	Cochrane Database of Systematic Reviews
CI	confidence interval
CRD	Centre for Reviews and Dissemination
DARE	Database of Abstracts of Reviews of Effectiveness
dB	decibel
DS	docusate sodium
ENT	ear, nose and throat
EQ-5D	European Quality of Life-5 Dimensions
EVPI	expected value of perfect information
EVPPI	expected value of partial perfect information
GP	general practitioner
HRQoL	health-related quality of life
HTA	Health Technology Assessment
HUI	Health Utility Index
ICD-9-CM	*International Classification of Diseases*, Ninth Edition, Clinical Modification
ICER	incremental cost-effectiveness ratio
ITT	intention to treat
N/A	not applicable
NHS	National Health Service
NHS EED	National Health Service Economic Evaluation Database
NS	normal saline
ns	not significant
OTC	over the counter
OTL	otolaryngologist
PEVPI	population expected value of perfect information
PSA	probabilistic sensitivity analysis
QALY	quality-adjusted life-year
r	discount rate
RCT	randomised controlled trial
SAE	serious adverse event
SAND	Suffolk and Norfolk Research and Development Consortium
SD	standard deviation
SF-6D	Short Form-6 Dimensions
SHTAC	Southampton Technology Assessments Centre
TM	tympanic membrane
TP	triethanolamine polypeptide
VAS	visual analogue scale

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background

Earwax is a normal secretion, the purpose of which is generally thought to be to protect the ear from particles entering the deeper part of the ear. Normally, earwax moves these particles to the outer ear. Sometimes this process fails and significant build-up of earwax can occur. This can affect anyone, but appears to be more prevalent in the elderly, children and those with learning disabilities. Estimates suggest anything from 700,000 to 2 million adults in England and Wales may have a build-up of earwax. While not all of these people will consult with a health-care practitioner, it is believed to be a common reason for attendance in primary care. Current practice for the removal of earwax varies. In general, a softening agent is usually recommended, leading up to irrigation of the ear if required. However, there are a variety of different agents for softening the earwax, and with no national guidelines on the removal of earwax many procedures are based on local custom and practice rather than a strong clinical evidence base. The relative safety and benefits of the different methods of removal are not known for certain.

Objectives

The objectives of this evidence synthesis were to conduct a systematic review of the evidence, assessing the clinical effectiveness and cost-effectiveness of the interventions that are currently available for softening and/or removing earwax in children or adults. To systematically search for, appraise and summarise clinical trial and observational evidence for the harms or adverse events (AEs) associated with interventions for softening or removing earwax. To construct an economic model for the UK to estimate the relative cost-effectiveness of those interventions that are considered to be clinically effective. To identify future cost-effective research in the management of earwax through a value of information analysis, specifying key elements in the design of future studies.

Methods

A systematic review of the evidence on the clinical effectiveness and cost-effectiveness and an economic evaluation were undertaken using a priori methods.

Data sources

Eleven electronic resources (including MEDLINE, EMBASE, CINAHL, BIOSIS, etc.) were searched from inception to November 2008. Bibliographies of related papers were assessed and experts were contacted to identify additional published and unpublished references. These were used for the systematic review and to inform the development and population of the economic model.

Study selection

Studies were included if they fulfilled the following criteria:

- *Interventions* All methods of earwax removal or softening, including drops, irrigation, other mechanical removal, other methods and combinations of these methods.
- *Participants* Adults or children presenting with build-up of earwax requiring removal.
- *Outcomes* Measures of hearing, adequacy of clearance of wax, quality of life, time to recurrence or further treatment, AEs and measures of cost-effectiveness.
- *Design* Randomised controlled trials (RCTs) and controlled clinical trials (CCTs) for clinical effectiveness, cohort studies for AEs and cost-effectiveness, and costing studies for cost-effectiveness.

Studies identified were assessed for inclusion through two stages, with titles and abstracts and full papers of retrieved studies assessed by two reviewers, with differences in decisions resolved through discussion or through recourse to a third reviewer.

Data extraction and quality assessment

Data were extracted by two reviewers using data extraction forms developed a priori, with any disagreements resolved through discussion or through recourse to a third reviewer. The methodological quality of the studies included in the systematic review of clinical effectiveness and cost-effectiveness was assessed using recognised quality assessment tools. The quality criteria used were applied by two reviewers, with any disagreements resolved through discussion or through recourse to a third reviewer.

Data synthesis

Studies were synthesised through a narrative review with full tabulation of the results of all included studies.

Economic model

The economic evaluation developed a deterministic decision tree model to evaluate three alternative options, specifically the use of softeners followed by irrigation in primary care, softeners followed by self-irrigation and a 'no treatment' option. It assumed a UK National Health Service (NHS) perspective, focused on an adult population aged 35–44 years with no contraindications to treatment and assessed outcomes over different time horizons (7 weeks to 45 years). Outcomes were assessed in terms of benefits to patients (i.e. successful removal of earwax and quality of life) and costs incurred, with costs presented in terms of a cost–utility analysis [cost per quality-adjusted life-year (QALY) and incremental cost-effectiveness ratio (ICER)].

Results

Clinical effectiveness

A total of 26 clinical trials conducted in primary care (14 studies), secondary care (8 studies) or other care settings (4 studies), met the inclusion criteria for the review. Of these studies, there were 22 RCTs and 4 CCTs. A range of interventions was used in the studies – some 16 different softeners with or without irrigation in various different comparisons were used. In addition to the wide range of interventions used, studies were diverse in terms of the participants and outcomes used, and also varied on timing of the intervention, duration of follow-up and methodological quality (in part a reflection of the age of many of the included studies), including use or not of any statistical analysis of their data.

Considering the studies that report statistical significance testing and ignoring any variations in methodological quality, results assessing clearance of wax show that: Cerumol, sodium bicarbonate, olive oil and water are all more effective than no treatment; triethanolamine polypeptide (TP) is better than olive oil; wet irrigation is better than dry irrigation; sodium bicarbonate drops followed by irrigation by nurse is more effective than sodium bicarbonate drops followed by self-irrigation; softening with TP and self-irrigation is more effective than self-irrigation only; and endoscopic de-waxing is better than microscopic de-waxing. Results assessing ease of subsequent irrigation as the outcome show that: Cerumol is better than dioctyl, TP and sodium bicarbonate and Audax are better than Earex. AEs appear to be minor and limited in extent, and mainly related to irrigation. No studies reported serious adverse events (SAEs). Minor pain, discomfort and irritation/itching of the ear were the main AEs.

Cost-effectiveness

The systematic review of cost-effectiveness did not identify any economic evaluations. The de novo economic model developed for this assessment found that softeners followed by self-irrigation were more likely to be cost-effective (£24,433 per QALY) than softeners followed by irrigation at primary care (£32,130 per QALY) when compared with no treatment. Comparison of the two active treatments showed that the additional gain associated with softeners followed by irrigation at primary care over softeners followed by self-irrigation was at a cost of £340,000 per QALY. When compared over a lifetime horizon to the 'no treatment' option, the ICERs for softeners followed by self-irrigation and of softeners followed by irrigation at primary care were £24,450 per QALY and £32,136 per QALY, respectively. Sensitivity and scenario analyses showed the results are fairly robust to changes in the cost of irrigation in primary care, although changes in the utility associated with loss of hearing may have some effect. However, caution should be taken in interpreting the results of the economic evaluation due to the paucity of evidence on the safety, benefits and costs of the different strategies. As a consequence, the results of the economic evaluation should be regarded as exploratory and

should not be used as a basis for changing policy and practice.

Conclusions

The systematic review of clinical effectiveness and cost-effectiveness found limited good-quality evidence, making it difficult to differentiate between the various methods for removing earwax in terms of clearing wax, improving quality of life and satisfaction, AEs or cost-effectiveness. Although it showed that softeners have an effect in clearing earwax in their own right and as precursors to irrigation, which specific softeners have an effect remains uncertain. Evidence on the effectiveness of methods of irrigation or mechanical removal was equivocal. The limited evidence on benefits and costs of methods of earwax removal meant that the economic evaluation was speculative and for illustration only. Its findings should not be used for policy decisions. As such, further research is required to improve the evidence base. A well conducted RCT incorporating an economic evaluation would appear to provide the most appropriate method to assess the different ways of providing the service (i.e. practice nurse provision in primary care versus self-care) as well as the effectiveness of the different methods of removal (i.e. softeners and mechanical removal). As part of such research it would be important to assess the acceptability of the different approaches to patients and practitioners to ensure the most appropriate structure to the research. Other studies could be considered to improve specific data (e.g. a costing study of primary care costs); however, the poor quality of the evidence suggests additional research would be required.

Chapter 1
Aim and background

Aim

The project will evaluate the clinical effectiveness and cost-effectiveness of the different methods for the removal earwax in adults and children. It will review systematically the evidence assessing the clinical effectiveness and cost-effectiveness of interventions that are currently available for softening and/or removing earwax, including the use of drops, irrigation, mechanical removal and other methods. The project will systematically search for, appraise and summarise evidence on the safety of the different methods, identifying any significant harms or adverse events (AEs). If the systematic review of cost-effectiveness shows that there are no appropriate good-quality economic evaluations, a new economic model relevant to the UK setting will be developed. Also, it will identify any research needs and use value-of-information approaches to help in prioritising them.

Description of the health problem

Earwax (cerumen) is a normal secretion in the external ear canal, produced by small glands in the ear. The purpose of earwax is generally thought to be to protect the ear by trapping any particles in the ear canal and preventing them from entering the deeper part of the ear. Particles may include dirt, dead skin or other fragments. Normally, earwax moves particles to the outer ear at a rate that prevents any significant build-up. When this process fails, there can be an excessive build-up of wax, which can block or occlude the auditory canal.[1,2] Although this can be a relatively minor problem, it can result in several other related problems, including hearing loss, discomfort, balance disorders, tinnitus and even infection.[3,4] It is often these symptomatic conditions that are the key concern for the person suffering from excessive earwax.

Although people with an excessive build-up of earwax can experience any of these conditions, hearing loss and the associated discomfort are probably the most frequent that occur.[5] The effects on hearing can be significant. Severity of hearing loss is measured by how well an individual can hear the frequencies or intensities of sound [measured by decibel (dB)] most often associated with speech. A person who can hear within the normal range can perceive sounds at a threshold intensity as low as 20 dB. Blockage of the ear from wax may elevate the hearing threshold to 40–45 dB.[6,7] In those presenting with age-related hearing loss, some will have earwax that, if removed, can reduce the hearing loss by around 10 dB.[8] The sense of blockage of the ear, the effects of hearing loss and the other comorbidities can cause discomfort and irritation to the person.

The occurrence of these related comorbidities provide evidence of the extent and severity of the build-up of earwax. Often people will present prior to the development of severe symptoms. In such instances, assessment of their condition is usually made based on the degree of occlusion of the auditory canal or tympanic membrane (TM), the extent of impaction of earwax, and the nature and characteristics of the earwax itself. These are often thought to be proportionally related to the severity of comorbidities.[7] Assessment of these symptoms is usually undertaken through direct visualisation of the ear canal with an otoscope.[9] There do not appear to be any documented standard criteria on which to base such judgements, meaning that they are open to variation in their measurement, reporting and interpretation. Such differences make judging the extent and severity of the earwax uncertain.

Aetiology

There are a number of possible causes of excess earwax or of the retention of earwax.[5,10–12] Small amounts of earwax are normal in the ear canal and excessive cleaning may interfere with the natural production of earwax. Other factors, such as the rate of earwax accumulation,[10] use of hearing aids,[11] small ear canals or skin conditions may also increase the risk of a build-up of earwax. In addition, different people appear to be at a higher risk of suffering from accumulation of earwax, with an increased risk for the elderly, men, people with intellectual impairment and secondary-care populations.[5,12]

As people age, the cerumen glands atrophy (decline in effectiveness) and earwax becomes drier, making it a more extensive problem in the older age group.[1] Excessive earwax may also present as a problem in hearing assessments, blocking the view of the TM (or ear drum) during examination, and it can interfere with the fitting of hearing aids. Some 80% of patients attending a hearing aid repair department do so because of problems with earwax.[13] Recurrence of the problem does not seem uncommon and it is suggested that around 30% of elderly and mentally impaired individuals[14] require regular treatment.

Pathology

Earwax is composed of the outer layers of the skin, which are discarded as part of a normal process of skin turnover and glandular secretions.[11] The skin is made up of three different layers, with the epidermis being the outermost layer.[15] The epidermis consists of different cells, the major cell type of which is keratinocytes. As part of the normal cycle of skin turnover, these cells push up through the epidermis and are eventually shed.[15] An over production of keratin or a failure in the separation of keratinocytes are thought to be possible factors leading to excessive earwax. For example, in a study of 20 patients with earwax, keratin was seen to account for up to 60% of the earwax plug.[16] Other research suggests that carotenoids (fat-soluble pigments) might contribute to the mechanism of the production of excessive earwax, but this requires further confirmation.[10,11]

Earwax has two phenotypes. Wet wax is far more common in Caucasians[17] and Africans,[18] consisting of approximately 50% lipid (fat).[10] Dry wax is more frequent in East Asians,[19] and only contains about 20% lipids.[20] There appear to be few other biochemical differences between the two types of wax.[10] Also, wax colour may vary from person to person.

Epidemiology

Although earwax and its associated problems are thought to be a common reason for attending primary care practices, data on its epidemiology in the general population are limited. Prevalence rates appear to vary widely, due in part to the different population groups under study, the likely variation in the interpretation of the degree of earwax present, and differences in the methods used to ascertain the data.

In an adult hearing screening study in Denmark, earwax was judged to be occluding in 2.1% of participants aged between 30 and 49 years.[21] This is similar to the rate of acoustically obstructing earwax (2.3%) identified in an earlier UK adult hearing screening study.[22] However, another estimate suggests that excessive or 'impacted' earwax is likely to be present in up to 5% of normal healthy adults, with higher rates in children, older people living in nursing homes and those with learning difficulties (approximately 10%, 57% and 36% of people in these three groups, respectively).[9,14] One of the limitations of the two screening studies is that the populations were those who agreed (from a random sample) to be screened for hearing loss and hence the estimates may not be representative of the general population. The latter study was a review of a number of different epidemiological studies but the estimates are also limited owing to differences in the methodologies, sample sizes and age of their included studies. This may explain the wide variation in ranges seen.

In a single-centre study of children aged 3–10 years in one region of the UK, the prevalence of partially occluding or totally occluding earwax was reported to be 43%.[23] The study suggested that the prevalence tends to decrease with age and that there is no difference in prevalence between gender. The authors of the study point out, however, that the sample was not a random one and the collection of data was undertaken during the winter months, which may explain the higher rates of earwax.

In older people who are admitted to an elderly care evaluation unit, 19% of those found to have a hearing impairment on assessment (55% of the total sample) had earwax occluding both ears.[24] The prevalence of bilateral earwax increased with age, from 9% in those aged 55–64 years and 65–74 years, to 13% in those aged 75–84, and to 27% in those over the age of 85 years. A UK survey of 300 consecutive general practice referrals of patients >60 years for hearing aids found a 29% prevalence of occluding wax.[25] However, it should be noted that these rates are from those with hearing impairment, rather than general population rates. It is also not clear whether the earwax was the cause of the hearing impairment. In another study of elderly participants (mean age 81 years) who had been identified as having hearing loss on screening, the occurrence of 'impacted' earwax was reported as 15.7% of ears.[26] One further study of hospitalised elderly patients

in the USA reported that 35% of its sample suffered with 'impacted' earwax, 15% unilaterally and nearly 20% bilaterally.[5] Similar caveats apply to these latter two studies regarding the generalisability of their populations with that of the general population.

It is clear that these studies show a wide variation in their estimates of the prevalence of earwax and also their definition of the extent of the earwax. It is unclear, however, whether all of these people would have viewed their earwax as problematic or symptomatic, particularly in the studies that identified their estimates from a screened population. However, to generate an estimate of the numbers of people in the general population with earwax that potentially may be problematic ('impacted' or 'occluding'), these estimates have been applied to the UK population size. An estimate of the prevalence in adults (aged 16–59 years) based on a figure of 2–5%[9,21,22] and a UK adult population of 36,122,100 (taken from mid-2006 estimates[27]) suggests somewhere between 722,000 and 1,800,000 adults may have problematic earwax. Taking a range of 10–43%[9,23] in children aged less than 16 years and a UK child population of 11,537,100,[27] the range of the prevalence of potentially problematic earwax would be in the region of 1,154,000–4,961,000. In those older than 60 years there may be somewhere between 2,069,000 and 7,369,000 people with potentially problematic earwax (based on a range of 16–57%[9,24,26] and a population of 12,928,100[27]). The wide ranges of these estimates, based on a number of different prevalence rates from different studies, each with their own particular limitations, illustrate the difficulty of pinpointing the extent of the earwax problem in the UK. Not all of these people will consult a health-care professional, but recent estimates suggest that health professionals perform up to 2 million ear irrigations in England and Wales per year.[11]

Current service provision and description of interventions

Despite the problems associated with the accumulation of excessive earwax and the demands placed upon primary care within the UK National Health Service (NHS), it appears that there are no nationally agreed guidelines for its diagnosis and treatment. As a consequence, it is likely that services will vary with many based primarily on local custom and practice rather than a strong clinical evidence base. Some locally and internationally based guidelines have been developed[28] and these, along with opinions from clinicians, including practice nurses, provide a basis for understanding the clinical pathway that may be followed by people who are suffering from the problems associated with excessive earwax. Problems that may lead a person to seek help include a feeling of a blockage, discomfort, hearing loss in one or both ears, tinnitus and/or dizziness.

In the UK, people requiring the removal of earwax have traditionally attended primary care practices for confirmation of the diagnosis and treatment. The method of treatment should take account of the severity of the condition, the possibility of any contraindications (e.g. perforations) or comorbidities (e.g. tinnitus), the skills of the practitioner and the setting for treatment. The majority of practitioners currently advise the use of some form of drops or softeners as a first stage. The *British National Formulary* (BNF) lists several preparations, including almond oil, olive oil, sodium bicarbonate drops, Cerumol®, Exterol®, Molcer®, Otex® and Waxsol®. Other softeners may also be used. A summary of different preparations is presented in *Table 1*, grouping them into water-based, oil-based or non-water-non-oil-based products, using the classification adopted by Hand and Harvey.[29] Not all of these preparations are currently available in the UK. Brand names will be used throughout the report unless those are unclear, when the generic name will be reported.

The intention of these remedies or drops is to either soften the wax prior to removal at the clinic or to help remove the wax on its own. Their specific action varies. For example, in vitro studies suggest that preparations including urea or glycerine increase water penetration of the earwax, while preparations including peroxide break up the earwax through the release of gas/bubbles, therefore aiding mechanical removal.[30] Limited data are available to guide people's choice of drops in particular clinical situations. AEs differ for each intervention but are generally thought to be mild. It is usually suggested that people allow between 3 and 7 days for these remedies or drops to take effect, although for some it may take longer (i.e. 14 days of drops) or several cycles.

If the wax has not dissolved or dissipated using drops or remedies, people are recommended to attend the primary care practice to have the

TABLE 1 *Summary of investigated preparations*

Key ingredient	Preparation	Background information
Water-based preparations		
Acetic acid (otic)	EarCalm	Acetic acid (glacial) ear spray. Ph Eur 2% w/w, ethoxylated, stearyl alcohol, ethylparahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), purified water. Supply 5 ml *Dose*: 1 metered dose (60 mg, 0.06 ml) sprayed into the affected ear at least 3 times daily, maximum 1 spray every 2–3 hours for 2 days after symptoms have disappeared but for no longer than 7 days (from age 12 years) *Side effects/allergic reaction*: Hives, difficulty breathing, swelling of face, lips, tongue or throat *Contraindication*: Hypersensitivity to acetic acid otic solution or perforated TM *Internet price*: Around £5.99
Docusate sodium	Molcer®	Docusate sodium 5%. Includes propylene glycol. Supply 15 ml *Dose*: Fill ear with solution and remain in position for a few minutes, repeat for 2 nights after which the wax can be removed (from age 12 years) *Side effects/allergic reaction*: Occasional skin irritations *Contraindication*: Perforated TM *OTC cost*: Around £1.90
	Waxsol®	Docusate sodium 0.5%. Glycerine, water and phenonip (a preservative). Supply 10 ml *Dose*: 2 drops per night (from age 6 years) *Side effects/allergic reaction*: Occasional stinging or soreness *Contraindication*: Perforation of the TM or inflammation of the ear *OTC cost*: Around £1.26
	Colace®	Liquid docusate sodium stool softener (not available in the UK)
	Dioctyl-medo® or Diocytl	Liquid docusate sodium stool softener and maize oil (not available in the UK)
Sodium bicarbonate	Care® (generic sodium bicarbonate may be used in practice)	Sodium bicarbonate BP 5% w/v. Supply 10 ml *Dose*: 3–4 drops, 3–4 times per day, for 3–5 days (from age 5 years) *Side effects/allergic reaction*: Dryness inside the ear, mild stinging sensation *Contraindication*: Unknown *OTC cost*: Around £2.20
Triethanolamine polypeptide oleate condensate *No longer available in the UK and discontinued in the USA*	Cerumenex® or Xerumenex®	Triethanolamine polypeptide oleate condensate (10%). Inactive ingredients – chlorobutanol 0.5%, propylene glycol and water. Supplied in 6 ml and 12 ml *Dose*: 5 drops, 2–3 times daily, for up to 3 days; limit exposure to the ear canal to 15–30 minutes (age unknown) *Side effects/allergic reaction*: Temporary burning, skin rash, itching, pain in or around the ears, dizziness or hearing trouble *Contraindication*: Perforated TM, otitis media or hypersensitivity to triethanolamine polypeptide, seborrhoeic dermatitis and eczema affecting the external ear Only available over the internet *Cost*: Around £3.08 (not OTC)
Sodium chloride (saline)	Generic solutions available	Sodium chloride 0.9%. Supply 20 × 0.5 ml *Dose*: 3–4 drops, 3–4 times per day, for 3–5 days (from age 6 months). *Side effects/allergic reaction*: None reported *Contraindication*: Unknown. *OTC cost*: Around £4.92

TABLE 1 *Summary of investigated preparations (continued)*

Key ingredient	Preparation	Background information
Oil-based preparations		
Chlorobutanol solution	Cerumol®	Chlorobutanol 5%, paradichlorobenzene 2%, arachis (peanut) oil 57.3%. Supply 11 ml *Dose*: 5 drops twice per day for 3 days (adults and children) *Side effects/allergic reaction*: Uncommon – can experience tingling sensation or temporary mild deafness when applied *Contraindication*: Otitis externa, seborrhoeic dermatitis and eczema affecting the outer ear, perforated TM and allergy to peanuts *OTC cost*: Around £2.85
Glycerine/glycerin	Earex (same as Otocerol)	Almond oil BP 33.33%, *Arachis* (peanut) oil BP 33.33% and rectified camphor oil 33.33%. Supply 10 ml *Dose*: 4 drops twice daily for up to 4 days (from the of age 1 year) *Side effects/allergic reaction*: Temporarily stinging or burning when first applied *Contraindication*: Allergy to peanuts or soya, inflamed or infected ear *OTC cost*: Around £2.29
Almond oil	Generic solutions available	Almond oil. Supply 10 ml *Dose*: 3–4 drops, 3–4 times per day, for 3–5 days (from age of 6 months) *Side effects/allergic reaction*: None reported *Contraindication*: Allergy to almonds *OTC cost*: Around £2.07
Olive oil	Earol (generic olive oil may be used in practice)	Olive oil ear drops. Supply 92 ml with 10-ml dropper *Dose*: 3–4 drops, 3–4 times per day, for 3–5 days (from age of 6 months) *Side effects/allergic reaction*: None reported *Contraindication*: Unknown *OTC cost*: Around £2.25
Non-water-non-oil-based preparations		
Choline salicylate solution	Audax®	Choline salicylate 21.61%, glycerol 12.62%. Supply 10 ml *Discontinued from use*
	Earex Plus (same as Audax®)	Choline salicylate 21.6% and glycerol 12.62%. Supply 10 ml *Dose*: Fill ear twice daily for up to 4 days (from age 1 year) *Side effects/allergic reaction*: None reported *Contraindication*: Perforated or bleeding TM *OTC cost*: Around £4.29
Urea–hydrogen peroxide	Otex (UK brand name, same as Exterol®)	Urea–hydrogen peroxide complex 5%, ear drops: 8-hydroxy-quinoline and glycerol. Supply 8 ml *Dose*: 5 drops twice daily for at least 3–4 days (from the age of 5 years) *Side effects/allergic reaction*: Unpleasant taste in mouth, temporary bubbling sensation, can aggravate the painful symptoms of excessive earwax, including some loss of hearing, dizziness and tinnitus *Contraindication*: Damaged TM, dizziness, pain, discharge, inflammation, infection and tinnitus within 2–3 days of irrigation or with history of ear problems *OTC cost*: Around £1.83

continued

TABLE 1 *Summary of investigated preparations (continued)*

Key ingredient	Preparation	Background information
Carbamide peroxide *Not available in the UK; available as OTC ear drops in the USA*	Debrox®	Carbamide peroxide 6.5% (urea peroxide). Supply 15 ml *Dose*: 5–10 drops twice per day for up to 4 days (from the age of 12 years) *Side effects/allergic reaction*: rare or uncommon – burning, itching, redness, worsening ear pain, rash, abnormal sensation while putting the drops in the ear and temporary reduction in hearing *Contraindication*: Perforated TM any signs of infection or injury, pain or other irritation, drainage, discharge or bleeding from the ear *Internet cost*: Around US$7.89 (around £5.28)
	Murine Ear®	Carbamide peroxide 6.5% and otic solution. Supply 15 ml *Dose*: 5–10 drops twice daily for up to 4 days (from the age of 12 years) *Side effects/allergic reaction*: Temporary decrease in hearing, dizziness, ear pain or other irritation, decreased hearing for a prolonged period of time, or discharge or bleeding from the ear *Contraindication*: Perforated TM, ear drainage, discharge, pain, rash, irritation or dizziness *Internet cost*: Around US$6.49 (around £4.35)

BP, British Pharmaceutical grade; OTC, over the counter; Ph Eur, *European Pharmacopeia*; w/v, weight to volume; w/w, weight to weight.

wax removed by mechanical removal, through either irrigation or curettage.[11] In irrigation, a pressurised flow of water is used to remove the earwax. Although flushing wax with metal piston syringes (e.g. Reiner-Alexander ear syringe) was common practice in primary care practices, these have largely been replaced with electronic irrigators, such as the oral jet irrigator, nebuliser or Propulse ear irrigator.[31,32] The use of metal piston syringes is no longer recommended.[33] Irrigation is contraindicated in people with perforated ear drums, history of ear surgery or chronic ear conditions. Reported harms of irrigation are pain, infection and injury to the ear, including TM perforation and tinnitus.[34,35] Curettage, which allows the removal of earwax under direct vision, using various implements, such as cerumen spoons, hooks, loops and probes, is rarely undertaken in primary care practices. Although it has the advantage of not using water to remove the earwax, and so perhaps lessening the risk of infection, it can be a difficult procedure, requiring specialist skill and time.[36]

Increasingly the role of the general practitioner (GP) has been taken over by the practice nurse (or, for the house-bound, the district nurse), who can confirm the problem by examination of the ear, recommending/prescribing the use of the drops or remedies and then removing any wax by irrigation.[31] On most occasions irrigation will successfully remove earwax on the first attempt; however, for a limited proportion of people it may prove more difficult and these people may need to attend on several occasions. Rarely, when it proves impossible for the primary care practice to remove the earwax, the person will be referred to a hospital-based specialist.

With the availability of several different softeners and proprietary drops, some people decide to self treat. As with their use in primary care practices, drops provide the possibility of treating the wax to allow it to dissipate or dissolve without further treatment. While such preparations offer the opportunity for self-treatment, caution needs to be exercised when used in combination with cotton wool swabs, as inadvertent damage to the inner ear canal or TM can occur. People may make several attempts to clear the wax with drops before consulting their primary care practice. Having self-treated with drops, people subsequently consulting the primary care practice for treatment may be able to have their earwax removed without further delay. Although not currently recommended, and not widely available within the UK, some forms of syringes for self-treatment are available. Soft bulb irrigators can be used by people after drops to flush their own ears. These can be purchased from suppliers through the internet and over the counter (OTC) in some European countries and in the USA. Other syringes for self-treatment are available, including plastic piston syringes (e.g. The Real McCoy and Master Blaster).

A minority of people who are unable to have their ears cleared through self-care or at the primary care practice, or have particular clinical conditions (e.g. cholesteatoma), or contraindications to standard treatment (e.g. pre-existing perforations of the TM) may be referred to specialist care. Ear, nose and throat (ENT) or otolaryngology departments use techniques such as microsuction or curettage through direct microscopic or endoscopic vision to clear earwax.[33,37,38] These methods are used in combination with suction or the use of a Jobson-Horne probe and a St Bartholomew's wax hook, or crocodile forceps.[38] This requires specialist equipment and considerable skill.[33,39] In very rare instances where clearance of earwax is prevented due to a narrowing of the external auditory canal, for example, surgery may be required.[11]

In addition to the above technologies, complementary therapies can also be used (e.g. ear candling).

Chapter 2
Methods

Methods for reviewing effectiveness

The a priori methods for systematically reviewing the evidence of clinical effectiveness and cost-effectiveness are described in the research protocol (Appendix 1), which was sent to experts for comment. Although helpful comments were received relating to the general content of the research protocol, there was none that identified specific problems with the methods of the review. The methods outlined in the protocol are briefly summarised below. Methods for the economic evaluation are outlined in Chapter 5 (see Methods of the economic valuation).

Search strategy

A sensitive search strategy was developed, tested and refined by an experienced information specialist. Separate searches were conducted to identify studies of clinical effectiveness, cost-effectiveness, quality of life, AEs, resource use/costs and epidemiology/natural history. Sources of information and search terms are provided in Appendix 2. The most recent search was carried out in November 2008.

Searches for clinical effectiveness and cost-effectiveness were from database inception. Electronic databases searched included: The Cochrane Database of Systematic Reviews (CDSR); The Cochrane Central Register of Controlled Trials (CENTRAL); Centre for Reviews and Dissemination (CRD) (University of York) Database of Abstracts of Reviews of Effectiveness (DARE); Health Technology Assessment (HTA) database and the NHS Economic Evaluation Database (NHS EED); MEDLINE (OVID), PREMEDLINE In-Process & Other Non-Indexed Citations (OVID), EMBASE (OVID); CINAHL; BIOSIS; Web of Knowledge Science Citation Index (SCI); Web of Knowledge ISI Proceedings; Current Controlled Trials and the National Research Register (Historical).

Primary care conferences were searched for recent abstracts (from 2004). The searches had no language restrictions. Any non-English language articles were set to one side in a separate foreign language reference database (see Appendix 2). Bibliographies of related papers were screened for relevant studies, and experts were also contacted to identify any additional relevant published or unpublished studies that were not identified on searches.

Inclusion and data extraction process

Titles and abstracts of studies identified by the search strategy were assessed for potential eligibility by two independent reviewers. The full text of relevant papers was then obtained and inclusion criteria were applied by two independent reviewers. Any disagreements over eligibility were resolved by consensus or, if necessary, by arbitration to a third reviewer. Data were extracted by one reviewer using a standard data extraction form and checked by a second reviewer.

Inclusion criteria

Patients

Adults or children presenting with build-up of earwax requiring removal.

Interventions

All methods of earwax removal or softening, including:

- drops
- irrigation (e.g. syringing, electronic irrigators)
- mechanical removal other than syringing (e.g. suction, probes and forceps)
- other methods
- combinations of above methods.

Outcomes

Studies were included if they reported one or more of the following outcome measures:

- measures of hearing
- adequacy of clearance of wax
- quality of life
- time to recurrence or further treatment
- AEs
- cost-effectiveness.

It was noted that measures assessing the extent or severity of earwax and the adequacy of clearance are often related to the degree of impaction. Although this term is frequently used, there is often no clear definition provided. It may or may not refer to wax that occludes the TM, to wax that is symptomatic to the individual and/or to a hardened plug of wax. As such, this systematic review will only use the term 'impacted' when there is either no definition or a lack of clarity in the definition provided in the study report. Also, where other outcomes are used with no clear definition this will be highlighted in the reporting of results.

Types of studies

Randomised controlled trials (RCTs) and controlled clinical trials (CCTs) (i.e. prospective non-randomised studies with a concurrent control group) were included for the assessment of the clinical effectiveness and, additionally, cohort studies were included for the assessment of AEs. Studies published only as abstracts or conference presentations were also considered for eligibility if sufficient information was presented to allow an appraisal of the methodology and assessment of results. Systematic reviews were used for background and as a source of references. For the review of cost-effectiveness any costing studies or cost-effectiveness evaluations (including modelling studies) were also eligible for inclusion.

Quality assessment

The quality of included RCTs and CCTs was assessed using criteria recommended by CRD.[40] Quality criteria were applied by one reviewer and checked by a second reviewer. At each stage, any differences in opinion were resolved through discussion or consultation with a third reviewer.

Data synthesis

Data were synthesised through a narrative review with tabulation of results of all included studies. Full data extraction forms are presented in Appendices 3–5. It was not considered appropriate to combine the included studies in a meta-analysis due to heterogeneity of the patient groups and comparator treatments (see Chapter 3, Quantity and quality of research available, for further details).

Chapter 3
Assessment of clinical effectiveness

Quantity and quality of research available

A total of 202 records of publications were identified through literature searching. Of these, 158 were excluded on title and abstract. Full reports for the remaining 45 were requested for more in-depth screening. Of these, 19 were excluded (see list of excluded studies in Appendix 6). An inclusion flow chart can be seen in Appendix 2.

Twenty-six published studies met the inclusion criteria – of these, 22 were RCTs and four were CCTs. These trials fell into three categories: studies undertaken in primary care (14 studies[41–54]), studies undertaken in secondary care (eight studies[4,54–60]), and studies of self-care or those undertaken in other care settings (four studies[61–64]). Where the setting was in emergency care this has been grouped under primary care in the present review because it was assumed that this was the first point of contact with a health professional. In some other cases the setting was not made explicit within the publication; where this was the case an assumed grouping was used based on the author(s) affiliation (e.g. if they worked in an outpatient clinic this was assumed to be a secondary care setting). Additionally, studies are also grouped by participant group (children, mixed adults and children, and adult groups). In some cases the study did not indicate who the target population was and these were classed under the mixed group as population 'unknown'. In some of these studies a mean age of the study participants was given but no range or measure of variance was reported and so these were also classed under the mixed population group. The subsequent discussion of these studies (below) will follow these conventions (*Table 2*).

There is very little consistency among the included studies, which makes it difficult to fully summarise the results and in many studies some basic data were not available. Across all of these studies there are variations in the characteristics of the participants recruited, in terms of age and, to some extent, gender, and in terms of the extent of the earwax problem. In many studies there is very limited discussion of baseline characteristics, which makes it difficult to establish the representativeness of the respective populations. Many of the included studies (eight studies[4,42,43,46,51,55,57,61]) were presented as either a short paper format (less than two sides), an abstract format or a conference proceeding, and, where this was the case, the available data were further limited.

Study sample sizes were typically small, varying from 36 participants[45] to 237 participants,[63] and only a few studies reported undertaking a sample size calculation (7 out of 24 studies[45,47,49,52,53,56,63]). In some studies the overall population sample size was not reported, rather the numbers of ears were presented.[42,43,60] Seventeen studies were two-arm comparisons,[41–45,48–54,56,58,59,63,64] five were three-arm studies,[46,47,55,57,62] and there was one study each with four,[4] five[61] and six[60] intervention arms.

There were also a wide range of interventions used between the included studies and differences in the length of follow-up used. For ease of understanding the review that follows is also divided into studies of immediate follow-up and delayed follow-up (the exact length of follow-up will be discussed for each study individually) and into studies where the intention was to use a softening agent alone (even when subsequent irrigation was used, if this was after initial outcome assessment) and those where the intention was always to use a softening agent and an irrigation as the intervention. Owing to the wide variation in interventions and comparisons used in the included studies the review has not been split by the different comparisons. However, each comparison is reported in sequence, in line with the conventions discussed above (setting, population, follow-up, softening agent with or without irrigation).

The outcome measures used also varied across the included studies. Often information concerning the definitions of the outcome measures used was limited and in many cases it was not possible to assess how valid, objective or consistently applied these different measures were. In the instances where this was clear the review has made note of this; for all other studies it should be assumed that care is required in the interpretation of the

outcomes. For the purpose of this review, the range of outcomes have been categorised as far as possible into those measuring the degree of occlusion; those measuring the ease of wax removal; those measuring participant satisfaction; those measuring recurrence of earwax; and AEs. Measures of the type and consistency of earwax removed were tabulated but not reported in the narrative synthesis. In many cases the baseline values were not presented for a particular outcome, which makes the interpretation of the evidence of the effectiveness of the interventions more difficult. Where pretreatment and post-treatment measurements of an outcome were reported this has been discussed (e.g. a study might report the varying degrees of occlusion before and after intervention). However, in many cases it is not clear how the final outcome is related to the finding at baseline (how many in the 'no change category' post intervention started in the fully occluded category pretreatment, how many were in the partially occluded and so on). Many of the studies also did not report measures of variance around the estimates presented.

A number of studies also did not report results of any statistical significance testing, and, of those that did, a number did not report the statistical analytical approach taken. As noted above, in some cases the allocation to interventions was undertaken on the basis of the number of ears rather than the number of participants. Also, in some studies where allocation was based on the number of participants, the analysis was undertaken on the number of ears. Where this is the case the present review has identified these studies. Care is recommended when interpreting the outcomes of these studies, as it is unclear whether valid statistical analyses (where reported) will have been undertaken (see *Cochrane Handbook for Systematic Reviews of Interventions* for discussion of appropriate analyses of these types of data[65]). Finally, there was a wide range in the publication dates of the included studies (1950–2007), and eleven studies were undertaken more than 20 years ago,[41,43,48,50,51,54,57,59–61,64] which may affect the generalisability of the studies to current practice (and account for some of the other issues already raised above). It is likely in current practice that an irrigator rather than a metal syringe will be used for the removal of earwax; however, syringes were used for many of the included studies, although this may not always be clear because 'syringing' and 'irrigation' may sometimes be used interchangeably. The present report refers to 'syringing' only where this was the term reported by the included study. In the case of self-treatment, the present report uses the term 'irrigation' when a soft bulb was used, as these are not syringes, even if the study authors have referred to this as a self-syringe.

Studies in primary care settings

Characteristics of the primary care studies are shown in *Table 3*. Seven RCTs[41,42,46–49,51] followed participants up immediately after interventions, and seven RCTs[43–45,50,52–54] had a delay between intervention and follow-up.

Two RCTs[46,47] compared docusate sodium (DS) versus triethanolamine polypeptide (TP) versus saline in children, while one RCT compared DS versus TP in a mixed population of adults and children.[49] Another trial[51] compared TP versus carbamide peroxide in an unspecified population. All of these had immediate follow-up after treatment.

Of two RCTs[44,50] comparing Cerumol, Dummer and colleagues[44] compared Cerumol with Audax in an adult population. This RCT had a delayed follow-up, averaging 4 days between the first and second visit (range 3–7 days). The second study by Jaffe and Grimshaw[50] compared Cerumol with Otocerol in a mixed population of adults and children. This study had a delayed follow-up, but the length was unspecified, with participants requested to revisit after three instillations. Cerumol was further compared with Waxsol in an RCT[48] with a mixed population of adults and children. This RCT had an immediate follow-up after treatment. Another comparison, of Audax with Earex,[45] was an RCT in a population of adults aged 16 years and above, and had a delayed follow-up of 5 days. A CCT by Fahmy and Whitefield[54] compared Exterol with Cerumol in an unspecified population and had a delayed follow-up of 1 week. The trial consisted of three studies, but only study three was in a primary care setting (for study one and study two see Studies in secondary care settings, below).

One RCT[52] compared aqueous sodium bicarbonate with aqueous acetic acid in a mixed population of children and adults. This trial had a delayed follow-up of 14 days. An RCT by the General Practitioner Research Group,[41] as well as a CCT by Burgess,[43] compared dioctyl-medo ear drops with oil in adults. These studies had an immediate follow-up and delayed follow-up of between 2 and 7 days after the intervention, respectively.

TABLE 2 *Overview of the study classifications used in the report*

Study	Settings	Population	Primary objective (SO or SI)
Primary care			
Studies with immediate follow-up for softeners only			
Meehan, 2002[46]	Emergency care	Children	SO
Whatley, 2003[47]	General paediatric clinic and children's hospital emergency department	Children	SO
Singer, 2000[49]	Emergency department in care centre	Adults and children	SO
Studies with delayed follow-up for softeners only			
Dummer, 1992[44]	Primary care	Adults	SO
Jaffe, 1978[50]	Primary care	Adults and children	SO
Carr, 2001[52]	Primary care – self treatment	Adults and children	SO
Fahmy, 1982[54]	Primary care[a]	Unknown	SO
Studies with immediate follow-up for softeners plus irrigation			
General Practitioner Research Group, 1965[41]	Primary care	Adults	SI
Pavlidis, 2005[42]	Primary care	Adults	SI
General Practitioner Research Group, 1967[48]	Primary care	Adults and children	SI
Amjad, 1975[51]	Primary care	Unknown	SI
Studies with delayed follow-up for softeners plus irrigation			
Burgess, 1966[43]	Primary care	Adults	SI
Lyndon, 1992[45]	Primary care	Adults	SI
Eekhof, 2001[53]	Primary care (follow-up: oil delayed, water immediate)	Unclear	SI
Secondary care			
Studies with delayed follow-up for softeners only			
Keane, 1995[4]	Secondary care	Unknown	SO
Fahmy, 1982[54]	Secondary care[a]	Unknown	SO
Studies with immediate follow-up for softeners plus irrigation			
Caballero, 2005[55]	Secondary care	Adult	SI
Dubow, 1959[57]	Secondary care	Children	SI
Chaput de Saintonge, 1973[59]	Secondary care	Unknown	SI
Studies with delayed follow-up for softeners plus irrigation			
Fraser, 1970[60]	Secondary care	Unknown	SI
Studies with delayed follow-up for other types of extraction			
Pothier, 2006[56]	Otolaryngology outpatient clinic (follow-up: immediate, but delayed if softeners used for endoscopic de-waxing)	Adult	N/A
Saloranta, 2005[58]	Secondary care plus community home (preventative study)	Adults and children	N/A

continued

TABLE 2 *Overview of the study classifications used in the report (continued)*

Study	Settings	Population	Primary objective (SO or SI)
Other care			
Studies with immediate follow-up for softeners plus irrigation			
Hinchcliffe, 1955[61]	Military research	Adults	SI
Roland, 2004[62]	Corporate research clinic	Adults	SI
Studies with delayed follow-up for self-care			
Coppin, 2008[63]	Self-treatment/primary care (self-irrigation/nurse irrigation)	Adults	N/A
Harris, 1968[64]	Self-treatment/primary care	Adults	N/A

N/A, not applicable; SI, 'softeners plus irrigation' as the primary objective; SO, 'softeners only' as primary objective – treatment can include subsequent irrigation.

a Fahmy and Whitefield[54] reported three separate studies within their publication: one based in primary care and two in secondary care.

Eekhof and colleagues[53] compared the instillation of water at body temperature with a group self-administering oil. The population for this RCT was unspecified, but had a mean age of 51 years for all participants. Follow-up was immediate after the water treatment, but delayed by 3 days for the oil arm of the study. There was only one RCT[42] comparing either 'wet' (with prior instillation of warm tap water) syringing or 'dry' syringing (no prior instillation of water) in an adult population. Follow-up was immediately after treatment.

The methodology and quality of reporting of included studies was generally poor (*Table 4*). A number of studies pre-date RCT reporting guidelines, but this may also reflect set word limits for some of the publications. Only three RCTs[47,49,52] were assessed as adequate for their randomisation procedure, with one assessed as partially meeting this criteria.[42] For several studies the method was judged inadequate,[46,51,53] but for the majority[41,44,45,48,50] it was not possible to judge due to a distinct lack of information. The same three studies[47,49,52] that were judged adequate for their randomisation procedures were also judged as adequate in their concealment allocation. For the remaining RCTs, concealment of allocation was either inadequate[42,53] or unknown,[41,44–46,48,50,51] making it impossible to rule out selection bias.

None of the studies were judged as adequate in their method for blinding caregivers or participants. While the difficulties in blinding for some of the interventions could have been addressed somewhat by blinding the assessor of the outcomes, none of the studies did so adequately. Measurement bias can therefore not be ruled out for the majority of included studies. With only 4 out of 14 studies reporting baseline characteristics,[42,47,49,50] it is also not possible to judge the similarities between the treatment groups at baseline for the majority of the studies. Four studies were judged adequate for the description of missing values,[45,47,49,52] but none of the studies reported an adequate intention-to-treat (ITT) analysis. Caution should be exercised in the interpretation of the results of these studies, as overall these appear to be at a high risk of bias, which may affect the direction of any effects shown.

Likewise, the CCTs (*Table 5*) appear at risk to bias and their results have to be interpreted with care. The two included studies[43,54] were of low quality, with unreported baseline characteristics in both and blinding of outcome assessors adequate in only one study.[43] Neither study was judged to be adequate for eligibility criteria, primary outcome results, ITT analysis, missing values or representativeness of the populations.

Results of studies in primary care with immediate follow-up

The results of the studies in primary care are reported in *Table 6*.

TABLE 3 *Table of characteristics of studies, primary care*

Study	Interventions	Participants	Outcomes
Immediate follow-up			
Author: Meehan and colleagues, 2002[46] Country: USA Number of centres: 1 Design: RCT Setting: Emergency care Follow-up: Immediate	1. DS: 1 ml (n = 15) 2. TP: 1 ml (n = 17) 3. NS: 1 ml (n = 16)	*Target population*: Cooperative patients, aged 1–18 years, presenting in a paediatric emergency department, with complete or partial TM occlusion *Baseline characteristics*: Age, mean years: 4.6 overall (no individual group details) Gender, M/F: 24:24 overall (no individual group details)	Amount of TM visualised AEs
Author: Whatley and colleagues, 2003[47] Country: USA Number of centres: 2 Design: RCT Setting: Children's hospital emergency department or large general paediatric clinic in same town Follow-up: Immediate	1. DS: 1 ml (n = 35) 2. TP: 1 ml (n = 30) 3. Saline control: 1 ml (n = 28)	*Target population*: Children aged 6 months to 5 years with complete or partial cerumen obstruction of the TM *Baseline characteristics*: Age, mean (SD): 1. 36.4 (19.1) months 2. 30.9 (15.2) months 3. 36.7 (19.5) months Overall range: (16 months–5 years) Gender M/F (%): 1. 14:20 (41:59) 2. 13:17 (43:57) 3. 15:13 (54:46)	Proportion achieving complete visualisation of the TM AEs
Author: Singer and colleagues, 2000[49] Country: USA Number of centres:1 Design: RCT Setting: Emergency department Follow-up: Immediate	1. DS: 1 ml (n = 27) 2. TP: 1 ml (n = 23)	*Target population*: (e.g. inclusion criteria) ≥ 1 year with ear canal partially or totally occluded by cerumen, medically requiring visualisation of ear canal (i.e. earache, hearing loss, fever) and presenting in the emergency department *Baseline characteristics*: Age, mean years (SD): 1. 38.7 (30.7) 2. 46.1 (29.1) Gender M/F (%): 1. 16 (59):11 (41) 2. 16 (70):7 (30)	Proportion of ears in which TM totally visible with or without irrigation or irrigation with 100 ml of irrigant Presence of AEs
Author: General Practitioner Research Group, 1965[41] Country: UK Number of centres: 14 Design: RCT Setting: Primary care Follow-up: Immediate	1. Dioctyl-medo (oil based), no dose stated (n = 77) 2. Control: Oil-base alone, no dose stated (n = 73)	*Target population*: UK primary care practice patients, no details on severity of occlusions *Baseline characteristics*: Age, maximum incidence: Males: 31–50 years Females: 51–70 years 32% new patients, 53% without syringing for over 12 months Gender, all patients, M/F: 1.3:1	Volume of water for syringing and syringefuls used Ease of wax removal Character of syringed wax

continued

TABLE 3 *Table of characteristics of studies, primary care (continued)*

Study	Interventions	Participants	Outcomes
Author: Pavlidis and Pickering, 2005[42] Country: Australia Number of centres: 1 Design: RCT Setting: Primary care Follow-up: Immediate	1. Wet syringing ($n = 22$ ears) 2. Dry syringing ($n = 17$ ears)	*Target population*: UK adult patients with earwax partially or totally occluding one or both ears, which would normally be syringed by their GP *Baseline characteristics*: Age, mean years (SD): 1. 63 (8) 2. 65 (20) Gender M/F (%): 1. 15 (68) : 7 (32) 2. 11 (65) : 6 (35)	Mean number of syringing attempts Mean time to syringing (minutes) AEs
Author: General Practitioner Research Group, 1967[48] Country: UK Number of centres: 10 Design: RCT Setting: Primary care Follow-up: Immediate	1. Waxsol: 6–7 drops self administered nightly ($n = 47$) 2. Cerumol: 6–7 drops self administered nightly ($n = 60$)	*Target population*: UK primary care practice patients with all cases of earwax apart from minor degrees of wax easily removed without softening agent *Baseline characteristics*: Age groups, % of all patients: 10–30 years, 27 31–50 years, 34 51–70 years, 31 71 years and over, 8 Gender: Not reported	Volume of water for syringing Ease of wax removal Character of wax AEs
Author: Amjad and Scheer, 1975[51] Country: USA Number of centres: Not reported Design: RCT Setting: Primary care Follow-up: Immediate	1. TP: 1 dose (amount not reported) ($n = 40$) 2. Carbamide peroxide: 1 dose (amount not reported) ($n = 40$)	*Target population*: Patients with hard or impacted earwax *Baseline characteristics*: Age: Not reported Gender: Not reported	Degrees of wax removal AEs (subjective and observations of objective side effects)
Delayed follow-up			
Author: Dummer and colleagues, 1992[44] Country: UK Number of centres: 1 Design: RCT Setting: Primary care Follow-up: Median number of days between visits 1 and 2 was 4 days (range 3–7 days)	1. Audax: Dose not reported ($n = 27$) 2. Cerumol: Dose not reported ($n = 23$)	*Target population*: Adults between 19–90 years presenting in primary care practice with impacted or hardened earwax *Baseline characteristics*: Age, mean (years): 1. 51 2. 55 Gender M/F: 1. 18:9 2. 14:9	Amount, colour and consistency of wax Symptoms Hearing Global impression of treatment efficacy (patient and investigator) Tolerability of treatment

TABLE 3 *Table of characteristics of studies, primary care (continued)*

Study	Interventions	Participants	Outcomes
Author: Jaffe and Grimshaw, 1978[50] Country: UK Number of centres: Up to 15 Design: RCT Setting: Primary care Follow-up: Patients asked to revisit GP after 3 instillations	1. Otocerol: 4 drops at night for 3 nights (n = 53) 2. Cerumol: 5 drops at night for 3 nights (n = 53)	*Target population*: Patients presenting at primary care practice with earwax and who would normally be prescribed a cerumenolytic *Baseline characteristics*: Age distribution (years): group 1, group 2 0–9: 0, 1 10–19: 5, 1 20–29: 4, 9 30–39: 8, 6 40–49: 7, 5 50–59: 12, 15 60–69: 9, 6 70–79: 7, 7 80–89: 1, 3 Gender M/F: 1. 32:21 2. 25:28	Ease of syringing Doctors overall impression AEs
Author: Fahmy and Whitefield, 1982[54] Country: UK Number of centres: Multicentre, but number of centres not reported Design: CCT Setting: Studies 1 and 2 in secondary care, study 3 in primary care Follow-up: 1 week	Study 3:* n = 160 (286 ears) 1. Exterol: 5–10 drops × 2 daily (ears = 157) 2. Cerumol: 5–10 drops × 2 daily (ears = 129) *Studies 1 and 2 are reported in *Table 7* – assessing earwax removal in secondary care settings	*Target population*: Patients presenting with earwax problems in secondary care for studies 1 and 2 and primary care in study 3 *Baseline characteristics*: Age: Not reported Gender: Not reported	Wax occlusion Wax consistency Ease of syringing
Author: Carr and Smith, 2001[52] Country: USA and/or Canada Number of centres: Unclear Design: RCT Setting: Primary care – self-treatment Follow-up: 14 days	1. Aqueous sodium bicarbonate (10%): 4 drops daily for 14 days (n = 35, 70 ears) 2. Aqueous acetic acid (2.5%): 4 drops daily for 14 days (n = 34, 68 ears)	*Target population*: Those suffering with occlusive cerumen in at least 1 ear (most presenting with other complaints and ceruminosis was noted incidentally) *Baseline characteristics*: Age, mean years for all (36 children and 33 adults): 1. 27.0 2. 25.3 Age, mean years for children: 1. 8.7 2. 7.26 Gender: Not reported	Degree of cerumen

continued

TABLE 3 *Table of characteristics of studies, primary care (continued)*

Study	Interventions	Participants	Outcomes
Author: Lyndon and colleagues, 1992[45] Country: UK Number of centres: Unclear Design: RCT Setting: Primary care Follow-up: 5 days	1. Audax: self administered AM and PM for 4 days (n = 19, 38 ears) 2. Earex: self administered) AM and PM for 4 days (n = 17, 34 ears)	*Target population*: Patients aged 16 years or over presenting in general practice with symptoms of hardened earwax, in either or both ears, requiring cerumenolytic treatment *Baseline characteristics*: Age, mean years for all patients (range): 52 (19–86) Gender, M/F for all patients: 19:17	Degree of impaction Ease of syringing Global impression of efficacy Side effects/discomfort
Author: Burgess 1966[43] Country: UK Number of centres:1 Design: CCT Setting: Primary care Follow-up: Between 2 and 7 days	1. Dioctyl-medo (in maize oil): 1 capsule (0.5 ml) AM and PM (n = 33 ears)* 2. Maize oil capsules: (n = 41 ears)* *Patients received 1 box (10 capsules) and capsules were instilled 4–10 times	*Target population*: Patients in primary care with more than one-half of an ear occluded by wax *Baseline characteristics*: Age range for all patients, years: 18–75 Gender, M/F all patients: 32:18	Average total of water used Ease of removing wax Character of wax Side effects
Author: Eekhof and colleagues, 2001[53] Country: The Netherlands Number of centres: 4 Design: RCT Setting: Primary care Follow-up: Immediate for water group but 3 days for oil group	1. Water at body temperature (n = 22) 2. Self administered 'oil' (n = 20)	*Target population*: All patients with complaints resulting from earwax were offered syringing. After each attempt at syringing the auditory canal was checked with an auriscope and the extent of blocking was noted (obstruction levels of 0–25%, 25–49%, 50–74% and 75–100% were used). If earwax was persistent (>75% after 5 attempts at syringing) patients were eligible to be included in the study *Baseline characteristics*: Age, mean years for all patients (SD): 51 (16) Gender, M/F for all patients: 20:22	Number of syringing attempts needed to remove wax

DS, docusate sodium; F, female; M, male; NS, normal saline; SD, standard deviation; TM, tympanic membrane; TP, triethanolamine polypeptide.

Softeners only studies

Adults

No studies were identified assessing an adult population comparing the use of softeners alone, with an immediate participant follow-up after treatment.

Children

Two studies[46,47] with immediate follow-up in children aimed to assess the use of a softening agent alone and fall under the softener-only category. After initial assessment of the outcome from the use of the softening agent both of these studies subsequently used an irrigation technique and reassessed outcomes. Both studies compared DS, TP and saline.

Measures of occlusion

Meehan and colleagues[46] reported the number of children with complete, partial or no occlusion after DS, TP or saline alone in attendees at an emergency care department. Thirteen per cent of children were rated as clear in the DS treatment group; 41% were clear in the TP treatment group and 13% in the saline treatment group. The corresponding proportions with complete obstruction at baseline for the three groups, respectively, were 73%, 65% and 56%, with 27%, 35% and 44%, respectively, having partial obstruction of the TM. While it would appear that more children in the TP group had clear TMs after treatment, no statistical significance testing was reported of the difference between effects of

TABLE 4 *Quality of studies, primary care*

Study	Randomisation	Concealment of allocation	Baseline characteristics	Eligibility	Blinding of assessors	Care-provider blinding	Patient blinding	Reporting outcomes	ITT	Withdrawals explained
Meehan, 2002[46]	In	Un	Un	In	Un	Par	Par	In	In	In
Whatley, 2003[47]	**Ad**	**Ad**	Rep	**Ad**	Par	Par	Par	**Ad**	In	**Ad**
Singer, 2000[49]	**Ad**	**Ad**	Rep	**Ad**	Un	In	Par	In	In	**Ad**
General Practitioner Research Group, 1965[41]	Un	Un	Un	Un	Un	Par	Par	In	In	In
Pavlidis, 2005[42]	Par	In	Rep	**Ad**	In	In	In	In	In	In
General Practitioner Research Group, 1967[48]	Un	Un	Un	In	Un	Par	Par	In	In	In
Amjad, 1975[51]	In	Un	Un	In	Un	Par	Par	In	In	In
Dummer, 1992[44]	Un	Un	Un	Par	In	In	In	In	In	In
Jaffe, 1978[50]	Un	Un	Rep	Par	Un	Par	Par	In	In	In
Carr, 2001[52]	**Ad**	**Ad**	Un	**Ad**	Un	Par	Par	In	In	**Ad**
Lyndon, 1992[45]	Un	Un	Un	**Ad**	Un	Un	Un	In	In	**Ad**
Eekhof, 2001[53]	In	In	Un	**Ad**	Un	Un	Un	**Ad**	In	Un

Ad, adequate; In, inadequate; Par, partial; Rep, reported; Un, unknown. (See Appendix 1.)

TABLE 5 *Quality assessment of CCTs, primary care*

Study	Baseline characteristics	Eligibility	Blinding of assessors	Reporting outcomes	ITT	Withdrawals explained	Representativeness
Fahmy, 1982[54]	Un	Par	Un	Par	Un	Un	Un
Burgess, 1966[43]	Un	Par	**Ad**	In	In	In	Un

Ad, adequate; In, inadequate; Par, partial; Rep, reported; Un, unknown. (See Appendix 1.)

the different softening agents. Thirty-three per cent, 29% and 31% of participants, respectively, for DS, TP and saline were still completely occluded, and 53%, 29% and 56% partially occluded for the three groups, respectively. Of these participants, irrigation was then used with varying results (*Table 6*). In around 50% of participants in all three groups the TM remained occluded or partially occluded after two irrigations.

Whatley and colleagues[47] also reported the number and proportion of children with clear TM after use of the treatments. Twelve per cent of participants in the DS treatment group, 13% in the TP and 4%

in the saline treatment group were reported as clear after softening treatment. The corresponding proportions of participants with complete occlusion of the TM at baseline for the three groups, respectively, were 91%, 80% and 79%. Similarly to the Meehan and colleagues study,[46] some 32–57% of participants remained occluded after two irrigations. This study reported statistical testing only for the proportions clear after the second irrigation, which was not statistically significant.

Measures of ease of wax removal
Meehan and colleagues[46] and Whatley and colleagues[47] did not report this outcome.

Measures of patient satisfaction
Meehan and colleagues[46] and Whatley and colleagues[47] did not report this outcome.

Measures of recurrence
Meehan and colleagues[46] and Whatley and colleagues[47] did not report this outcome.

Adverse events
Ten (21%) participants in the Meehan study[46] had pain with irrigation and one (1%) participant in the Whatley study[47] had a small ear bleed after irrigation.

Mixed or unknown populations
One study[49] was identified assessing a mixed population with the a priori intention of comparing softeners alone, coupled with an immediate participant follow-up after treatment. This study compared DS with TP.

Measures of occlusion
Singer and colleagues[49] assessed the number of ears with complete visualisation after DS or TP in a mixed population of adults and children. The TM was completely visualised in 19% of DS and 9% of TP treated participants, respectively; however, the difference was not statistically significant [% difference DS–TP 9.8; 95% confidence interval (CI) –8.8 to 28.5]. At baseline 78% of participants in the DS arm and 78% of participants in the TP arm had completely obstructed TMs. Complete TM visualisation after treatment, with or without subsequent irrigation with normal saline solution, was statistically significantly greater for DS than TP [82% versus 35%, respectively; difference 46.7% (95% CI 22.3–71.1%)]. Results were also presented for numbers with a clear TM after a first and then second irrigation. This showed that a higher proportion of participants in the TP arm (79%) than the DS arm (42%) were still not completely clear after two irrigations. However, this was not tested for statistical significance between the two groups.

Measures of ease of wax removal
Singer and colleagues[49] did not report this outcome.

Measures of patient satisfaction
Singer and colleagues[49] did not report this outcome.

Measures of recurrence
Singer and colleagues[49] did not report this outcome.

Adverse events
Singer and colleagues[49] found no cases of pain, vertigo, nausea or hearing loss.

Softeners and irrigation studies
Adults
There were two studies where the intention was to compare different softeners, which were then followed by syringing in an adult population, with an immediate participant follow-up after treatment.[41,42] The General Practitioner Research Group[41] compared dioctyl-medo with an oil-based control, and Pavlidis and Pickering[42] compared use of water prior to syringing (wet syringing) to no water prior to syringing (dry syringing). Neither of these studies reported on the baseline degree of occlusion in their populations.

Measures of occlusion
Neither the General Practitioner Research Group[41] or Pavlidis and Pickering[42] reported on these outcomes.

Measures of ease of wax removal
The General Practitioner Research Group[41] study reported on the number (or fractions) of syringefuls required to remove wax after using dioctyl-medo drops or an oil-based control. The mean amount of water required for the dioctyl-medo treatment group was 122 ml compared with 165.5 ml for the oil-based control group. The statistical significance of the difference between the two groups was, however, not tested. The study does report that there was an outlier for the control group and that removal of the outlier resulted in there being little difference between the treatment groups. Syringe capacity varied – 57, 85 and 112 ml – and the authors state that an exact analysis in relation to the number of syringefuls used, and in respect of each syringe size, was made. The

study also categorised ease of wax removal (easy or difficult, partial or failed), with wax removal classed as easy for 70% of participants receiving dioctyl-medo and 57% of control participants receiving oil-based control treatment. The study did not report any statistical significance testing on these data. No baseline values of the degree of earwax were reported.

Pavlidis and Pickering[42] reported on the mean number of syringing attempts for those in the 'wet' and 'dry' syringing groups. Wet syringing needed 7.5 attempts (mean), while dry syringing needed 25.4. This was seen to be statistically significantly different ($p = 0.043$). Pavlidis and Pickering[42] suggest that the number of syringing attempts are unusually high due to the small volume of the syringe used (25 ml), which is smaller than syringes used by GPs (> 120 ml). No baseline values of the degree of earwax were reported

Measures of patient satisfaction
The General Practitioner Research Group[41] reported that 92% of the dioctyl-medo group and 86% of the oil-based control group found the procedure tolerable. Pavlidis and Pickering[42] did not report on this outcome.

Measures of recurrence
Neither the General Practitioner Research Group[41] nor Pavlidis and Pickering[42] reported on these outcomes.

Adverse events
The General Practitioner Research Group[41] found no AEs in 91% of the dioctyl-medo group and 89% of the oil-based control group. AEs were entirely related to the procedure of syringing, but no further details about the nature of these are reported. Pavlidis and Pickering[42] reported transient dizziness for one participant only, after having both ears syringed, with all TM being intact at the end of syringing.

Children
No studies were identified assessing children and comparing softeners followed by syringing, with an immediate participant follow-up after treatment.

Mixed or unknown populations
Two studies[48,51] were included that assessed the use of a softening agent and a syringing agent in mixed populations over a delayed period of follow-up. The General Practitioner Research Group[48] study compared Waxsol with Cerumol, and the Amjad and Scheer[51] study compared TP with carbamide peroxide.

Measures of occlusion
Amjad and Scheer[51] assessed degree of wax removal using TP and carbamide peroxide in an unspecified population. Excellent removal was reported for 68% of TP participants and 5% of carbamide peroxide participants, with good removal in 20% and 12% of participants, respectively. Effective removal (combining excellent and good) was reported for 88% of the TP-treated participants and 17% in the carbamide peroxide-treated participants. At baseline, 90% of participants in the TP group and 80% of participants in the carbamide peroxide group had complete obstruction of the TM, with 10% and 20% having partial obstruction for the two groups, respectively. The study also reports degree of wax removal as a function of pretreatment wax. This showed that in the TP group effective (rated as excellent or good) wax removal was achieved in 100% of participants with soft or loose pretreatment wax, whereas the corresponding value in the carbamide peroxide group was 33%. In those with hard or impacted wax at baseline some 88% and 84% (for the two categories respectively) in the TP group had 'effective' clearance. The corresponding rates in the carbamide peroxide group were 19% for those with hard wax pretreatment and 11% for those with impacted wax pretreatment. The study did not report any statistical significance testing of the data (*Table 6*).

Measures of ease of wax removal
The General Practitioner Research Group[48] assessed the volume of water needed for syringing after the use of Waxsol and Cerumol in a population of adults and children. The mean volume per participant for the Waxsol treatment group was 156 ml [5.5 fluid ounces (fl oz)] per participant and for the Cerumol treatment group was 240 ml (8.4 fl oz). Ease of wax removal (easy or difficult removal, partly or failed removal) was also assessed by this study, with 83% of participants in the Waxsol treatment group and 80% in the Cerumol treatment group judged to have easily removed earwax. The study did not report if this outcome was tested for statistical significance. No baseline degree of occlusion were reported in the General Practitioner Research Group[48] study. Amjad and Scheer[51] did not report on this outcome.

TABLE 6 *Outcomes of studies, primary care*

Immediate follow-up – children – softeners alone as primary objective

Meehan and colleagues, 2002[46]

	DS	**TP**	**Saline**	***p*-value**
TM occlusion				
	n = 15	*n* = 17	*n* = 16	
Complete	5	5	5	Not reported
Partial	8	5	9	
Clear	2	7	2	
TM occlusion after first irrigation				
	n = 13	*n* = 15	*n* = 15	
Complete	4	4	4	Not reported
Partial	6	3	5	
Clear	3	8	6	
TM occlusion after second irrigation				
	n = 12	*n* = 15	*n* = 15	
Complete	3	4	3	Not reported
Partial	4	3	4	
Clear	5	8	8	

Whatley and colleagues, 2003[47]

	DS	**TP**	**Saline**	***p*-value**
	n = 35	*n* = 30	*n* = 28	
Clear TM after agent, *n* (%)	4 (12)	4 (13)	1 (4)	Not reported
Clear TM after first irrigation, *n* (%)	13 (38)	12 (40)	12 (43)	Not reported
Clear TM after second irrigation, *n* (%)	18 (53)	13 (43)	19 (68)	Not significant

Immediate follow-up – mixed population – softeners alone as primary objective

Singer and colleagues, 2000[49]

	DS (*n* = 27)	**TP (*n* = 23)**	**Difference (95% CI)**
Completely visualised ears after solvent only, *n* (%)	5 (19)	2 (9)	9.8 (–8.8 to 28.5)
Completely visualised ears after solvent with or without irrigation, *n* (%)	22 (82)	8 (35)	46.7 (22.3 to 71.1)

TM visualisation, n (%)

	Complete	**Incomplete**	**Complete**	**Incomplete**	**Not reported**
After solvent only	5 (19)	22 (81)	2 (9)	21 (91)	
First 50-ml ear irrigation	10 (45)	12 (55)	2 (10)	19 (90)	
Second 50-ml ear irrigation	7 (58)	5 (42)	4 (21)	15 (79)	

TABLE 6 *Outcomes of studies, primary care (continued)*

Immediate follow-up – adult population – softeners and irrigation at primary objective

General Practitioner Research Group, 1965[41]

	Dioctyl-medo (*n* = 77)			**Oil-based control (*n* = 73)**			
	No. of cases	**Total quantity (ml)**	**Mean per case**	**No. of cases**	**Total quantity (ml)**	**Mean per case**	***p*-value**
Number of syringefuls used							
0.25–1	35	2123	60	26	1732	65	Not tested
1.25–2	13	1718	130.5	17	2329	136	Not tested
2.5–4	12	2243	187.5	17	3487	207	Not tested
5–15	6	2045	341	4	2613	653	Not tested
Total	66	8129	122	64	10,181	165.5	Not tested
Ease of wax removal, N (%)							
Easy		54 (70)			42 (57)		
Difficult		17 (22)			23 (32)		
Partial		3 (4)			6 (8)		
Failed		2 (3)			2 (3)		
Character of syringed wax, N (%)							
Liquid		14 (19)			10 (14)		
Shredded		34 (46)			28 (40)		
Hard lumps		26 (35)			32 (46)		
Failed		3			2		
Not recorded		0			1		

Pavlidis & Pickering, 2005[42]

	Wet syringing (*n* = 22)	**Dry syringing (*n* = 17)**	***p*-value**
Mean number of syringing attempts (SD)	7.5 (7.3)	25.4 (39.4)	0.043
Mean time to syringing (minutes)	6.5	15.4	ns but *p*-value not reported

Immediate follow-up – mixed populations – softeners and irrigation as primary objective

General Practitioner Research Group, 1967[48]

	Waxsol (*n* = 47)		**Cerumol (*n* = 60)**		
Volume of water (fl oz)	**No. of participants**	**Total volume**	**No. of participants**	**Total volume**	***p*-value**
0.5	0	0	1	0.5	Not reported
1	6	6.0	2	2.0	
2	13	26.0	4	8.0	
2.5	1	2.5	1	2.5	
3	3	9.0	5	15.0	
4	3	12.0	8	32.0	

continued

TABLE 6 *Outcomes of studies, primary care (continued)*

5	0	0	1	5.0	
6	6	36.0	4	24.0	
7	2	14.0	2	14.0	
8	3	24.0	12	96.0	
9	0	0	2	18.0	
10	1	10.0	2	20.0	
12	6	72.0	8	96.0	
14	1	14.0	2	28.0	
16	2	32.0	2	32.0	
18	0	0	1	18.0	
24	0	0	1	24.0	
26	0	0	1	26.0	
40	0	0	1	40.0	
Totals	47	257.5	60	501.0	
Mean volume per participant:	5.5 fl oz (156 ml)		8.4 fl oz (240 ml)		Not reported
	No. of participants (%)		**No. of participants (%)**		***p*-value**
≤ 56 ml (2 fl oz)	19 (40)		7 (12)		$p < 0.05$
> 56 ml	28 (60)		53 (88)		
Proportion of participants needing: 14–112 ml:	55%		35%		$p < 0.05$
Ease of removal, n (%)					
Easily removed	39 (83)		48 (80)		No *p*-values reported
Removed with difficulty	6 (13)		9 (15)		
Partly removed	1 (2)		1 (2)		
Failed	1 (2)		2 (3)		
Character of wax (% of participants)					
Liquid	17		17		No *p*-values reported
Shredded	46		35		
Hard lumps	37		24		
***Amjad and Scheer, 1975*[51]**					
Degree of wax removal, n (%)					
	TP (*n* = 40)		**Carbamide peroxide (*n* = 40)**		***p*-value**
Excellent (E)	27 (68)		2 (5)		Not reported
Good (G)	8 (20)		5 (12)		
Fair (Fr)	2 (5)		4 (10)		
Poor (Pr)	3 (7)		29 (73)		
Effective (E + G: excellent + good)	35 (88)		7 (17)		

TABLE 6 *Outcomes of studies, primary care (continued)*

Efficacy to pretreatment wax

	No.	E+G	Fr	Pr	E+G (%)	No.	E+G	Fr	Pr	E+G (%)	*p*-value
Impacted	19	16	1	2	84	18	2	0	16	11	Not reported
Hard	16	14	1	1	88	16	3	2	11	19	
Loose	1	1	0	0	100	3	1	0	2	33	
Soft	4	4	0	0	100	3	1	2	0	33	
Complete obstruction	36	31	2	3	86	32	4	3	25	13	
Partial obstruction	4	4	0	0	100	8	3	1	4	38	

Delayed follow-up – adult population – softeners alone as primary objective

Dummer and colleagues, 1992[44]

	Audax (*n* = 27, ears *n* = 54)	Cerumol (*n* = 23, ears *n* = 46)	*p*-value
Amount of wax (n, ears)			
Increased	0	0	Not reported across groups
No change	24 (44%)	22 (48%)	
Decreased	28 (52%)	24 (52%)	
Missing data	2 (4%)	0	
Colour of wax (n, ears)			
Darkened	0	0	States ns, but *p*-value not reported
No change	10	9	
Lightened	42	36	
Missing data	2	1	
Consistency (n, ears)			
Hardened	0	0	States ns, but *p*-value not reported
No change	6	5	
Softened	46	40	
Missing data	2	1	
Objective hearing (n, ears)			
Improved	7 (13%)	2 (4%)	States ns, but *p*-value not reported
No change	45 (83%)	44 (96%)	
Worsened	0	0	
Missing data	2 (4%)	0	
Overall assessment			
Investigator rated 'effective' (*n*, pts)	36	22	Unclear if tested
Overall assessment			
Participant rated 'effective' (*n*, pts)	25 (93%)	23 (100%)	States ns, but *p*-value not reported

continued

TABLE 6 *Outcomes of studies, primary care (continued)*

Delayed follow-up – mixed populations – softeners alone as primary objective

Jaffe and Grimshaw, 1978[50]

	Otocerol (*n* = 53)	**Cerumol (*n* = 53)**	***p*-value**
Syringing needed	Yes: 39, no 14	Yes: 47, no 6	*N* requiring syringing $p < 0.05$
Syringing needed by grade at entry			
Mild	Yes 6, no 7	Yes 6, no 4	Not reported
Moderate	Yes 19, no 7	Yes 30, no 2	
Severe	Yes 14, no 0	Yes 11, no 0	
Doctor reported ease of syringing			
	30/39 (76.9%)	34/47 (72.3%)	$\chi^2 = 0.25$, ns
Ease of syringing by grade at entry			
Mild	Easy 5, not easy 1	Easy 5, not easy 1	Not reported
Moderate	Easy 14, not easy 5	Easy 25, not easy 5	
Severe	Easy 11, not easy 3	Easy 4, not easy 7	
Overall judgement effectiveness			
Success	38	33	ns
Failure	10	13	
Partial	5	7	

Fahmy and Whitefield, 1982[54] (see Table 10 for study 1 and 2 results in secondary care)

	Exterol (*n* = 157)		**Cerumol (*n* = 129)**		***p*-value**
	Initially hard	**Initially soft**	**Initially hard**	**Initially soft**	
Wax dispersed without syringing	45	19	12	15	$p < 0.001$
Syringed easily	60	22	52	14	
Syringed with difficulty	9	2	33	3	

Carr and Smith, 2001[52]

	10% sodium bicarbonate (*n* = 35)	**2.5% acetic acid (*n* = 34)**	***p*-value**
Mean change degree of cerumen	0.66	0.78	States ns but *p*-value not reported
Mean maximum change	1.00	1.00	

Delayed follow-up – adult populations – softeners and irrigation as primary objective

Lyndon and colleagues, 1992[45]

	Audax (*n* = 19, 38 ears)	**Earex (*n* = 17, 34 ears)**	***p*-value**
Degree of impaction			
None	10	6	States ns but *p*-value not reported
Mild	17	11	
Moderate (Mod)	9	12	
Severe (Sev)	2	3	
Missing data	0	2	

TABLE 6 *Outcomes of studies, primary care (continued)*

	Post-treatment				**Post-treatment**				
	None	**Mild**	**Mod**	**Sev**	**None**	**Mild**	**Mod**	**Sev**	***p*-value**
Degree of impaction at end point by pretreatment score									
None	1	1	0	0	1	0	0	0	States ns but *p*-value not reported
Mild	3	4	0	0	2	4	0	0	
Moderate	6	12	8	0	3	7	11	1	
Severe	0	0	1	2	0	0	1	2	
	Audax (*n* = 38 ears)				**Earex (*n* = 34 ears)**				***p*-value**
Ease of syringing, ears									
Not required	15				7				$p < 0.005$ for score of 'not required' or 'easy'
Easy	22				12				
Difficult	1				11				
Impossible	0				0				
Missing data	0				4				
	Audax (*n* = 19)				**Earex (*n* = 17)**				
Global impression of efficacy, investigator n = pts*									
Completely effective	8				5				
Very effective	9				1				
Fairly effective	2				7				
Not effective	0				3				
Missing data	0				1				
Total	19				17				
Global impression of efficacy, participant n = pts*									
Completely effective	8				5				
Very effective	9				2				
Fairly effective	2				7				
Not effective	0				2				
Missing data	0				1				
Total	19				17				
*Investigators' and participants' own global impression of efficacy merged categories (not effective and fairly effective) were significantly in favour of Audax ($p < 0.01$).									
Burgess, 1966[43]									
	Dioctyl-medo (*n* = 33 ears)				**Maize oil (*n* = 41 ears)**				***p*-value**
Average water used									
	111 ml				81 ml				Not reported
Ease of removal, N ears									
Easy	19				33				Not reported
Difficult	11				5				
Partial	3				3				
Failed	1				0				

continued

TABLE 6 *Outcomes of studies, primary care (continued)*

Character wax, N ears			
Liquid	1	4	Not reported
Shredded	5	6	
Lumps	27	31	
Delayed follow-up – mixed populations – softeners and irrigation as primary objective			
Eekhof and colleagues, 2001[53]			
	Water (*n* = 22)	**Control 'oil' (*n* = 20)**	***p*-value**
Mean number syringing attempts			
	3.0 (95% CI 2.4 to 3.6)	2.4 (95% CI 1.7 to 3.1)	Difference 0.6 (95% CI –0.3 to 1.5); $p = 0.18$
Mean number syringing attempts per participant by number earwax removed			
	Number removed	**Number removed**	***p*-value**
1	4	6	Not reported to be tested
1.5	1	2	
2	2	5	
2.5	3	1	
3	2	2	
3.5	4	0	
4	2	0	
5	3	4	
6	1	0	

CI, confidence interval; DS, docusate sodium; ns, not significant; SD, standard deviation; TP, triethanolamine polypeptide.

Measures of patient satisfaction

Eighty-nine per cent of participants in the Waxsol treatment group and 95% in the Cerumol treatment group were reported to have found the treatment tolerable in the General Practitioner Research Group study.[48] No statistical analysis of the differences in this data was provided, however. Amjad and Scheer[51] did not report on this outcome.

Measures of recurrence

The General Practitioner Research Group[48] and Amjad and Scheer[51] did not report on this outcome.

Adverse events

Seven per cent of participants in the Waxsol and 5% in the Cerumol treatment group reported AEs in the General Practitioner Research Group study, but no details about the nature of these events or statistical testing of results are given.[48] There were no reported cases of AEs in the Amjad and Scheer study.[51]

Results of studies in primary care with delayed follow-up

The results of the studies in primary care are reported in *Table 6*.

Softeners only studies

Adults

One study[44] in adults, which had the initial objective to use softeners alone to clear the earwax, was included. Dummer and colleagues[44] compared Audax and Cerumol and delayed participant follow-up for 4 days.

Measures of occlusion

Dummer and colleagues[44] measured the number of ears with post-treatment changes in the amount of wax present (increased, no change and decreased). Fifty-two per cent of ears for both treatments (Audax 28 ears, Cerumol 24 ears) were judged to have a reduced amount of wax. In both groups there were more than 40% with no change in the amount of wax present after treatment. No

statistical analysis of the differences across the groups appeared to have been undertaken on these outcomes, however, and no baseline values of the degree of wax present were reported. Post-treatment performance-based hearing and change in performance-based hearing were assessed through a variety of tests. In the Audax group 13% of ears demonstrated improved hearing, whereas in the Cerumol group the figure was only 4%. There was no change in objective hearing in 83% of ears in the Audax group and 96% of ears in the Cerumol group. The paper states that there were no statistically significant differences between the groups; however a *p*-value was not reported. A global investigator impression of efficacy for the treatments was also undertaken; however, there appears to be a reporting error in terms of the number of participants in the groups and therefore care should be taken in the interpretation of this outcome. It is also unclear how this outcome was assessed.

Measures of ease of wax removal
Dummer and colleagues[44] did not report on this outcome.

Measures of patient satisfaction
In a global impression assessment of the efficacy of the treatments, Dummer and colleagues[44] found that 93% of participants rated the treatment as effective in the Audax treatment group and 100% rated it as effective in the Cerumol treatment group. The authors reported no statistically significant difference between the treatment groups, but no *p*-value was given. It was also unclear how this assessment was measured.

Measures of recurrence
Dummer and colleagues[44] did not report on this outcome.

Adverse events
In the study by Dummer and colleagues,[44] a slight irritation to the ear was reported by two participants in the Audax treatment group, while in the Cerumol treatment group one participant experienced a slight itch and another a buzzing noise shortly after use. No further details of these events were reported.

Children
No studies were identified assessing children in a comparison of softeners alone, with a delayed participant follow-up.

Mixed or unknown populations
Three studies[50,52,54] with mixed or unknown populations were included. All had a delayed follow-up and an intention to assess outcomes after softeners only. Carr and Smith[52] compared a 10% solution of aqueous sodium bicarbonate with a 2.5% solution of acetic acid. The study had a 14-day follow-up. Fahmy and Whitefield[54] compared Exterol and Cerumol, and participants were followed-up 1 week later. This study was one of three and, as previously mentioned, study one and two are covered under Studies in secondary care settings, below. Jaffe and Grimshaw[50] assessed Otocerol and Cerumol with a revisit after three instillations of the interventions.

Measures of occlusion
Carr and Smith[52] measured the change in the degree of earwax, based on a scale of 1–4, where higher scores relate to higher degrees of occlusion. The mean change in the degree of cerumen was reported to be 0.66 in the 10% sodium bicarbonate group and 0.78 in the 2.5% acetic acid group. The study reports that the difference was not statistically significant, but no *p*-value was provided. No baseline values of the degree of occlusion were presented in the study.

Fahmy and Whitefield[54] found the number of ears not requiring syringing was statistically significantly greater after treatment with Exterol ($p < 0.001$), with wax dispersal occurring in 41% of ears in the Exterol treatment group and 21% of ears in the Cerumol treatment group.

Jaffe and Grimshaw[50] did not report on these outcomes.

Measures of ease of wax removal
After treatment, Fahmy and Whitefield[54] found that ears were syringed easily in 52% of ears in the Exterol treatment group and 51% in the Cerumol treatment group. No data analysis of the differences between groups was presented. Exterol was statistically significantly superior to Cerumol, when the number of ears not requiring syringing (above) was combined with the number syringed easily ($p < 0.001$). Seven per cent of ears in the Exterol treatment group and 28% of ears in the Cerumol treatment group remained difficult to syringe after treatment. At baseline, 97 ears in the Exterol group and 86 ears in the Cerumol group were reported to be totally or subtotally occluded with earwax. The remaining ears (60 Exterol,

43 Cerumol) were rated as partially occluded at baseline. There are no data reporting post-treatment outcome in relation to pretreatment outcome, however.

Jaffe and Grimshaw[50] wanted to establish if, after treatment with Otocerol or Cerumol, syringing was required. There was a statistically significant difference in favour of Otocerol, only 73% of Otocerol participants needed syringing compared with 89% of Cerumol participants ($p < 0.05$). At baseline the grade of impaction was assessed as mild, moderate or severe in 13, 26 and 14 participants in the Otocerol group, respectively, and in 10, 32 and 11 participants in the Cerumol group, respectively. Of the 26% of participants in the Otocerol group that did not require syringing after treatment, all of these were rated as mild or moderate at the start of the study. However, 11% of participants categorised as mild at baseline and 36% of participants categorised as moderate at baseline did require syringing after treatment with Otocerol. All of the participants in the Otocerol group with severe impaction at baseline (26%) required syringing post-treatment. In the Cerumol group a similar pattern emerged. Of the 11% of participants that did not require syringing after treatment, all had been rated as mild or moderate at the start of the study. However, 11% and 57% of participants rated as mild or moderate occlusion at baseline did require syringing after treatment. Finally, all of the 21% of participants with severe impaction at baseline required syringing post-treatment. No statistical analysis of this data was reported, however. Where syringing was required, the clinician's rating of the ease of syringing was also reported (76.9% Otocerol versus 72.3% Cerumol were 'easy to syringe'). This was not statistically significantly different between the treatment groups.

In the Jaffe and Grimshaw study,[50] an overall judgement of effectiveness was categorised into success (defined as those in whom syringing was not required or where it was easy and no reports of side effects), failure (defined as those in whom syringing was difficult with or without side effects) and partial (defined as those who reported side effects, but in whom the doctor found it easy to syringe and had no reservations about using the product again). In the Otocerol group 72% were judged to be successes, 19% were judged to be failures and 9% were classed as partial successes. In the Cerumol group these figures were 62%, 25% and 13% for success, failure and partial categories, respectively. The overall judgement of effectiveness between the treatment groups was not statistically significant.

Carr and Smith[52] did not report on this outcome.

Measures of patient satisfaction

These outcomes were not reported by Carr and Smith,[52] Jaffe and Grimshaw[50] or Fahmy and Whitefield.[54]

Measures of recurrence

These outcomes were not reported by Carr and Smith,[52] Jaffe and Grimshaw[50] or Fahmy and Whitefield.[54]

Adverse events

Adverse events were divided into pain (0% Otocerol; 2% Cerumol) and irritation (6% Otocerol, 15% Cerumol) on application, and pain (2% Otocerol, 2% Cerumol) and irritation (8% Otocerol, 8% Cerumol) during use in the Jaffe and Grimshaw study.[50] There was one case (2%) of slight giddiness (no further details) in the Otocerol group. Thirteen per cent of participants suffered AEs in the Otocerol treatment group and 19% in the Cerumol treatment group, but one case included under Cerumol AEs was related to the unpleasant smell of the treatment.[50] The most common AEs were irritation on application, pain during use and irritation during use. The result was reported as statistically non-significant, but no *p*-value was given. Carr and Smith[52] reported no cases of otitis externa or external auditory canal dermatitis for their treatments groups, while Fahmy and Whitefield[54] did not report AEs.

Softeners and irrigation studies

Adults

There were two studies[43,45] in which the intention was to compare different softeners, which were then followed by syringing in an adult population, with a delay in participant follow-up after treatment. Lyndon and colleagues study[45] compared self-administered Audax and Earex followed by syringing, with a delayed follow-up of 5 days. Burgess[43] compared dioctyl-medo and maize oil followed by syringing, with a delayed follow-up of 2–7 days.

Measures of occlusion

Lyndon and colleagues' study[45] measured the degree of impaction from none to severe. After treatment, 26% of ears in the Audax treatment group and 18% of ears in the Earex treatment

group had no wax impaction, but no *p*-value was reported. At baseline, 5% of ears in the Audax treatment group and 3% of ears in the Earex group had no impaction. Eighteen per cent, 68% and 8% of ears in the Audax group were rated as having mild, moderate and severe impaction at baseline, respectively. In the Earex group, these figures were 24%, 65% and 9%, respectively. Analysis of pre- and post-treatment impaction scores between the groups was reported as non-significant, with a trend towards less impaction for the Audax treatment; however, no *p*-value was given. Investigators also completed a global impression of efficacy rating (completely effective, very effective, fairly effective and not effective). This was statistically significant in favour of Audax ($p < 0.01$) for the merged categories of 'not effective' and 'fairly effective', but it was unclear whether this was for the investigator rating alone, participant rating alone (see below) or a combination of the two.

Measures of ease of wax removal
Burgess[43] measured ease of removal and average water used. The diocytl-medo treatment group used on average 111 ml and the maize oil treatment group used 81 ml for syringing the wax. Ease of wax removal was measured for the number of ears, categorised as easy (58% dioctyl-medo, 80% maize oil) or difficult (33% dioctyl-medo, 12% maize oil), partial (9% diocytl-medo,7% maize oil) or failed. The only reported case of failure was for the dioctyl-medo group. This study did not report any statistical significance testing on the data. Burgess[43] only reported baseline characteristics for all participants combined, where the study reports that 80% of ears were completely occluded at baseline. Consequently, there were no data reporting post-treatment outcome in relation to pretreatment outcome. Lyndon and colleagues[45] also measured ease of syringing and found a statistically significant difference in favour of Audax, in that syringing was more frequently scored as 'not required' or 'easy' (97% ears in the Audax group, 56% ears in the Earex group, $p < 0.005$).

Measures of patient satisfaction
In the study by Lyndon and colleagues,[45] participants completed a global impression of efficacy rating. Forty-two per cent of participants in the Audax treatment group and 29% of participants in the Earex treatment group rated the treatment as completely effective. The authors state that there was a statistically significant difference in favour of Audax ($p < 0.01$) for the 'not effective' and 'fairly effective' categories merged together, but it was unclear from the report whether this included the investigator rating alone (as above), participant rating alone or a combination. Burgess[43] did not report on this outcome.

Measures of recurrence
Burgess[43] and Lyndon and colleagues[45] did not report on this outcome.

Adverse events
There were no AEs found for either treatment in the Burgess study.[43] Lyndon and colleagues[45] report two AEs for Earex alone, one being a slight irritation and one based on the unacceptable smell of the treatment.

Children
There were no studies assessing children in a comparison of softeners followed by syringing, with a delayed participant follow-up.

Mixed or unknown populations
One study[53] assessed an unspecified population (although reported a mean age of 51 years for all participants). Warm water as a softener was compared with oil, followed by syringing for both treatment groups. The study had an immediate follow-up for the warm water intervention, but a delayed follow-up of 3 days for the control group using oil.

Measures of occlusion
Eekhof and colleagues[53] did not report on this outcome.

Measures of ease of wax removal
Eekhof and colleagues[53] reported the mean number of syringing attempts between the water and oil-control groups [water: 3.0 (95% CI 2.4 to 3.6), oil-control: 2.4 (95% CI 1.7 to 3.1)]. As the difference between means was not statistically significant ($p = 0.18$), warm water was reported to be as effective as oil as a softening agent. However, the study was not powered to test for statistical equivalence and so caution is required in interpreting this outcome. No baseline degree of earwax was reported.

Measures of patient satisfaction
Eekhof and colleagues[53] did not report on this outcome.

Measures of recurrence
Eekhof and colleagues[53] did not report on this outcome.

TABLE 7 *Characteristics of included studies in secondary care*

Study	Interventions	Participants	Outcomes
Immediate follow-up			
Author: Caballero and colleagues, 2005[55] Country: Spain Number of centres: One Design: RCT Setting: Secondary care Follow-up: Immediate	1. Chlorobutanol: 2 ml ($n = 32$) 2. Sodium carbonate: 2 ml ($n = 29$) 3. Saline: 2 ml ($n = 28$)	*Target population*: Adults with total cerumen obstruction *Baseline characteristics*: Age: 19–78 years Gender: Not reported	Primary outcomes: Proportion of TM completely visualised
Author: Dubow, 1959[57] Country: USA Number of centres: At least two Design: RCT Setting: Secondary care Follow-up: Immediate	1. Hydrogen peroxide 3% solution: dose not reported ($n = 20$) 2. Mineral oil: Dose not reported ($n = 20$) 3. TP: Dose not reported ($n = 20$)	*Target population*: Children with at least one completely cerumen-occluded ear canal, disregarding other disorders, presenting in a paediatric clinic and in 'office practice' *Baseline characteristics*: Age range, years: 3–12 overall (no individual group details) Gender: Not reported	Wax clearance
Author: Chaput De Saintonge and Johnstone, 1973[59] Country: UK Number of centres: One Design: RCT Setting: Secondary care Follow-up: Immediate	1. TP: dose not reported ($n = 32$) 2. Olive oil: Dose not reported ($n = 35$)	*Target population*: any patient with impacted wax attending outpatients *Baseline characteristics*: Age: Not reported Gender: Not reported	Total volume of water Amount of wax removed
Delayed follow-up			
Author: Keane and colleagues, 1995[4] Country: Ireland Number of centres: One Design: RCT Setting: Secondary care Follow-up: 5-day trial	1. Cerumol: 4 drops twice daily ($n = 24$, 40 ears) 2. Sodium bicarbonate: 4 drops twice daily ($n = 25$, 39 ears) 3. Sterile water: 4 drops twice daily ($n = 24$, 38 ears) 4. Control: No treatment ($n = 38$)	*Target population*: Hospitalised patient with one or both ears impacted *Baseline characteristics*: Age: not reported Gender: not reported	Primary outcomes: Percentage clearance and number of ears (clearance is explained by the 'natural expulsion of earwax') Secondary outcomes: AEs
Author: Fahmy and Whitefield, 1982[54] Country: UK Number of centres: One Design: CCT Setting: Studies 1 and 2 in secondary care Follow-up: 1 week	*Study 1*: $n = 40$ (80 ears) 1. Exterol: 5–10 drops × 2 daily ($n = 20$) 2. Glycerol control: 5–10 drops × 2 daily ($n = 20$) *Study 2*: $n = 50$ (100 ears) 1. Exterol: 5–10 drops × 2 daily ($n = 25$) 2. Cerumol: 5–10 drops × 2 daily ($n = 25$) *Study 3*: Reported in *Table 3*	*Target population*: patients presenting with earwax *Baseline characteristics*: Age: Not reported Gender: Not reported	Wax occlusion Wax consistency Ease of syringing

TABLE 7 *Characteristics of included studies in secondary care (continued)*

Study	Interventions	Participants	Outcomes
Author: Fraser, 1970[60] Country: UK Number of centres: Six hospitals Design: RCT Setting: Secondary care Follow-up: At least 3 days	1. Sodium bicarbonate: Once daily for 3 days (dose not stated) (*n* = 124 ears) 2. Olive oil: Once daily for 3 days (dose not stated) (*n* = 25 ears) 3. Cerumol: Once daily for 3 days (dose not stated) (*n* = 24 ears) 4. Waxsol: Once daily for 3 days (dose not stated) (*n* = 26 ears) 5. TP: 15–30 minutes prior to syringing (n = 24 ears) 6. Dioctyl capsules: Once daily for 3 days (dose not stated) (*n* = 25 ears) One ear per person provided a test and control ear	*Target population*: Geriatric attendees at hospitals, with bilateral hard earwax that occludes the external auditory meatus in both ears *Baseline characteristics*: Age: Not reported Gender: Not reported	Ease of syringing Frequency of syringing Appearance of wax removed
De-waxing techniques			
Author: Pothier and colleagues, 2006[56] Country: UK Number of centres: One Design: RCT Setting: Otolaryngology outpatient clinic Follow-up: Treated and assessed on initial visit, unless cerumenolytics used and then unspecified delay	1. Endoscopic otoendoscope de-waxing (diode light source) (*n* = 50) 2. Microscopic de-waxing (aural speculum) (*n* = 50)	*Target population*: Patients requiring removal of earwax from the ear canal to allow full view of TM, with a history of earwax *Baseline characteristics*: Age, mean years (SD, range): 1. 57.2 (16.86, 16–87) 2. 58.3 (17.3, 18–91) Gender M/F: 1. 60:40 2. 62:38	Levels of pain and discomfort for patient Ease of de-waxing Time taken to de-wax
Prevention of recurrence after removal earwax			
Author: Saloranta and colleagues, 2005[58] Country: Finland Number of centres: Two Design: RCT Setting: Secondary care and community home for people with learning difficulties Follow-up: 12 months (visits also at 3 months and at a point of recurrence)	1. Skin oil Ceridal lipolotion: 2 ml, self administered, except in those with learning difficulties (*n* = 20) 2. No treatment (*n* = 19)	*Target population*: Patients with learning difficulties. Had to have a history of impacted cerumen with symptoms like impaired hearing or sensation of blocked ear canal more often than once per year, and earwax completely obstructing the ear canal at the point of inclusion *Baseline characteristics* (learning difficulties): 1. *n* = 13, 16 ears (*n* = 9) 2. *n* = 19, 29 ears (*n* = 10) Age, mean years (range): 1. 34 (4–52) 2. 44 (1–74) Gender M/F: 1. 7:6 2. 8:10	Recurrence of cerumen impaction AEs

AEs, adverse events; CCT, controlled clinical trial; F, female; M, male; SD, standard deviation; TM, tympanic membrane.

Adverse events

Eekhof and colleagues[53] did not report on this outcome.

Studies in secondary care settings

Eight studies undertaken in secondary care settings were identified (*Table 7*): seven were RCTs and one was a CCT. Three RCTs[55,57,59] followed participants up immediately after interventions. One[57] was a three-arm trial in children, of hydrogen peroxide, mineral oil or TP; one other[55] was a three-arm trial in adults, of chlorobutanol, sodium carbonate and saline. The third study[59] compared TP with olive oil; the participant group was not described in this study. Three included studies had a longer delay in their follow-up. Keane and colleagues'[4] RCT, which appears to be in elderly adults, was a four-arm trial of Cerumol, sodium bicarbonate, sterile water and no treatment (control). The interventions were administered for 5 days, after which the participants were reassessed. Fraser[60] assessed sodium bicarbonate, olive oil, Cerumol, Waxsol, TP and dioctyl to a within-participant control (one ear test, one ear control) in elderly participants over a period of 3 days follow-up. The third study, a CCT by Fahmy and Whitefield,[54] included three separate studies, one of which was in participants from primary care and was discussed previously (Chapter 3, Studies in secondary care settings). Of the other two studies, one compared Exterol with glycerol and the other Exterol with Cerumol. The target population for these studies was not clear in the publication, but the ear drops were given over a one-week period before follow-up. In addition to the studies comparing the use of different softening agents, two other studies were included that either compared two de-waxing techniques[56] or the application of a skin oil with no treatment.[58] In the first of these RCTs adults in an otolaryngology clinic requiring removal of earwax were randomised to endoscopic otoendoscopic de-waxing or microscopic de-waxing. In the second RCT, participants had their earwax removed and were then randomised to either Ceridal lipolotion skin oil or no treatment to assess the recurrence of cerumen. This study was undertaken in adults and children with learning difficulties and follow-up was for 12 months.

The quality of reporting and methodology of the included studies was generally poor (see *Tables 8* and *9*). Of the seven RCTs, none of the studies was assessed as having an adequate generation of the randomisation sequence. In one RCT the generation of the randomisation schedule was judged to be partially met,[56] in three this was judged to be inadequate,[57,58,60] and in the remainder it was not possible to judge due to a lack of information.[4,55,59] Only one RCT adequately met the criteria for concealment of allocation.[59] Therefore, most of these studies may be subject to selection bias, with the allocation sequence open to possible manipulation. Double-blinding (participant and caregiver) was assessed as being adequate only in one study.[59] While double-blinding may have been difficult for some interventions, blinding of the outcome assessors could have been undertaken; however, there were no studies that were assessed as adequately blinding the outcome assessors. This factor is particularly important when subjective outcome measures are used and therefore this may mean the studies are subject to measurement bias. Many studies did not present baseline characteristics of the participants within their intervention arms so it is unclear how similar the groups were at baseline. The description of withdrawals were assessed as being adequate in four studies,[4,56–58] but only one of these studies also described an adequate ITT analysis.[56] Overall these studies are at a high risk of bias, which may affect the direction of any effects shown, and care should be taken in the interpretation of the results.

The CCT[54] was similarly judged to be only of low quality, the baseline characteristics between the study arms were unknown, the blinding of outcome assessors was unclear, and the report does not refer to withdrawals and dropouts or any ITT analysis. The results of this study should also be interpreted cautiously due to the high risk of bias.

Results of studies in secondary care with immediate follow-up

The results of studies in secondary care are reported in *Table 10*.

Softeners only studies

There were no studies that assessed the use of softeners alone and followed participants up immediately.

Softeners and irrigation studies

Adults

One study[55] was included that compared the use of chlorobutanol, sodium carbonate and saline (and subsequent irrigation) in an adult population and followed participants immediately afterwards.

TABLE 8 *Quality of included RCTs, secondary care studies*

Study	Randomisation	Concealment of allocation	Baseline characteristics	Eligibility	Blinding of assessors	Care-provider blinding	Patient blinding	Reporting outcomes	ITT	Withdrawals explained
Caballero, 2005[55]	Un	Un	Un	Par	Un	Un	Un	In	In	In
Dubow, 1959[57]	In	Un	Un	**Ad**	Un	Un	Un	In	In	**Ad**
Chaput de Saintonge, 1973[59]	Un	**Ad**	Un	In	Un	**Ad**	**Ad**	In	In	In
Keane, 1995[4]	Un	Un	Un	Un	Un	Un	Un	In	In	**Ad**
Fraser, 1970[60]	In	In	Un	Un	In	In	In	In	In	In
Pothier, 2006[56]	Par	In	Rep	**Ad**	In	In	In	In	**Ad**	**Ad**
Saloranta, 2005[58]	In	Un	Un	**Ad**	Un	Un	Un	In	In	**Ad**

Ad, adequate; In, inadequate; ITT, intention to treat; Par, partial; Rep, reported; Un, unknown. (See Appendix 1.)

TABLE 9 *Quality of included CCT, secondary care studies*

Study	Baseline characteristics	Eligibility	Blinding of assessors	Reporting outcomes	ITT	Withdrawals explained	Representativeness
Fahmy, 1982[54]	Un	Par	Un	Par	Un	Un	Un

ITT, intention to treat; Par, partial; Rep, reported; Un, unknown. (See Appendix 1.)

Measures of occlusion

Caballero and colleagues[55] reported the proportion of participants in which the TM was completely visualised after treatment and irrigation. The study reports that there were no statistically significant differences among treatments with chlorobutanol, sodium carbonate or saline (66%, 55% and 43% for the three groups, respectively), although it was unclear from the study what the statistical analysis was testing. No baseline measures of the degree of occlusion were presented.

Measures of ease of wax removal

Caballero and colleagues[55] did not report these outcomes.

Measures of participant satisfaction

Caballero and colleagues[55] did not report these outcomes.

Measures of recurrence

Caballero and colleagues[55] did not report these outcomes.

Adverse events

Caballero and colleagues[55] did not report AEs.

Children

One study[57] comparing hydrogen peroxide, mineral oil or TP in children, with an immediate follow-up, was included.

Measures of occlusion

Dubow[57] reported the number of children with clearance of cerumen after treatment and syringing. The proportions of children rated as clear were 35% in the hydrogen peroxide group, 42% in the mineral oil group, and 70%

in the TP group. The study did not report statistical significance testing on this data. No baseline measures of the degree of occlusion were presented.

Measures of ease of wax removal
Dubow[57] did not report these outcomes.

Measures of participant satisfaction
Dubow[57] did not report these outcomes.

Measures of recurrence
Dubow[57] did not report these outcomes.

Adverse events
One child in the Dubow[57] study was reported to have an itching erythematous eruption of the external auditory meatus and surrounding area of the pinna of the ear. It was not clear to which group this child was allocated.

Mixed or unknown populations
One study[59] in a mixed-population group immediately followed up participants having either TP or olive oil and subsequent syringing.

Measures of occlusion
Comparing TP with olive oil, Chaput de Saintonge and Johnstone[59] reported that 63% of participants in the TP group and 60% of participants in the olive oil group had complete removal of earwax at immediate follow-up. Rates of those with partial wax removal were 38% and 29% for the two groups, respectively. There were no participants in the TP group and 11% of participants in the olive oil group for whom the amount of wax removed was classified as negligible. The study reports that there were no statistically significant differences between the two intervention groups but the *p*-value was not presented. No baseline measures of the degree of occlusion were presented.

Measures of ease of wax removal
Chaput de Saintonge and Johnstone[59] report that the volume of water used for syringing was statistically significantly less in the TP intervention arm than in the olive oil arm of their study; $p < 0.05$.

Measures of participant satisfaction
Chaput de Saintonge and Johnstone[59] did not report these outcomes.

Measures of recurrence
Chaput de Saintonge and Johnstone[59] did not report these outcomes.

Adverse events
Chaput de Saintonge and Johnstone[59] did not report AEs.

Results of studies in secondary care with delayed follow-up

The results of studies in secondary care are reported in *Table 10*.

Softeners only studies
Adults
One study[4] was included that included adults and had the intention to assess outcomes after the use of only a softening agent, after a period of follow-up. The study compared Cerumol, sodium bicarbonate, water and no treatment, and follow-up was after 5 days.

Measures of occlusion
Keane and colleagues'[4] comparison of Cerumol, sodium bicarbonate, water and no treatment assessed the proportion of ears still impacted after treatments. The proportions appear to be similar between the groups (Cerumol 16%, sodium bicarbonate 21%, water 18%, no treatment 26%), except for a slightly higher proportion remaining impacted in the 'no treatment' group. No *p*-values or baseline measures of the degree of occlusion were reported. The proportion of ears assessed as moderately clear were statistically significantly different between the Cerumol (15%) and the 'no treatment' group (10%) only; $p < 0.05$. The proportion of ears assessed as completely clear was reported to be statistically significantly different between the Cerumol versus control group, the sodium bicarbonate versus control group and the water versus control group (Cerumol 9%, sodium bicarbonate 8%, water 8%, no treatment 2%) – all $p < 0.05$.

Measures of ease of wax removal
Keane and colleagues[4] did not report these outcomes.

Measures of participant satisfaction
Keane and colleagues[4] did not report these outcomes.

Measures of recurrence
Keane and colleagues[4] did not report these outcomes.

Adverse events
No participants were reported to have any irritation or contact sensitivity from any of the treatments in the Keane and colleagues[4] study.

Children

There were no studies in children that assessed the use of softeners alone with a delayed follow-up.

Mixed or unknown populations

One study[54] was included that assessed the use of a softening agent after a follow-up period of 1 week in an unknown population. Fahmy and Whitefield[54] undertook two comparisons in secondary care (see Chapter 3, studies in secondary care settings, for primary care comparison). In one, a comparison of Exterol and glycerol was made and in the second a comparison of Exterol and Cerumol was made.

Measures of occlusion

In the study comparing Exterol with glycerol, Fahmy and Whitefield[54] found that in 15% of ears in the Exterol group the earwax had dispersed at follow-up; however, no ears in the glycerol group were identified where the earwax had dispersed after treatment. No statistical significance testing was reported. Participants with earwax remaining then went on to receive syringing (see below). In this study at baseline some 90% of participants in both the Exterol and the glycerol group had total occlusion of the TM. The remaining 10% in each group were rated as having partial occlusion at baseline. There were no data reporting post-treatment outcome in relation to pretreatment assessment in this study, however.

In the second study undertaken by Fahmy and Whitefield,[54] comparing Exterol with Cerumol, the number of ears not requiring syringing was markedly greater (40%) with Exterol than with Cerumol (10%), $p < 0.001$. Participants with earwax remaining then went on to receive syringing (see below). In this study 46% of participants in the Exterol group were considered to have total or subtotal occlusion at baseline. The corresponding figure for the Cerumol group at baseline was 38%. The remaining 54% and 62% for each group, respectively, were rated as having partial occlusion at baseline. There were no data reporting post-treatment outcome in relation to the pretreatment outcome in this study.

Measures of ease of wax removal

In the first Fahmy and Whitefield[54] study comparing Exterol with glycerol, the proportion of ears that were subsequently syringed easily were 85% in the Exterol group and 50% in the glycerol group. No statistical significance testing was reported. The number of ears that were syringed with difficulty was higher in the glycerol group (50%) than the Exterol group (15%), but no statistical significance testing was undertaken. The study reports that when the number of ears not requiring syringing (above) was added to the number syringed easily, Exterol was statistically significantly superior to the control group; $p < 0.001$.

In the Fahmy and Whitefield[54] study comparing Exterol with Cerumol, the number of ears syringed easily were greater in the Exterol group (90%) than the Cerumol group (42%) (p-value not stated) and hence the number of ears syringed with difficulty was greatest in the Cerumol group (58% Cerumol versus 10% Exterol; p-value not stated). The authors report that when the number of ears not requiring syringing (see above) was added to the number syringed easily, Exterol was statistically significantly superior to Cerumol; $p < 0.001$.

Measures of participant satisfaction

Fahmy and Whitefield[54] did not report these outcomes in either of their studies in secondary care.

Measures of recurrence

Fahmy and Whitefield[54] did not report these outcomes in either of their studies in secondary care.

Adverse events

Fahmy and Whitefield[54] did not report AEs.

Softeners and irrigation studies

Adults

There were no studies in adult populations that assessed the use of softeners and irrigation with a delayed follow-up.

Children

There were no studies in children that assessed the use of softeners and irrigation with a delayed follow-up.

Mixed or unknown populations

One study,[60] that assessed the use of a softening agent and irrigation over a delayed period of time in an unknown population, was included. This study compared sodium bicarbonate, olive oil, Cerumol, Waxsol, TP and dioctyl with a same participant control (of no treatment in one ear) over a 3-day period.

Measures of occlusion

Fraser[60] did not report these outcomes.

Measures of ease of wax removal

Ease of syringing was tested between each of the interventions and their corresponding same participant control in the Fraser[60] study and then differences (between intervention and control) were tested across the interventions. No baseline values for the degree of earwax were presented in this study. Cerumol, olive oil and Waxsol showed a positive difference in ease of syringing rating than their respective controls, suggesting that the treatment ear was syringed more easily. TP and dioctyl showed a negative difference suggesting that the control ear was syringed more easily. Sodium bicarbonate was reported to be equivalent to the control. In addition, when the mean differences (between each intervention and same participant control) were compared across interventions, the study author reports that Cerumol differed statistically significantly from sodium bicarbonate ($p < 0.05$), but that all other comparisons were not statistically significant. When the mean rank of the differences (between each intervention and same participant control) were compared across interventions, Cerumol was statistically significantly better than dioctyl and TP ($p < 0.05$).

Similar patterns were seen in the frequency of syringing successes and failures with Cerumol, olive oil and Waxsol rated better than controls, and TP and dioctyl rated worse than controls. However, it should also be pointed out that a number of participants in each of these groups were scored equal to control on the frequency of syringing success and failure.

Measures of participant satisfaction

Fraser[60] did not report these outcomes.

Measures of recurrence

Fraser[60] did not report these outcomes.

Adverse events

Frequency of otitis externa (inflammation of the external meatus) was reported by Fraser.[60] There were 12 ears (4%) that had otitis externa: in three ears it was reported to be bilateral and probably not due to the study; of the remaining six ears, three ears had received sodium bicarbonate, two Waxsol and one TP.

Additional studies

Along with the above studies in secondary care (*Table 10*), two additional studies were included which do not fit into the categories of softeners alone or softeners and syringing, owing to their interventions. The first (Pothier and colleagues[56]) compared two different de-waxing techniques: endoscopic otoendoscope de-waxing and microscopic de-waxing. The second (Saloranta and colleagues[58]) treated participants who had earwax removed by syringing at an initial evaluation with either a skin oil or no treatment, to evaluate recurrence over a 12-month period.

De-waxing techniques

Pothier and colleagues[56] compared two different de-waxing techniques; endoscopic otoendoscope de-waxing and microscopic de-waxing. On a visual analogue scale (VAS) of 0–100 the difficulty of de-waxing was rated as less difficult in the endoscopic group (score 9) than in the microscopic group (score 20); $p = 0.005$. This corresponds to the difference in time taken to perform the de-waxing, which was also statistically significantly different between the two groups, where the endoscopic de-waxing took less time (1.8 versus 3.3 minutes; $p = 0.001$). Endoscopic de-waxing was also rated by participants (on a scale of 0–100) as causing less discomfort (score 5 versus 25) and less pain (score 3.5 versus 10) than the microscopic de-waxing procedure respectively (p-values for statistical significance = 0.002 and 0.075, respectively). At baseline 40% of participants in the endoscopic de-waxing arm and 52% of participants in the microscopic de-waxing arm had complete occlusion of the TM but this difference was not statistically significantly different; $p = 0.69$.

No complications were reported during de-waxing; however, one participant from each group sustained minor bleeding from ear canals. Five participants from the endoscopic group required conversion to microscopic de-waxing (three were successfully de-waxed, two were sent home with cerumenolytics) and two participants in the microscopic group were converted to endoscopic de-waxing (one was successfully de-waxed, one was sent home with cerumenolytics).

Prevention of recurrence

Saloranta and colleagues[58] treated participants who had earwax removed by syringing at initial evaluation with either a skin oil (self-administered in those without learning difficulties) or no treatment, to evaluate recurrence over a 12-month period. Recurrence of impacted cerumen was seen in 23% of the Ceridal skin-oil-treated participants compared with 61% in those participants with no treatment ($p < 0.05$). The recurrence in treated ears was also statistically significantly less in the skin-

TABLE 10 *Outcomes of treatments in secondary care*

Immediate follow-up – adult population – softeners and irrigation as primary objective

Caballero and colleagues, 2005[55]

Proportion of TM completely visualised

Chlorobutanol (*n* = 32)	Sodium carbonate (*n* = 29)	Saline (*n* = 28)	*p*-value
21/32 (65.6%)	16/29 (55.2%)	12/28 (42.9%)	$p = 0.209$

Immediate follow-up – child population – softeners and irrigation as primary objective

Dubow, 1959[57]

Clearance: no. of cases (%)

Hydrogen peroxide (*n* = 20)	Mineral oil (*n* = 19)	TP (*n* = 20)	*p*-value
7 (35%)	8 (42%)	(14) 70%	Not reported

Immediate follow-up – mixed populations – softeners and irrigation as primary objective

Chaput de Saintonge and Johnstone, 1973[59]

	TP (*n* = 32)	Olive oil (*n* = 35)	*p*-value
Amount of wax removed (n)			
Complete	20	21	States ns, but *p*-value not reported
Partial	12	10	
Negligible	0	4	
Volume of water used (*n*): (estimated by reviewer)			
150 ml	7	1	Overall $p < 0.05$
300 ml	14	14	TP needed smaller volumes of water than olive oil
450 ml	4	6	
600 ml	2	2	
750 ml	0	2	
900 ml	1	7	

Delayed follow-up – adult population – softeners alone as primary objective

Keane and colleagues, 1995[4]

	Cerumol (*n* = 24)	Sodium bicarbonate (*n* = 25)	Water (*n* = 24)	Control (*n* = 38)	*p*-value
Impacted, % (*n*, ears)	40.0 (16)	53.8 (21)	47.4 (18)	68.4 (26)	
Moderately clear, % (*n*, ears)	37.5 (15)	25.6 (10)	31.6 (12)	26.3 (10)	$p < 0.05$, Cerumol vs control
Completely clear, % (*n*, ears)	22.5 (9)	20.6 (8)	21.0 (8)	5.3 (2)	$p < 0.05$, Cerumol vs control $p < 0.05$, sodium bicarbonate vs control $p < 0.05$, water vs control

continued

TABLE 10 *Outcomes of treatments in secondary care (continued)*

Delayed follow-up – mixed populations – softeners alone as primary objective

Fahmy and Whitefield, 1982[54] (see* Table 6 *for results of study in primary care)

Study 1

	Exterol (*n* = 20, ears *n* = 40)		**Glycerol control (*n* = 20, ears *n* = 40)**		
	Initially very hard wax	**Initially hard wax**	**Initially very hard wax**	**Initially hard wax**	***p*-value**
Wax dispersed without syringing, ears	–	6	–	–	Not stated
Syringed easily, ears	15	14	2	18	Not stated
Syringed with difficulty, ears	5	–	14	6	Not stated

Study 2

	Exterol (*n* = 25, ears *n* = 50)			**Cerumol (*n* = 25, ears *n* = 50)**			
	Initially v hard	**Initially hard**	**Initially soft**	**Initially v hard**	**Initially hard**	**Initially soft**	***p*-value**
Wax dispersed without syringing, ears	4	14	2	–	–	5	$p < 0.001$
Syringed easily, ears	6	18	3	–	10	9	
Syringed with difficulty, ears	2	1	–	8	17	1	

Delayed follow-up – mixed populations – softeners and irrigation as primary objective

Fraser, 1970[60] (n = ears)

Ease of syringing

	Sum scores		
	Test ears	**Control ears**	**Difference (mean rank)**
Cerumol (24 ears)	92	122	+30[a] (+11.9)[b]
Olive oil (25 ears)	116	140	+24 (+3.4)
Waxsol (26 ears)	110	128	+18 (+2.8)
Sodium bicarbonate (124 ears)	Control		0 (–3.5)
TP (24 ears)	118	107	–11 (–9.0)
Dioctyl (25 ears)	119	107	–12 (–9.1)

A positive difference indicates that the test were easier to syringe than the control ears.

a Cerumol differed significantly from sodium bicarbonate ($p < 0.05$); all other comparisons were not significant.
b When mean ranks were compared, Cerumol was significantly better than dioctyl and TP ($p < 0.05$).

Frequency of syringing successes and failures

	Product better (*n* participants)	**Scores equal (*n* participants)**	**Control better (*n* participants)**
Cerumol (24 ears)	15	5	4
Olive oil (25 ears)	10	6	9
Waxsol (26 ears)	11	6	9
TP (24 ears)	7	7	10
Dioctyl (25 ears)	8	5	12

TABLE 10 *Outcomes of treatments in secondary care (continued)*

No. of ears in which very forceful syringing failed

	Test ears	**Control ears**
Cerumol (24 ears)	1	5
Olive oil (25 ears)	2	4
Waxsol (26 ears)	3	5
TP (24 ears)	5	3
Dioctyl (25 ears)	5	2

Appearance of wax removed by syringing

	Percentage of lumps	**Percentage partially broken up**	**Percentage completely broken up**
Cerumol (24 ears)	46	37	17
Olive oil (25 ears)	40	44	16
Waxsol (26 ears)	15	46	39
Sodium bicarbonate (124 ears)	33	43	24
TP (24 ears)	42	25	33
Dioctyl (25 ears)	36	44	20

De-waxing techniques

Pothier and colleagues, 2006[56]

	Endoscopic otoendoscope de-waxing (*n* = 50)	**Microscopic de-waxing (*n* = 50)**	***p*-value**
Discomfort – median score on VAS (0–100)	5	25	$p = 0.002$
Pain – median score on VAS (0–100)	3.5	10	$p = 0.075$
Difficulty in de-waxing – median score on VAS (0–100)	9	20	$p = 0.005$
Time taken to perform de-waxing (minutes)	1.8	3.3	$p = 0.001$

Prevention of recurrence after removal of cerumen

Saloranta and colleagues, 2005[58]

	Ceridal skin-oil (*n* = 13)	**No treatment (*n* = 18)**	***p*-value**
Recurrence of cerumen impaction	3 (23%)	11 (61%)	$p < 0.05$
Recurrence in treated ears	3/16 (19%)	15/29 (52%)	$p < 0.05$

ns, not significant; TP, triethanolamine polypeptide; VAS, visual analogue scale.

TABLE 11 *Characteristics of studies of self-care*

Study	Interventions	Participants	Outcomes
Author: Coppin and colleagues, 2008[63] Country: UK Number of centres: Seven primary care practices Design: RCT Setting: Self-care/primary care Follow-up: 1–2 weeks for comparison of interventions; within 6 weeks for assessment of further treatment AEs, rates and reasons for non-participation or non-compliance	1. Sodium bicarbonate for ≥ 2 days (dose not reported) and self-irrigation (n = 118) 2. Sodium bicarbonate for ≥ 2 days (dose not reported) and irrigation by practice nurse (n = 119)	*Target population*: Adults consulting a GP or practice nurse with symptoms of occluding earwax (itching, sensation of blockage, reduced hearing) consenting to inclusion in study *Baseline characteristics*: Age, mean years (SD): 1. 57 (14) 2. 55 (16) Gender M/F: 1. 66:34 2. 63:37	*Primary outcomes*: Reported symptoms and wax clearance *Secondary outcomes*: Further treatment required and acceptability of treatment
Author: Harris 1968[64] Country: Ireland Design: RCT Number of centres: One Setting: Self-care/primary care Follow-up: 1 day	1. TP (enough ear drops to fill the ear and left in overnight) plus self-irrigation with warm water (maximum of 12 squirts) the morning after (n = 24) 2. Control: No softener, self-irrigation with warm water (maximum of 12 squirts) in the morning only (n = 21)	*Target population*: All participants attending surgery and complaining of symptoms directly attributable to ceruminosis *Baseline characteristics*: Age and gender not reported	*Primary outcomes*: (Not stated as primary or secondary) Wax clearance Meati clearance Colour cerumen Symptoms AEs

AEs, adverse events; F, female; M, male; RCT, randomised controlled trial; SD, standard deviation; TP, triethanolamine polypeptide.

oil-treated group (19%) than the non-treated group (52%); $p < 0.005$. The study also reports that there were no AEs observed in either group.

Studies of self-care

Two RCTs[63,64] investigated the use of self-irrigation after participants had been assessed for earwax in primary care. One[63] compared self-irrigation to nurse irrigation in adult participants who had been given sodium bicarbonate to use for at least 2 days. The follow-up was 1–2 weeks later for the comparison of interventions. A later follow-up (within 6 weeks) was undertaken to assess the need for further treatment and for the assessment of AEs and adherence to treatment. The other study[64] randomised participants to either TP overnight and self-irrigation in the morning, or just self-irrigation in the morning. Both studies used soft bulb irrigators and followed up participants subsequent to the irrigation attempts. *Table 11* shows the characteristics of the two self-care studies.

The quality of the included RCT of self-irrigation[63] (*Table 12*) compared with nurse irrigation was assessed as having reasonable quality. The method of generating the randomisation sequence and the concealment of allocation were rated as being adequate. These factors limit the risk from selection bias. Blinding of the participants and care-providers was not possible due to the nature of the intervention; however, the outcome assessors could have been blinded to the treatment allocation and this was therefore judged as inadequate. Withdrawals were reported but there appeared to be additional numbers missing in the analysis of many of the outcomes and there was no discussion of the application of an ITT principle to the analysis of data. The RCT of self-irrigation with or without a previous softener[64] was assessed to be of low methodological quality. Details of the randomisation schedule and allocation were not adequately described and it is also unclear whether the outcome assessors were blinded to treatment allocation.

TABLE 12 *Quality of included RCT of self-care*

Study	Randomisation	Concealment of allocation	Baseline characteristics	Eligibility	Blinding of assessors	Care-provider blinding	Patient blinding	Reporting outcomes	ITT	Withdrawals explained
Coppin, 2008[63]	**Ad**	**Ad**	Rep	Un	In	N/A	N/A	**Ad**	In	Par
Harris, 1968[64]	Un	Un	Un	Par	Un	Un	Un	In	In	**Ad**

Ad, adequate; In; inadequate; ITT, intention to treat; Par, partial; Rep, reported; Un, unknown; N/A, not applicable. (See Appendix 1.)

Results of studies in self-care settings

The results of studies in self-care are reported in *Table 13*.

Measures of occlusion

In the study by Coppin and colleagues,[63] at baseline 63% of participants in the self-irrigation group had a completely occluded right ear and 67% a completely occluded left ear. In the nurse irrigation group these proportions were similar (62% with completely occluded right ear and 69% with a completely occluded left ear). After treatment the degree of obstruction was rated on a 4-point scale (0 = no or minimal wax with TM fully visible; 1 = minor amount of wax with TM essentially visible; 2 = moderate amount of wax with TM partially obscured; 3 = complete occlusion of TM) by a treatment nurse. Based on this nurse-evaluated score, wax 'clearance' (a combined score of 0 and 1) was seen in 48% of those in the self-irrigation group compared with 63% in the nurse-irrigation group; $p = 0.03$. There were no baseline data of the degree of obstruction using this particular scale hence no data on the post-treatment outcome in relation to the pretreatment outcome were presented. This score was reported to have been used in a pilot study by the report authors, and a reference is provided, although it is also not clear if this was a fully validated measure.

The proportion assessed as not requiring further clearance in the Coppin and colleagues[63] study was higher in the nurse-irrigation group (69%) compared with those in the self-irrigation group (51%); $p < 0.01$. This assessment was undertaken by a GP or a nurse who may or may not have carried out the pretreatment assessment (28% were by the same nurse).

Harris[64] reported the number of participants with complete clearance versus partial or incomplete clearance of earwax, with statistically significantly higher proportions of participants seen with completely cleared ears in the TP softened group ($p < 0.005$). Of those with completely obscured TM at baseline ($n = 14$ per treatment group) in the TP softening group, eight participants were completely cleared after treatment. In the self-irrigation only group no participants were completely cleared after treatment. Of those with partially obscured TM at baseline ($n = 10$) in the TP softening group, all 10 were reported to be cleared at follow-up. In the self-irrigation-alone group, seven participants had partially obscured TM at baseline and just one was cleared at follow-up (*Table 13*). Subsequent to follow-up, six TP participants had softened wax cleared in primary care with gentle syringing and 19 participants in the control group had wax cleared with normal syringing after examination at the surgery.

Measures of ease of wax removal

Coppin and colleagues[63] and Harris[64] did not assess these measures.

Measures of participant satisfaction

On a self-reported symptom score that ranged from 0 (no symptoms) to 6 (severe symptoms) which had previously shown high internal reliability in a pilot study, the mean change in score from baseline in the Coppin and colleagues[63] study was better in those participants in the nurse-irrigation group than the self-irrigation group [difference –0.45 (95% CI –0.11 to –0.79; $p = 0.01$)].

In the Coppin and colleagues study,[63] satisfaction with treatment was assessed on a 7-point scale that had previously been used in a pilot study.

TABLE 13 *Outcomes of studies with a self-care setting*

Coppin and colleagues, 2008:[63] self-irrigation vs nurse irrigation					
	Sodium bicarbonate + self-irrigation (*n* = 118)		**Sodium bicarbonate + nurse irrigation (*n* = 119)**		**Difference groups (95% CI); *p*-value**
Wax clearance (obstruction score 0 or 1), *n* (%)	50/104 (48)		64/102 (63)		15% (1% to 28%); $p = 0.03$
Requires no further clearance (based on normal clinical practice), *n* (%)	51/100 (51)		66/95 (69)		18% (5% to 32%); $p < 0.01$
Mean (SD) change in symptom score from baseline	–0.81 (1.44)		–1.26 (1.15)		–0.45 (–0.11 to –0.79); $p = 0.01$
Satisfied with treatment, *n* (%) (agreed slightly or more)	78/110 (71)		105/106 (99)		28% (19% to 29%); $p < 0.001$
Use same treatment again, *n* (%) (agreed slightly or more)	82/110 (75)		106/106 (100)		25% (17% to 25%); $p < 0.001$
Treatment convenient, *n* (%) (agreed slightly or more)	84/110 (76)		95/105 (90)		14% (4% to 24%); $p < 0.01$
Harris, 1968:[64] softeners and self-irrigation vs self-irrigation alone					
Clearance					
	TP (*n* = 24)		**Control (*n* = 21)**		***p*-value**
Completely cleared	18		1		$p < 0.005$
Partially or not cleared	6		20		
State of meati	**Completely obscured**	**Partially obscured**	**Completely obscured**	**Partially obscured**	
Before treatment					
	14	10	14	7	ns
After treatment					
Meati cleared	8	10	0	1	
Meati not cleared	6	0	14	6	

CI, confidence interval; ns, not significant; SD, standard deviation; TP, triethanolamine polypeptide.

TABLE 14 *Treatment discomfort and AEs from studies with a self-care setting*

Coppin and colleagues, 2008[63]			
	Sodium bicarbonate + self-irrigation (*n* = 118)	**Sodium bicarbonate + nurse irrigation (*n* = 119)**	**Difference groups (95% CI); *p*-value**
Treatment discomfort (slight or more), *n* (%)	43/100 (39)	35/108 (32)	7% (–6% to 19%); $p = 0.30$
Treatment dizziness (slight or more), *n* (%)	14/100 (13)	14/108 (13)	0% (–9% to 9%); $p = 0.96$
Infection, *n* (%)	1/97 (1)	1/93 (1)	0% (–3% to 3%); $p = 1.00$
Perforation, *n* (%)	1/97 (1)	1/94 (1)	0% (–3% to 3%); $p = 1.00$
Signs of trauma, *n* (%)	1/97 (1)	1/94 (1)	0% (–3% to 3%); $p = 1.00$

CI, confidence interval.

The proportion of participants who rated their satisfaction with treatment as satisfied slightly or more was higher in the nurse-irrigation group than the self-irrigation group, a difference of 28% (95% CI 19% to 29%); $p < 0.001$. It was unclear whether this scale was a fully validated measure of satisfaction with treatment.

Harris[64] did not report satisfaction as an outcome.

Measures of recurrence

Neither Coppin and colleagues[63] or Harris[64] assessed these measures.

Adverse events

There were no statistically significant differences between the two groups in the rating of treatment discomfort [difference of 7% (95% CI –6% to 19%)] in the Coppin and colleagues[63] study (*Table 14*). There were also no statistically significant differences between rates of dizziness, infection, perforation or signs of trauma (differences between groups for each type = 0%). One participant in the nurse-irrigation group had bilateral otitis externa. Of the two participants that had perforations (one in each group), one had old scarring on the TM and one had pre-existing cholesteatoma (unclear which group each belonged to). In the Harris[64] study, AEs were reported as one participant in the TP arm suffering erythema around the external auditory meatus. No other AEs were reported.

Studies in other care settings

One RCT[62] was undertaken in a corporate research clinic in adult volunteers with excessive or impacted cerumen on examination (*Table 15*). The study compared TP, Murine and placebo with saline, and follow-up was immediate. One CCT[61] was undertaken in a military research unit in a population of adult entrants to the Royal Air Force who had impacted cerumen (*Table 15*). The study compared sodium bicarbonate, Cerumol, hydrogen peroxide, olive oil and 'no treatment' control. Follow-up was also immediate. Both studies also followed the softening agents with an irrigation procedure before assessing the outcomes.

The quality of reporting and methodology of the included studies was generally poor (*Tables 16* and *17*). In the RCT the randomisation schedule and the concealment of allocation were unknown, which

TABLE 15 *Characteristics of studies in other care settings*

Corporate research unit: adult population with immediate follow-up			
Author: Roland and colleagues, 2004[62] Country: USA Number of centres: One Design: RCT Setting: Corporate research clinic Follow-up: Immediate	1. TP: Dose not reported (n = 24) 2. Murine: Dose not reported (n = 26) 3. Placebo: Dose not reported (n = 24)	*Target population*: ≥ 18-year-old company employees, volunteering with excessive or impacted cerumen, required to have mild, moderate or complete cerumen occlusion *Baseline characteristics*: Age, mean years (range): 45 (22–66) overall (no individual group details) Gender M/F 51:23 (M/F ratio): (2.2:1)	*Main outcome*: Post-treatment level of occlusion *Other outcome*: Otological signs and symptoms
Military research unit: adult population with immediate follow-up			
Author: Hinchcliffe, 1955[61] Country: UK Number of centres: One Design: CCT Setting: Military Follow-up: Immediate	1. Sodium bicarbonate BPC: 5 drops (*n* = 37 ears) 2. Cerumol: 5 drops (*n* = 37 ears) 3. Hydrogen peroxide BPC: 5 drops (*n* = 37 ears) 4. Olive oil BP: 5 drops (*n* = 37 ears) 5. Control: No treatment (*n* = 37 ears)	*Target population*: Adult entrants to the Royal Air Force in the 1950s, found to have hard wax obscuring the meatus in one or both ears on entrant examination *Baseline characteristics*: Age: Not reported Gender: Not reported	No. of occasions wax meatus was not cleared within specified 5 minutes No. of cases with symptoms of discomfort

BP, British Pharmaceutical grade; BPC, British Pharmaceutical Codex; CCT, controlled clinical trial; F, female; M, male; RCT, randomised controlled trial; TP, triethanolamine polypeptide.

TABLE 16 *Quality of RCT in other care setting*

Study	Randomisation	Concealment of allocation	Baseline characteristics	Eligibility	Blinding of assessors	Care-provider blinding	Patient blinding	Reporting outcomes	ITT	Withdrawals explained
Roland, 2004[62]	Un	Un	In	**Ad**	**Ad**	Par	**Ad**	**Ad**	In	**Ad**

Ad, adequate; In; inadequate; ITT, intention to treat; Par, partial; Rep, reported; Un, unknown; N/A, not applicable. (See Appendix 1.)

TABLE 17 *Quality of CCT in other care setting*

Study	Baseline characteristics	Eligibility	Blinding of assessors	Reporting outcomes	ITT	Withdrawals explained	Representativeness
Hinchcliffe, 1955[61]	Un	**Ad**	Par	In	In	Un	Un

Ad, adequate; In; inadequate; ITT, intention to treat; Par, partial; Rep, reported; Un, unknown; N/A, not applicable. (See Appendix 1.)

may lead to an increased risk of selection bias. Blinding of outcome assessors and the participant were judged to be adequate, with blinding of the caregiver judged as partially met. The number of withdrawals was discussed, but there was no discussion on an analysis based on the ITT principle. The CCT was judged to meet the criteria only partially for blinding of outcome assessors, but the reporting of outcomes and any withdrawals values was inadequate. These studies are at a high risk of bias, which may affect the direction of any effects shown. Caution is therefore required when interpreting the results.

Results of studies in other care settings

The results of studies in other care settings are reported in *Table 18*.

Measures of occlusion

Participants in the RCT by Roland and colleagues[62] were assessed for the degree of occlusion after treatment and syringing. The proportion of participants classified as having no occlusion was highest in the placebo group (41.7%). In the TP group the proportion with no occlusion was 29.2% and in the Murine group this was 15.4%. The proportion of participants classified as having mild, moderate or complete occlusion were subsequently lower in the placebo group and higher in the TP and Murine groups. While these data suggest that the placebo group had better outcomes than the TP and Murine groups, there were no statistically significant effects shown ($p = 0.06$). The change from baseline in the degree of occlusion was presented in a figure and estimated by a reviewer. This suggests that there was resolution of the earwax in 30% of the TP arm, 16% in the Murine arm and 42% in the placebo arm, but the differences were not tested statistically. The proportion rated as having an improvement in the amount the earwax was also higher in the placebo group (8% TP, 7% Murine, 22% placebo), and the proportion rated as having no change or a worsening of earwax was lower in the placebo group (62% TP, 77% Murine, 38% placebo), although again this was not tested for statistical significance. The degree of occlusion seen at baseline was not presented per intervention group,

but the level of occlusion across all participants was presented.

Measures of ease of wax removal

In the Hinchcliffe CCT[61] the outcome assessed was the number of occasions the wax meatus was not cleared within a prespecified 5 minutes. In all groups the proportions not cleared in the time frame were generally low (sodium bicarbonate 16%, Cerumol 19%, hydrogen peroxide 11%, olive oil 5% and control 24%), although the control arm appeared to have more participants 'not cleared' than the other comparisons. The study reports that olive oil was statistically significantly better than no treatment at all, but no *p*-value was reported to support this.

Measures of participant satisfaction

These outcome measures were not assessed by Roland and colleagues[62] or Hinchcliffe and colleagues.[61]

Measures of recurrence

These outcome measures were not assessed by Roland and colleagues[62] or Hinchcliffe and colleagues.[61]

Adverse events

In the Roland and colleagues[62] RCT, rates of related AEs were low in all groups. One participant in the TP group and two in the Murine group had ear pruritis. One participant in the placebo group had ear discomfort and one participant in the TP group had contact dermatitis. There was only one AE classed as unrelated by the study authors, this was a case of vertigo seen in the TP group.

In the Hinchcliffe[61] CCT AEs were only reported as numbers, no details of specific AEs were reported. All treatments except the control were associated with some AEs; these appeared to be higher in the Cerumol treatment arm ($n = 22$) than in the other treatments (sodium bicarbonate $n = 4$; hydrogen peroxide $n = 6$; olive oil $n = 4$), but no statistical significance testing was undertaken. The study author reports that symptoms of discomfort occurred significantly more often for Cerumol than for any other preparation, but no further data were reported to support this.

Outcomes of the above two studies are shown in *Table 18*.

TABLE 18 *Outcomes of studies in other care settings*

Roland and colleagues, 2004[62]						
Degree of occlusion						
	TP (*n* = 24)		**Murine (*n* = 26)**		**Placebo (*n* = 24)**	***p*-value**
None, *n* (%)	7 (29.2)		4 (15.4)		10 (41.7)	TP vs placebo $p = 0.37$
Mild, moderate or complete occlusion	17 (71)		22 (85)		14 (58)	Murine vs placebo $p = 0.06$
Change from baseline in occlusion (estimated by reviewer)						
	Resolved: 30%		Resolved: 16%		Resolved: 42%	Not tested
	Improved: 8%		Improved: 7%		Improved: 22%	
	No change/worse: 62%		No change/worse: 77%		No change/worse: 38%	
Hinchcliffe, 1955[61] (*n* = ears)						
	Sodium bicarbonate (*n* = 37)	**Cerumol (*n* = 37)**	**Hydrogen peroxide (*n* = 37)**	**Olive oil (*n* = 37)**	**Control (*n* = 37)**	***p*-value**
No. of occasions wax meatus was not cleared within specified 5 minutes	6 (16%)	7 (19%)	4 (11%)	2 (5%)	9 (24%)	

TP, triethanolamine polypeptide.

Summary of results of the systematic review of clinical effectiveness

Quantity, quality and nature of evidence

- Twenty-six clinical trials conducted in primary care (14 studies), secondary care (eight studies) or other care settings (four studies), met the inclusion criteria for the review. Of these studies, there were 22 RCTs and four CCTs.
- The evidence on the clinical effectiveness of the different methods of earwax removal was diverse in terms of the people, interventions, comparators and outcomes assessed. Many of the studies suffered from limitations associated with the completeness of reporting of methods and results. For those where information was presented, they were generally considered to be of poor quality, with many studies providing only partial or inadequate consideration of potential biases. Many of the differences and inadequacies may reflect the long period during which the research findings have emerged (1950–2007), with changes to clinical practice and developments in the principles for the conduct of research evident.
- A range of interventions have been used in the studies involving 16 different softeners with or without irrigation in various different comparisons. Most comparisons are of different oil-based softeners against water-based softeners. Doses are not always reported and timing of the intervention and follow-up assessment varies across the studies.
- Participants in the trials also varied across the studies, in terms of age, sex and extent of earwax problem. In some cases few details of baseline characteristics are given in the study reports, so interpretation of results is difficult.
- A range of outcome measures were reported across the studies often with limited information on the definition of these outcomes, making it difficult to assess their validity and objectivity, and how consistently they were applied. For example, measures of earwax removal might be reported in terms of clearance or visualisation of TM (described as complete, partial or negligible) or in terms of impaction or occlusion (described as none, mild, moderate or severe). Ease of earwax removal was reported in terms of number of attempts or the amount of liquid needed to achieve some degree of success. As a consequence, a pragmatic approach was taken to classify outcomes under these categories despite no evidence that these are directly comparable between studies.
- Some studies reported measures of participant satisfaction, but these were not always assessed with valid measures. Measures of recurrence were rarely reported as most studies were of a short time frame. AEs were rarely reported.
- Data analysis conducted in the trials was also variable with several studies not reporting the analytic approach used or results of statistical tests.
- Due to these methodological issues, summarising the results of included studies was difficult and meta-analysis impossible. As such, care should be taken in interpreting the findings of the studies.

Results

- Considering the studies that report statistical significant differences in outcomes *measuring clearance of earwax* (*Tables 19* and *20*) and ignoring any variations in methodological quality, results assessing the extent and ease of clearance of wax show that Cerumol, sodium bicarbonate, olive oil and water are all more effective than no treatment at removal of earwax; Cerumol is better than dioctyl, TP and sodium bicarbonate for ease of subsequent irrigation; TP is better than olive oil in the volume of water used in syringing; Audax is better than Earex for ease of removal by subsequent irrigation; Exterol and Otocerol are better than Cerumol in terms of the number of people requiring irrigation after treatment with softeners.
- Other comparisons show that wet irrigation is better than dry irrigation for *ease of removal*; sodium bicarbonate drops followed by nurse irrigation is more effective than sodium bicarbonate drops followed by self-irrigation; softening with TP and self-irrigation is more effective than self-irrigation only; endoscopic de-waxing is better than microscopic de-waxing; recurrence of earwax and impacted earwax is less in ears that are treated with skin oil than those not treated.
- *Patient satisfaction* was assessed in five studies through several different measures. Over 85% of people in two studies found the use of dioctyl-medo, oil-based softeners, Waxsol and Cerumol tolerable. In two other studies the effectiveness of softeners as judged by patients ranged from 29% for Earex to between 42% and 93% for Audax and 100% for Cerumol.

TABLE 19 *Summary of results on measures of occlusion by interventions*

Comparison	Study	Measure(s)[a]	Statistical significance
Audax			
1. Audax 2. Earex	1. Lyndon and colleagues 1992[45]	Degree of impaction: None, mild, moderate or severe	Not statistically significant (no *p*-value reported)
Cerumol			
1. Cerumol 2. Exterol	1. Fahmy and Whitefield 1982[54] (study 2)	Wax dispersal without syringing	Statistically significant in favour of Exterol ($p < 0.001$)
	2. Fahmy and Whitefield 1982[54] (study 3)	Wax dispersal without syringing	Statistically significant in favour of Exterol ($p < 0.001$)
1. Cerumol 2. No treatment	1. Keane and colleagues 1995[4]	Clearance: Impacted, moderately clear or completely clear	Statistically significant in favour of Cerumol for completely clear ($p = 0.05$)
Murine			
1. Murine 2. Placebo	1. Roland and colleagues 2004[62]	Occlusion: None or 'mild-moderate-complete'	Not statistically significant ($p = 0.06$)
TP			
1. DS 2. TP	1. Singer and colleagues 2000[49]	TM visualisation: Complete or incomplete	Not statistically significant
1. TP 2. Olive oil	1. Chaput de Saintonge and Johnstone 1973[59]	Amount of wax removed: Complete, partial or negligible	Not statistically significant (no *p*-value reported)
1. TP 2. Murine	1. Roland and colleagues 2004[62]	Occlusion: None or 'mild-moderate-complete'	Not statistically significant ($p = 0.37$)
Sodium bicarbonate preparations			
1. Aqueous sodium bicarbonate 2. Aqueous acetic acid	1. Carr and Smith 2001[52]	Mean change in degree of cerumen	Not statistically significant (no *p*-value reported)
1. Sodium bicarbonate 2. No treatment	1. Keane and colleagues 1995[4]	Clearance: Impacted, moderately clear or completely clear	Statistically significant in favour of sodium bicarbonate for completely clear ($p = 0.05$)
Olive oil			
1. Olive oil 2. No treatment	1. Hinchcliffe 1955[61]	No of times wax meatus not cleared within 5 minutes	Statistically significant in favour of olive oil (no *p*-value reported)
Water			
1. Water 2. No treatment	1. Keane and colleagues 1995[4]	Clearance: Impacted, moderately clear or completely clear	Statistically significant in favour of water for completely clear ($p = 0.05$)

TM, tympanic membrane; TP, triethanolamine polypeptide.
a A number of included studies did not report measures of occlusion as an outcome and a number of other studies did not report any data analyses.

TABLE 20 *Summary of results on measures of ease of wax removal by interventions*

Comparison	Study	Measure(s)[a]	Statistical significance
Audax			
1. Audax 2. Earex	1. Lyndon and colleagues 1992[45]	Ease of syringing: not required, easy, difficult or impossible	Statistically significant in favour of Audax ($p < 0.005$)
Cerumol			
1. Cerumol 2. Dioctyl capsules	1. Fraser 1970[60]	Ease of syringing	Mean ranks comparison statistically significant in favour of Cerumol ($p < 0.05$)
1. Cerumol 2. Sodium bicarbonate	1. Fraser 1970[60]	Ease of syringing	Statistically significant in favour of Cerumol ($p < 0.05$)
1. Cerumol 2. TP	1. Fraser 1970[60]	Ease of syringing	Mean ranks comparison statistically significant in favour of Cerumol ($p < 0.05$)
1. Cerumol 2. Waxsol	2. Fraser 1970[60]	Ease of syringing	Not statistically significant (no *p*-value reported)
1. Cerumol 2. Otocerol	1. Jaffe and Grimshaw 1978[50]	Number of people needing syringing	Statistically significant in favour of Otocerol ($p = 0.05$)
TP			
1. TP 2. Olive oil	1. Chaput de Saintonge and Johnstone 1973[59]	Ease of syringing: volume of water used for syringing	Statistically significant in favour of TP ($p = 0.05$)
Sodium bicarbonate preparations			
1. Sodium bicarbonate 2. Olive oil	1. Fraser 1970[60]	Ease of syringing	Not statistically significant (no *p*-value reported)
Water			
1. Water 2. Self-administered oil	1. Eekhof and colleagues 2001[53]	Mean number of syringing attempts	Not statistically significant ($p = 0.18$)
Olive oil			
1. Olive oil 2. No treatment	1. Hinchcliffe 1955[61]	No. of times wax meatus not cleared within 5 minutes	Statistically significant in favour of olive oil (no *p*-value reported)
Dioctyl-medo			
1. Dioctyl-medo 2. Oil	2. Fraser 1970[60]	Ease of syringing	Not statistically significant (no *p*-value reported)

TP, triethanolamine polypeptide.

a A number of included studies did not report measures of ease of wax removal as an outcome, and a number of other studies did not report any data analyses.

TABLE 21 *Summary of research in progress*

Contact name	Title	Funding body
Dr K Schroeder	Olive oil vs ear syringing for the removal of earwax in primary care: pragmatic randomised trial	Scientific Foundation Board, Royal College of GPs, UK
Mr S Gillett	Microsuction vs instruments for de-waxing: a randomised controlled trial	Royal United Hospital Bath NHS Trust, UK
Dr M Caballero	Chlorobutanol, potassium carbonate, and irrigation in cerumen removal	Hospital Clinic of Barcelona, Spain
Mr S MacKeith	The use of wax softeners (cerumenolytics) before de-waxing: a randomised clinical study	NHS R&D Support Funding, UK
Dr C Hand	The treatment of symptomatic earwax in primary care	None

In another study, people undergoing nurse irrigation were more satisfied than those self-irrigating their ears (difference 28%).

- *Adverse events* appear to be minor, limited in extent and mainly related to irrigation. None of the studies reported perforation of the TM or serious infections. In the majority of studies fewer than 10% of people suffered any AE. Minor pain (0–21%) and irritation/itching of the ear (4–15%) were the main AEs.

Conclusion

Despite the relative benefits of certain softeners in aiding the extent and ease of earwax clearance, it is not possible to say that any one type of softener is superior in clearing earwax with or without subsequent irrigation on the evidence available. Separate studies have found significant benefits from wet syringing compared with dry syringing, from nurse irrigation rather than self-irrigation, and from endoscopic than microscopic de-waxing.

Research in progress

We identified a total of five ongoing trials from our searches (*Table 21*). Schroeder and colleagues aimed to evaluate olive oil as a softening agent, comparing the usual care of self-administered olive oil for 5 days prior to irrigation versus 3 weeks. The primary outcome of the trial was ear canal clearance and the trial was set to finish in 2006.

Gillett and colleagues aimed to investigate the differences in discomfort and/or complications between microsuction and the use of instruments. The trial was set to finish in July 2008, although no subsequent publication has been identified at the time of writing.

The third study by Caballero and colleagues was set in a hospital clinic in Spain and aimed to compare Otocerum® ear drops, Taponoto® ear drops and placebo. This is reported to be a phase IV trial, non-randomised, double-blind and parallel-assignment trial. The primary outcome was the proportion with a completely visualised TM, with either the treatments alone or with irrigation if needed. The study was expected to finish in October 2008 and no publication has so far been identified.

Two other controlled trials were identified from searches of the National Research Register. A study by MacKeith and colleagues was sited at the Bristol Royal Infirmary and aimed to evaluate wax softening agents used immediately prior to de-waxing by microsuction. The outcome was the impact of softening agents on the pain or discomfort of the procedure. The trial was anticipated to end in June 2007 and the trial status is shown as completed.

The second study, by Hand and the Suffolk and Norfolk Research and Development Consortium (SAND), aimed to compare preparations for the treatment of symptomatic earwax. No further details are provided and the trial was set to end in January 2007.

No publication of the trial data for any of the five studies has been found so far.

Chapter 4
Adverse events

Adverse outcomes that are reported to be associated with the removal of earwax, especially from ear irrigation, are well documented in the descriptive literature of the condition[66–68] and also in studies reporting litigation and compensation claims that are related to earwax removal.[34,69,70] These include more serious adverse events (SAEs), which can be broadly grouped into ear infections (otitis externa, otitis media); damage to the ear (external auditory canal, perforation of TM), various levels of discomfort and noises (pain, vertigo, fullness of ear and tinnitus), and both temporary and permanent hearing impairment.[6,67,70] Some literature also suggests that people with diabetes may have an increased risk of suffering from malignant otitis externa as a result of irrigation. This is an infection of the external auditory canal and deep periauricular tissues, and may progress into skull base osteomyelitis with cranial nerve paralysis, and, in rare cases, may result in death.[71,72]

However, despite the perception that there is a potential risk from earwax removal there were very few serious adverse outcomes reported in the RCTs that were identified in the systematic review of clinical effectiveness above (see Chapter 3). This may be due to factors relating to the study design, including small sample sizes and, in many cases, the short duration of follow-up. As such, a wider search of the literature was undertaken to identify any additional studies.

Searching

A targeted search of the literature was undertaken to identify additional studies reporting AEs associated with the removal of earwax, to assess the safety of earwax removal and to inform the economic modelling of the problem. The search was not restricted by study design. The following section complements the clinical effectiveness section, reporting overall results from both the RCTs identified, and any relevant observational studies. No systematic critique of the studies was undertaken; however, key methodological limitations of the studies are discussed in the relevant sections below. In addition, only AEs that the study authors attributed to the interventions were included. The studies were assessed on an ITT basis.

Adverse events from drops alone

Four RCTs[4,44,50,52] were identified that included AEs from using drops alone with no irrigation. These RCTs are all critically assessed and data extracted in the clinical effectiveness section above (see Chapter 3). Two of these RCTs, by Carr and Smith[52] and Keane and colleagues,[4] did not find any AEs. The other two RCTs are shown in *Table 22*. One observational study by Midani and colleagues[73] was identified and data is also summarised in *Table 22*. This was an open-label study of Sofenz cerumenolytic solution in 109 participants with excessive and impacted cerumen. A total of 58 AEs were reported, but only 16 were reported to be directly related to the treatment.

There were major differences in all of the studies in terms of population, drops used, care setting and methodologies used. Therefore, no formal meta-analysis of this data was attempted. However, an estimated probability for individually defined AEs from relevant studies was generated for illustration. An overall probability of an AE occurring was also calculated from the studies that included AEs as outcomes. Caution is required therefore in the interpretation of this data. The ranges of AEs reported for each condition and overall proportion for all AEs from the studies and the one observational study are reported in *Table 22*.

The overall number of AEs was 43 out of a total study population of 407 participants from the RCTs and observational study. The probability of minor AEs occurring was 10.57%. It is worth noting, however, that the probability of AEs may be variable depending on the type of drops used. The Cerumol arm of the Jaffe and colleagues RCT,[74] for example, accounts for 13 AEs, whereas the arm using Otocerol accounts for a further eight AEs out of the total of 43. However, due to

TABLE 22 *Percentage of adverse outcomes due to ear drops alone*

Adverse outcome	Overall probability of AEs in study population (%)	Range of AEs across studies (%)	References
Defined AEs from studies			
Giddiness	0.94	–	Jaffe and Grimshaw[50]
Pain	2.83	–	Jaffe and Grimshaw[50]
Itchiness/pruritus	2.51	2.00–2.75	Dummer and colleagues,[44] Midani and colleagues[73]
Skin irritation/erythema	9.43	4.00–17.92	Jaffe and Grimshaw,[50] Midani and colleagues,[73] Dummer and colleagues[44]
Oedema	3.67	–	Midani and colleagues[73]
Buzzing	2.00	–	Dummer and colleagues[44]
Other ear disorders	4.59	–	Midani and colleagues[73]
All studies that assessed AEs			
	10.57	0–17.92%	Jaffe and Grimshaw,[50] Carr and Smith,[52] Keane and colleagues[a],[4] Dummer and colleagues,[44] Midani and colleagues[73]

AEs, adverse events.
a Control arm with no treatment not included.

the heterogeneity of the studies it is not possible to draw any reliable conclusions about which drops are likely to cause more adverse outcomes than others. Based on data available it would seem that AEs from drops are relatively rare and tend to be of a mild nature.

Adverse events for drops and irrigation

An assumption was made that the reporting of AEs from drops and irrigation would be split into major AEs (those events that would be more likely to require additional treatment or resource use), and minor AEs (those that were likely to be transient and would not require additional treatment).

Major adverse events from drops and irrigation

Sixteen RCTs that included AEs as outcomes were identified. Three of these RCTs did not explicitly state what AEs had occurred and so it was not possible to assess whether the AEs were major or minor in nature, and so they are discussed separately, below. One other study, by Burgess[43] was excluded because only the number of ears syringed were reported and it was not possible to tell how many participants were involved in the trial. Therefore, 12 RCTs were included.

In addition, two observational studies were identified. The first study was a retrospective analysis of 2400 patient records from a tinnitus clinic in the USA, who had experienced severe tinnitus. Eleven participants reported that their tinnitus started as a result of cerumen removal. However, it was not clear how many of the 2400 participants with severe tinnitus had actually received ear irrigation, and there was no clear association between the two events, and so the study was excluded.[75] The other study[76] was a large prospective observational study (952 ears in 622 subjects) of people attending an ENT clinic in Nigeria, who were using drops to soften earwax and then undergoing irrigation of the ear with a Propulse II irrigation system. The only adverse outcomes reported were one participant with vertigo and another with a TM perforation. No minor AEs were reported. The study was undertaken in a different care setting to the UK, and the majority of participants were children, therefore this may limit the generalisability of the studies results. However, the equipment used and the 'wet' phenotype of cerumen is similar to both countries and populations and, as such, the study was included.

As described, the individual RCTs and the one observational study results were used to produce a probability for individually defined AEs. An overall probability of major AEs from drops and irrigation was also generated from all studies that included AEs as outcomes. Caution is recommended in the interpretation of these data. The RCTs were also heterogeneous, with reports from a variety of settings and using several different types of drops and irrigation techniques as active treatments and controls. Furthermore, the external validity of the Nigerian observational study to a UK context requires caution in its interpretation. The ranges of AEs reported for all major AE from the studies are reported in *Table 23*.

There were nine occurrences of AEs in a total study population of 1515 participants. The overall probability of major adverse outcome was therefore 0.59%. Six of the nine AEs came from the Fraser and colleagues study[60] (all otitis externa) involving 124 participants. If this study was excluded then the incidence of AEs would drop to 0.22%. This would be close to the Sharp and colleagues'[6] estimation a 0.1% incidence of major complications based on their otolaryngological unit in Scotland. No incidence of tinnitus, otitis media and hearing loss were reported in any of the included studies.

It would seem that major AEs occur relatively infrequently, but, given the heterogeneous nature of the studies included, this result should be interpreted with caution.

Minor adverse events from drops and irrigation

The same 12 RCTs that were identified for the major AEs section above were all included in this section. No observational studies were identified reporting rates of minor AEs from the literature search. As mentioned above an estimate of the probabilities of minor AEs from drops and ear irrigation were generated. These need to be treated as illustrative only. The ranges of AEs reported for each condition and overall proportion for all AEs from the studies are reported in *Table 24*.

There were 128 occurrences of AEs from a total study population of 893. Overall, the incidence of minor AEs was 14.33% from all the included studies. The Coppin and colleagues' study reported 108 out of the 128 incidences of AEs.[63] The higher incidence of AEs in this study, especially for discomfort and dizziness suggest a more sensitive inclusion of AEs than the other studies.[63] One of

TABLE 23 *Proportion of major adverse outcomes due to drops and ear irrigation*

Adverse outcome	Overall probability of AEs in study population (%)	Range of AEs across studies (%)	References
Defined AEs from studies			
Tinnitus	0	–	No incidence in included studies
Vertigo	0.16	–	Ogunleye and Awobem[76]
Perforated ear drum	0.16	–	Ogunleye and Awobem[76]
Otitis media	0	–	No incidence in included studies
Otitis externa	1.94	0.85–4.84	Coppin and colleagues,[63] Fraser[60]
Permanent hearing loss	0	–	No incidence in included studies
Temporary hearing loss	0	–	No incidence in included studies
All studies that assessed AEs			
	0.59	0–4.84	Ogunleye and Awobem,[76] Coppin and colleagues,[63] Meehan and colleagues,[46] Whatley and colleagues,[47] Singer and colleagues,[49] Pavlidis and Pickering,[42] Amjad and Scheer,[51] Lyndon and colleagues,[45] Saloranta and colleagues[a],[58] Roland and colleagues,[62] Fraser,[60] Dubow,[57] Harris[64]

AEs, adverse events.
a Control arm with no treatment not included.

TABLE 24 *Proportion of minor adverse outcomes due to drops and ear irrigation*

Adverse outcome	Overall probability of AEs in study population (%)	Range of AEs across studies (%)	References
Defined AEs from studies			
Pain	20.83	0	Meehan and colleagues[46]
Itchiness/pruritus	3.01	1.69–4.05	Roland and colleagues,[62] Dubow[57]
Skin irritation/dermatitis	1.94	1.35–2.78	Roland and colleagues,[62] Lyndon and colleagues,[45] Harris[64]
Dizziness	11.03	3.85–11.81	Pavlidis and Pickering,[42] Coppin and colleagues[63]
Discomfort	25.40	1.35–32.91	Roland and colleagues,[62] Coppin and colleagues[63]
Ear bleed	1.09	–	Whatley and colleagues[47]
Ear trauma	0.84	–	Coppin and colleagues[63]
All studies that assessed AEs			
	14.33	0–32.91	Coppin and colleagues,[63], Meehan and colleagues,[46] Whatley and colleagues,[47] Singer and colleagues,[49] Pavlidis and Pickering,[42] Amjad and Scheer,[51] Lyndon and colleagues,[45] Saloranta and colleagues[a],[58] Roland and colleagues,[62] Fraser,[60] Dubow,[57] Harris[64]

AEs, adverse events.
a Control arm with no treatment not included.

the arms in the trial was a self-syringing group and this may also explain the higher number of AEs in the study. If this study was excluded then the probability of minor AEs would fall to 3.05% for the remaining included studies.

Three further RCTs[41,48,61] reported an overall rate of AEs but did not define the adverse outcomes that had occurred therefore it was not possible to determine whether they were major or minor AEs. One of these studies, by Hinchcliffe and colleagues, reported only the number of ears treated and as it was not possible to determine how many participants there were in this trial it was excluded. There was a total 257 participants in the two remaining RCTs.[41,48] There were an estimated 21 AEs (the studies reported AEs only as a percentage of each arm with or without AE). This gave an overall probability of 8.17% for the occurrence of AEs. Another study[76] in Nigeria using drops to soften earwax, and then irrigation of the ear, reported that there were no minor AEs.

The incidence of minor AEs is relatively common compared to the major AEs, but it is unclear how long many of these AEs last. It is likely, however, by their very nature, that they will be relatively transient and have little or no impact on resource use.

Conclusion

The evidence from the included RCTs and the two observational studies suggest that using both drops and ear irrigation are safe techniques for the removal earwax, with the number of SAEs being low. However, some studies may have been more sensitive at including AE data than others, and in many the length of follow-up was not suitable for capturing AEs. These factors and the methodological issues noted above (and in Chapter 3) suggest that care is required before interpreting earwax removal techniques as safe procedures. The probabilities of more SAEs obtained from this simple aggregation technique were not thought to be reliable enough to put into the economic model. The minor incidence rates were felt unlikely to have a major impact on either health-related quality of life (HRQoL) or resource use and so were also not used.

Chapter 5
Economic analysis

The aim of this section is to evaluate the cost-effectiveness of methods of earwax removal. A systematic review of the literature was conducted to identify economic evaluations on the use of softeners with or without irrigation and other methods of earwax removal. An economic model was then developed to compare different strategies to achieve earwax removal. This section will report the results of the systematic review, the rationale and the components of the economic evaluation, including the structure of the model, the sources of data on costs and benefits, assumptions underlying the model, and results of the analysis.

Systematic review

A systematic review of the literature was undertaken to identify economic evaluations considering the treatment of earwax. The methods for the systematic review are described in Chapter 2. The details of the inclusion and exclusion criteria are shown in Appendix 1 and the search strategies are shown in Appendix 2.

No cost-effectiveness studies were identified that met the inclusion criteria for the review.

Southampton Health Technology Assessments Centre (SHTAC) economic analysis

A modelled economic evaluation was undertaken to estimate the comparative cost-effectiveness of three alternative treatment strategies for earwax removal in adults, without any known contraindications to the use of softeners or irrigation.

Rationale for the model structure

With no nationally accepted guidelines for the management of symptomatic earwax in the UK (see Chapter 1, Current service provision and description of interventions), it was recognised that current practice would vary. Reflecting such variations in the economic model would be difficult, if not impossible. As a consequence a simplified model structure was developed using information from available practice guidelines, other published evidence and expert advice from clinicians and other health professionals. The model was developed from the NHS perspective, with each alternative treatment option involving primary care practitioners in diagnosing the condition and recommending subsequent treatment options.

Three options were considered in the economic model with the intention of reflecting current practice for the population under consideration and possible alternatives. The options considered in the model following presentation at primary care are (1) use of softening drops (softeners) for a week with return to the primary care practice for ear irrigation if no spontaneous earwax clearance occurs (current standard practice); (2) use of softeners for a week followed by self-irrigation and return to primary care if unsuccessful for professional irrigation; and (3) 'no treatment'. The 'no treatment' or 'do nothing' option was included in the model as a universal comparator. It represents a hypothetical situation when no treatment is available or offered to the patient or the patient decides not to undergo treatment. Some anecdotal evidence suggests that some primary care practices no longer offer professional irrigation, with the suggestion that the condition will resolve itself. Details of the treatment strategies are provided in Chapter 5 (Model structure).

Population included in the model

The target population includes adults aged 35–44 years with earwax, who are eligible for any of the evaluated treatment alternatives. Patients who have a known contraindication for irrigation (such as current or pre-existing otitis media, vertigo, recurrent ear infection, history of ruptured TM, permanent hearing loss, acute illness or fever) are considered outside the scope of this economic evaluation. Although excessive earwax is more prevalent in older age groups, the 35–44 age group was selected as this was the group for whom evidence of effectiveness was available.

Perspective of the economic evaluation

As already stated, the perspective of the cost-effectiveness analysis is predominately that of the NHS; however, the out-of-pocket expenses on the OTC medications and equipment are also included. The out-of-pocket expenditures include softeners for all patients undergoing active treatments, bulb irrigators for patients choosing self-irrigation, and painkillers and antibiotics for those patients who had a SAE associated with irrigation. These cost items were added to the total cost of health-care resources associated with the treatment of earwax. However, out-of-pocket expenses are relatively small in comparison with the cost of resources used at primary and secondary care in the treatment of earwax.

Outcomes

Results of the model are reported as incremental costs and incremental benefits in terms of successful removal of earwax and additional quality-adjusted life-years (QALYs), and the incremental cost-effectiveness ratio (ICER) calculated with respect to 'no treatment'.

Methods of the economic evaluation

Model structure

This section describes in detail the clinical pathways associated with each active treatment alternative introduced in Chapter 5 (SHTAC economic analysis) above. *Figure 1* presents the structure of the model.

In the base-case scenario it was assumed that patients in each of the active treatments follow a GP's advice to apply softeners for 1 week. The use of softeners has two advantages: first, the softeners assist any subsequent irrigation by softening earwax and, second, they facilitate a spontaneous earwax clearance in some patients, after which no irrigation is required. Use of softeners is considered to be the first line of treatment followed by irrigation as the second line of treatment. Finally, if the earwax is still not removed after three rounds of applying softeners and syringing, patients may be referred to secondary care for removal of earwax by a specialist otolaryngologist (OTL). In the first active treatment alternative (current or standard practice), patients presenting at primary care for earwax treatment are initially assessed by a GP (assumption used in the base-case analysis) or a nurse (a scenario analysis); they are advised to use olive oil or sodium bicarbonate for a week and if spontaneous earwax clearance does not occur then return to the practice for irrigation. The irrigation is administered by a practice nurse using an electric irrigator.

Alternatively, in the second active treatment option, patients may be advised to apply softeners for a week, and if spontaneous earwax clearance has not occurred they should proceed with self-irrigation using a bulb irrigator, which is available from chemists. Patients for whom self-irrigation does not result in earwax removal return to primary care for a second irrigation. Unlike the first irrigation, the second and third irrigations are administered professionally by a practice nurse using an electric irrigator. The second (and the third, if required) irrigation attempts do not require prior assessment by a GP.

The base-case scenario includes both active treatment alternatives, as well as a conventional 'no treatment' comparator.

There are no data to estimate the proportion of patients given each of the treatment options; therefore for the purpose of an economic evaluation the treatment strategies listed above represent the decision choices available for GPs and their patients.

Assumptions used in the model

The economic evaluation does not differentiate between patients who present with one or both ears occluded. Although this is a simplifying assumption, there were no reliable data that would allow differentiation of the outcomes with respect to unilateral or bilateral presentation of earwax.

While there is a non-zero probability of experiencing spontaneous earwax clearance associated with the first application of softeners, it is not the case for severely impacted and hardened earwax. In such instances, spontaneous earwax clearance assisted by softeners is unlikely to occur. Severely occluding and/or hardened earwax may not even be successfully removed at the first irrigation attempt at primary care and will require a second, and sometimes third, round of using softeners followed by irrigation in primary care. In such instances it is assumed that the use of drops merely facilitates the next professionally administered irrigation attempt, and is not associated with the probability of achieving a spontaneous earwax clearance.

If the first irrigation attempt was unsuccessful, the probability of a successful earwax removal at the second and the third irrigation attempt at primary care would not depend on whether the first irrigation was administered by a practice nurse or the patients themselves.

Most patients achieve the desired outcome (earwax removal) without a SAE associated with irrigation. It is assumed that the use of softeners alone as well as the 'do nothing' option are not associated with a SAE. In the base-case scenario the probability of a SAE is assumed to be the same regardless of the mode of irrigation (self-irrigation or administered by a practice nurse) and whether irrigation is undertaken for the first, second or the third time.

The published clinical evidence used to populate the model[4,63] does not report an incidence of SAEs. However, the occurrence of a SAE was viewed as a clinically important factor, which can also affect the results of an economic evaluation. By including the likelihood of a SAE in the model we have effectively reduced the benefits that occur following successful removal of earwax.[4,63]

As there are no published estimates of the incidence of SAEs associated with irrigation, an expert OTL's opinion was obtained. The probability estimate of having a SAE as a result of irrigation was based on the observed rate of presentation to secondary care for treatment of a TM puncture/rupture or a serious ear infection. The corresponding assumption used in the model is that all the SAE patients are referred and treated at secondary care. However, it is possible that some patients with a TM puncture/rupture or a serious ear infection are monitored and treated by their GPs. If this is the case the estimate used in the model is an underestimate.

The patients who had a SAE associated with irrigation (typically a TM perforation or an infection) experience pain and discomfort. However, following the experts' advice it was assumed that after 1 week the pain subsides and in 2 weeks most patients experience a spontaneous healing of a TM or resolution of a serious ear infection.

As discussed in Chapter 3, irrigation is a fairly safe procedure, with only a small proportion of patients experiencing minor complications such as superficial erythema and dizziness. Minor complications are assumed to be short-lasting and not significant enough to be associated with a measurable decrease in HRQoL or an additional use of health-care resources. Therefore, the minor complications are not included in the modelled economic evaluation. There is paucity of evidence on the incidence of more serious and possibly lasting complications such as tinnitus. These are not included in the modelled economic evaluation.

Apart from the temporary loss of hearing in the affected ear(s), there are a few other symptoms such as aural fullness, vertigo, itching and tinnitus that affect HRQoL of patients being treated for earwax problems. However, there are no published estimates of utility values associated with symptoms other than loss of hearing. Therefore, the estimated loss of utility for the model is limited to the loss of hearing that was applied to all patients until the earwax is cleared. In addition, utility decrements are applied to patients who experienced a SAE that involves both loss of hearing and pain.

Model type and characteristics

We developed an economic model of treatment alternatives for a single event of earwax removal. A deterministic decision tree (*Figure 1*) analysis was conducted, focusing on binary outcomes representing earwax that was removed or not removed, with results expressed as incremental cost per patient with earwax safely removed. Analysis also incorporated loss of utility associated with temporary loss of hearing due to occlusion, and for pain and loss of hearing due to a SAE, with results presented as incremental cost per QALY. The base-case analysis was conducted in a population aged 35–44 years, with the corresponding age-adjusted utility value of 0.91 (Kind and colleagues[77]).

Results of the deterministic decision-analytical model in terms of QALYs were extrapolated to a lifetime horizon (45 years) using an EXCEL spreadsheet. The major assumption in these calculations was that, according to clinical experts, the recurrence rate of earwax is 0.35, which is close to one episode occurring every 3 years or 15 single presentations over the assumed time horizon. The age-specific utility values were used for the estimated effects (QALYs)[77] as the cohort, aged 35 years at the baseline, was progressing through the different age categories. Both costs and outcomes were discounted using a 3.5% discounting rate. The calculations also take the UK age-adjusted annual mortality rate into account. Although the assumption of no treatment over this

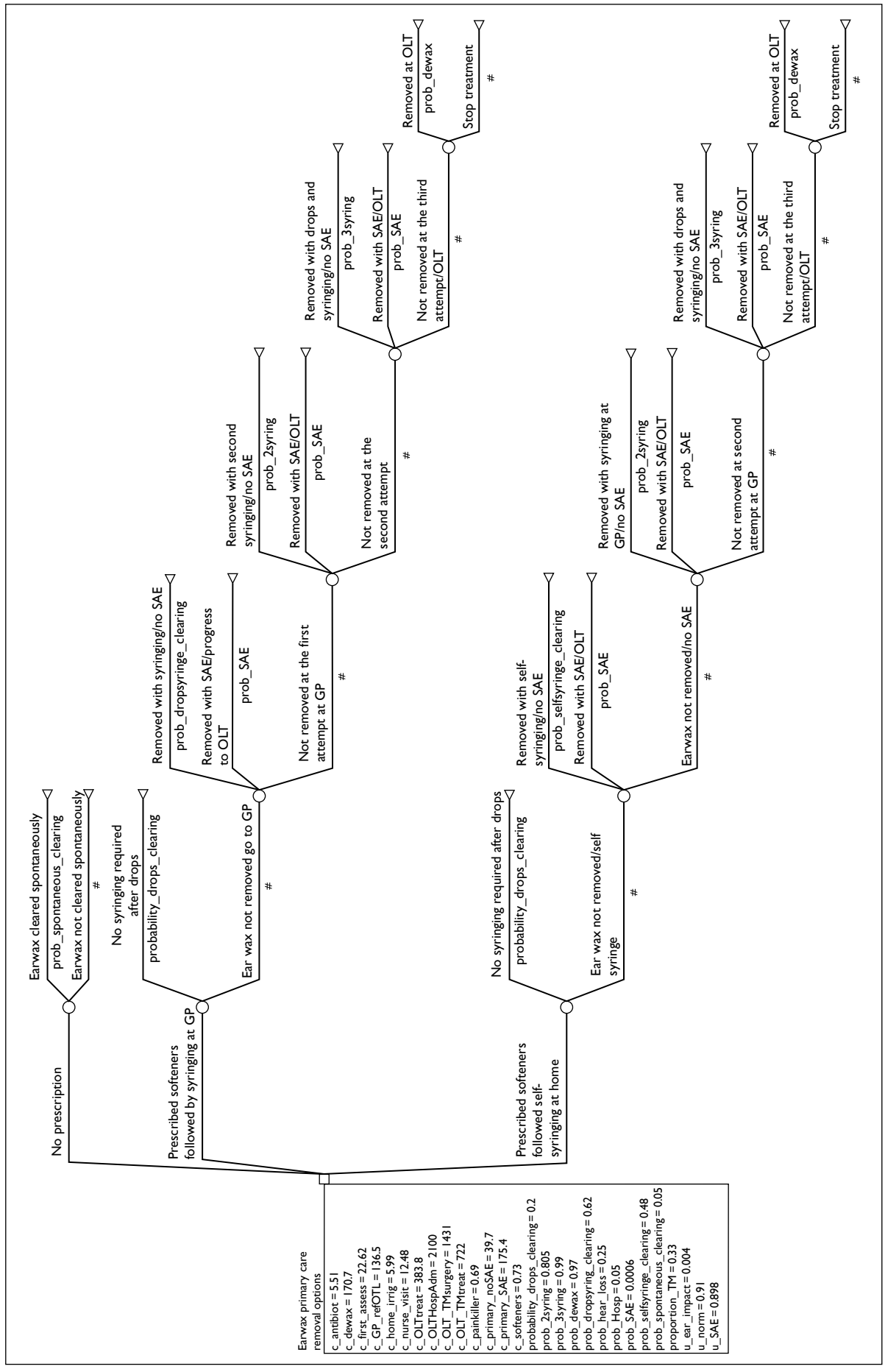

FIGURE 1 *The structure of the economic model of earwax treatment alternatives; OLT, otolaryngologist, a specialist doctor providing treatment at secondary care; SAE, serious adverse event.*

period of time is unlikely to be realistic, the no treatment alternative is included in the analysis for the purpose of maintaining consistency across all stages of an economic analysis. *Table 25* presents characteristics of the decision-tree model and the lifetime extrapolation.

Assessment of uncertainty (sensitivity analysis)

A deterministic sensitivity analysis was used to address particular areas of uncertainty in the model. We investigated the uncertainties around the probability estimates that were expected, a priori, to have a disproportionate impact on the study results.

Scenario analysis was used to address the uncertainty associated with some aspects of the chosen structure of the model.

Parameter uncertainty is addressed using probabilistic sensitivity analysis (PSA). Probability distributions are assigned to the point estimates used in the base-case analysis. The point estimates for treatment effects are reported in *Tables 26* and *27*.

The purpose of this analysis was to test the robustness of the cost-effectiveness results to variation in structural assumptions and parameter inputs.

Data sources used in the model

This section of the report describes the inputs to the model, provides justification for their use, details their respective sources and explains their role in the model. The data used in the model have been collected from a variety of sources, chosen on the basis of appropriateness to the UK and the quality of the data as assessed by the reviewers and in consultation with clinical experts.

Clinical effectiveness data

As can be seen in Chapter 3, there is limited clinical effectiveness data available for the model. Two studies can be used: one study of the use of softeners alone by Keane and colleagues,[4] which involved a 'no treatment' comparator, and one study by Coppin and colleagues,[63] which compared self-irrigation with irrigation in primary care and estimated patient-relevant outcomes. Other estimates are from clinical evidence and experts' advice, which suggests that earwax is eventually resolved in the majority of patients. Therefore, in the base-case analysis both active treatment arms are associated with a very high probability of successful earwax removal. *Table 26* presents

TABLE 25 *Characteristics of the modelled economic evaluation*

Type of the model	Treatment alternatives/ pathways	Outcome	Time horizon	Discounting
Deterministic decision tree	No treatment Softeners followed by self-irrigation Softeners followed by irrigation administered by a practice nurse	Binary outcome 'earwax removed' (yes/no)	7 weeks[a]	Not applicable
Deterministic decision tree	No treatment Softeners followed by self-irrigation Softeners followed by irrigation administered by a practice nurse	QALY	7 weeks[a]	Not applicable
EXCEL model with interactive inputs from the deterministic decision tree[b]	No treatment Softeners followed by self-irrigation Softeners followed by irrigation administered by a practice nurse	QALY	Lifetime (until the baseline cohort of 35-year-olds reaches the age of 80)	3.5% applied to both costs and outcomes

QALY(s), quality-adjusted life-years; SAE, serious adverse event.

a Seven weeks is a minimally acceptable time horizon to allow time for up to three presentations at primary care for irrigation, which, including the first week of using softeners, takes 4 weeks, and may be followed by 2 weeks of monitoring a SAE and at least 1 week to include the outcomes of a hospital admission of the patients for whom a SAE was not resolved.

b The base-case calculations were repeated four times using the age-adjusted utility values[77] to obtain age-adjusted estimates of QALYs for each of the treatment alternatives.

TABLE 26 *Estimates of clinical effectiveness used in the base-case analysis*

Treatment alternatives including 'no treatment' option	Probability of earwax removed (range used in the sensitivity analysis)[a]	Source	Comments
No treatment (spontaneous earwax removal)	0.05 (0.035–0.065)	[b]Keane and colleagues, 1995[4]	The outcomes were assessed on an ordinal scale with three categories: 'impacted', 'moderately clear' and 'completely clear'. The model outcome 'earwax removed' corresponds to the 'completely clear' (of wax) outcome in Keane and colleagues[4]
Use of softeners preceding irrigation at primary care	0.20 (0.14–0.26)	[b]Keane and colleagues, 1995[4]	
Softeners followed by self-irrigation	0.48 (0.34–0.62)	Coppin and colleagues, 2007[63]	The outcomes were initially assessed on an ordinal 4-point scale assessing the degree of obstruction of the membrane (see Chapter 3, Research in progress). Coppin and colleagues[63] reported a binary outcome of the degree of wax clearance. The model outcome 'earwax removed' corresponds to the combined scores of 0 (no or minimum wax with TM fully visible) and 1 (minor amount of wax with TM essentially visible)
Softeners followed by irrigation administered by nurse at primary care	0.62[c] (0.43–0.81)	Coppin and colleagues, 2007[63]	
Second irrigation – at primary care	0.805 (0.69–0.91)	Linear extrapolation	
Third irrigation – at primary care	0.99 (0.95–1.0)	Expert advice	Remaining patients assumed to undergo de-waxing in secondary care
Successful de-waxing at secondary care without SAE	0.97 (0.8–1.0)	Pothier and colleagues, 2006[56]	

SAE, serious adverse event; TM, tympanic membrane.
a The range of estimates used in the sensitivity analysis was calculated by varying the point estimate by 30%.
b The outcomes were originally reported with respect to number of impacted ears and were subsequently converted into the outcomes with respect to patients.
c In total, 14% of patients in softeners and nurse irrigation arm were lost to follow-up in the Coppin and colleagues[63] study. It is reasonable to assume that patients did not present for the professionally administered irrigation because the earwax was resolved after application of softeners.

probability estimates of clinical effectiveness and *Table 27* presents probabilities associated with a SAE used in the model.

Health states/utilities

A systematic literature search did not result in any published estimates of utility loss due to symptomatic earwax. As discussed in Chapter 5 (Assumptions used in the model), reduction in the quality of life associated with the range of symptoms caused by impacted earwax is limited to the loss of hearing and, for the small proportion of patients experiencing SAE, to the loss of hearing and pain. A targeted literature search identified some published utility decrements associated with the loss of hearing due to reasons other than symptomatic earwax. *Table 28* presents the results.

One study[78] reports utility decrement of 0.006 derived from patients with a range of conditions that result in mild to severe hearing loss [*International Classification of Diseases*, Ninth Edition, Clinical Modification (ICD-9-CM) diagnosis code 389], which can be used for an estimate of temporary hearing loss. The other study[79] reports a utility gain associated with hearing improvement due to provision of a hearing aid. In this study the mean postintervention changes in European Quality of Life-5 Dimensions (EQ-5D) and Short Form-6 Dimensions (SF-6D) were similar, although the change in mean utility scores assessed by EQ-5D was not statistically different from zero. The mean utility score assessed by Health Utilities Index (HUI)3 demonstrated a significantly higher improvement of 0.06. As there is only a limited understanding of the degree of hearing loss associated with symptomatic earwax, it is not certain whether the estimates of utility gain due to the provision of hearing aid is comparable with the utility gain associated with earwax removal.

TABLE 27 *Base-case analysis probabilities associated with a SAE*

Event/treatment	Probability of event/ treatment (range used in sensitivity analysis)	Source	Comments
SAE associated with irrigation administered by nurse at primary care	0.0006 (0.0003–0.0009)	Expert advice	The base-case estimate is based on 11 SAEs observed in secondary care, servicing the population of 300,000[a] The upper limit in the range is based on 18 SAEs observed annually in secondary care, servicing a population of 280,000[a]
SAE associated with self-irrigation	0.0006 (0.0003–0.0009)	Expert advice	Assumed to be the same as the probability of SAE in primary care
Hospital admission for either myringoplasty or treatment of a serious infection	0.05 (0.035–0.065)	Expert advice	
Probability of partial permanent hearing loss if myringoplasty is only partially successful	0.25 (0.18–0.33)	Expert advice	
Proportion of patients with TM perforation in the total number of patients with SAE	0.333 (0.23–0.43)	Expert advice	There are two types of SAE: a TM perforation and a serious ear infection. These SAEs differ with respect to treatment pathways and costs

SAE(s), serious adverse event(s); TM, tympanic membrane.
a The following assumptions were made in the calculation of the estimated rate of SAEs: the incidence of symptomatic earwax is 8%[7] and 80% of the population with earwax require irrigation.

TABLE 28 *Published utility decrements associated with the loss of hearing*

Source	Characteristics of the population	Method	Disutility value (standard error)	Degree of the hearing loss	Comments
Sullivan and Ghushchyan, 2006[78]	*N* = 320; *USA patients with the ICD-9-CM 389 condition*[a]	SF-12 converted into EQ-5D	0.006 (0.0001)	As defined by the ICD-9-CM diagnosis code 389	The disutility estimate represents the marginal decrement in EQ-5D index scores after controlling for age, comorbidity, gender, race ethnicity income and education
Barton and colleagues, 2004[79]	*N* = 609 *UK patients with mean age of 68.4 who are eligible for a hearing aid*	HUI3, SF-6D and EQ-5D	0.06,[b] 0.014,[b] 0.005,[b] respectively	Not reported	

EQ-5D, European Quality of Life-5 Dimensions; HUI, Health Utilities Index; ICD-9-CM, *International Classification of Diseases*, Ninth Edition, Clinical Modification; SF-12, Short Form-12 items; SF-6D, Short Form-6 Dimensions
a The regression analysis with EQ-5D as a dependent variable was conducted on the much larger sample involving patients with the range of ICD-9-CM conditions.
b Assessed by comparing utility score before and after fitting hearing aids.

Table 29 shows the utility values used in the model for each health state in the cohort of 35- to 44-year-old patients presented at baseline with earwax. The age-specific population norm for the cohort of 35- to 44-year-old patients is 0.91.[77] In the base-case analysis the disutility value of 0.006 for the loss of hearing and the disutility value of 0.012 for the duration of SAE were used as, according to expert opinion, these estimates correspond to the loss of quality of life associated with symptomatic earwax. It should be noted that the experts were informed of the disutility value when asked to estimate the impact of a SAE on utility; therefore, this value was not obtained independent of the 0.006 disutility.

TABLE 29 *Utility values used for each health state in the model*

Health state	Utility	Source	Time interval to which utility applies
Earwax causing temporary loss of hearing	0.904	Sullivan and Ghushchyan, 2006[78]	From the baseline and until earwax is removed and hearing restored
Earwax removed/hearing restored	0.910	Kind and colleagues, 1999[77]	Applies at the point of a successful earwax removal and until the exit from the model
SAE (serious infection and TM perforation)	0.898	Expert advice	Applies for 2 weeks from the SAE onset
Permanent slight loss of hearing as a result of TM perforation	0.904	Assumption	Applies for life to the 25% of patients for whom myringoplasty was not completely successful

SAE, serious adverse event; TM, tympanic membrane.

TABLE 30 *Health-care resource use associated with earwax treatment at primary care*

Resource	Amount used	Unit cost (£) (2006–7 prices)	Source	Cost (£)
Pharmaceuticals (not NHS cost borne by patients)				
Softeners – olive oil	10 ml	0.73	NHS electronic drug tariff[a]	0.73
Equipment and consumables				
Electric irrigator (Propulse III) used for irrigation at primary care	1 item	78.99 (excluding VAT)	www.medisave.co.uk/instruments-ear-syringe-c-240 241.html (price was valid until September 2008)	2 × 78.99/2000 = 0.08[a]
Cleansing tablets for electric irrigator (assuming the machine is cleaned after each application)	1 pack × 200	20 (including postage)	Expert advice (based on the actual primary care practice expenditures)	20/200 = 0.1
Cost of annual services of an irrigator	Annually	60	Expert advice	2 × 60/2000 = 0.06[a]
Disposable jet tips for an electric irrigator	1 pack 100	44.00	www.medisave.co.uk/instruments-ear-syringe-c-240 241.html	44/100 = 0.44
Otoscope (including bulbs)	1 item	319.00	Expert advice (assumed 4 years of use)	319/4000 = 0.08[a]
Disposable tips for an otoscope	1 pack × 850	47.00 (including postage)	Expert advice	47/850 = 0.056
Head torch (including bulbs)	1 item	60	Expert advice (assumed to be replaced annually)	60/1000 = 0.06
Other disposable and non-disposable equipment (e.g. Noots Tank, Propulse reservoir, Jobson-Horne probe, capes)	Various	N/A	Uppal and colleagues[80] (adjusted for 2006/07 prices)	2.12
(A) Subtotal: equipment and consumables				**3.00**
Staff cost				
GP consultation (primary assessment)	5 minutes	2.90 per minute	PSSRU,[81] expert advice	14.50
(B) GP consultation + 20% clinical staff overhead[80]				**17.40**
GP SAE – related consultation (referral to secondary care)	15 minutes	2.90 per minute	PSSRU,[81] expert advice	43.50

TABLE 30 *Health-care resource use associated with earwax treatment at primary care (continued)*

Resource	Amount used	Unit cost (£) (2006–7 prices)	Source	Cost (£)
(C) GP SAE – related consultation + 20% clinical staff overhead[80]				**52.2**
Practice nurse consultation	15 minutes	0.383 per minute	PSSRU,[81] expert advice	8.00
(D) Practice nurse consultation + 20% clinical staff overheads[80]				**9.6**
Subtotal				
Direct clinical cost of GP initial assessment				17.40
Direct clinical cost of GP referral and follow-up (used in self-irrigation with SAE)				52.2 × 2 = 104.4
Direct clinical cost of nurse session (used in the second and third irrigation episode)				9.6
Direct clinical cost of earwax treatment without SAE				30.0 = [(A) + (B) + (D)]
Direct clinical cost of earwax treatment with SAE				134.4 = [(A) + (B) + (D) + 2 × (C)]
Total costs (direct, indirect and private patient costs)[a]				
Cost of GP assessment				22.62
GP referral and follow-up only (used in self-irrigation-related SAE)				136.45[b]
Nurse session (used in the second and third irrigation)				12.48
Earwax treatment without SAE				39.70[b]
Earwax treatment with SAE (includes one GP referral one follow-up)				175.40[b]

N/A, not applicable; PSSRU, Personal Social Services Research Unit; SAE, serious adverse event; VAT, value added tax.
a The total cost includes direct and indirect costs. Indirect costs such as estates, domestics and non-clinical personnel are assumed to be 30% of direct cost.[80]
b Includes the cost of softeners = £0.73 (paid by the patients).

The HUI3 value reported in the study of Barton and colleagues[79] was used in the scenario analysis.

Assuming that the life expectancy of a person of 35 years of age is 45 years, the disutility value of 0.006,[78] if assessed using the time trade-off method, would correspond to a half year of life traded for the symptomatic earwax being removed. By implication the disutility value of 0.06[79] would correspond to 5 years of life traded for living without symptomatic earwax.

Resource use and cost data

As the analysis reflects an NHS perspective, UK specific resource use and costing data have been used where available. Cost data were obtained from a number of primary and secondary sources.

Table 30 shows categories of health-care resource use, the amount used, the unit prices and the associated cost of earwax presentation at primary care.

The following assumptions were made in calculating the costs:

- With respect to the cost of electric irrigator per patient (£0.08), the estimated annual number of patients presenting with earwax problems at the typical primary care practice was assumed to be about 1000. This was based on the mean number of three presentations per day. It was assumed that two electronic irrigators in use in the typical primary care practice (2 × £78.99) are replaced every 2 years during which time about 2000 patients are treated for earwax.
- With respect to the cost of a nurse consultation (an ear irrigation session), the estimated average nurse time is an arithmetic mean between 10 minutes that are typically spent on irrigating one ear and 20 minutes spent on irrigating both ears. See Chapter 5 (Assumptions used in the model), which outlines assumptions of the model.

Different cost components are used in the model depending on the treatment option and the patients' progression along the alternative treatment pathways as depicted in the decision tree (*Figure 1*). The 'no prescription' option is associated

only with the cost of an initial assessment conducted either by a GP (base-case analysis) or a nurse (scenario analysis). Treatment of patients who applied softeners following consultation at the primary care practice and achieved a spontaneous earwax removal is associated with the cost of initial assessment and the cost of softeners (e.g. £22.62 + £0.73 = £23.35). Those patients who achieve clearance following a single professional irrigation at primary care incur the cost of the initial assessment, the softener cost and the cost of the irrigation administered by a practice nurse (£39.70 = earwax treatment without SAE in *Table 30*). Those patients suffering an AE incur, in addition to the above costs, a GP consultation in order to refer the patient to secondary care (OTL) and a follow-up consultation (£175.40 = earwax treatment with SAE in *Table 30*). Both consultations are assumed to take 15 minutes of GP time. The exact same costing process is followed for the second and third attempts at syringing in primary care, if required.

Table 31 shows the category of health-care resources associated with self-irrigation at home. Patients self-irrigating at home incur the cost of an initial consultation in primary care, the cost of softeners and a bulb irrigator. For those patients experiencing spontaneous clearing of earwax the costs include the cost of initial assessment and the cost of softeners only. Patients who are not successful at self-irrigation are assumed to present at primary care for the second and, if necessary, third irrigation that is administered by a practice nurse. Subsequent costs are incurred as per the option for attending primary care for syringing.

Table 32 shows the health-care resources used for dewaxing and treating SAE in secondary care.

Patients presenting at secondary care for treatment-related SAEs incur additional costs. As discussed above, two categories of SAE were included in the economic evaluation: TM perforation and serious infection. Following expert advice, all patients with SAEs experience pain and need to use painkillers for 1 week, incurring the associated cost. In addition, all patients with serious infection are prescribed antibiotics for 2 weeks, incurring the cost.

Treatment for SAEs by an OTL consists of initial and follow-up appointments, with a series of investigations (*Table 32*). Those treated on an outpatient basis require either two presentations for treatment of TM or four presentations for treatment of a serious infection. Those patients requiring hospital admission (5% of those referred to the OTL) for myringoplasty (surgical treatment of TM perforation) require on average either a day-case admission or an overnight admission, while a serious ear infection requires, on average, a 2-day

TABLE 31 *Health-care resources associated with self-irrigation at home*

Resource	Amount used	Unit cost (£) (2006–7 prices)	Source	Cost (£)
GP consultation (primary assessment)				
GP consultation including 20% staff overheads and 30% indirect cost	5 minutes	2.90 per minute	PSSRU, expert advice	22.62
Pharmaceuticals				
Softeners – olive oil	10 ml	0.73	NHS electronic drug tariff[a]	0.73
Equipment				
Bulb irrigator (25 ml)	1 item[b]	5.99	Online cost[c]	5.99
Total cost of earwax self-irrigation				**22.62 + 0.73 + 5.99 = 29.34**

a Available at: www.ppa.org.uk/edt/September_2008/mindex.htm (last accessed on 28 May 2008).
b With recurrent rate of earwax of 0.35 (expert advice), the shelf-life of a bulb irrigator should be about 3 years, to be used more than once, which may not be a realistic assumption. Therefore, the total cost of a bulb irrigator is included in the calculations.
c http://shop.ypproducts.co.uk/acatalog/Enemas_Tubes.html (last accessed on 28 May 2008).

TABLE 32 *Health-care resources used in de-waxing and treating a SAE*

Resource	Amount used	Unit cost (£) (2006–7 prices)	Source	Total cost (£) (comments)
Pharmaceuticals				
Analgesics, paracetamol 500 mg	32 tablets	0.69	NHS electronic drug tariff[a]	0.69 (applied to 100% of TM perforation patients assuming 1–2 tablets, 3 times per day, for 7 days)
Antibiotics, ofloxacin 200 mg	10	5.51	NHS electronic drug tariff[a]	5.51 (applied to 100% of serious infection patients)
Antibiotic/steroid ear drops –clioquinol 1%/flumetasone 0.02%	7.5 ml	1.47	NHS electronic drug tariff[a]	1.47 (applied to 18% of SAE patients whom Hussain[82] used in scenario analysis)
Investigations				
The total cost of investigations, such as audiometry, ear swabs for culture and sensitivity	N/A	N/A	Uppal and colleagues[80] (adjusted for 2006–7 prices)	42.40 (applied to 100% of SAE patients)
The total cost of a new and the follow-up appointments	Various	N/A	Uppal and colleagues[80] (adjusted for 2006–7 prices)	170.7[b] (applied to 100% of SAE patients)
Myringoplasty = minor ear procedure without CC (day case CZ08Y)	N/A	705	DHS[c]	705 (applied to 5% of SAE patients in the model who were referred to OTL)
Hospital admission for a serious infection treatment = intermediate ear procedure without CC		1377	DHS[c]	1377 (applied to 5% of SAE patients in the model patients who were referred to OTL)
Total cost of OTL treatment				
De-waxing without a SAE				170.7
Treatment of serious infection without hospital admission[d]				42.4 + (2 × 170.7) + 5.51 + (0.18 × 1.47) = 389.57
Treatment of serious infection with hospital admission				42.4 + (2 × 170.7) + 1377 + 5.51 + (0.18 × 1.47) = 1766.57
Treatment of TM perforation without surgery[d]				42.4 + (4 × 170.7) + 0.69 = 725.89
Treatment of TM perforation with surgery				42.4 + (4 × 170.7) + 705 + 0.69 = 1430.89

CC, complications and comorbidities; N/A, not applicable; OTL, otolaryngologist; SAE, serious adverse event; TM, tympanic membrane.

a Available at: www.ppa.org.uk/edt/September_2008/mindex.htm (last accessed on 28 May 2008).

b This includes clinical staff cost, overheads, equipment and indirect costs.

c National Schedule of Reference Costs 2006–7: NHS Trusts. Available via www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_082571 (last accessed on 28 May 2008).

d According to the experts, a TM perforation involves four presentations to secondary care, whereas a serious infection requires two presentations.

hospital admission (expert opinion). The total secondary care cost of treating a TM perforation without admission is higher than that for a serious infection. In contrast, if a patient is admitted to hospital the cost of treatment of a serious infection becomes more expensive than for a TM perforation.

Base-case results of a single presentation model

Results of the base-case deterministic decision analysis of alternative approaches to earwax removal are presented in *Table 33*. The results are reported in terms of incremental costs and incremental gains: a gain in likelihood of earwax being successfully removed and additional QALYs.

TABLE 33 *Base-case cost-effectiveness results comparing 'no treatment' alternative with softeners followed by self-irrigation and softeners followed by professional irrigation*

Treatment alternative	Cost (£) (2006–7 prices)	Probability of earwax being removed at the end of the seventh week	Incremental cost per successfully treated patient[a]	QALYs	Incremental cost per QALY (ICER)[a]
No treatment	22.62	0.05	–	0.121727	–
Softeners followed by self-irrigation	37.28	0.999977	14.66	0.122327	24,433
Softeners followed by irrigation at primary care	42.38	0.999983	19.76	0.122342	32,130

ICER, incremental cost-effectiveness ratio; QALY(s), quality-adjusted life-year(s).
a ICER are calculated with respect to the comparator – 'no treatment'.

Table 33 shows results of the base-case analysis using a deterministic decision-analytic model with a 7-week time horizon. The ICER is calculated with respect to the conventional comparator 'no treatment'.

In comparison with the 'no treatment' option, the additional cost of successful treatment of a patient with an earwax problem is £14.66 for the alternative beginning with the use of softeners and self-irrigation, and £19.76 for the alternative beginning with the use of softeners followed by irrigation at primary care. However, when two active treatment options are compared, the incremental cost of treating an additional patient with softeners followed by professional irrigation, as opposed to treating with a combination of softeners and self-irrigation, is about £850,000 per successful earwax removal. With the additional QALY gain of only 0.000015, this gives an ICER of £340,000 per QALY. This is because the additional gain associated with the option of softeners followed by irrigation at primary care is small, at 0.000006, or 6 additional patients in every 1,000,000 patients treated for earwax problems.

Both active treatment alternatives are associated with a very high probability of achieving an outcome (i.e. earwax removal), which, for all practical purposes, is not different from 1.0 (i.e. virtual certainty). Therefore, the above results can be interpreted within a cost-minimisation framework, which demonstrated that the same outcome can be achieved at a lesser cost if patients use softeners first, followed by self-irrigation, and present at primary care only if self-irrigation did not result in earwax removal. However, as further discussed in Chapter 7, the self-irrigation alternative may not be appropriate for every patient presenting at primary care with an earwax problem.

Although it was assumed in the base-case scenario that the probability of SAE in both active treatment alternatives is the same, there was no published clinical evidence to support this assumption. Neither was there consensus between the experts who provided feedback on the results of this study. Some clinical experts consider self-irrigation using a soft rubber bulb irrigator to be a completely safe alternative to the current practice involving professional irrigation. However, one expert advised that although a TM puncture is unlikely to occur when a soft rubber bulb irrigator is used, self-irrigation may not necessarily exclude the probability of having a SAE, such as displacing the ear drum and exerting traumatic pressure on the inner ear.

Two principal factors contributed to the base-case results: the difference in the estimated clinical effectiveness between the two active treatment options as reported by Coppin and colleagues[63] (0.42 versus 0.68) and a small incremental gain in terms of QALYs. This was not surprising, given that in the base-case analysis the size of the disutility associated with hearing loss was only 0.006.[78] These and other parameter uncertainties are explored in the univariate and bivariate sensitivity analyses reported in Chapter 5 (Deterministic sensitivity analysis).

Lifetime extrapolation of results of a single presentation modelling

Table 34 shows the results of the lifetime extrapolation of the outcomes of the modelling of

TABLE 34 *Lifetime cost-effectiveness results comparing softeners followed by self-irrigation and softeners followed by professional irrigation (in 2006–7 prices)*

Treatment alternatives	No treatment	Softeners followed by self-irrigation	Softeners followed by irrigation at primary care
Total discounted cost (£)[a]	178.85	294.84	335.17
Total discounted QALYs[a]	20.671636	20.676380	20.676500
Incremental cost (£)[b]	–	115.99	156.32
Incremental effect[b]	–	0.004744	0.004864
ICER (£/QALY)[b]		£24,450	£32,136

ICER, incremental cost-effectiveness ratio; QALY(s), quality-adjusted life-year(s).
a Both lifetime cost and QALY estimates were adjusted for all-cause mortality.
b Calculated with respect to the comparator 'no treatment'.

a single presentation with an earwax problem in 2006–7 prices.

In comparison with no treatment, the difference in total discounted cost over 45 years is £116 for the treatment alternative involving self-irrigation and £156 for the treatment alternative involving professional irrigation. The corresponding discounted QALY gains are 0.004744 and 0.004864 for self-irrigation and the professional irrigation treatment alternatives, respectively. This translates into the estimated ICER of about £24,450 per QALY for the treatment alternative involving self-irrigation and £32,136 per QALY for the treatment alternative involving professional irrigation. The slight difference between base-case results and lifetime model results is due to rounding error in the very small effect differences between the three treatment pathways. When two active treatments are compared with each other the incremental cost of £40.30 and incremental QALY of 0.0001202 resulted in the ICER of more than £335,000.

Deterministic sensitivity analysis

Table 35 shows the variables that were included in the sensitivity analyses.

1. In the first sensitivity analysis the rate of AEs associated with irrigation administered by a practice nurse at primary care was kept at the same level as in the base-case analysis, while the rate of SAE associated with self-irrigation was increased until it reached the level at which the treatment alternative of softeners followed by irrigation at primary care became more cost-effective in terms of QALYs.
2. In the second sensitivity analysis both clinical effectiveness estimates associated with active treatments were altered, with the clinical effectiveness of self-irrigation decreasing and irrigation administered by a practice nurse increasing until the combination of the parameter values reached the level at which the alternative associated with self-irrigation was dominated by softeners followed by irrigation administered by a practice nurse at primary care.
3. In the remaining sensitivity analyses the model parameters were varied as indicated in *Table 35*.

Table 36 shows results of the sensitivity analyses.

The threshold analysis indicated that the results of a base-case scenario (a single event model) are robust to the small variations in the probability of SAE associated with self-irrigation. The probability of a SAE associated with self-irrigation needs to be increased approximately 10 times from the base-case value of 0.0006 to 0.00596 (while maintaining the probability of SAE associated with professional irrigation at the baseline level) before the treatment alternative associated with self-irrigation became dominated by the treatment alternative involving irrigation at primary care.

The threshold analysis indicated that the results are also robust with respect to the small variations in clinical effectiveness parameters (the probability of earwax removed). The cost of treatment involving self-irrigation remains less expensive, albeit fractionally less effective, until the probability of successful earwax removal using self-irrigation is decreased from 0.48 in the base case to 0.25 (ie. assumed to be two times less effective), while the probability of successful earwax removal using professional irrigation is increased from 0.62 to 0.92. When both extreme values are used in

TABLE 35 *Variables included in the sensitivity analyse*

Variable(s)	Base-case point estimate (range tested in the sensitivity analysis)	Type of analysis
1. Probability of SAE associated with self-irrigation was varied	0.0006 (0.0006–0.059)	Bivariate threshold analysis to identify the SAE value associated with softeners and self-irrigation being dominated by softeners and irrigation at primary care
2.Clinical effectiveness of self-syringing	0.48 (0.15–0.25)	Threshold analysis to identify the clinical effectiveness values associated with softeners and self-irrigation being dominated by softeners and irrigation at primary care
3. Clinical effectiveness of irrigation at primary care	0.62 (0.60–95)	Threshold analysis to identify the clinical effectiveness values associated with softeners and self-irrigation being dominated by softeners and irrigation at primary care
4. Clinical effectiveness of softeners	0.2 (0.01–0.5)	Univariate analysis
5. Cost of self-irrigation (including softeners)	6.72 (2.00–9.00)	Univariate analysis

SAE, serious adverse event.

the base-case analysis, the treatment alternative involving self-irrigation is dominated by the treatment alternative involving irrigation at primary care.

Results of the one-way sensitivity analysis indicated that the outcomes are sensitive to the variation in the rate of successful earwax removal from the use of softeners. When the clinical effectiveness of the use of softeners increased from 0.01 to 0.5 the ICER decreased by about two times in both the active treatment arm in comparison to the 'no treatment' alternative. The ICER comparing softeners followed by irrigation at primary care remained unacceptably high when compared with treatment associated with self-irrigation (ICER = £329,098 per QALY at the value of clinical effectiveness of softeners equal to 0.5).

Results of the one-way sensitivity analysis indicated that the outcomes are not very sensitive to the variation in the cost of self-irrigation. When the cost was varied from £2.00 to £9.00 the ICER comparing treatment involving self-irrigation to no treatment changed from around £19,000 per QALY to almost £28,500 per QALY compared with the base-case estimate of ICER £24,433 per QALY. The ICER comparing softeners followed by irrigation at primary care remained unacceptably high when compared to treatment associated with self-irrigation (ICER = £534,933 per QALY at the cost of self-irrigation of £2; ICER = £173,819 per QALY at the cost of self-irrigation of £9.00).

Scenario analyses

Two scenario analyses were undertaken. In the first it was no longer assumed that a GP conducts the first assessment of patients presenting with an earwax problem; instead, the patients from all treatment arms were assessed by a nurse. In the second scenario analysis, as discussed in Chapter 5 (Health states/utilities) the estimate of a disutility value associated with the loss of hearing was taken from the study by Barton and colleagues,[79] which used a HUI3 quality-of-life assessment tool.

By substituting a GP assessment cost with a nurse assessment cost, the total cost of earwax treatment without SAE at primary care decreased from £39.70 to £29.60. The latter estimate comprised the costs of softeners (£0.73) and initial assessment by a nurse (£12.48), followed by the cost of a professional irrigation session (£16.38). No changes in the GPs' involvement in treating patients with SAE were assumed. *Table 37* shows the results of this scenario analysis.

Reduction in the cost of assessment resulted in a reduction of the total cost of all treatment alternatives. However, the incremental costs in comparison with the 'no treatment' alternative have not changed significantly when translating into the ICER values, which are not substantially different from the base-case analysis results. When two active treatment options are compared, the estimated ICER is £462,670 per QALY, which is higher than the £340,000 per QALY in the base-case analysis.

TABLE 36 *Results of the sensitivity analysis*

Parameter(s) tested	Parameter value(s) (base-case parameter-value)	Cost per successfully treated patient (£/successful earwax removal)[a]		QALYs gained per successfully treated patient		Incremental cost per QALY (ICER) (£/QALY)[a]	
		Softeners followed by self-irrigation	Softeners followed by irrigation at primary care	Softeners followed by self-irrigation	Softeners followed by irrigation at primary care	Softeners followed by self-irrigation	Softeners followed by irrigation at primary care
Base-case results		**14.66**	**19.76**	**0.122327**	**0.122342**	**24,433**	**32,130**
1. The threshold analysis of SAE associated with self-irrigation[b]	0.00596 (0.0006)	19.19	19.76	0.122324	0.122342	32,144	32,130
2.The threshold analysis of clinical effectiveness of self-irrigation	0.25 (0.48)	18.56	19.76	0.122301	0.122342	32,334	32,130
3. The threshold analysis of clinical effectiveness of irrigation at primary care	0.92 (0.62)	14.66	15.78	0.122327	0.122376	24,433	24,314
4. Clinical effectiveness of softeners	0.01–0.5 (0.2)	17.97–9.44	24.29–12.63	0.122313–0.122349	0.122332–0.122358	30,655–15,186	40,122–20,006
5. Cost of self-irrigation	£2.00– 9.00 (£5.99)	11.47–17.07	19.76	0.122327–0.122327	0.122342–0.122342	19,119–28,455	32,130

ICER, incremental cost-effectiveness ratio; QALY(s), quality-adjusted life-year(s); SAE, serious adverse event.
a ICER is calculated with respect to the comparator – 'no treatment'.
b The probability of SAE associated with self-irrigation was varied, whereas the probability of SAE associated with professional irrigation remained as in the base-case scenario.

TABLE 37 *Results of the scenario analysis of comparing 'no treatment' with two active treatment alternatives, while assuming the reduced cost of irrigation at primary care*

Treatment alternative	Cost (£) (2006–7 prices)	Probability of earwax being removed at the end of the seventh week	Incremental cost per successfully treated patient[a]	QALYs	Incremental cost per QALY (ICER)[a]
No treatment	12.48	0.05	–	0.121727	–
Softeners followed by self-irrigation	27.53	0.999977	15.05	0.122327	25,083
Softeners followed by irrigation at primary care	34.70	0.999983	22.22	0.122342	36,130

ICER, incremental cost-effectiveness ratio; QALY(s), quality-adjusted life-year(s).
a ICER is calculated with respect to the comparator – 'no treatment'.

TABLE 38 *Results of the scenario analysis assuming that the disutility associated with the loss of hearing is 0.06 rather than 0.006, as assumed in the base-case analysis*

Treatment alternative	Cost (£) (2006–7 prices)	Probability of earwax being removed at the end of the seventh week	Incremental cost per successfully treated patient[a]	QALYs	Cost per QALY (ICER)[a]
No treatment	22.62	No change	–	0.114769	–
Softeners followed by self-irrigation	37.28	No change	No change	0.120768	2444
Softeners followed by irrigation at primary care	42.38	No change	No change	0.120923	3211

ICER, incremental cost-effectiveness ratio; QALY(s), quality-adjusted life-year(s).
a ICER is calculated with respect to the comparator – 'no treatment'.

This is because the differences in cost between two active treatments increased from £5.10 in the base-case analysis to £7.17 in the scenario analysis, rendering the less expensive treatment strategy involving self-irrigation more cost-effective relative to strategy based solely on professional irrigation.

Table 38 shows the results of the second scenario analysis using the disutility values from Barton and colleagues.[79]

When the disutility associated with the loss of hearing is assumed to be 0.06 (Barton and colleagues)[79] or 10 times higher than the disutility estimate assumed in the base-case analysis, the ICER gained is substantially reduced for either of the active treatment alternatives when compared with no treatment. When these options are compared with each other the ICER is about £32,910 per QALY. The large difference between the ICER estimates in the base case and the scenario analysis is explained by the nature of the measurement instruments. Barton and colleagues[79] commented that, unlike the EQ-5D, the HUI3 explicitly asks about a person's capability to hear, and therefore it is not surprising that people with impaired hearing have lower levels of utility according to the HUI3 than according to the EQ-5D and SF-6D. Other studies on the clinical effectiveness and cost-effectiveness of digital hearing aids have identified similar differences.[83]

Probabilistic sensitivity analysis

Table 39 reports the mean costs and outcomes from the PSA of results of a single presentation model. The PSA generated cost and QALY estimates for each active treatment alternative that were similar to those for the base-case analysis (see *Table 33* for base-case analysis). Variables included in the PSA, distributions and parameters of distributions used can be seen in Appendix 7.

TABLE 39 *Probabilistic sensitivity analysis (single presentation)*

Treatment alternative	Mean cost (£)	SD	Mean effects (QALY)	SD
No treatment	22.62	2.3	0.121727	0.000014
Softeners followed by self-irrigation	37.20	2.6	0.122327	0.000011
Softeners followed by irrigation at primary care	42.30	3.6	0.122342	0.000009

SD, standard deviation; QALY, quality-adjusted life-year.

Figure 2 shows the cost-effectiveness acceptability curves for all alternative treatments. The chart indicates the probability that a given treatment option is optimal compared with the alternatives. This suggests that a 'no treatment' option is a cost-effective option at lower threshold levels of willingness-to-pay for health outcomes (QALYs). At the threshold above £30,000 per QALY, the treatment involving self-irrigation becomes more likely an optimal option among the three alternative treatments. As the threshold is increased, softeners followed by irrigation at primary care is increasingly likely to be the optimal treatment alternative. At the threshold of about £330,000 per QALY both active treatment alternatives are equally likely to be optimal.

Summary of economic analysis

- A systematic review of the literature found no existing economic evaluations that met the inclusion criteria of the review.
- We developed a deterministic decision tree model from an NHS perspective to estimate comparative cost-effectiveness of treatment options for earwax following presentation at primary care. It focused on an adult population aged 35–44 years, with no contraindications to treatment options considered.
- The decision tree model compares use of softeners for 1 week with return to the primary care practice for irrigation if no earwax clearance occurs (standard practice), use of softeners for 1 week followed by self-irrigation and return to primary care if unsuccessful for professional irrigation, and no treatment.
- The structure and data inputs of the model were based on our systematic review of the literature on clinical effectiveness and cost-effectiveness of treatment, systematic searches on HRQoL and AEs associated with earwax and hearing loss, other published literature for costs, and consultation with clinical experts.
- Results from the decision tree model were extrapolated over different time horizons to give an estimate of lifetime cost-effectiveness of treatment alternatives.

FIGURE 2 *Cost-effectiveness acceptability curves comparing no treatment, softeners followed by irrigation and softeners followed by self-irrigation.*

- Base-case cost-effectiveness results suggest that the ICER for softeners followed by self-irrigation is about £24,400, and for softeners followed by irrigation at primary care it is about £32,100, compared with no treatment.
- The ICER is over £340,000 when comparing the two active treatments as the additional gain associated with professional irrigation is very small, but at an additional cost.
- The lifetime model ICERs are virtually the same as the base-case ICERs due to a constant recurrence rate of wax used in all three treatment pathways. The slight difference in base case and lifetime ICERs is due to rounding errors in the small effectiveness gains between treatment pathways. If there had been evidence that treatment reduced the frequency or likelihood of recurrence then the lifetime model would have been more informative.
- Sensitivity analyses show results are mostly robust although outcomes are sensitive to variation in the rate of successful earwax removal from the use of softeners.
- Scenario analyses show that results are not sensitive to reduced cost of irrigation in primary care, but are sensitive to changes in disutility value associated with loss of hearing.
- Caution should be taken in interpreting the results of the economic evaluation. The paucity of evidence on the safety, benefits and costs of the different strategies necessitated the use of different assumptions developed from available evidence and expert advice. Uncertainty about the structure and inputs in the model brings into question the reliability of the results. With the focus on a selected population group (people aged 35–44 years with no contraindications) and the evaluation of an intervention which may only have relevance to a specific patient group, the findings may have limited applicability to the general population. As a consequence, the results of the economic evaluation should be regarded as exploratory and should not be used as a basis for changing policy and practice.

Chapter 6
Value of information analysis

Value of information analysis was used to help identify future research priorities.[84,85] Our first step was to calculate the population expected value of perfect information (PEVPI). This equates to the difference between the expected value of a decision based on perfect information and a decision based on currently available information. Calculating PEVPI provides a 'preliminary screen' with the purpose of eliminating research designs that have costs in excess of the PEVPI. In the event that no research designs were to pass this screening test further research investment would not be recommended.

For those research designs that do pass the initial screening test, the groups of parameters that may be investigated should be examined in terms of expected value of partial perfect information (EVPPI) for parameters. If the EVPPI exceeds the cost of the research design for a particular group of parameters, subsequent investment may be deemed worthwhile, whereas if the cost of a new study design exceeds the EVPPI then the additional research should not be undertaken. Both PEVPI and EVPPI are decision threshold specific, and will vary depending upon the health-care payer's perspective of this threshold.

The analysis was conducted in the statistical package R. The decision tree model was replicated in R and code written to estimate the PEVPI and EVPPI. This acted as a technical validation of the original TREEAGE model and facilitated reduced run times for the value of information analysis than could have been obtained with EXCEL.

Figure 3 shows the PEVPI by decision threshold based on an annual population of 2 million[67] and assuming that each patient is treated a mean of 1.25 times to achieve clearance. When the decision threshold is low the technology is not expected to be cost-effective and additional information is unlikely to change the decision. The PEVPI reaches a maximum when the threshold is equal to the ICER of the treatment options (the ICER for self-irrigation versus no treatment is £24k, whereas the ICER for GP irrigation versus self-irrigation is around £340k); that is where we are most uncertain about whether to adopt or reject the technology based on existing evidence. This analysis in *Figure 3* assumes a 10-year lifespan of the technology.

Figure 4 shows the PEVPI for a range of lifespan thresholds for the technology. These assume the technology will last for this period of time before a new technology comes along and replaces it. PEVPI is calculated as follows:

$$PEVPI = EVPI \sum_{t=1}^{T} \frac{I_t}{(1+r)^t}$$

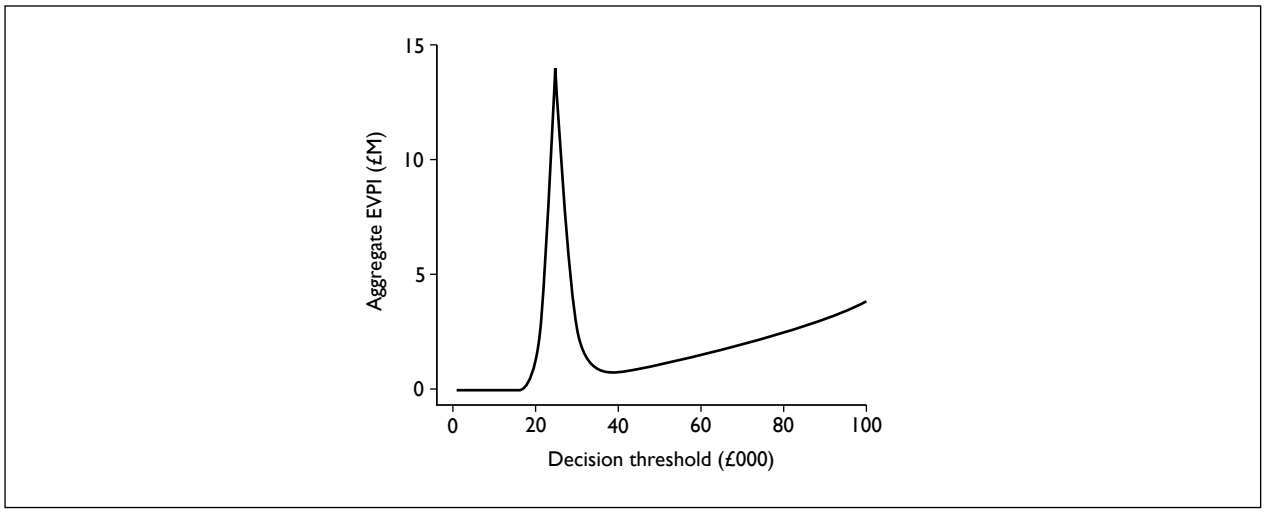

FIGURE 3 *Population expected value of perfect information.*

where T is the technology lifespan, r is the discount rate and I is the population incidence. The recent debate over the threshold to adopt for the lifespan of a technology is acknowledged,[86] although a 10-year lifespan would seem a reasonable proxy for the estimation of uncertainty given the historical longevity of the technology revealed in the clinical effectiveness review. An alternative would have been to conduct an empirical exercise or solicit expert opinion perhaps through a Bayesian process, both of which Phillips and colleagues[85] profess also have their weaknesses.

Figures 3 and *4* suggest that the decision problem passes the initial screening test for a common range of thresholds. Thus we proceed to calculate the EVPPI with the purpose of informing future research priorities and study designs.

Figure 5 shows the EVPPI conducted on selected groups of parameters. To reduce computational burden we followed the advice of Brennan and colleagues[87] and used a higher number of runs in the inner loop (750) than the outer loop (500) for a total of 375,000 iterations per group of EVPPI parameters.

Choice of parameter groups was informed by potential study designs that could feasibly be conducted: utilities; primary care costs; secondary care costs; irrigation efficacy; softener efficacy; and frequency of AEs. The EVPPI is, again, a function of the choice of decision threshold.

Figure 6 shows the EVPPI in more detail around the generally accepted decision threshold adopted in the UK (i.e. between £20,000 and £30,000

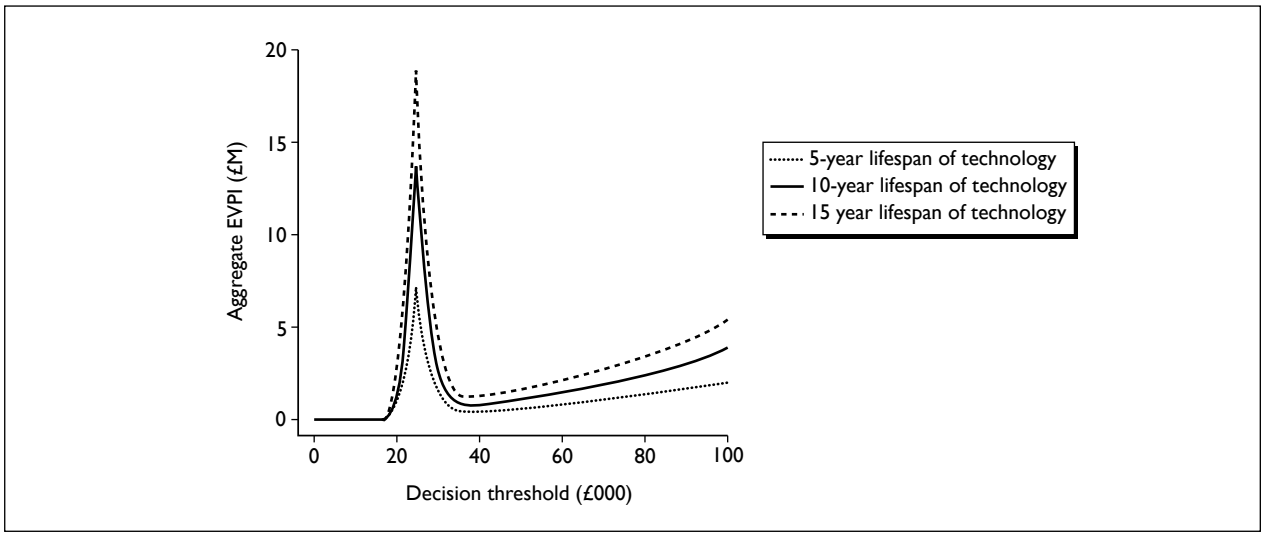

FIGURE 4 *Population expected value of perfect information for a range of lifespan thresholds.*

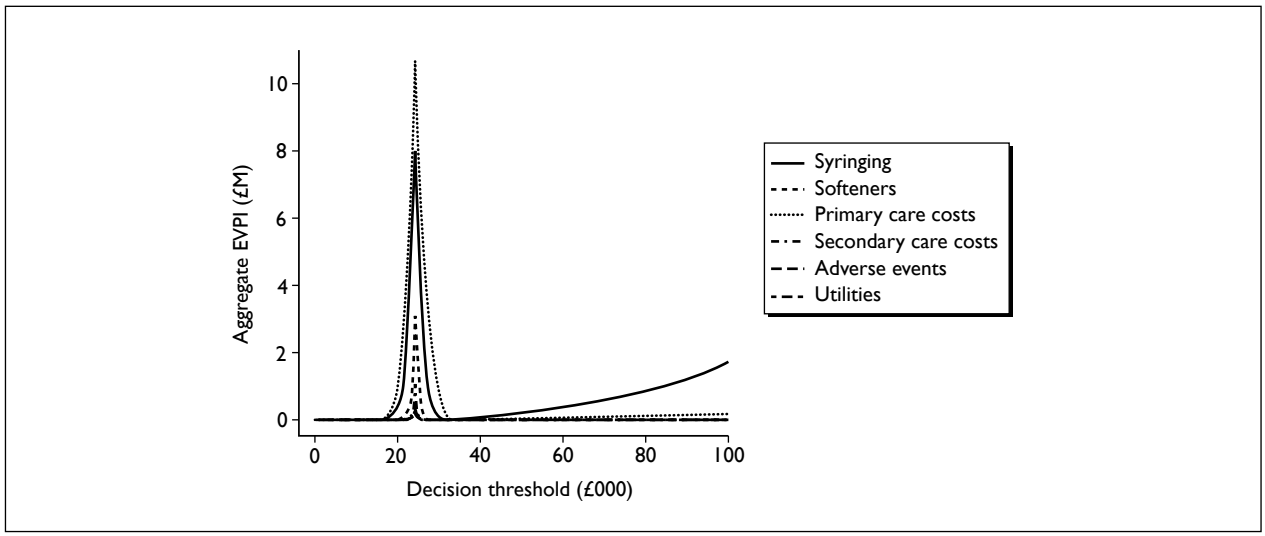

FIGURE 5 *Expected value of population perfect information for selected parameter groups.*

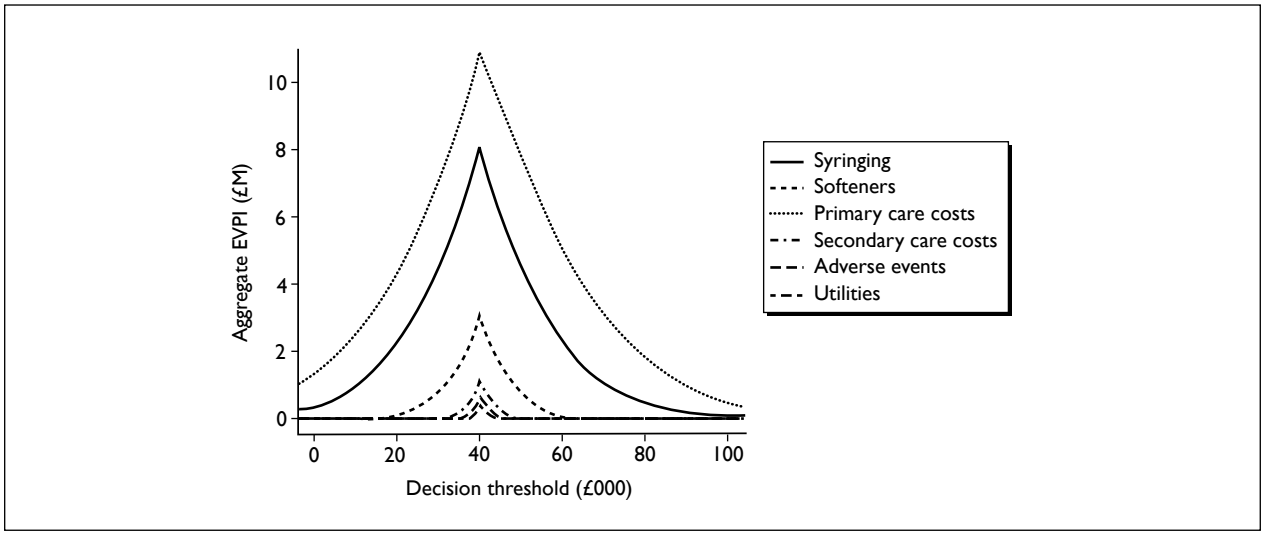

FIGURE 6 *Expected value of population perfect information for selected parameter groups, highlighted for a decision threshold between £20,000 and £30,000.*

per QALY). The figure illustrates that if future research is to be commissioned, it should prioritise improving the estimates of the costs of primary care and the efficacy of irrigation. These results are unsurprising as they are the principal drivers of the model. Secondary care costs are of far less importance as they are related to the management of AEs, which are deemed so rare as to have negligible impact on the analysis.

Whether this research should be undertaken depends upon the cost of the study into the groups of parameters and the exact threshold under which the decision is to be made. In this case it is likely that a prospective costing study or chart review for primary care costs and a clinical trial or observational study for irrigation efficacy would be required. If the threshold is £20,000 per QALY, it is unlikely that a clinical trial to inform irrigation efficacy could be undertaken, but a costing study could be performed within the EVPPI upper bound. However, if the adopted decision threshold is closer to the level of maximum uncertainty then investment in a clinical trial may be well founded. Investment in other groups of parameters is far less certain dependent upon the decision threshold.

A caveat is that the CIs around many of the parameters included in the model have been estimated, rather than informed by published evidence, and it is these estimates which inform the analysis. Furthermore, the analysis does not strongly suggest further research on utilities would be warranted, as the published utility estimate used in the model is accompanied by a low variability. Perhaps, in retrospect, if there is doubt as to the validity of this estimate in the UK, as attested by expert advice, then a Bayesian model could have been used in which a prior probability was used to identify current expectations.

Chapter 7
Discussion

Statement of principal findings

Clinical effectiveness

Twenty-six clinical trials (22 RCTs and four CCTs) met the inclusion criteria of the review and were included for the assessment of the clinical effectiveness of methods for earwax removal. A range of interventions have been used in the studies, such as softeners with or without irrigation, in different populations and in different settings. Participants in the trials also varied across the studies in terms of age, sex and extent or severity of earwax. In some cases few details of baseline characteristics are given in the study reports, so interpretation of results was difficult. Outcomes also vary across studies often with limited information on the definitions used, making it difficult to assess their validity and objectivity, and how consistently they were applied. For example, measures of earwax removal might be reported in terms of clearance or visualisation of TM (described as complete, partial or negligible) or in terms of impaction or occlusion (described as none, mild, moderate or severe). Ease of earwax removal was reported in terms of number of attempts or the amount of liquid needed to achieve some degree of success. Methods of data analysis were also variable with several studies not reporting the analytic approach used or results of statistics tests. Due to these methodological issues, summarising the results of included studies was difficult and meta-analysis was judged inappropriate.

Considering the studies that report statistical significance, results from these studies suggest that Cerumol, sodium bicarbonate, olive oil and water are all more effective than no treatment for removal of earwax; Cerumol is better than dioctyl, TP and sodium bicarbonate for ease of subsequent irrigation; TP is better than olive oil in the volume of water used for syringing; Audax is better than Earex for ease of removal by subsequent irrigation; Exterol and Otocerol are better than Cerumol in terms of the number of people requiring irrigation after treatment with softeners; wet irrigation is better than dry irrigation for ease of removal; sodium bicarbonate drops followed by nurse irrigation is more effective than sodium bicarbonate drops followed by self-irrigation; endoscopic de-waxing is better than microscopic de-waxing; and recurrence of earwax and impacted earwax is less likely in ears treated with skin oil than those not treated.

Patient satisfaction with the different treatment options was rarely assessed. Comparisons of different softeners, including dioctyl-medo, oil-based softeners, Waxsol and Cerumol, showed that over 85% of people found them tolerable. When considering the effectiveness of different softeners, people's responses ranged more widely, with 29% assessing Earex as effective compared with between 42% and 93% for Audax and 100% for Cerumol. Another comparison of nurse-versus-self-irrigation found that people were more satisfied with nurse irrigation (difference 28%). AEs were rare (usually < 10% of patients affected) and minor in nature. Most were limited to those associated with irrigation, such as minor pain (0–21%) and irritation/itching (4–15%). None of the studies reported perforation of the TM or infection. Although there was evidence assessing the comparative benefits of different interventions for removing earwax, it was of poor quality and equivocal. As a consequence it was not possible to identify a particular softener as being superior in clearing wax either with or without subsequent irrigation. Although separate studies have found benefits of wet syringing over dry syringing, from nurse-provided irrigation rather than self-irrigation and, endoscopic compared with microscopic de-waxing, the evidence was limited in nature and quality, so only tentative conclusions should be drawn.

Economic evaluation

Although we conducted a systematic review of the cost-effectiveness of the different methods for earwax removal, no economic evaluations were identified. As a consequence, a de novo economic model was developed to examine the cost-effectiveness of different alternative strategies, including softeners followed by irrigation in primary care (primary care option), softeners followed by self-irrigation (self-care option) and a 'no treatment' option. The results indicated

that the self-care option (£24,433 per QALY) is likely to be more cost-effective than the primary care option (£32,130 per QALY) when compared with the 'no treatment' option over a 7-week time horizon. When the two active treatment options were directly compared, the incremental cost of treating an additional patient with the primary care option as opposed to self-care option was £340,000 per QALY. When assessed over a lifetime horizon (45 years) the cost per QALY compared to the 'no treatment' option was £24,450 for the self-care option to £32,136 for the primary care option. Similarly, when comparing the two active treatments over a lifetime horizon, the resultant incremental cost per QALY was over £335,000 for the primary care option. A constant recurrence rate of wax was assumed for all three treatment pathways due to a lack of data to model an alternative assumption. Therefore, the lifetime results are merely an extrapolation of costs and outcomes from the base-case model out to a 45-year period.

The results were fairly robust to a range of sensitivity and scenario analyses undertaken to explore parameter uncertainties of the modelled economic evaluation. Variations in measures of clinical effectiveness, rates of AE and costs resulted in cost per QALYs ranging between £15,000 and £40,000 for the two options compared to no treatment, and between £170,000 and £535,000 when the two active treatment options were compared. However, interpretation of these results should be undertaken with caution. Uncertainties as to current clinical practice and the paucity of clinical and economic evidence are considerable limitations to the economic evaluation. As a result the economic evaluation should be considered exploratory and not as a justification for any changes in practice.

Strengths and limitations of the assessment

The assessment has certain strengths:

- It was independent of any vested interest.
- The review brings together the evidence for the clinical effectiveness and cost-effectiveness of different methods of earwax removal using consistent methods of critical appraisal, presentation and transparency. In addition a de novo economic model has been developed, following recognised guidelines.
- The evidence synthesis was guided by the principles for undertaking systematic reviews and economic evaluations. Prior to undertaking the assessment, the methods were set out in a research protocol (Appendix 1), and this was commented on by an advisory group. The protocol defined the research question, inclusion criteria, quality criteria, data extraction process and methods used to undertake the different stages of the assessment.
- An advisory group has informed the review from its initiation, through the development of the research protocol and completion of the report.
- Systematic searches were undertaken to identify data for the economic model, and main results were summarised and presented.
- The quality of the clinical effectiveness studies was assessed using criteria recommended by the NHS CRD.

In contrast, the assessment was affected by certain limitations:

- The studies identified by the systematic review of clinical effectiveness were published over a considerable period, from 1950 to 2007. Inevitably the nature of clinical trials in terms of their methods and their reporting in publications has changed significantly during this period. Of the trials included in this systematic review, those early published studies tended to provide very limited details of their methods and results. As a consequence, it was difficult to assess the quality of the studies and interpret their results appropriately. In addition, the technologies have continued to develop, with new softeners, methods of irrigation and changes in the nature of the service used to deliver the interventions. Again, this limits the comparability of the evidence.
- Limited details are given in many of the studies of the participants involved in the studies, the dose and frequency of softeners used and the length of follow-up. All affect the generalisability of the findings.
- The effectiveness of the different interventions for removing earwax was assessed through a range of different outcomes. While many of the outcomes assessed the extent and ease of clearance, the specific nature of the different outcomes varied considerably. The extent of clearance was assessed by outcomes such as amount of TM visualised, proportion achieving complete visualisation of the TM, degree of

wax removal, hearing, wax clearance, wax occlusion, degree of impaction, amount of wax removed, recurrence of cerumen impaction and further treatment required. Ease of removal of earwax was assessed through outcomes such as volume of water for syringing and syringefuls used, mean number of syringing attempts, mean time to syringe, ease of wax removal, ease of syringing, frequency of syringing, and time taken to de-wax. In many of the studies there was no clear description or definition of these outcome measures. Many are open to subjective measurement and interpretation. As a consequence, it was difficult to directly compare and synthesise the outcomes from the different studies. No studies assessed benefits of the different interventions on quality of life. Although a limited proportion of studies did examine different measures of patient satisfaction, these were limited to whether patients were satisfied with the intervention and if they found them effective and tolerable. Again, these outcomes were not clearly defined or described and open to subjective interpretation.

- Some studies used a different unit of allocation to that used for the analysis (e.g. participants compared with ears). Although there are methods for handling the analysis of such data, it was unclear whether these were followed by the primary studies.
- Although recurrence of earwax is thought to be a common problem for sufferers, it was not considered in the studies included in the systematic review. Recurrence may be a consequence of differences in the anatomical structure of different people's ears, a result of damage that has been caused to the mechanism that allows earwax to be removed or to the use of medical devices (e.g. hearing aids). Inevitably people within this group will use a disproportionate amount of services and research should focus on identifying methods for diagnosing, treating and, if possible, preventing further problems. The economic evaluation assumed a recurrence rate of one event every 3 years. Inevitably this was a simplification and some people will incur a higher recurrence rate.
- Follow-up with authors to clarify details of their methods and results was not routinely undertaken. Given that the majority of studies that lacked such information were those published nearly 60 years ago, it was considered of limited value to do so as authors would be difficult to trace and further details of studies are unlikely to be available. As technologies have developed and practice has changed, these early studies may have been of more limited relevance to current practice. Where there were uncertainties in key aspects in more recent publications, contact was attempted and was beneficial in some cases.
- Synthesis of the studies included in the systematic review of clinical effectiveness was through narrative review. Due to the limitations of the literature, meta-analysis was not possible.
- The limitations evident in the systematic review of clinical effectiveness and cost-effectiveness and in the evidence on the epidemiology and aetiology of earwax have impacted upon the development of the de novo economic evaluation. With studies either lacking detail of study characteristics or being heterogeneous in nature, the evidence base was limited. As a consequence, assumptions were used to develop the structure of the clinical pathway and to populate the different elements of the model (see Chapter 5, Assumptions used in the model). This has rendered the economic evaluation as exploratory, from which definitive recommendations for changing clinical practice should not be drawn.
- The economic evaluation was developed from a NHS perspective, with patients having to attend primary care for assessment prior to decisions about subsequent treatment. Inevitably, some people will not attend primary care for assessment and/or treatment and will either suffer from the problem untreated or decide to self treat. These people are not included within the evaluation. The rationale for excluding these people was that the intention of providing evidence to decision-makers as to possible future guidance to the NHS, and, as such, the research had to focus on aspects of current provision that could be affected by policy. This led to the exclusion of the evaluation of a service where advice from the NHS on self-syringing is provided without attendance at primary care practice (e.g. NHS Direct or through advice from pharmacists) or the effects of personal costs to the patient. Also, limited evidence was available as to the safety and effectiveness of self diagnosis and treatment.
- With no definitive guidelines identified for the management of symptomatic earwax in the UK, the clinical pathway used to structure the economic evaluation was developed using assumptions based on available evidence and advice from clinical experts. As a consequence,

it was uncertain if the clinical pathway used in the model was representative of current practice. For example, it was unclear who undertakes the first assessment within primary care, whether a practice nurse or a GP. Opinion appears to vary and it is likely that different primary care practices adopt different approaches. Also, the duration of the use of softeners was uncertain. Expert advice indicates that people use softeners for a week prior to self-based or primary-care-practice-based irrigation. Others have suggested that the effectiveness of softeners may not depend on the duration of their use[49] with spontaneous clearance achieved in a short period (e.g. 20 minutes). Although alternatives have been examined through sensitivity and scenario analyses where possible, in some instances a pragmatic approach has been taken.

- Similar concerns affect the parameter inputs used to populate the economic evaluation. No published evidence was found on the incidence of SAE associated with either professional irrigation or self-irrigation. As a consequence the base-case estimate was based on expert advice from an OTL. This may be an underestimate of the probability of SAE as it is based on the assumption that all patients are referred to secondary care. It is possible that some patients with SAE are first treated in primary care, and only those whose infection or TM perforation does not heal within the expected time are referred to secondary care. It was also assumed that the probability of SAE in both active treatment alternatives is the same regardless of the mode of irrigation (self-irrigation or administered by a primary care practice nurse) and whether irrigation is undertaken for the first, second or the third time, which may not correspond to actual clinical practice.
- There were no published estimates of the loss of HRQoL associated with symptomatic earwax. The utility decrement of 0.006 (standard error = 0.0001) was obtained from Sullivan and Ghushchyan.[78] This was based on SF-12 quality-of-life estimates in the general US population, with the loss of hearing as defined by the ICD-9-CM diagnosis code 389. The original estimates were then converted into EQ-5D values. The estimates are not specific to patients presenting with earwax, although earwax is associated with temporary loss of hearing, as well as other symptoms. The utility decrement does not reflect minor complications, such as itching and tinnitus, and other minor symptoms, such as aural fullness and vertigo that affect HRQoL of patients with earwax problem. The direction of bias in the results of an economic evaluation associated with the use of utility decrement of 0.006 based on the ICD-9-CM diagnosis code 389 is unknown. An alternative utility estimate of 0.06[79] obtained in the population eligible for a hearing aid was used in the scenario analysis. The results indicated that the ICER estimates are sensitive to the choice of value of the utility gain.
- The economic evaluation was conducted for a general population of adults aged 35–44 years without any known contraindications to irrigation, reflecting the participants in the primary studies of efficacy used to develop the economic evaluation. Although limited epidemiological data were available, it was felt that this group may not represent those in which the condition is most prevalent. As such, the results may not necessarily apply to other population groups, such as the elderly, children and people with disabilities. This is particularly important when considering the use of new technologies, such as self-irrigation, which require care in their use and adherence to instruction. It is likely that self-irrigation will only be relevant to a subgroup of the general population and therefore it should not necessarily be considered as an option for all groups.

Comparison with previous reviews

The findings of our evidence synthesis are generally in line with those of other systematic reviews in the area. We identified four previous reviews,[1,29,37,74] each with slightly different methodologies and therefore different number of included studies. One review[74] included nine RCTs, as well as seven in vitro studies and centred on commercially available products obtainable to facilitate ear syringing. All included RCTs were quality assessed and date of last searching was 2002. Excluding the findings of the in vitro studies, the review found that no one product was superior to another.

A Cochrane Collaboration review updated in 2009, which included nine RCTs, centred on the effectiveness of ear drops only.[88] All included RCTs were quality assessed. Although most studies were judged not to be comparable and of poor

quality, two[46,47] of the nine included trials were meta-analysed. While the overall findings of the review were inconclusive, results from the meta analysis suggest TP is statistically superior to saline in preventing the need for syringing. A third review[29] included 18 RCTs and concentrated on the effectiveness of topical preparations for the treatment of earwax. Trials were quality assessed and the date of last searching was January 2004. Preparations in this review were categorised into water-, oil- and non-water-based. Although the review undertook a meta-analysis, it also found that no one preparation was superior to another in either clearing earwax or facilitating syringing.

A more recent review[37] included trials and systematic reviews,[1,29] and considered treatments for both ear syringing and manual removal. The review carried out a grade evaluation of interventions for earwax on four of the included RCTs.[4,42,56,62] Date of last searching was June 2007. Similarly to our conclusion, the overall conclusion of the review was that there was not enough evidence showing softeners alone to be effective or that one type of softener is superior to another.

Our review differed from these previous reviews, in that we assessed studies by setting, intention to use softening agent alone or as part of the irrigation procedure, followed by population and subgrouped into immediate or delayed follow-up. We assessed all methods of treatment, including self-syringing, all available preparation comparisons and each study was assessed for methodological quality. We did not feel that quantitative pooling of the data was appropriate. In the Hand and Harvey study,[29] data was combined. However, with such diverse outcomes and participant groups, we question whether this is appropriate. Furthermore, it is also questionable whether pooled data based on such poor quality studies provides reliable evidence about the effectiveness of these products.

Research recommendations

The systematic review of clinical effectiveness and cost-effectiveness and the development of the de novo economic evaluation have highlighted the paucity of good-quality evidence available to identify the most appropriate methods for the removal of earwax. This is a key concern given the prevalence of the condition, its implications for the use of health service resources and the apparent need to provide national guidance for practitioners. In addition, the potential for litigation has an influence on the provision of the service and unequivocal evidence is required to provide a safe, effective and efficient service. To provide clearer guidance, there will be a need for further research.

Much of the research identified in the systematic review has focused on the use of different drops to soften, dissipate or dissolve the wax, with limited attention being given to other facets, such as the method of mechanical removal, the role of the provider of the service, the effects of variations in practice and the importance of patient choice. Inevitably, it will be helpful to have clear evidence on the safety and effectiveness of the different drops and of the different methods for mechanical removal of earwax. However, a key concern that requires further research is how the different interventions are delivered and to which patient groups. Current practice, although thought to be variable nationally, tends to involve people attending primary care practices for diagnosis and treatment. Self-treatment with drops and then self-irrigation may offer a less costly alternative, with people only attending primary care practices if they are unable to clear the problem to their satisfaction. As a condition with a high recurrence rate, this would have the potential for reducing costs considerably. However, uncertainty remains as to whether self-irrigation is a safe and effective option that would be acceptable to patients and practitioners. By the nature of the process involved and concerns about litigation against the health service, it may be that the use of self-irrigation would be limited to a specific patient subgroup able to consent to its use and self treat. It would be helpful to identify this group and the safety, benefits and costs of the use of self-irrigation compared to current practice.

As such, it would be helpful to have an RCT to assess the clinical effectiveness and cost-effectiveness of self-treatment through the provision of drops and use of a soft bulb irrigator compared with standard practice. With the variation in current practice within the UK, the trial should focus on the role of the practice nurse in assessing the condition, recommending drops and irrigating the ears within the comparator. Where appropriate, it should consider the possibility of using different drops for softening the earwax, different durations of the use of softeners and the particular methods for irrigation. However, these should be considered secondary to the use of self-treatment and the provision of the service. The patient groups included in the trial should be representative of those currently attending primary

care, with a predominance of more elderly patients. Recurrence is common among people with earwax and this aspect will need to be encompassed with any evaluation. The outcomes to be used in the RCT will be important and will need to be objective, clearly defined and assessed by validated outcome assessors to improve comparability. They should include relief from patient reported symptoms, measures of clearance, quality of life and patient satisfaction and AE.

An economic evaluation will be a key part of any subsequent research. It is evident that the data that would normally underpin an economic evaluation are very limited. Further evidence is required on the epidemiology of the condition in terms of the prevalence of the condition, levels of recurrence and its natural history. It will be important to measure the patient's quality of life using an appropriate and validated measure (e.g. EQ-5D or HUI3) focusing on people with symptomatic earwax rather than surrogates associated with hearing loss. AEs are thought to be important factors in providing the service and it will be important to collect data from any RCT. Given their apparent rarity and limited length of follow-up of most RCTs, there will need to be additional research to collect data on SAEs from primary and specialist care databases (e.g. serious infections and perforations of the TM). Accurate data on the costs of the different treatment options will be important to the evaluation and should be collected prospectively as part of any study.

While an RCT incorporating an economic evaluation provides the most robust form of evidence, it is possible that investment in other forms of study design would provide appropriate data to help develop the current evaluation and allow decisions concerning policy to the NHS. A value of information analysis assessed the value of further research on utilities, primary care costs, secondary costs, irrigation efficacy, softener efficacy and frequency of AEs. At a decision threshold of between £20,000 and £30,000 the EVPPI identified improvements in estimates of costs associated with primary care and the efficacy of methods of irrigation as the key inputs for improved information. As such, a prospective costing study or chart review of primary care costs may provide useful data to improve the current economic evaluation within the bounds of acceptable research costs. Improving data on the efficacy of different methods of irrigation is likely to require a clinical trial which would be more costly, but could provide information for other parameters.

Chapter 8
Conclusions

The systematic review has shown limited good-quality evidence assessing the clinical effectiveness and cost-effectiveness of the different methods of earwax removal. As a consequence, it has proved difficult to differentiate between the different methods of earwax removal in terms of their effectiveness in clearing earwax, improving patient quality of life and satisfaction, or AEs. It appears that softeners do have some effect in helping to clear earwax in their own right or as a precursor to irrigation. However, which specific softeners are most effective remains unclear. There was limited consideration of the most effective method of irrigation or mechanical removal of earwax. Although irrigation was a key part of the treatment within many of the trials, the specific methods were not a focus of the analyses. Where the methods of irrigation or mechanical removal were assessed, the evidence was limited in quantity and/or methodological quality, so no clear guidance can be provided. The paucity of evidence on the benefits and costs of the different methods for the removal of earwax rendered the economic evaluation limited in its scope, and speculative, with many uncertainties remaining. Although it found self-treatment more cost-effective than primary care practice-based care, it focused on a limited population group (i.e. people 35–44 years with no contraindications) and was underpinned by several speculative assumptions (e.g. comparable clinical effectiveness). As such, the economic evaluation should be considered illustrative of the possible analysis that could be undertaken if a satisfactory evidence base were available. It does not provide evidence for recommendations that can be used to change clinical practice.

As a consequence, further research is required to identify the most effective method for the removal of earwax for different groups of people. The research should focus on those elements where uncertainty remains and that have the potential to impact on patients, the provision of the service and value for money. Although much of the research so far has looked at the role of softeners, perhaps the more important aspect for research is consideration of the method of mechanical removal and provision of the service. Traditionally, this has relied upon the patient attending the primary care practice for consultation, followed by the use of softeners and a further visit to have the earwax removed. Self-treatment may provide an alternative option for a specific group of people who find it acceptable and are able to undertake the procedure. It would provide the opportunity for those people to treat themselves when required, with the possibility of removing some of the burden from the health service. For many people professional care from the health service will continue to provide the most appropriate method for the removal of earwax and research should assess the role of the practice nurse and other members of the nursing team in the provision of care. In both instances research should assess the clinical effectiveness and cost-effectiveness of the different approaches, focusing on efficacy, acceptability to patients and practitioners, possible AEs and costs. While a RCT incorporating an economic evaluation would provide the most robust method for assessing several aspects of the removal of earwax, a prospective study of the costs of the provision of care within primary care may provide a less costly option in the first instance.

Acknowledgements

Contributions of authors

AJ Clegg: Developed the original research grant application, acted as principal investigator and project managed the research, developed the research protocol, assisted in the development of the search strategy, assessed studies for inclusion, extracted data from and quality assessed included studies, synthesised evidence, and drafted and edited the final report.

E Loveman: Developed the research protocol, led the systematic review of clinical effectiveness, assisted in the development of the search strategy, assessed studies for inclusion, extracted data from and quality assessed included studies, synthesised evidence, and drafted and edited the final report.

E Gospodarevskaya: Developed the research protocol, assisted in the development of the search strategy, assessed studies for inclusion and extracted data for the economic evaluation, led the development of the economic evaluation and drafted the final report.

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A Bird: Developed the research protocol, assisted in the development of the search strategy, assessed studies for inclusion and extracted data from included studies, synthesised evidence, developed the economic evaluation and drafted the final report.

J Bryant: Developed the original research grant application, developed the research protocol, and drafted and edited the final report.

DA Scott: Developed the original research grant application, acted as guarantor for the economic evaluation, developed the research protocol, developed the economic evaluation and drafted the final report.

P Davidson: Developed the original research grant application, developed the research protocol and assisted in the drafting of the final report.

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We would like to thank members of our advisory group panel who provided expert advice and comments on the protocol and/or a draft of this report:

Professor George Browning, Emeritus Professor of Otorhinolaryngology, MRC Institute of Hearing Research, University of Glasgow, Glasgow Royal Infirmary, Glasgow, UK.

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We are also grateful to Karen Welch, Information Specialist (SHTAC, University of Southampton), for conducting the searches; Elizabeth Hodson, Information Assistant (Wessex Institute, University of Southampton), for retrieving references; Mr Jonathan Blanshard, Consultant ENT Surgeon

(Basingstoke and North Hampshire NHS Foundation Trust, Basingstoke), Mr Paul Spraggs, Consultant ENT Surgeon (Basingstoke and North Hampshire NHS Foundation Trust, Basingstoke), Dorothy Wicke, Research Nurse (Oakley and Overton Partnership, Basingstoke), Joanne Nesbitt, Practice Nurse (Denton Park Medical Group, Newcastle PCT, Newcastle) and Julia Johns, Practice Nurse (Padnell Road Surgery, Hampshire PCT) for data for the economic model; and, Dr Jill Colquitt, Senior Research Fellow (SHTAC, University of Southampton), for reviewing a draft of this report.

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Appendix 1
Protocol methods

Systematic review

A systematic review will be undertaken in accordance with the NHS Centre for Reviews and Dissemination (CRD) guidelines,[40] published guidelines on meta-analysis,[89] and criteria for appraising economic evaluations.[90,91]

Literature searches

Literature will be identified from several sources including electronic databases, bibliographies of articles, grey literature and consultation with experts in the area. A comprehensive database of relevant published and unpublished articles will be constructed using the REFERENCE MANAGER software package. The searches carried out will include:

1. General health and biomedical databases, including MEDLINE, EMBASE, Science Citation Index and BIOSIS.
2. Specialist electronic databases: DARE and The Cochrane Library.
3. Grey literature and conference proceedings.
4. Contact with individual experts and those with an interest in the field.
5. Checking of reference lists.
6. Research in progress: National Research Register (historical), UKCRN, Current Controlled Trials (CCT) and ClinicalTrials.gov.

All databases will be searched from their inception to the current date. In the first instance searches will be conducted in all languages, with non-English language articles set to one side in a separate foreign language reference database. Thereafter, an assessment of the volume of non-English language literature will be made and, translation and time restrictions permitting, these will be included in the review. Letters will be sent to experts to ask if they know of any relevant published or unpublished studies that we have not identified.

Study inclusion

Studies will be selected for inclusion in the review in a two-stage process using the predefined and explicit selection criteria outlined in Table 1 below. The full literature search results will be screened independently by two reviewers to identify all citations that may meet the inclusion criteria. Full manuscripts of all selected citations will be retrieved and assessed by two independent reviewers against the inclusion criteria. These criteria will be piloted on a sample of papers. Any disagreements over study inclusion will be resolved by consensus or if necessary by arbitration involving a third reviewer.

Planned inclusion/exclusion criteria

The planned inclusion/exclusion criteria for the systematic review are shown in *Table 1*.

Data extraction

The extraction of studies' characteristics, methods and findings will be conducted by one reviewer and checked by a second reviewer using a predesigned and piloted data extraction form to avoid any errors. Any disagreements between reviewers will be resolved by consensus or, if necessary, by arbitration by a third reviewer.

Quality assessment

The methodological quality of all included studies will be appraised using a formal quality assessment criteria recommended by CRD[40] (see below) and criteria for appraising economic evaluations.[90,91] Study quality will be assessed by one reviewer and checked by a second reviewer. Any disagreements between reviewers will be resolved by consensus or if necessary by arbitration involving a third reviewer.

Data synthesis

The results of included studies will be tabulated and summarised in a narrative review. The methods of data synthesis will be determined by the nature of the studies identified through searches and included in the review. Quantitative synthesis of results will be considered if there are several high-quality studies of the same design, but specific details are not possible until the data has been obtained. Sources of heterogeneity will be investigated using appropriate methods.

Economic evaluation

Cost-effectiveness will be assessed through a two-stage process. First, a systematic review of cost-effectiveness studies (full economic evaluations) will be undertaken to address the question of the

TABLE 1 *Inclusion criteria for systematic reviews*

Interventions	All methods of earwax removal or softening, including:
	• Drops
	  • Almond oil
	  • Olive oil
	  • Sodium bicarbonate drops
	  • Cerumol
	  • Exterol
	  • Molcer
	  • Otex
	  • Waxsol
	• Irrigation (e.g. syringing, electronic irrigators)
	• Mechanical removal other than irrigation (e.g. suction, probes and forceps)
	• Other methods
	• Combinations of above methods
	[Note: Interventions specify methods of removal and softening. Although it does not outline methods of visualisation (e.g. microscope, endoscope and head light loop) these will be identified in data extraction as they will be important elements of removal.]

Population	Adults and children presenting with build-up of earwax requiring removal
Outcomes	Measures of hearing Adequacy of clearance of wax (e.g. visualisation of tympanic membrane) Quality of life Time to recurrence or further treatment Adverse events (AEs) Measures of costs and cost-effectiveness (e.g. cost per quality-adjusted life-year) (Note: Studies must report summary statistics or present sufficient raw data to allow these to be calculated.)
Study design	Randomised controlled trials Controlled clinical trials Cohort studies (AEs) Costing studies, cost-effectiveness evaluations (including modelling studies) (Note: Where there is evidence from different types of study design for a specific intervention, only those studies with the most rigorous designs will be included and data extracted.)

AEs, adverse events.

cost-effectiveness of different methods for earwax removal in the different patient groups. The methods for the review will be analogous to those presented for the review of clinical effectiveness and results will be presented using a narrative synthesis. Quality assessment of cost-effectiveness studies will be conducted using a checklist adapted from those developed by Drummond and colleagues[90] and Philips and colleagues.[91]

Second, if no economic evaluation relevant to the UK setting is identified, construction of a de novo economic model will be considered where appropriate, with the aim of establishing the relative cost-effectiveness of the different interventions for removing earwax. The structure of the model will reflect current treatment pathways employed by clinicians and other health professionals for the removal of earwax. Any proposed alternatives to current practice identified in the literature or through consultation with practicing clinicians and other health professionals will also be considered. The structural validity of the model will be checked through consultation with clinicians and other health professionals in the UK who are experienced in earwax removal. The model will be either a decision tree or a Markov process model, although its design will be determined, in part, by the data available to populate it. Health states will likely comprise: occlusion, complete clearance and adverse events (AEs) (e.g. perforation leading to long-term

hearing loss). It is expected that the model will be populated with the data from the systematic review of clinical effectiveness and cost-effectiveness, and from other routinely collected data sources [e.g. unit costs from the Personal Social Services Research Unit (PSSRU)]. If data are not identified from these sources, we will consider performing additional targeted searches and/or consultation with experts on all model inputs to provide appropriate data. The model will be from the perspective of the NHS and will include, where possible, all costs and consequences related to the NHS perspective and all patient-related benefits.

The base-case model will aim to focus on adults who are eligible for the entire range of treatment alternatives for earwax removal, although the model will aim to assess those interventions shown to be effective in the systematic review of clinical effectiveness. Subject to data availability, alternative versions of the model may be developed to examine subgroups that may respond differently to treatment. Possible subgroups will be identified through consultation with clinical advisors and through the evidence from the systematic review. Each alternative treatment pathway is likely to be quantified in terms of the success of treatment, symptom recurrence, serious AEs suffered, the resource cost of treatment and impact on patients' quality of life. Costs will be presented in a base year and discounting of costs and benefits will be performed. Incremental costs and benefits will then be measured for alternative treatments. If possible, the outcome measure from the economic evaluation will be cost per quality-adjusted life-year (QALY).

The model's underlying assumptions will be assessed through sensitivity analyses and threshold analysis for a range of parameters at which reasonable cost-effectiveness levels could be achieved. Probabilistic sensitivity analysis, whereby parameters are varied within reported ranges and distributions, will be undertaken to determine the impact of uncertainty upon the model.

Value of information analysis will be undertaken where possible to help identify future research priorities quantified by the value of reducing decision uncertainty (and its consequences in terms of the opportunity costs), which could be derived from additional research investment on earwax removal technologies.[84,85] It is intended that this approach will systematically appraise which future research would be most valuable and also assist in identifying appropriate research designs.[92]

The model will be constructed in TREEAGE PRO 2007 or Microsoft EXCEL and will be made as transparent as possible in order that it can be readily updated when new data emerge. The modelling work will follow guidelines for good practice as reported by Philips and colleagues.[91] Building a model is an iterative process and quality control checks will be included at several points during the process to ensure that appropriate structure and data are applied. This is necessary to ensure that the results can be relied upon to inform decision-makers regarding the cost-effectiveness of the intervention. There are several steps to this formal process:

- A comparison of the model results with those from any other relevant models identified from our systematic review. Any differences between the results will be explored and, if necessary, appropriate modifications made to the model.
- Model results will be analysed to ensure they accurately reflect the inputs used in the model. This ensures that the data used to populate the model are being applied at the correct times and locations. Extreme parameter values can be used to test whether the model behaves as expected.
- The model will be critically appraised by a second health economist/modeller. This will allow the approach to be validated and permits any areas of disagreement to be resolved prior to generation of model results.

These three steps help ensure that all aspects of potential error in the model – a lack of internal validity, a lack of external validity and any omissions or biases from an individual health economist – are addressed.

Types and sources of information for economic evaluation

Epidemiology Information on the epidemiology of hearing impairment including the incidence, prevalence and prognosis of the condition will be identified from the literature and supplemented if necessary with clinical expertise.

Treatment efficacy and safety Efficacy and safety data will be extracted from the clinical studies identified in our systematic review of clinical effectiveness. If there is a paucity of data on parameters, clinicians may need to be consulted in order to obtain estimates of, or variability around, the parameters included in the model. The outcomes are likely to be assessed in terms of symptom relief, AEs suffered and symptom recurrence.

Quality of life In order to calculate cost per QALY the estimates of utility decrements for patients who suffer symptoms of hearing impairment and AEs typically associated with wax removal will be sought. Ideally utility weights for common adverse effects will be obtained from patient-based estimates (or, potentially, 'guardian-based' estimates in the case of children). These decrements may be reported in literature and preference will be given to the utility weights expressed in age- and sex-specific EQ-5D population norms for the UK.[77] Separate targeted searches will be undertaken to try and identify relevant data. If necessary, however, they will be obtained from alternative sources such as clinical opinion through contact with clinicians.

Cost and resource use measurement The pattern of resource use and their associated costs may be identified from published or official sources. If necessary these data will be supplemented by contact with clinicians and NHS trust finance departments. Major resource components will include treatment costs in terms of primary and/or secondary care visits (including staff costs, equipment and overheads), treatment of AEs and follow-up visits. All drug costs will be obtained from the *British National Formulary* (BNF) online. Inpatient days and outpatient visits costs will also be obtained from NHS reference costs. Unit costs for home visits by GPs or district nurses will be obtained from published data.[93]

Quality assessment criteria

Quality criteria for assessment of experimental studies

1. Was the assignment to the treatment groups really random?
2. Was the treatment allocation concealed?
3. Were the groups similar at baseline in terms of prognostic factors?
4. Were the eligibility criteria specified?
5. Were outcome assessors blinded to the treatment allocation?
6. Was the care-provider blinded?
7. Was the patient blinded?
8. Were the point estimates and measure of variability presented for the primary outcome measure?
9. Did the analyses include an ITT analysis?

Some instructions for using a checklist for RCTs

Quality item	Coding	Explanation
1. Was the assignment to the treatment groups really random?		
Random sequence generation	Adequate Partial Inadequate Unknown	*Adequate*: Random numbers table or computer and central office or coded packages *Partial*: Envelopes (sealed) without further description or serially numbered opaque, sealed envelopes *Inadequate*: Alternation, case record number, birth date, or similar procedures *Unknown*: Just the term 'randomised' or 'randomly allocated', etc.
2. Was the treatment allocation concealed?		
Concealment of randomisation The person(s) who decide on eligibility should not be able to know or be able to predict with reasonable accuracy to which treatment group a patient will be allocated. In trials that use good placebos this should normally be the case; however, different modes or timing of drug administration in combination with the use of small block sizes of known size may present opportunities for clinicians who are also involved in the inclusion procedure to make	Adequate Inadequate Unknown	*Adequate*: When a paper convinces you that allocation cannot be predicted (separate persons, placebo really indistinguishable, clever use of block sizes (large or variable). Adequate approaches might include centralised or pharmacy-controlled randomisation, serially numbered identical containers, on-site computer-based system with a randomisation sequence that is not readable until allocation, and other approaches with robust methods to prevent foreknowledge of the allocation sequence to clinicians and patients

Quality item	Coding	Explanation
accurate guesses and selectively exclude eligible patients in the light of their most likely treatment allocation; in centres with very low inclusion frequencies combined with very brief follow-up times this my also present a potential problem because the outcome of the previous patient may serve as a predictor of the next likely allocation		I*nadequate*: This option is often difficult. You have to visualise the procedure and think how people might be able to circumvent it. Inadequate approaches might include use of alternation, case record numbers, birth dates or week days, open random numbers lists, serially numbered envelopes (even sealed opaque envelopes can be subject to manipulation) and any other measures that cannot prevent foreknowledge of group allocation *Unknown*: No details in text; disagreements or lack of clarity should be discussed in the review team
3. Were the groups similar at baseline regarding the prognostic factors?		
Baseline characteristics Main aim is to enable the reviewer to see which patients were actually recruited. It enables one to get a rough idea on prognostic comparability. A real check on comparability requires multivariable stratification (seldom shown)	Reported Unknown	Consult the list of prognostic factors or baseline characteristics (not included in this appendix). Reviewer decides
4. Were the eligibility criteria specified?		
Prestratification Consult the list of prognostic factors or baseline characteristics (not included in this appendix)	Adequate Partial Inadequate Unknown	*Single-centre study* *Adequate*: Prestratification on at least one factor from the list or no prestratification if the number of patients exceeds a prespecified number *Partial*: Leave judgement to reviewer *Inadequate*: Stratification on a factor(s) not on our list or no stratification, whereas the number of patients is less than the prespecified number *Unknown*: No details in text and no way to deduce the procedure from the tables *Multicentre study* *Adequate*: Must prestratify on centre. Within each centre the criteria for single-centre studies also apply *Partial*: Impossible option *Inadequate*: No prestratification on centre or violating the criteria for single-centre studies (see above) *Unknown*: No details in text and no way to deduce the procedure from the tables
5. Were outcome assessors blinded to the treatment allocation?		
Blinding of assessors The assessor may be the patient (self report), the clinician (clinical scale, blood pressure) or, ideally, a third person or a panel. Very important in judgement of cause of death but unimportant in judgement of death	Adequate Inadequate Unknown	*Adequate*: Independent person or panel or (self) assessments in watertight double-blind conditions *Inadequate*: Clinician is assessor in trial on drugs with clear side effects or a different influence on laboratory results, ECGs, etc. *Unknown*: No statements on procedures and not deducible
6. Was the care-provider blinded?		
Blinding of caregivers Look out for good placebos (see, hear, taste, feel, smell), tricky unmasking side effects accounting for the subjectivity of the outcome measurements and the accessibility of co-interventions by the caregivers	Adequate Partial Inadequate Unknown	*Adequate*: Placebo described as 'indistinguishable' and procedures watertight (use your imagination with the 'cheat' in mind; e.g. statement that sensitive/unmasking laboratory results were kept separate from ward personnel)

Quality item	Coding	Explanation
		Partial: Just 'double-blind' in text and no further description of procedures or nature of the placebo *Inadequate*: Wrong placebo (e.g. fructose in trial on ascorbic acid) *Unknown*: No details in text
Co-interventions Register when they may have an impact on any of the outcome phenomena. Consult the list of cointerventions (not included in this appendix).	Adequate Partial Inadequate Unknown	*Adequate*: Percentages of all relevant interventions in all groups *Partial*: One or more interventions omitted or omission of percentages in each group *Inadequate*: Not deducible *Unknown*: No statements
7. Was the patient blinded?		
Blinding of patients This item is hard to define. Just the statement 'double-blind' in the paper is really insufficient if the procedure to accomplish this is not described or reasonably deducible by the reviewer. Good placebos (see, hear, taste, feel, smell), tricky unmasking side effects accounting for the subjectivity of the outcome measurements and the accessibility of co-interventions by the patient are required	Adequate Partial Inadequate Unknown	*Adequate*: Placebo described as 'indistinguishable' and procedures watertight *Partial*: Just 'double-blind' in text and no further description of procedures or nature of the placebo *Inadequate*: Wrong placebo *Unknown*: No details in text
Compliance Dosing errors and timing errors	Adequate Partial Inadequate Unknown	*Adequate*: Medication Event Monitoring System (MEMS or eDEM) *Partial*: Blood samples, urine samples (use of indicator substances) *Inadequate*: Pill count or self report *Unknown*: Not mentioned
Check on blinding Questionnaire for patients, caregivers, assessors and analysis of the results; the (early) timing is critical because the treatment effect may be the cause of unblinding, in which case it may be used as an outcome measure	Reported Unknown	Reviewer decides
8. Were the point estimates and measure of variability presented for the primary outcome measure?		
Results for the primary outcome measure	Adequate Partial Inadequate Unknown	*Adequate*: Mean outcome in each group together with mean difference and its standard error (SE) or standard deviation (SD) or any CI around it or the possibility to calculate those from the paper. Survival curve with log-rank test and patient numbers at later time points *Partial:* Partially reported *Inadequate*: No SE or SD, or SD without N (SE=SD/N) *Unknown*: Very unlikely

Quality item	Coding	Explanation
9. Did the analysis include an intention-to-treat (ITT) analysis?		
ITT Early dropout can make this very difficult. Strictest requirement is sensitivity analysis including early dropouts	Adequate Inadequate	Reviewers should not just look for the term ITT but assure themselves that the calculations were according to the ITT principle
Dealing with missing values The percentage missing values on potential confounders and outcome measurements (seldom given) is a rough estimate of a trial's quality. One can carry them forward, perform sensitivity analysis assuming the worst- and best-case scenarios, use statistical imputation techniques, etc. Note that the default option (deletion) assumes that the value is randomly missing, which seems seldom justified	Adequate Partial Inadequate Unknown	*Adequate*: Percentage of missing values and distribution over the groups and procedure of handling this stated *Partial*: Some statement on numbers or percentages *Inadequate*: Wrong procedure (a matter of great debate) *Unknown*: No mentioning at all of missing and not deducible from tables
Loss to follow-up This item examines both numbers and reasons; typically an item that needs checking in the methods section and the marginal totals in the tables. Note that it may differ for different outcome phenomena or time points. Some reasons may be reasons given by the patient when asked and may not be the true reason. There is no satisfactory solution for this	Adequate Partial Inadequate Unknown	*Adequate*: Number randomised must be stated. Number(s) lost to follow-up (dropped out) stated or deducible (from tables) for each group and reasons summarised for each group *Partial*: Numbers, but not the reasons (or vice versa) *Inadequate*: Numbers randomised not stated or not specified for each group *Unknown*: No details in text

Appendix 2

Literature searches and flow chart of included studies

The following databases were searched for published studies and recently completed and ongoing research. Searches were updated in December 2008.

1. General health and biomedical databases, including MEDLINE, EMBASE, Science Citation Index and BIOSIS.
2. Specialist electronic databases: DARE and the Cochrane library.
3. Grey literature and conference proceedings.
4. Contact with individual experts and those with an interest in the field.
5. Checking of reference lists.
6. Research in progress: National Research Register (historical), UK Clinical Research Network (CRN), Current Controlled Trials (CCT) and ClinicalTrials.gov.

Clinical effectiveness searches

The following strategies were used to search MEDLINE (OVID), 1966–2008. These were translated to search the other databases listed above.

1. cerumen/(578)
2. cerum*.tw. (531)
3. (ear* and wax*).tw. (581)
4. earwax*.tw. (60)
5. or/1–4 (1280)
6. randomized controlled trial.pt. (248764)
7. controlled clinical trial.pt. (76414)
8. randomized.ab. (160990)
9. placebo.ab. (103272)
10. clinical trials as topic.sh. (135286)
11. randomly.ab. (117274)
12. trial.ti. (71485)
13. exp Cohort Studies/(648803)
14. cohort.tw. (102947)
15. or/6–14 (1169187)
16. 5 and 15 (114)
17. humans.sh. (10090140)
18. 16 and 17 (105)
19. from 18 keep 1–105 (105)

Figure 7, shows the identification of studies for inclusion in the systematic review of clinical effectiveness.

Foreign language publications

Two foreign language publications were identified on searches and are listed below. From their English language abstracts it would appear that neither of these had a comparator group, and would therefore not meet the inclusion criteria of our review. However, we were unable to fully screen these for inclusion.

1. Cassano P, Mora E, Damiani V, Passali FM, Passali D. Valutazione dell'efficacia cerumenolitica di Audispray. *Otorinolaringol* 2002;**52**:131–5.
2. Cavallazzi GM, Bottero A. Impiego clinico di un nuovo ceruminolitico: considerazioni preliminary. *Riv Orl Aud Fon* 1988;**8**:197–200.

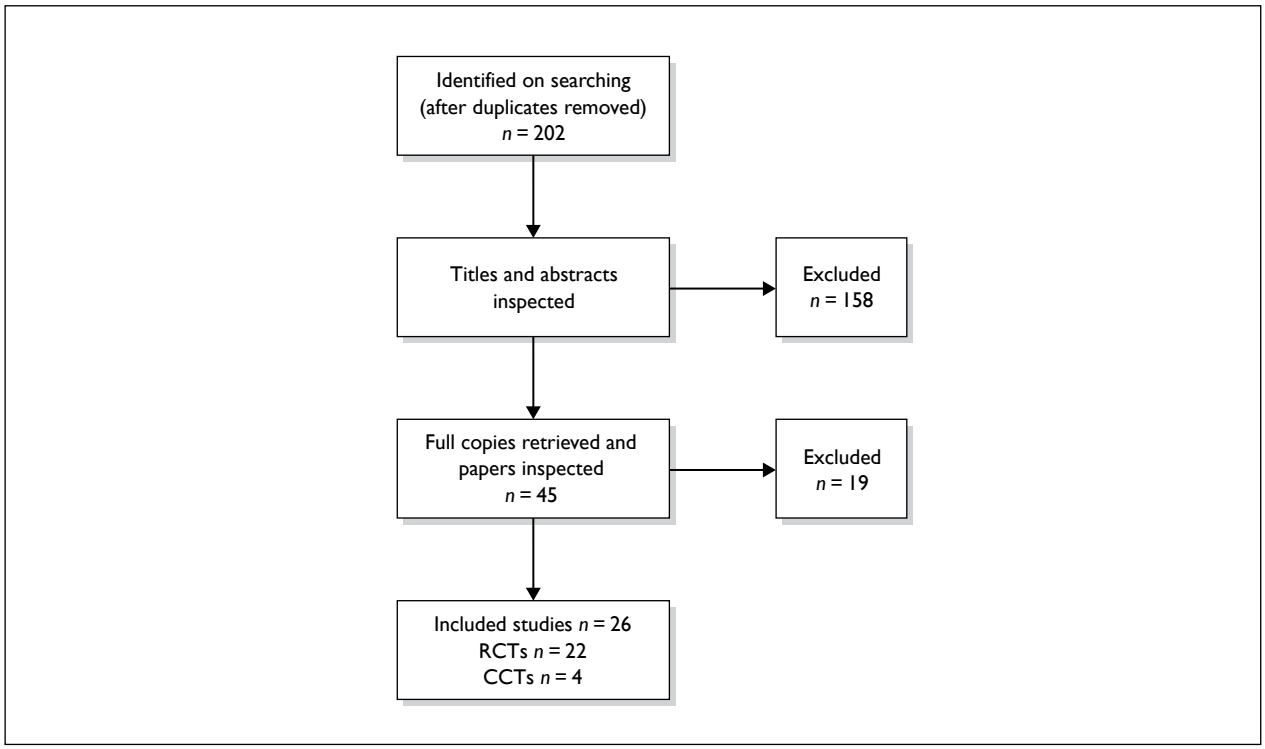

FIGURE 7 *Flow chart of identification of studies for inclusion in the systematic review of clinical effectiveness. CCTs, controlled clinical trials; RCTs randomised controlled trials.*

Appendix 3

Data extraction forms: primary care setting

Meehan and colleagues[46]

Extracted by: PH		**Checked by: EL**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Meehan and colleagues:[46] Abstract *Year*: 2002 *Country*: USA *Study design*: Double-blind RCT *Number of centres*: One *Setting*: Emergency care *Funding*: None reported	1. DS (Colace): 1 ml 2. TP (Cerumenex): 1 ml 3. NS: 1 ml *Duration of treatment*: 15 minutes *Other interventions used*: Irrigation with 50 ml of saline if TM was still occluded after treatment, repeated once if needed	*Number of participants*: 48 DS: *n* = 15 TP: *n* = 17 Saline: *n* = 16 *Sample attrition/dropout*: None reported, but numbers of participants in secondary outcomes are lower *Inclusion criteria for study entry*: Cooperative participants aged 1–18 presenting to a paediatric emergency department, with complete or partial TM occlusion *Exclusion criteria for study entry*: None reported	*Primary outcomes*: Amount of TM visualised *Secondary outcomes*: AEs *Method of assessing outcomes*: Grades of TM occlusion – complete, partial or clear *Length of follow-up*: Immediate

Baseline characteristics of participants

	All	**DS (*n* = 15)**	**TP (*n* = 17)**	**Saline (*n* = 16)**	***p*-value**
Gender M/F	24 : 24				No *p*-values reported
Mean age	4.6				
Median age	3.5				
TM occlusion – complete		11	11	9	
TM occlusion – partial		4	6	7	

Results

Primary outcomes

TM occlusion	**DS (*n* = 15)**	**TP (*n* = 17)**	**Saline (*n* = 16)**	***p*-value**
Complete	5	5	5	No *p*-values reported
Partial	8	5	9	
Clear	2	7	2	

Comments: after solvent (intervention) only

Secondary outcomes

	DS (*n* = 15)	**TP (*n* = 17)**	**Saline (*n* = 16)**	***p*-value**
TM occlusion after one irrigation:	*n* = 13	*n* = 15	*n* = 15	No *p*-values reported
Complete	4	4	4	
Partial	6	3	5	
Clear	3	8	6	

TM occlusion after two irrigations:	*n* = 12	*n* = 15	*n* = 15	No *p*-values reported
Complete	3	4	3	
Partial	4	3	4	
Clear	5	8	8	
Comments: The most common AE was pain with irrigation overall (10/48)				
Methodological comments				
Allocation to treatment groups: RCT – no other details reported				
Blinding: Study states double-blind evaluation, but no details reported				
Comparability of treatment groups: no details reported				
Method of data analysis: The abstract reports a trend for the efficacy of Cerumenex without irrigation and that adding irrigation improves the effectiveness of Colace, while a second irrigation does not improve outcomes. No data analysis or p-values are reported to support this				
Sample size/power calculation: None reported				
Attrition/dropout: None reported, but numbers of participants reported in secondary outcomes are lower				
General comments				
Generalisability: No breakdown of baseline characteristics for the three groups is provided, population consists of American children attending a university paediatric emergency department				
Outcome measures: It is unclear how valid or objective the measure was, or how consistent the assessments were.				
Intercentre variability: N/A				
Conflict of interests: None reported				

AEs, adverse events; DS, docusate sodium; F, female; M, male; N/A, not applicable; NS, normal saline; RCT, randomised controlled trial; TM, tympanic membrane; TP, triethanolamine polypeptide.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Inadequate
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Inadequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Partial
7. Was the patient blinded?	Partial
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Whatley and colleagues[47]

Extracted by: EL		**Checked by: PH**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Whatley and colleagues[47] *Year*: 2003 *Country*: USA *Study design*: RCT *Number of centres*: Two *Setting*: Children's hospital emergency department or large general paediatric clinic in same town *Funding*: Not stated	1. DS (docusate): 1 ml 2. TP (triethanolamine polypeptide): 1 ml 3. Saline control: 1 ml *Duration of treatment*: Between 15 and 30 minutes depending on number of irrigations *Other interventions used*: In all groups, if, after 15-minutes, the TM was not completely visualised, the ear was irrigated with 50 ml of tepid tap water (85–95°F). If still not clear another irrigation was undertaken A 60-ml syringe with a 18-gauge angiocatheter precut to 1.5 cm in lengths was used for irrigation	*Number of participants*: 96 assessed for eligibility, 3 refused to participate, 93 randomised 1. DS: 35 2. TP: 30 3. Control: 28 *Sample attrition/dropout*: DS one discontinued study, one excluded from analysis (protocol violation). *Inclusion criteria for study entry*: Aged 6 months to 5 years with complete or partial cerumen obstruction of the TM (assessed by 1 of 4 investigators) *Exclusion criteria for study entry*: Otitis externa Myringotomy tubes presently or placed within the last 2 years Suspected perforation of TM Severe healing loss in 1 or both ears Known allergy to study agents Prior complication from irrigation	*Primary outcomes*: Proportion achieving complete visualisation of the TM *Secondary outcomes*: Adverse events *Method of assessing outcomes*: Wax (based on colour and consistency) was characterised as soft, hard or mixed Complete obstruction defined as inability to visualise any of the TM, partial ability to visualise part of the TM but not all membrane landmarks, including light reflex, ossicles and mobility. To determine interobserver variability each investigator examined the same 26 ears prior to study initiation. A kappa value of 0.72 was obtained *Length of follow-up*: Immediate

Baseline characteristics of participants

	DS (*n* = 34)	**TP (*n* = 30)**	**Saline (*n* = 28)**	***p*-value**
Mean (SD) age, months	36.4 (19.1)	30.9 (15.2)	36.7 (19.5)	$p = 0.38$
Gender, M/F (%)	14:20 (41:59)	13:17 (43:57)	15:13 (54:46)	$p = 0.59$
Race, n (%)				
African American	26 (76)	15 (50)	19 (68)	$p = 0.16$, between all groups
White	8 (24)	14 (47)	8 (29)	
Other	0	1 (3)	1 (3)	
Wax, n (%)				
Hard	11 (32)	12 (40)	7 (25)	$p = 0.57$, between all groups
Soft	11 (32)	12 (40)	11 (39)	
Mixed	12 (35)	6 (20)	10 (36)	
Complete obstruction at enrolment, *n* (%)	31 (91)	24 (80)	22 (79)	$p = 0.33$

Results: Mean age (SD) in months for all participants 34.7 (18.1) gender for all (%) M 42 : F 50 (36 : 58)

Primary outcomes	**DS (*n* = 34)**	**TP (*n* = 30)**	**Saline (*n* = 28)**	***p*-value**
Clear TM after agent, *n* (%)	4 (12)	4 (13)	1 (4)	*p*-value not reported
Clear TM after first irrigation, *n* (%)	13 (38)	12 (40)	12 (43)	
Clear TM after second irrigation, *n* (%)	18 (53)	13 (43)	19 (68)	Between the 3 groups, p = ns

Comments: Potential confounders, including study site, different investigators and type of wax were analysed. The difference in the success rate between sites was not statistically significant ($p = 0.64$), nor was the difference between investigators ($p = 0.58$). The only trend was that the success rate for soft wax (68%) was higher than for mixed (50%) or hard (43%); $p = 0.13$.

Secondary outcomes	DS ($n = 34$)	TP ($n = 30$)	Saline ($n = 28$)	p-value

Comments: AEs – one patient had a small amount of ear canal bleeding after irrigation, but was able to complete the study (not reported which intervention group the participant was in).

Methodological comments

Allocation to treatment groups: A computerised, random-number program was used. Syringes were placed in consecutively numbered envelopes by a hospital pharmacist. Each enrolled participants was then assigned the next numbered envelope

Blinding: States double-blind, pharmacist loaded and sealed the syringes into envelopes, but not clear if any distinguishing factors between syringes or when the code was broken. Treatments were a different colour and any residues after drainage could enable investigators to determine which treatment a participant had received

Comparability of treatment groups: No statistically significant differences in baseline characteristics. Compared with the paediatric clinic, a higher proportion of patients enrolled in the emergency department received TP (42% vs 15%) and fewer patients received saline (22% vs 45%). Visually race appears to be dissimilar; however, differences are shown as statistically not significant

Method of data analysis: Categorical variables analysed using a chi-squared test or a Fisher's exact test. Continuous variables analysed using ANOVA. $p < 0.05$ was considered statistically significant. SAS statistical software version 8.02 (SAS Institute, Cary, NC) was used

Sample size/power calculation: A sample size of 90 was estimated to achieve 80% power to detect a 40 percentage-point difference between the treatment groups (= 0.05; χ^2 with d = 2). A 40 percentage-point difference was considered to be significant, based on previous studies

Attrition/dropout: In the docusate group 1 patient discontinued (due to the ear being irrigated before an agent was placed) and one was excluded

General comments

Generalisability: Population was young children, predominantly of African American race (64%). Convenient sample, only assessed when an investigator was available

Outcome measures: Inter-rater reliability assessed and reasonable

Intercentre variability: No significant differences noted by investigators. There was an imbalance of the TP and normal saline treatment groups between the 2 sites, with a higher percentage of participants enrolled in the emergency department TP group (42% vs 15%) and fewer participants in the normal saline group (22% vs 45%). Participants in the DS treatment group at each site were evenly distributed (36% vs 39%). The differences in success rates between sites was not significant ($p = 0.64$) nor the differences between investigators ($p = 0.58$)

Conflict of interests: None noted

AEs, adverse events; ANOVA, analysis of variance; F, female; M, male; RCT, randomised controlled trial; SD, standard deviation; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Adequate
2. Was the treatment allocation concealed?	Adequate
3. Were the groups similar at baseline in terms of prognostic factors?	Reported
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Partial
6. Was the care-provider blinded?	Partial
7. Was the patient blinded?	Partial
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Adequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, not reported, unclear.

Singer and colleagues[49]

Extracted by: PH		**Checked by: EL**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Singer and colleagues, [49] *Year*: 2000 *Country*: USA *Study design*: Double-blind RCT *Number of centres*: One *Setting*: Emergency department *Funding*: None reported	1. DS (Colace): 1 ml in liquid form 2. TP (Cerumenex): 1 ml in liquid form *Duration of treatment*: 10–15 minutes *Other interventions used*: If membrane was still obscured, ear irrigated with 50 ml of lukewarm normal saline solution. Repeated for a second time if TM was still obscured (50-ml syringe with 18-gauge angiocatheter at tip)	*Number of participants*: 50 (1 ear only per patient) 1. DS: 27 2. TP: 23 *Sample attrition/dropout*: None reported *Inclusion criteria for study entry*: ≥ 1 year, medially required visualisation of ear canal (i.e. earache, hearing loss, fever) and ear canal partially or totally occluded by cerumen *Exclusion criteria for study entry*: Known or suspected TM perforation, overt ear infection, uncooperative or allergy to solvent agents.	*Primary outcomes*: Proportion of ears in which membrane totally visible with or without irrigation or irrigation with 100 ml irrigant. *Secondary outcomes*: Presence of AE *Method of assessing outcomes*: Partially or totally obscured TM not stated but an interobserver agreement on patients independent patient set was good, $p = 0.79$ (reference given) *AE*: Participants/parents were asked to indicate AEs during procedure *Length of follow-up*: Immediate

Baseline characteristics of participants

	DS (*n* = 27)	**TP (*n* = 23)**	***p*-value**
Mean age years (SD)	38.7 (30.7)	46.1 (29.1)	No *p*-values reported
Gender M/F (%)	16 (59), 11 (41)	16 (70), 7 (30)	
Children ≤ 5 years (%)	9 (33)	4 (17)	
Completely occluded ears	21 (78)	18 (78)	

Results: 13% of participants ≤ 5 years old

Primary outcome: *n* (%)	**DS (*n* = 27)**	**TP (*n* = 23)**	**Percentage difference, DS–TP (95% CI)**	***p*-value**
Completely visualised ears after solvent only	5 (19)	2 (9)	9.8 (–8.8 to 28.5)	No *p*-values reported
Completely visualised ears after solvent with or without irrigation	22 (82)	8 (35)	46.7 (22.3 to 71.1)	

TM visualisation, number (%)[a]

	Complete	**Incomplete**	**Complete**	**Incomplete**	***p*-value**
After solvent only	5 (19)	22 (81)	2 (9)	21 (91)	No *p*-values reported
First 50-ml ear irrigation	10 (45)	12 (55)	2 (10)	19 (90)	
Second 50-ml ear irrigation	7 (58)	5 (42)	4 (21)	15 (79)	

Comments:

a Subsets of same data as above.

Secondary outcomes	**DS (*n* = 27)**	**TP (*n* = 23)**	**Percentage difference, DS–TP (95% CI)**	***p*-value**
AEs (i.e. pain, vertigo, nausea or hearing loss)	0 (0)	0 (0)	0 (–7.8 to –7.8)	No *p*-values reported

Comments:

Methodological comments

Allocation to treatment groups: Assignment was generated by computerised random numbers program. A series of opaque consecutively numbered syringes were prepared by hospital pharmacy, unconnected to the emergency department or enrolment process

Blinding: States double-blind, but as solutions differ in colour (Colace = pink, Cerumenex = yellow) solvent likely to have become obvious when used

Comparability of treatment groups: Groups are reported to be similar in age, sex and proportion of completely obscured TMs, but no *r*-values given. However, the mean age of the Colace group was lower, most likely because it included more than double the amount of children

Method of data analysis: SPSS version 8.0 was used for statistical analysis and demographics were compared using chi-squared test, *t*-tests for continuous variables. No *p*- or *r*-values are reported. Outcomes are presented as point and interval estimates with the difference in proportions and 95% CI for the difference. Post hoc subgroup analysis based on participants' age was performed. It is uncertain if the study was powered for a subgroup analysis and authors provide no data. Data not extracted

Sample size/power calculation: 80% power to detect differences between groups in main outcome chi-squared test, $\alpha = 0.05$), assuming after application of control solvent 40% of membranes completely visualised

Attrition/dropout: No dropouts are reported and all 50 participants finished treatment

General comments

Generalisability: American cooperative paediatric and adult patients

Outcome measures: Unclear how valid, objective or consistently applied the outcome measures were. Interobserver agreement was from an independent patient set

Intercentre variability: N/A

Conflict of interests: None reported

AE(s), adverse event(s); CI, confidence interval; F, female; M, male; N/A, not applicable, RCT, radomised controlled trial; SD, standard deviation; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Adequate
2. Was the treatment allocation concealed?	Adequate
3. Were the groups similar at baseline in terms of prognostic factors?	Reported
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Inadequate
7. Was the patient blinded?	Partial
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

General Practitioner Research Group[41]

Extracted by: PH **Checked by: EL**

Reference and design	Intervention	Participants	Outcome measures
Author: General Practitioner Research Group[41] *Year*: 1965 *Country*: UK *Study design*: Double-blind RCT *Number of centres*: 14 *Setting*: Primary care *Funding*: None reported	1. Dioctyl-medo ear drops: Gelatine capsules with 5% of dioctyl sodium sulphosuccinate in a maize oil base 2. Control: Oil-based alone *Duration of treatment*: Half an hour before ear syringing *Other interventions used*: Syringing (standardised method of syringing, only metal type of ear syringe was used and size recorded)	*Number of participants*: 150 1. Dioctyl-medo: 77 2. Control: 73 *Sample attrition/ dropout*: None reported *Inclusion criteria for study entry*: None reported *Exclusion criteria for study entry*: None reported	*Primary outcomes*: Volume of water for syringing and syringefuls used *Secondary outcomes*: Ease of wax removal Character of syringed wax *Method of assessing outcomes*: Removal: 1 = easy or difficult, 2 = partial or failed Earwax: 1 = liquid, 2 = shredded, 3 = hard lumps *Length of follow-up*: Immediate

Baseline characteristics of participants

Age, maximum incidence	**All (*n* = 150)**	***p*-value**
Males	31–50 years	
Females	51–70 years	
Gender M/F	1.3 : 1	

Results: 32% of participants were new cases, 53% without syringing for over 12 months

Primary outcomes

	Dioctyl (*n* = 77)			**Control (*n* = 73)**			***p*-value**
No. of syringefuls used	**No of cases**	**Total quantity (ml)**	**Mean per case**	**No of cases**	**Total quantity (ml)**	**Mean per case**	**No analysis conducted**
0.25–1	35	2123	60	26	1732	65	
1.25–2	13	1718	130.5	17	2329	136	
2.5–4	12	2243	187.5	17	3487	207	
5–15	6	2045	341	4	2613	653	
Totals	66	8129	122	64	10,181	165.5	

Note: Difference in mean caused by one participant in control group requiring 15 syringefuls of water to remove the wax. After exclusion of this case virtually no differences between groups in respect of this factor.

Comments: Maximum incidence for males in 31–51 year group, for females 51–70 year group. Syringes hold 2, 3 or 4 oz of water (57, 85 or 112 ml) and exact analyses was made in respect of each size syringe and number of syringefuls.

Secondary outcomes

Removal, *n* (%)	**Dioctyl (*n* = 77)**	**Control (*n* = 73)**	***p*-value**
Easy	54 (70)	42 (57)	
Difficult	17 (22)	23 (32)	
Partial	3 (4)	6 (8)	
Failed	2 (3)	2 (3)	

Comments: partial or failed removal combined was 8% for the dioctyl-medo group and 11% for the control group. Study reports differences, but no evidence of any statistical analysis.

Character of wax, *n* (%)	Dioctyl (*n* = 77)	Control (*n* = 73)	*p*-value
Liquid	14 (19)	10 (14)	
Shredded	34 (46)	28 (40)	
Hard lumps	26 (35)	32 (46)	
Failed	3	2	
Not recorded	0	1	

Comments: AEs were negligible and mostly related to syringing. 91% of dioctyl participants vs 89% control had no side effects. 92% of dioctyl participants vs 86% control found procedure tolerable.

Methodological comments

Allocation to treatment groups: Choice treatment by random selection. On 'breaking the code' it was found that 77 participants received dioctyl-medo and 73 participants were in the control group. No other details reported

Blinding: Authors report double-blind trial. Doctor administers drops, assessments and syringing, but no other details reported

Comparability of treatment groups: Distribution of participants between groups is reported to be 'even' in respect of age and sex, but only gender ration is reported

Method of data analysis: Not reported

Sample size/power calculation: Not reported

Attrition/dropout: Not reported

General comments

Generalisability: UK primary care practice patients, no details on severity of occlusions

Outcome measures: Outcome measures open to subjective interpretation. Comparative results between the 2 preparations are reported to be unaffected by sex, age or duration of wax, but no description analysis given. Results slightly better in males, younger participants and cases of shortest duration. No statistical data to support this.

Intercentre variability: Standardised syringing procedure reported, but no other details given.

Conflict of interests: None reported

AEs, adverse events; F, female; M, male; RCT, randomised controlled trial.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Unknown
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Partial
7. Was the patient blinded?	Partial
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Pavlidis and Pickering[42]

Extracted by: PH		**Checked by: EL**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Pavlidis and Pickering[42] *Year*: 2005 *Country*: Australia *Study design*: RCT *Number of centres*: One *Setting*: Primary care *Funding*: General Practice Education & Training, and General Registrars Association Registrar Scholarship & Research Fund funded consumables	1. Warm tap water and syringing (25-ml Luer-Lok syringe) 2. Dry syringing (25-ml Luer-Lok syringe) *Duration of treatment*: 1. 15 minutes[a] 2. Immediate[a] *Other interventions used*: Auroscopic ear canal inspection for all patients after each syringing attempt Patients with wax in both ears: a coin toss determined treatment for the left ear, with right ear receiving alternative	*Number of participants*: 26, 39 ears 1. *n* = 22 ears 2. *n* = 17 ears *Sample attrition/dropout*: None reported *Inclusion criteria for study entry*: ≥ 18 years old, with earwax partially or totally occluding one or both ears that GP would normally syringe *Exclusion criteria for study entry*: Actual or suspected TM perforation Previous ear surgery Current otitis media or otitis externa Swimming during previous 3 days Ear drops during previous 3 days Unable to lie down for 15 minutes Unable to consent	*Outcomes*: Mean number of syringing attempts Mean time to syringing (minutes) AEs *Method of assessing outcomes*: Syringing – 25 ml of water for each syringing attempt until visibly clear *Length of follow-up*: Immediate

Baseline characteristics of participants

	Wet syringing (ears = 22)	**Dry syringing (ears = 17)**	***p*-value**
Gender M/F (%)	15 (68), 7 (32)	11 (65), 6 (35)	
Age, mean years (SD)	63 (8)	65 (20)	ns[b]
Mean duration of symptoms, days (SD)	300 (421)	249 (353)	ns[b]

Comments: Patients aged between 37 and 90 years.

Results

Outcomes	**Wet syringing (ears = 22)**	**Dry syringing (ears = 17)**	***p*-value**
Mean no. of attempts (SD)	7.5 (7.3)	25.4 (39.4)	$p = 0.043$ (in favour of wet syringing)
Mean time to syringe ear, minutes[a]	6.5	15.4	ns[b]

Comments: 1 patient had both ears syringed and experienced dizziness (not vertigo). No other AEs were noted and all TMs were intact at end of syringing.

a It is stated that the number of syringing attempts is unusually high due to the small volume of the syringe used (25 ml), with GP being reported as normally using larger metal ear syringes (> 120 ml).
b For non-significant results no *p*-value is given.

Methodological comments

Allocation to treatment groups: Patients were randomised by the toss of a coin, but for those with wax in both ears the coin toss always determined the treatment for the left ear. Authors acknowledged that randomisation procedure could have led to selection bias

Blinding: Open, non-blinded trial

Comparability of treatment groups: Differences between groups for age and mean duration of symptoms reported as non-significant

Method of data analysis: Unpaired, two-tailed *t*-tests to compare group differences

Sample size/power calculation: Not reported. It is stated that the study was not powered to detect major complications (approximately 1 in 1000 ears syringed)

Attrition/dropout: Not reported

General comments

Generalisability: UK adult patients with earwax partially or totally occluding one or both ears, which would normally be syringed by their GP

Outcome measures: Unknown how valid or objective the outcome measures were. All patients had their ears syringed by one of the research group to maintain technique consistency. It is stated that most patients preferred 15-minute water treatment to using softening preparation for some days at home prior to syringing, but no data are reported to support this

Intercentre variability: N/A

Conflict of interests: None reported. General Practice Education & Training, and General Registrars Association Registrar Scholarship & Research Fund funded consumables

AEs, adverse events; F, female; M, male; N/A, not applicable; RCT, randomised controlled trial; SD, standard deviation; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Partial
2. Was the treatment allocation concealed?	Inadequate
3. Were the groups similar at baseline in terms of prognostic factors?	Reported
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Inadequate
6. Was the care-provider blinded?	Inadequate
7. Was the patient blinded?	Inadequate
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

General Practitioner Research Group[48]

Extracted by: PH **Checked by: EL**

Reference and design	Intervention	Participants	Outcome measures
Author: General Practitioner Research Group[48] *Year*: 1967 *Country*: UK *Study design*: Double-blind RCT *Number of centres*: 10 *Setting*: Primary care *Funding*: None reported	1. Waxsol (dioctyl sodium sulphosuccinate): 6–7 drops nightly* 2. Cerumol (*p*-dichlorobenzene and benzocaine): 6–7 drops nightly* *Duration of treatment*: 2 nights (10 minutes per treatment) *Other interventions used*: Syringing *Inserted with dropper by participants, following standardised instructions. If both ears are affected, procedure is repeated in the other ear	*Number of participants*: 107 1. Waxsol: 47 2. Cerumol: 60 *Sample attrition/dropout*: None reported *Inclusion criteria for study entry*: All cases of earwax *Exclusion criteria for study entry*: Minor degrees of wax easily removed without softening agent	*Outcomes*: Volume of water for syringing Ease of wax removal Character of wax AEs *Method of assessing outcomes*: Water volumes calculated from the number or fraction of syringefuls required Removal of wax: easy, difficult, partial or failed Character of wax: liquid, shredded or hard lumps *Length of follow-up*: Immediate

Baseline characteristics of participants

	All (*n* = 107)	***p*-value**
Age, %		
10–30 years	27	No *p*-values reported
31–50 years	34	
51–70 years	31	
71 years and over	8	
Elapsed time since last syringing, %		
≥ 12 months	32	
10–12 months	17	
7–9 months	5	
4–6 months	5	
1–3 months	1	
New cases	41	
Wax in left ear, %	31	
Wax in right ear, %	23	
Wax in both ears, %	46	

Results

Outcomes:	**Waxsol (*n* = 47)**		**Cerumol (*n* = 60)**		
Volume of water, fl oz	**No. of participants**	**Total volume**	**No. of particpants**	**Total volume**	***p*-value**
0.5	0	0	1	0.5	No *p*-values reported
1	6	6.0	2	2.0	
2	13	26.0	4	8.0	
2.5	1	2.5	1	2.5	
3	3	9.0	5	15.0	
4	3	12.0	8	32.0	

5	0	0	1	5.0	
6	6	36.0	4	24.0	
7	2	14.0	2	14.0	
8	3	24.0	12	96.0	
9	0	0	2	18.0	
10	1	10.0	2	20.0	
12	6	72.0	8	96.0	
14	1	14.0	2	28.0	
16	2	32.0	2	32.0	
18	0	0	1	18.0	
24	0	0	1	24.0	
26	0	0	1	26.0	
40	0	0	1	40.0	
Totals	47	257.5	60	501.0	
Mean volume per participant	5.5 fl oz (156 ml)		8.4 fl oz (240 ml)		Not reported
	No. of participants (%)		**No. of participants (%)**		***p*-value**
≤ 56 ml (2 fl oz)	19 (40)		7 (12)		$p < 0.05$[a]
> 56 ml	28 (60)		53 (88)		
Proportion of participants needing 14–112 ml (%)	55		35		$p < 0.05$[a]

Comments:

a Reported to be significant at 5% level in favour of Waxsol for cases ≤ 2 fl oz (56 ml), remaining 'in favour' of Waxsol at 4 fl oz (112 ml).

Ease of wax removal, no. of participants (%)

	Waxsol (*n* = 47)	**Cerumol (*n* = 60)**	***p*-value**
Easily removed	39 (83)	48 (80)	No *p*-values reported
Removed with difficulty	6 (13)	9 (15)	
Partly removed	1 (2)	1 (2)	
Failed	1 (2)	2 (3)	
Character of wax, % of participants			
Liquid	17	17	No *p*-values reported
Shredded	46	35	
Hard lumps	37	24	

Comments: Failed participant in Waxsol group – further syringing after a week cleared wax. Failed two participants in Cerumol group – one participant had wax removed after olive oil instillation and several attempts at syringing and instrumental means; the information for the other participant was not recorded.

	Waxsol (*n* = 47)	**Cerumol (*n* = 60)**	***p*-value**
AEs, % of participant[s]	7	5	No *p*-values reported
Treatment found tolerable, % of participants	89	95	

Comments:

a No details reported.

Methodological comments

Allocation to treatment groups: Choice treatment by random selection. On 'breaking the code' it was found that 47 participants received Waxsol and 60 participants received Cerumol. No other details reported

Blinding: Authors report double-blind trial, but no details reported

Comparability of treatment groups: No split for baseline characteristics of groups provided. Treatment groups are reported as reasonably matched, with the exception of a higher proportion of participants without prior treatment in the Cerumol group, but no data provided

Method of data analysis: Some statistical significant differences commented on, but minimal details reported and analysis based on post hoc division based on volume water

Sample size/power calculation: No details reported

Attrition/dropout: No details reported

General comments

Generalisability: UK Primary Care Practice patients, no details on severity of occlusions

Outcome measures: Unclear how valid, objective and consistently applied the measures were

Intercentre variability: Standardised instructions to patients reported, but no details given about possible variation in syringing procedure

Conflict of interests: None reported

AEs, adverse events; RCT, randomised controlled trial.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Inadequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Partial
7. Was the patient blinded?	Partial
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Amjad and Scheer[51]

Extracted by: PH		Checked by: EL	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Amjad and Scheer[51] *Year*: 1975 *Country*: USA *Study design*: Double-blind RCT *Number of centres*: Not stated *Setting*: Primary care *Funding*: None reported	1. 1 dose of TP (triethanolamine polypeptide) oleate condensate 2. 1 dose of carbamide peroxide *Duration of treatment*: Each affected ear was treated with 1 application of drops, which were left in the ear canal for 30 minutes *Other interventions used*: Irrigation with lukewarm water after treatment	*Number of participants*: 80 1. TP: *n* = 40 2. Control: *n* = 40 *Sample attrition/dropout*: None reported *Inclusion criteria for study entry*: Hard or impacted earwax *Exclusion criteria for study entry*: None reported	*Primary outcomes*: Degrees of wax removal *Secondary outcomes*: AE (subjective and observations of objective side effects) *Method of assessing outcomes*: Excellent (removal of all wax), good (removal of most wax), fair (removal of some wax) and poor (removal of little or no wax) Degree of obstruction: complete or partial *Length of follow-up*: Immediate

Baseline characteristics of participants

Pretreatment wax, number of ears

	TP (*n* = 40)	**Carbamide peroxide (*n* = 40)**	***p*-value**
Impacted	19	18	No *p*-values reported
Hard	16	16	
Loose	1	3	
Soft	4	3	
Complete obstruction	36	32	
Partial obstruction	4	8	

Results

Primary outcomes

Efficacy of treatment, *n* (%)	**TP (*n* = 40)**	**Carbamide peroxide (*n* = 40)**	***p*-value**
Excellent	27 (68)	2 (5)	No *p*-value reported
Good	8 (20)	5 (12)	
Fair	2 (5)	4 (10)	
Poor	3 (7)	29 (73)	
Effective ('excellent' plus 'good')	35 (88)	7 (17)	
Comments:			

Secondary outcomes

	TP (*n* = 40)	**Carbamide peroxide *n* = 40**	***p*-value**
AE	0	0	No *p*-value reported

Efficacy to pretreatment wax	No.	E+G	F	P	E+G%	No.	E+G	F	P	E+G%	*p*-value
Impacted	19	16	1	2	84	18	2	0	16	11	No *p*-value reported
Hard	16	14	1	1	88	16	3	2	11	19	
Loose	1	1	0	0	100	3	1	0	2	33	
Soft	4	4	0	0	100	3	1	2	0	33	
Complete obstruction	36	31	2	3	86	32	4	3	25	13	
Partial obstruction	4	4	0	0	100	8	3	1	4	38	

Comments: No., number of ears; E+G, effective ('excellent' plus 'good'); F, Fair; P, Poor.

Methodological comments

Allocation to treatment groups: 80 participants were randomly divided into equal intervention and control group

Blinding: Study states double-blind evaluation, but no details reported

Comparability of treatment groups: No details reported. Pretreatment wax appears similar

Method of data analysis: None reported. Only descriptive/frequency data presented

Sample size/power calculation: None reported

Attrition/dropout: None reported

General comments

Generalisability: No baseline characteristics provided, American population

Outcome measures: It is unclear how valid or objective the measure was, or how consistent the assessments were; study states that no comparison between treatments was intended, as carbamide peroxide needs multiple instillations

Intercentre variability: N/A – it appears to be a one-centre study

Conflict of interests: Cerumenex distributed by Purdue Frederick Co., New York, NY

AEs, adverse events; N/A, not applicable; RCT, randomised controlled trial.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Inadequate
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Inadequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Partial
7. Was the patient blinded?	Partial
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown

Dummer and colleagues[44]

Extracted by: EL		Checked by: PH	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Dummer and colleagues[44] *Year*: 1992 *Country*: UK *Study design*: RCT *Number of centres*: One *Setting*: Primary care *Funding*: Supported by Napp Laboratories Ltd	1. Audax ear drops, night and morning for 3 days* 2. Cerumol ear drops, night and morning for 3 days* *Duration of treatment*: 3 days *Other interventions used*: None reported *Drops for 3 days and assessed on 4th day in methods, drops for 4 days after which reassessment took place in summary	*Number of participants*: 50 Audax: 27 Cerumol: 23 *Sample attrition/dropout*: None reported *Inclusion criteria for study entry*: Aged between 19 and 90 years, presenting with impacted or hardened earwax *Exclusion criteria for study entry*: Those with inflammation or the external auditory meatus, seborrhoeic dermatitis and eczema affecting the external ear, a perforated TM, a pre-existing ear infection requiring treatment with systemic antibiotics, known salicylate sensitivity, instrumentation of the ears (hearing aids), regular swimmers	*Primary outcomes*: (Not defined as primary or secondary.) Outcomes included: amount, colour and consistency of wax, symptoms, hearing, global impression of treatment efficacy (patient and investigator) and tolerability *Method of assessing outcomes*: Amount of wax – considerable block to meatus, considerable but no blockage, medium, scanty Colour – black, brown, yellow, pale Consistency – concrete hard, firm, soft, runny Symptoms – none, deafness, blockage, pain, discharge, irritation Objective hearing – normal whispered voice test, abnormal whispered voice test, Rinne test abnormal, Weber test abnormal *Length of follow-up*: Median number of days between visits 1 and 2 was 4 days (range 3–7 days)
Baseline characteristics of participants			
	Audax (*n* = 27)	**Cerumol (*n* = 23)**	***p*-value**
Mean age, years	51	55	
Gender, M/F, *n*	18/9	14/9	
Results: primary outcomes			
Amount of wax			
	Audax (*n* = 27, ears = 54)	**Cerumol (*n* = 23, ears = 46)**	***p*-value**
Increased	0	0	Not reported across groups
No change	24 (44%)	22 (48%)	
Decreased	28 (52%)	24 (52%)	
Missing data	2 (4%)	0	
Colour of wax			
Darkened	0	0	States no significant differences, *p*-value not reported
No change	10	9	
Lightened	42	36	
Missing data	2	1	
Consistency of wax			
Hardened	0	0	States no significant differences, *p*-value not reported
No change	6	5	
Softened	46	40	
Missing data	2	1	
Objective hearing			
Improved	7 (13%)	2 (4%)	States no significant differences, *p*-value not reported
No change	45 (83%)	44 (96%)	
Worsened	0	0	
Missing data	2 (4%)	0	

Overall assessment			
Investigator rated 'effective'	36 participants[a]	22 participants	Unclear if tested
Overall assessment			
Participant rated 'effective'	25 (93%) participants	23 (100%) participants	States no significant differences, *p*-value not reported
Tolerability	2 (both slight irritation to the ear)	2 (1 slight itch, 1 buzzing noise after use)	
Subgroup data of 25 participants (12 Audax, 13 Cerumol) with abnormal hearing on entry.			
a It is unclear if this is an error, as there only 27 participants in the group or if this should have said number of ears instead of patients as stated in the study.			
Objective hearing			
Improved	7	2	$p < 0.05$ (*p*-value not reported for other change variables)
No change	4	11	
Worsened	0	0	
Missing data	1	0	
Comments: No baseline scores reported for any of these measures.			
Methodological comments			
Allocation to treatment groups: States 'allocated at random' but no further details of randomisation schedule or allocation concealment			
Blinding: States single-blind (investigator), but no details of how this was maintained			
Comparability of treatment groups: States treatment groups were well matched for age, sex and objective hearing			
Method of data analysis: Each ear was assessed separately (100 in total) and tests for differences between treatments were made between patients; $p < 0.05$ statistically significant. Mann–Whitney *U*-test for amount, colour, consistency, global efficacy. Fisher's exact test for hearing test. Demographics chi-squared test			
Sample size/power calculation: Not reported			
Attrition/dropout: Missing data shown in tables, but reasons for missing data unclear			
General comments			
Generalisability: Difficult to assess as minimal demographic characteristics presented			
Outcome measures: Unclear how valid, objective, or consistently applied the outcome measures used were			
Intercentre variability: Not applicable			
Conflict of interests: States supported by Napp Laboratories, who manufacture Audax			
F, female; M, male; RCT, randomised controlled trial; TM, tympanic membrane.			

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Partial
5. Were outcome assessors blinded to the treatment allocation?	Inadequate
6. Was the care-provider blinded?	Inadequate
7. Was the patient blinded?	Inadequate
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate
ITT, intention to treat.	
a Adequate, inadequate, partial, reported, unknown.	

Fahmy and Whitefield[54]

Extracted by: EL		Checked by: AC	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Fahmy and Whitefield[54] *Year*: 1982 *Country*: UK *Study design*: CCT *Number of centres*: One for study 1 and 2, multicentre for study 3, but number of centres not reported *Setting*: Studies 1 and 2 in secondary care, study 3 in primary care *Funding*: Not reported	*Study 1*: 1. Exterol[a] 2. Glycerol control *Study 2*: 1. Exterol 2. Cerumol[b] *Study 3*: 1. Exterol 2. Cerumol *Study 4*: 1. Exterol (data not reported here as no comparison) For all studies participants instilled 5–10 drops twice per day *Duration of treatment*: 1 week *Other interventions used*: a Urea hydrogen peroxide, 5% in anhydrous glycerol b Arachis oil preparation with 2% paradichlorobenzene, 5% chlorbutol, 10% turpentine oil	*Number of participants*: *Study 1*: 40 participants (80 ears) completed the study 1. Exterol: 20 people 2. Glycerol control: 20 people *Study 2*: 50 patients (100 ears) completed the study 1. Exterol: 25 2. Cerumol: 25 *Study 3*: 160 patients (286 ears) completed the study 1. Exterol 157 ears 2. Cerumol 129 ears *Sample attrition/dropout*: Not reported but reports numbers as those 'completing' the study. *Inclusion criteria for study entry*: States as far as possible the protocol remained identical (for all studies); patients presenting with earwax problems *Exclusion criteria for study entry*: Patients with inflammation of the external meatus, middle ear pathology, e.g. mastoid cavities, or perforation of the TM; a scarred membrane did not constitute a contraindication	*Primary outcomes*: (Not defined as primary or secondary.) Wax occlusion, wax consistency, ease of syringing *Method of assessing outcomes*: States each ear was assessed independently. No definitions of classification of outcomes noted *Length of follow-up*: 1 week

Baseline characteristics of participants

	Study 1, no. of ears		
	Exterol (*n* = 20, 40)	**Glycerol control (*n* = 20, 40)**	***p*-value**
Degree of wax occlusion (ears)			
Total	36	36	Not reported to be tested
Partial	4	4	
Consistency of wax (ears)			
Very hard	20	16	Not reported to be tested
Hard	20	24	

	Study 2, no. of ears		
	Exterol (*n* = 25, 50)	**Cerumol (*n* = 25, 50)**	***p*-value**
Degree of wax occlusion (ears)			
Total or subtotal	23	19	Not reported to be tested
Partial	27	31	
Consistency of wax (ears)			
Very hard	12	8	Not reported to be tested
Hard	33	27	
Soft	5	15	

	Study 3, no. of ears		
	Exterol (*n* = 157)	**Cerumol (*n* = 129)**	***p*-value**
Degree of wax occlusion (ears)			
Total or subtotal	97	86	Not reported to be tested
Partial	60	43	
Consistency of wax (ears)			
Hard	114	97	Not reported to be tested
Soft	43	32	

Results

	Study 1, no. of ears				
	Exterol (*n* = 20, 40 ears)		**Glycerol control (*n* = 20, 40 ears)**		
	Initially very hard wax	**Initially hard wax**	**Initially very hard wax**	**Initially hard wax**	***p*-value**
Wax dispersed without syringing	–	6	–	–	Not stated
Wax syringed easily	15	14	2	18	
Wax syringed with difficulty	5	–	14	6	

Comments: When the number of ears not requiring syringing is added to the number syringed easily, Exterol was statistically significantly superior to the control group; $p < 0.001$. After treatment with Exterol a significant number ears did not require syringing compared with glycerol.

	Study 2, no. of ears:						
	Exterol (*n* = 25, 50 ears)			**Cerumol (*n* = 25, 50 ears)**			
	Initially very hard	**Initially hard**	**Initially soft**	**Initially very hard**	**Initially hard**	**Initially soft**	***p*-value**
Wax dispersed without syringing	4	14	2	–	–	5	See comments
Wax syringed easily	6	18	3	–	10	9	
Wax syringed with difficulty	2	1	–	8	17	1	

Comments: the number of ears not requiring syringing is markedly greater with Exterol than with Cerumol, $p < 0.001$. When the number of ears not requiring syringing is added to the number syringed easily, Exterol was statistically significantly superior to Cerumol; $p < 0.001$.

	Study 3, no. of ears				
	Exterol (*n* = 157)		**Cerumol (*n* = 129)**		
	Initially hard wax	**Initially soft wax**	**Initially hard wax**	**Initially soft wax**	***p*-value**
Wax dispersed without syringing	45	19	12	15	See comments
Wax syringed easily	60	22	52	14	
Wax syringed with difficulty	9	2	33	3	

Comments: The number of ears not requiring syringing is markedly greater after treatment with Exterol than with Cerumol; $p < 0.001$. When the number of ears not requiring syringing is added to the number syringed easily, Exterol was statistically significantly superior to Cerumol; $p < 0.001$.

Methodological comments

Allocation to treatment groups: Participants presenting with earwax were treated with alternate preparations on a sequential basis

Blinding: Not reported

Comparability of treatment groups: No baseline characteristics reported

Method of data analysis: analysed by *t*-test and chi-squared test; appears to be selective statistical testing of differences

Sample size/power calculation: Not reported

Attrition/dropout: Text states numbers completing the study therefore unsure if any participants were potentially included, but not reported upon

General comments

Generalisability: No baseline demographic characteristics, UK population

Outcome measures: Unclear how valid, objective or consistently applied the outcome measures were

Intercentre variability: Not reported

Conflict of interests: Dermal Laboratories supplied the Exterol and control preparations

CCT, controlled clinical trial; TM, tympanic membrane.

Quality criteria for assessment of controlled clinical studies

Item	Judgement[a]
Were the groups similar at baseline in terms of prognostic factors?	Unknown
Were the eligibility criteria specified?	Partial
Were outcome assessors blinded to the treatment allocation?	Unknown
Were the point estimates and measure of variability presented for the primary outcome measure?	Partial
Did the analyses include an ITT analysis?	Unknown
Were withdrawals and dropouts completely described?	Unknown
Were participants likely to be representative of the intended population?	Unknown

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Jaffe and Grimshaw[50]

Extracted by: EL							**Checked by: AC**
Reference and design	**Intervention**			**Participants**			**Outcome measures**
Author: Jaffe and Grimshaw[50] *Year*: 1978 *Country*: UK *Study design*: RCT *Number of centres*: Up to 15 *Setting*: Primary care *Funding*: None reported	1. Otocerol,* 4 drops at night, for 3 nights 2. Cerumol,* 5 drops at night, for 3 nights *Duration of treatment*: 3 nights *Other interventions used*: Patients were asked to gently cleanse the ear with cotton wool the following morning *No details of constitution of the treatment			*Number of participants*: 106 *Otocerol*: 53 *Cerumol*: 53 *Sample attrition/dropout*: Not reported *Inclusion criteria for study entry*: Patients presenting with wax in their ears and who would normally be prescribed a cerumenolytic *Exclusion criteria for study entry*: Overt perforation of the drum or severe infection			*Primary outcomes*: (Not defined as primary or secondary). Ease of syringing, doctors overall impression, adverse effects *Secondary outcomes*: See above *Method of assessing outcomes*: Not reported *Length of follow-up*: Patients asked to revisit GP after three instillations
Baseline characteristics of participants							
	Otocerol (*n* = 53)			**Cerumol (*n* = 53)**			***p*-value**
Gender M/F	32/21			25/28			$\chi^2 = 1.86$, no *p*-value given
	Gender distribution						
Age	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	***p*-value**
0–9 years	0	0	0	1	0	1	Reports not statistically significant using the Kolmogorov–Smirnov test, but value itself not reported.
10–19 years	5	0	5	0	1	1	
20–29 years	3	1	4	6	3	9	
30–39 years	6	2	8	2	4	6	
40–49 years	5	2	7	1	4	5	
50–59 years	6	6	12	7	8	15	
60–69 years	5	4	9	3	3	6	
70–79 years	1	6	7	3	4	7	
80–89 years	1	0	1	2	1	3	
Grade of impaction							
Mild	13			10			Not statistically significant, $\chi^2 = 1.37$, no *p*-value given
Moderate	26			32			
Severe	14			11			
Comments: Degree of impaction classified as mild (soft wax, which could be syringed at once if necessary), moderate (small plug of hard wax for which a cerumenolytic would usually be used before syringing) or severe (large plug of hard wax for which a cerumenolytic would be essential). Grades on presentation were more widely spread in the Otocerol group with more mild and severe cases but this was not statistically significant.							
Duration of symptoms, median	21 days			14 days			
Results: primary outcomes							
Syringing needed							
	Otocerol (*n* = 53)			**Cerumol (*n* = 53)**			***p*-value**
	Yes 39, no 14			Yes 47, no 6			Difference in those requiring syringing $\chi^2 = 3.94$, $p < 0.05$

Syringing needed by grade at entry			
Mild	Yes 6, no 7	Yes 6, no 4	
Moderate	Yes 19, no 7	Yes 30, no 2	
Severe	Yes 14, no 0	Yes 11, no 0	
Comments:			

Results: secondary outcomes

Doctor reported ease of syringing, where required, n (%)

	Otocerol (*n* decline from 53)	**Cerumol (*n* declines from 53)**	***p*-value**
Ease of syringing by grade at entry			
	30/39 (76.9)	**34/47 (72.3)**	**$\chi^2 = 0.25$, not significant**
Mild	Easy 5, not easy 1	Easy 5, not easy 1	
Moderate	Easy 14, not easy 5	Easy 25, not easy 5	
Severe	Easy 11, not easy 3	Easy 4, not easy 7	
Adverse effects, total no, with side effects	7	10	Not statistically significantly different
Effects reported			
Pain on application	0	1	
Irritation on application	3	8	
Pain during use	1	1	
Irritation during use	4	4	
Slight giddiness	1	0	
Unpleasant smell such that patient would not use again	0	1	
Doctor reported would not use product again, *n* patients	8	9	
Overall judgement effectiveness success[a]	38	33	Overall response better for Otocerol, but not statistically significant[b]
Failure[c]	10	13	
Partial[d]	5	7	

Comments:

a Defined as those in whom syringing was not required or where it was easy and no reports of side effects.
b The ratio of success–failure was highly significant in each group ($p < 0.001$ Otocerol, $p < 0.01$ Cerumol).
c Defined as those in whom syringing was difficult (with or without side effects).
d Defined as those who reported side effects but in whom the doctor found it easy to syringe and had no reservations about using the product again.

Methodological comments

Allocation to treatment groups: States randomly allocated to either treatment according to a previously determined scheme (scheme not outlined)

Blinding: States double-blind, but no other descriptions given

Comparability of treatment groups: Slightly higher male–female ratio in the Otocerol group, but this was not statistically significant, neither was the age distribution between the two groups

Method of data analysis: By chi-squared test, no other details reported

Sample size/power calculation: Not reported

Attrition/dropout: Not reported, from numbers assume none. Some outcomes reported subsets of patients

General comments
Generalisability: Minimal detail of participant demographics, children and adults in sample
Outcome measures: Unclear how valid, objective or consistently applied the outcome measures were
Intercentre variability: 15 GPs took part in the trial, unclear if all from different centres, but the majority likely to be
Conflict of interests: None reported
F, female; M, male; NS, normal saline; RCT, randomised controlled trial.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Reported
4. Were the eligibility criteria specified?	Partial
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Partial
7. Was the patient blinded?	Partial
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Carr and Smith[52]

Extracted by: EL		Checked by: AC	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Carr and Smith[52] *Year*: 2001 *Country*: USA and/or Canada *Study design*: RCT *Number of centres*: Unclear *Setting*: Primary care – self-treatment *Funding*: Not reported	1. Aqueous sodium bicarbonate,10% 2. Aqueous acetic acid, 2.5% *Duration of treatment*: 4 drops daily for 14 days *Other interventions used*: No other ear drops during the duration of treatment	*Number of participants*: 69 *Sodium bicarbonate*: 35 *Acetic acid*: 34 *Sample attrition/dropout*: Two participants out of the acetic acid group discontinued due to stinging in the ear canal *Inclusion criteria for study entry*: Those with occlusive cerumen in at least 1 ear; most presented with other complaints and ceruminosis was noted incidentally *Exclusion criteria for study entry*: History of TM perforation, present ventilation tubes, a mastoid cavity, otitis externa, or unwillingness to participate in the 2-week treatment regimen	*Primary outcomes*: Degree of cerumen *Secondary outcomes*: *Method of assessing outcomes*: Degree of cerumen scored by 1 of the 2 examiners from 1–4 (1 = none, 2 = small amount on canal walls, 3 = TM visible but significant amount of cerumen present, 4 = occlusive cerumen). Reports based on scale used by Schwartz and colleagues[94] (study looked at otitis media). Tested for reliability by 3 observers measuring 60 ears of people not in the study. Average change in score was averaged across both ears if both ears initially scored > 1. Maximum change was the best score in each participant *Length of follow-up*: 14 days

Baseline characteristics of participants

	Sodium bicarbonate (*n* = 35)	**Acetic acid (*n* = 34)**	***p*-value**
Mean age, years	27.0	25.3	
N, ears	70	68	
Degree of cerumen	Not reported	Not reported	

Results

Primary outcomes	**Sodium bicarbonate (*n* = 35)**	**Acetic acid (*n* = 34)**	***p*-value**
Mean change degree of cerumen	0.66	0.78	No difference, *p*-value not given
Mean maximum change	1.00	1.00	

Comments: Multivariate analysis showed that differences in maximum scores were significantly related to age; children had higher average and maximum scores.

Subgroup analyses, children only[a]	**Sodium bicarbonate (*n* = 16, 26 ears)**	**Acetic acid (*n* = 20, 29 ears)**	***p*-value**
Mean age, years	8.7	7.26	
Mean change	0.92	0.93	
Mean maximum change	1.31	1.25	
Category change, n (ears)			
Change = 0	10	9	
Change = 1	10	15	
Change = 2	4	3	
Change = 3	2	2	

Comments:

a For the child group the power to detect a difference was measured a priori and therefore subgroup reported here. Change scores between children and adults also presented, but not extracted here as no evidence it was an a priori decision.

Adverse events: no cases of otitis externa or external auditory canal dermatitis.

Methodological comments

Allocation to treatment groups: Each participant was given a dropper bottle of the study solution chosen randomly by the patient from a box where only the identical bottle caps were visible

Blinding: Each bottle was marked as either A or B so that both patient and investigator were blinded to the solution used. Bottles were prepared by a hospital pharmacy, with unblinding occurring after completion of all data collection and analysis. Also states that although patients could detect the odour of acetic acid, in no case could the examiner detect it

Comparability of treatment groups: No discussion from authors. Minimal demographic information reported, ages appear to be similar. No baseline scores of the primary end point

Method of data analysis: Analysis done for average change in score and maximum change in score per patient using a Mann–Whitney *U*-test. Paediatric results were separated from the group and analysed independently. Interobserver difference in scoring cerumen was 0.76

Sample size/power calculation: The power to detect a difference of one category (paediatric group) (on the degree of cerumen) if it existed in the data was reported to be 85%. No other details of this calculation reported, nor any power calculation for the rest of the study

Attrition/dropout: Two participants in the acetic acid group were withdrawn and reasons given, unclear whether an ITT analysis was undertaken

General comments

Generalisability: Unclear as minimal characteristics of participants given

Outcome measures: Unclear how valid and objective the outcome measures were. Inter-rater reliability was assessed, however, and was good

Intercentre variability: Unclear how many centres were involved

Conflict of interests: None noted

ITT, intention to treat; RCT, randomised controlled trial; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Adequate
2. Was the treatment allocation concealed?	Adequate
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Partial
7. Was the patient blinded?	Partial
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.

a Adequate, inadequate, partial, reported, unknown.

Lyndon and colleagues[45]

Extracted by: EL		Checked by: AC	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Lyndon and colleagues[45] *Year*: 1992 *Country*: UK *Study design*: RCT *Number of centres*: Unclear *Setting*: Primary care *Funding*: Not reported	1. Audax* ear drops, AM and PM (self administered) 2. Earex** ear drops, AM and PM (self administered) *Duration of treatment*: 4 days (patients returned to clinic on fifth day for syringing) *Other interventions used*: States all centres used a standardised syringing procedure using tepid tap water *Choline salicylate (20%) and ethylene oxide-polyoxypropylene glycol (analgesics) combined with glycol and glycerol **Arachis oil, almond oil and rectified camphor oil	*Number of participants*: 36 *Audax*: 38 ears (19 participants) *Earex*: 34 ears (17 participants) *Sample attrition/dropout*: 35 attended on both assessment days (1 Earex participant failed to return) *Inclusion criteria for study entry*: Patients presenting in general practice with symptoms of hardened earwax in either or both ears requiring cerumenolytic treatment; patients aged 16 years or over *Exclusion criteria for study entry*: Inflammation of the external auditory meatus, middle ear pathology or perforation of the TM, pre-existing ear infection requiring treatment with systemic antibiotics, known salicylate sensitivity	*Primary outcomes*: (Not defined as primary or secondary.) Degree of impaction, ease of syringing, global impression of efficacy. Side effects/discomfort. *Secondary outcomes*: (see above) *Method of assessing outcomes*: Separate assessments were carried out at all times for the left and right ear. The degree of wax impaction was rated as non-existent (excluded the patient), mild (could be syringed once if necessary), moderate (small plug of hard wax) or severe (large plug of hard wax). Ease of syringing rated as not required, easy, difficult, impossible *Length of follow-up*: 5 days

Baseline characteristics of participants

	All participants	***p*-value**
Male–female ratio	19:17	
Mean age	52 years (range 19 to 86 years)	

Pretreatment degree of impaction

	Audax, no. of ears = 38	**Earex, no. of ears = 34**	***p*-value**
None	2	1	
Mild	7	8	
Moderate	26	22	
Severe	3	3	

Results

Post-treatment score

Degree of impaction	**Audax, no. of ears = 38**	**Earex, no. of ears = 34**	***p*-value**
None	10	6	See below
Mild	17	11	
Moderate (Mod)	9	12	
Severe (Sev)	2	3	
Missing data		2	

Degree of impaction at end point by pretreatment score	**Post-treatment**				**Post-treatment**				***p*-value**
	None	**Mild**	**Mod**	**Sev**	**None**	**Mild**	**Mod**	**Sev**	
None	1	1	0	0	1	0	0	0	See below
Mild	3	4	0	0	2	4	0	0	
Moderate	6	12	8	0	3	7	11	1	
Severe	0	0	1	2	0	0	1	2	

Comments: Although the difference between the two groups did not reach statistical significance, a trend was seen towards less impaction post-treatment in the Audax group than the Earex group.

Ease of syringing, ears			
Not required	15	7	$p < 0.005$[a]
Easy	22	12	
Difficult	1	11	
Impossible	0	0	
Missing data	0	4	
Comments: Paper states that six patients in the Audax group and three in the Earex group did not require syringing of either ear. This does not correspond with the number of ears reported as not requiring syringing in the table (and extracted above).			
a Significant difference in favour of Audax in that syringing was more frequently scored as 'not required' or 'easy'.			
Investigator's global impression efficacy (states no. ears, but n's do not add up so assume no. patients)			
Completely effective	8	5	
Very effective	9	1	
Fairly effective	2	7	
Not effective	0	3	
Missing data	0	1	
Total	19	17	
Participants' global impression efficacy (states no. ears, but n's do not add up so assume no. patients)			
Completely effective	8	5	
Very effective	9	2	
Fairly effective	2	7	
Not effective	0	2	
Missing data	0	1	
Total	19	17	
Comments: States there was a statistically significant difference in favour of Audax ($p < 0.01$). 'Not effective' and 'fairly effective' categories were merged for the analysis. Unclear if this is investigator rating alone, participant rating alone or some combination.			
AEs or discomfort	0	1 (slight irritation), 1 (smell unacceptable)	

Methodological comments

Allocation to treatment groups: States 'according to a pre-determined randomisation allocation schedule'

Blinding: Not reported

Comparability of treatment groups: No baseline characteristics reported between groups. Baseline degree of impaction appear to be similar

Method of data analysis: Chi-squared test to compare reduction in impaction from pretreatment to post-treatment for each treatment, and the difficulty of syringing between treatments

Sample size/power calculation: Study was designed to have 50 completing patients, although limited recruitment only generated complete data on 36 patients. This provided sufficient power, however, to differentiate between the two treatments. No details of sample size calculation to establish this is reported

Attrition/dropout: One participant failed to return (no reason documented)

General comments

Generalisability: People over 16 years (19 years and over)

Outcome measures: Unclear how valid, objective and consistently applied outcome measures were

Intercentre variability: Uncertain how many centres

Conflict of interests: None noted

AE, adverse event; RCT, randomised controlled trial; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Unknown
7. Was the patient blinded?	Unknown
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Burgess[43]

Extracted by: PH		**Checked by: EL**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Burgess[43] *Year*: 1966 *Country*: UK *Study design*: CCT *Number of centres*: One *Setting*: Primary care *Funding*: None reported	1. Dioctyl-medo (in maize oil): 1 capsule (0.5 ml) AM and PM* 2. Maize oil capsules* *Duration of treatment*: 4 days *Other interventions used*: Syringing (Bacon syringe) *Participants were supplied with 1 box (10 capsules) and capsules were instilled 4–10 times	*Number of participants*: 50 (74 ears) 1. Dioctyl-medo: 33 ears 2. Maize oil: 41 ears *Sample attrition/dropout*: Not reported *Inclusion criteria for study entry*: More than one-half of an ear occluded by wax *Exclusion criteria for study entry*: None reported	*Outcomes*: Average total of water used, ease of removing wax and character of wax, side effects *Method of assessing outcomes*: Number or fraction of syringefuls required. Removal of wax: easy, difficult, partial and failed. Character of wax removed: liquid, shredded and lumps *Length of follow-up*: Between 2 and 7 days

Baseline characteristics of participants

	All (*n* = 50, 74 ears)		***p*-value**
Age	18–75 years		No *p*-values reported
Gender M/F	32 : 18		
Ears completely occluded (%)	59 (79.7)		

Results

Outcomes	**Dioctyl-medo (ears = 33)**	**Maize oil (ears = 41)**	***p*-value**
Average water volume	111 ml	81 ml	No *p*-values reported
Removal of wax, number of ears			
Easy	19	33	
Difficult	11	5	
Partial[a]	3	3	
Failed[a]	1	0	
Character of removed wax, number of ears			
Liquid	1	4	
Shredded	5	6	
Lumps	27	31	
Side effects	0	0	

Comments:

a All the partially successful removals and the one failed removal occurred in ears not completely occluded at baseline.

Methodological comments

Allocation to treatment groups: Unknown – used coded capsules for treatment, with code unbroken until trial finished
Blinding: Both GP and patient blinded to treatment
Comparability of treatment groups: No details reported
Method of data analysis: None reported
Sample size/power calculation: None reported
Attrition/dropout: None reported

General comments

Generalisability: No breakdown of baseline characteristics between groups provided, adult UK population.
Outcome measures: It is unclear how valid or objective the measures are
Intercentre variability: N/A
Conflict of interests: Medo Chemicals Ltd supplied Dioctyl-medo ear drops

CCT, controlled clinical trial; F, female; M, male; N/A, not applicable.

Quality criteria for assessment of controlled clinical studies

Item	Judgement[a]
1. Were the groups similar at baseline in terms of prognostic factors?	Unknown
2. Were the eligibility criteria specified?	Partial
3. Were outcome assessors blinded to the treatment allocation?	Adequate
4. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
5. Did the analyses include an ITT analysis?	Inadequate
6. Were withdrawals and dropouts completely described?	Inadequate
7. Were participants likely to be representative of the intended population?	Unknown

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Eekhof and colleagues[53]

Extracted by: EL		**Checked by: PH**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Eekhof and colleagues[53] *Year*: 2001 *Country*: The Netherlands *Study design*: RCT *Number of centres*: Four *Setting*: Primary care *Funding*: Not reported	1. Water at body temperature 2. Control group – self administered 'oil' each night for 3 days *Duration of treatment*: 15 minutes *Other interventions used*: After 15 minutes a series of attempts at syringing was made (syringing methodology standardised, and method reported) for the intervention group, for the control group syringed after 3 days	*Number of participants*: 130 participants (224 ears) initially syringed of which 42 had persistent earwax and randomised (59 ears) *Intervention*: 22 *Control*: 20 *Sample attrition/dropout*: None reported *Inclusion criteria for study entry*: All patients with complaints resulting from earwax offered syringing. After each attempt at syringing the auditory canal was checked with an auriscope and the extent of blocking noted (obstruction levels of 0–25%, 25–49%, 50–74% and 75–100%) were used. If earwax was persistent (>75% after 5 attempts at syringing) then patient was eligible to be included in the study *Exclusion criteria for study entry*: TM perforation, middle ear operation, otitis externa, swimming within previous 72 hours, use of cerumenolytics in the previous 72 hours	*Primary outcomes*: Number syringing attempts needed to remove wax *Secondary outcomes*: None *Method of assessing outcomes*: Unclear *Length of follow-up*: Immediate for water group, but 3 days for oil group

Baseline characteristics of participants

	All patients	***p*-value**
Gender: M/F	20/22	
Mean age	51 years (SD 16)	

Results

Primary outcomes	**Water (*n*=22)**	**Oil (*n*=20)**	***p*-value**
Mean number syringing attempts	3.0 (95% CI 2.4, 3.6)	2.4 (95% CI 1.7, 3.1)	Difference between means 0.6 (95% CI –0.3, 1.5), $p=0.18$

Number of syringing attempts needed per patient by intervention group

	Number of patients in which the earwax was removed after each attempt at syringing		
Mean no. attempts	**Water group**	**Oil group**	***p*-value**
1	4	6	Not reported to be tested
1.5	1	2	
2	2	5	
2.5	3	1	
3	2	2	
3.5	4	0	
4	2	0	
5	3	4	
6	1	0	

Comments: Authors report, therefore, that water leads to comparable results; however, study not powered for equivalence but superiority.

Methodological comments

Allocation to treatment groups: States 'randomised' study – allocation to groups by birth year, even or odd. In patients with both ears having persistent wax, both had the same strategy

Blinding: None

Comparability of treatment groups: Not reported

Method of data analysis: Means compared with *t*-test. In patients with wax in both ears, the mean number of syringing attempts needed for both ears in one patient were used for the calculations. All ears still with persistent wax after 5 syringing attempts were given the value of 6 for the calculations

Sample size/power calculation: A difference of 2 syringing attempts between the mean of the groups was found to be clinically significant, 13 people were therefore needed in each group. With groups of 20 and 22 patients a difference of 1.6 between means would be statistically significant

Attrition/dropout: Not reported and *n*'s appear to add up

General comments

Generalisability: Minimal details of population group reported; however, all included studies had five failed syringing attempts

Outcome measures: Unclear how valid, objective and consistently applied the measures were. Number of attempts at syringing is a proxy for adequacy of clearance of wax

Intercentre variability: No details reported, four centres included

Conflict of interests: No funding source reported, reviewer assumes not funded directly (trainee GPs and no pharmaceutical agents used)

CI, confidence interval; F, female; M, male; RCT, randomised controlled trial; SD, standard deviation; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Inadequate
2. Was the treatment allocation concealed?	Inadequate
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Unknown
7. Was the patient blinded?	Unknown
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Adequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Unknown

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Appendix 4

Data extraction forms: secondary care setting

Caballero and colleagues[55]

Extracted by: EL		**Checked by: PH**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Caballero and colleagues[55] *Year*: 2005 *Country*: Spain *Study design*: RCT *Number of centres*: One *Setting*: Assume secondary care from author affiliation *Funding*: Not reported	1. Chlorobutanol: 2 ml, no further details 2. Sodium carbonate: 2 ml, no further details 3. Saline: 2 ml *Duration of treatment*: 15 minutes *Other interventions used*: after 15 minutes the ear was irrigated with 50ml of tepid water	*Number of participants*: 90: 1. Chlorobutanol $n = 32$ 2. Sodium carbonate $n = 29$ 3. Saline $n = 28$ *Sample attrition/dropout*: Not reported *Inclusion criteria for study entry*: Adults with total cerumen obstruction *Exclusion criteria for study entry*: Not reported	*Primary outcomes*: Proportion of TM completely visualised *Secondary outcomes*: Not reported *Method of assessing outcomes*: Not reported *Length of follow-up*: Immediate

Baseline characteristics of participants (all participants aged 19–78 years)

Results

Primary outcomes	**Chlorobutanol ($n = 32$)**	**Sodium carbonate ($n = 29$)**	**Saline ($n = 28$)**	***p*-value**
Proportion of TM completely visualised	21/32 (65.6%)	16/29 (55.2%)	12/28 (42.9%)	$p = 0.209$

Comments: unsure if *p*-value relates to comparison across all three groups

Secondary outcomes	**Chlorobutanol $n = 32$**	**Sodium carbonate $n = 29$**	**Saline $n = 28$**	***p*-value**

Comments:

Note: If reviewer calculates a summary measure or confidence interval *please indicate*.

Methodological comments

Allocation to treatment groups: States randomised, but no further details reported

Blinding: Not reported

Comparability of treatment groups: States groups were similar in age, race, sex, ear enrolled and wax consistency, but no data reported

Method of data analysis: States variables were analysed with chi-squared test; $p = 0.05$ was statistically significant

Sample size/power calculation: Not reported

Attrition/dropout: None reported but numbers do not add up to 90 so assume one withdrew/dropped out

General comments

Generalisability: Unclear population

Outcome measures: Unclear how valid the outcome measures were

Intercentre variability: Not applicable

Conflict of interests: Unknown

RCT, randomised controlled trial; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Partial
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Unknown
7. Was the patient blinded?	Unknown
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Dubow[57]

Extracted by: PH		**Checked by: EL**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Dubow[57] *Year*: 1959 *Country*: USA *Study design*: RCT *Number of centres*: At least two *Setting*: Assume secondary as paediatric clinic *Funding*: None reported	1. Hydrogen peroxide (USA household antiseptic of 3% solution) 2. Mineral oil 3. Cerumenex *Duration of treatment*: Treatment administered by parents and left in ear overnight, followed by irrigation with warm water the following morning *Other interventions used*: Dropper bottle of liquid test material and a 2-oz Davol rubber ball and nozzle-type syringe	Number of participants: 60 1. Peroxide solution: n = 20 2. Mineral oil: *n* = 20 3. Cerumenex: *n* = 20 Sample attrition/dropout: 1. *n* = 0 2. *n* = 1 3. *n* = 0 Inclusion criteria for study entry: children with at least 1 completely cerumen-occluded ear canal, without regard to other disorders, presenting in a paediatric clinic and in 'office practice' Exclusion criteria for study entry: acutely ill children, were the illness would prevent follow-up visit	*Primary outcomes*: Wax clearance *Secondary outcomes*: None reported *Method of assessing outcomes*: Otological examination prior and after treatment *Length of follow-up*: Immediate

Baseline characteristics of participants:

	All (*n* = 60)	***p*-value**
Age	3–12 years	No *p*-values reported
Race	All (including white, coloured and Chinese)	
Moderate – severe pain	3	

Results:

Primary outcomes	**Hydrogen peroxide (*n* = 20)**	**Mineral oil (*n* = 19)**	**Cerumenex (*n* = 20)**	***p*-value**
Clearance: *n* (%)	7 (35%)	8 (42%)	(14) 70%	No *p*-values reported

Comments: Number of patients calculated from percentages by reviewer.

Secondary outcomes	**Hydrogen peroxide (*n* = 20)**	**Mineral oil (*n* = 19)**	**Cerumenex (*n* = 20)**	***p*-value**

Comments: AE – one itching erythematous eruption of the external auditory meatus and surrounding area of the pinna of the ear.

Methodological comments

Allocation to treatment groups: Group was formed from children presenting themselves for paediatric examination. Children were randomly assigned to a group, unless there were language difficulties or other inability to achieve understanding by the parents, as procedure 'would not be carried out properly'

Blinding: No details reported.

Comparability of treatment groups: No details reported

Method of data analysis: None reported

Sample size/power calculation: None reported

Attrition/dropout: One child in mineral oil group refused to be treated by parents

General comments

Generalisability: No baseline characteristics provided, population based on American children in late 1950s

Outcome measures: It is unclear how the primary outcome was measured, how valid or objective the measure was or how many paediatricians took part in the examinations (consistency)

Intercentre variability: N/A

Conflict of interests: Cerumenex distributed by Purdue Frederick Co., New York, NY

AE, adverse event; N/A, not applicable; RCT, randomised controlled trial.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Inadequate
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Unknown
7. Was the patient blinded?	Unknown
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Chaput de Saintonge and Johnstone[59]

Extracted by: PH		**Checked by: EL**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Chaput de Saintonge and Johnstone[59] *Year*: 1973 *Country*: UK *Study design*: Double-blind RCT *Number of centres*: One *Setting*: Secondary care *Funding*: None reported	1. Triethanolamine polypeptide oleate condensate (TP) 2. Olive oil *Duration of treatment*: 20 minutes *Other interventions used*: Syringing by nursing staff with a hand syringe	*Number of ears*: 67 1. TP: $n = 32$ 2. Olive oil: $n = 35$ *Sample attrition/dropout*: Not reported *Inclusion criteria for study entry*: Any patient with impacted wax attending outpatients *Exclusion criteria for study entry*: None reported	*Outcomes*: Total volume of water and amount of wax removed *Method of assessing*: Water used in syringing measured to nearest 50 ml *Amount of wax removed*: Complete, partial or negligible *Length of follow-up*: Immediate

Baseline characteristics of participants: not reported

	TP ears = 32	**Olive oil ears = 35**	***p*-value**

Results

Outcomes

	TP ears ($n = 32$)	**Olive oil ears ($n = 35$)**	***p*-value**
Volume of water used[a]			
150 ml	7	1	$p < 0.05$
300 ml	14	14	TP needs smaller volumes water than olive oil
450 ml	4	6	
600 ml	2	2	
750 ml	0	2	
900 ml	1	7	
Amount of wax removed			
Complete	20	21	States not significant, but no *p*-values reported
Partial	12	10	
Negligible	0	4	

Comments:
a Estimated from graph by reviewer, TP needed a significantly smaller volume of water for syringing than olive oil.

Methodological comments

Allocation to treatment groups: Treatments were allocated in random order, no other details reported

Blinding: Study states double-blind method was used and treatments were supplied in identical coded bottles, with codes not broken until trial completion

Comparability of treatment groups: No details reported

Method of data analysis: Mann–Whitney *U*-test used to test for differences in volume of water used

Sample size/power calculation: None reported

Attrition/dropout: None reported

General comments

Generalisability: No baseline demographic characteristics, UK population

Outcome measures: It is unclear how valid or objective the measures were

Intercentre variability: N/A

Conflict of interests: None reported. HR Napp Ltd supplied TP ear drops and assisted in setting up the trial

N/A, not applicable; RCT, randomised controlled trial.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Adequate
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Inadequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Adequate
7. Was the patient blinded?	Adequate
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Keane and colleagues[4]

Extracted by: PH **Checked by: EL**

Reference and design	Intervention	Participants	Outcome measures
Author: Keane and colleagues[4] *Year*: 1995 *Country*: Ireland *Study design*: Double-blind RCT *Number of centres*: One *Setting*: Secondary care *Funding*: None reported	1. Cerumol:[a] 4 drops twice daily 2. $NaHCO_3$ (sodium bicarbonate):[b] 4 drops twice daily 3. Sterile water: 4 drops twice daily 4. Control: No treatment *Duration of treatment*: 5 days *Other interventions used*: [a]Cerumol: Chlorbutol 5%, paradichlorobenzene 2%, arachis oil 57.3% [b]Sodium bicarbonate: $NaHCO_3$ 5 g, glycerol and purified water	*Number of participants*: $n = 113$, 97 randomised (155 ears) *Cerumol*: $n = 24$ (40 ears) *Sodium bicarbonate*: $n = 25$ (39 ears) *Sterile water*: $n = 24$ (38 ears) *Control*: $n = 24$ (38 ears) *Sample attrition/dropout*: 13 went home and 3 died, 97 completed study *Inclusion criteria for study entry*: One or both ears impacted *Exclusion criteria for study entry*: Known pathology of the ear canal and/or TM and those already on ear drops	*Primary outcomes*: Percentage clearance and number of ears (clearance is explained by the 'natural expulsion of earwax') *Secondary outcomes*: AE *Method of assessing outcomes*: Auditory canal classification – 1. impacted wax in the external canal, 2. moderately clear external canal or 3. completely clear external canal. Examination and re-examination carried out by the same observer *Length of follow-up*: 5-day trial

Baseline characteristics of participants

None reported

Results

Primary outcomes: clearance % (no. of ears)

	Cerumol ($n = 24$)	$NaHCO_3$ ($n = 25$)	Water ($n = 24$)	Control ($n = 24$)	*p*-value
Impacted	40.0 (16)	53.8 (21)	47.4 (18)	68.4 (26)	
Moderately clear	37.5 (15)	25.6 (10)	31.6 (12)	26.3 (10)	$p < 0.05$ Cerumol vs control
Completely clear	22.5 (9)	20.6 (8)	21.0 (8)	5.3 (2)	$p < 0.05$ Cerumol vs control $p < 0.05$ $NaHCO_3$ vs control $p < 0.05$ water vs control

Comments: No significant differences between Cerumol, $NaHCO_3$ or water.

Secondary outcomes

	Cerumol ($n = 24$)	$NaHCO_3$ ($n = 25$)	Water ($n = 24$)	Control ($n = 24$)	*p*-value

Comments: AE – no cases of irritation or contact sensitivity.

Methodological comments

Allocation to treatment groups: Participants were randomly divided into four groups. States treatment was allocated in random order and the 'code was not broken until the trial was complete'. No other information provided. Unclear reporting over randomisation of participants in respect of number randomised

Blinding: Authors state double-blind trial. The only information provided is that the drops were administered by nursing staff and that ears were examined and re-examined by same observer

Comparability of treatment groups: Unknown, no baseline reported

Method of data analysis: *t*-test, paired samples only; no adjustment for multiple comparisons made

Sample size/power calculation: Not reported

Attrition/dropout: No dropouts after randomisation. Poor reporting means it is unclear whether the 16 additional participants received any treatment

General comments

Generalisability: Possibly elderly hospitalised patients, but exact patient group unclear

Outcome measures: Unclear how valid and objective the outcome classification was

Intercentre variability: N/A

Conflict of interests: None reported

AE, adverse event; N/A, not applicable; RCT, randomised controlled trial; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Unknown
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Unknown
7. Was the patient blinded?	Unknown
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Fraser[60]

Extracted by: AC **Checked by: PH**

Reference and design	Intervention	Participants	Outcome measures
Author: Fraser[60] *Year*: 1970 *Country*: UK *Study design*: RCT *Number of centres*: Six hospitals *Setting*: Secondary care *Funding*: Not stated	1. Sodium bicarbonate (BPC) 2. Olive oil 3. Cerumol 4. Waxsol 5. TP 6. Dioctyl capsules *Duration of treatment*: Ear drops were instilled once daily for 3 days prior to syringing for 15 minutes, except TP, which was used 15–30 minutes before syringing due to its claimed rapid action *Other interventions used*: None stated	*Number of participants*: 248 ears from 124 people, with 1 ear per person providing a test and control ear *Intervention*: 124 ears *Control*: 124 ears *Sample attrition/dropout*: 18 patients failed to complete the trial due to errors in the procedure and 3 died *Inclusion criteria for study entry*: Participants had bilateral hard earwax that occludes the external auditory meatus in both ears; patients were from geriatric attendees at hospitals *Exclusion criteria for study entry*: None stated	*Primary outcomes*: Ease of syringing, frequency of syringing, appearance of wax removed *Secondary outcomes*: see above *Method of assessing outcomes*: Not stated *Length of follow-up*: At least 3 days

Baseline characteristics of participants

None reported

Results

Outcomes

	Sum scores		
Ease of syringing	**Test ears**	**Control ears**	**Difference (mean rank)**
Cerumol (24 ears)	92	122	+30[a] (+11.9)[b]
Olive oil (25 ears)	116	140	+24 (+3.4)
Waxsol (26 ears)	110	128	+18 (+2.8)
Sodium bicarbonate (124 ears)	Control		0 (–3.5)
TP (24 ears)	118	107	–11 (–9.0)
Dioctyl capsules (25 ears)	119	107	–12 (–9.1)

Comments: The lower the score the easier the syringing. A positive difference indicates that the test were easier to syringe than the control ears.
a Cerumol differed significantly from sodium bicarbonate ($p < 0.05$), all other comparisons were not significant.
b When mean ranks were compared, Cerumol was significantly better than dioctyl and TP; $p < 0.05$.

	No. of patients in which:		
Frequency of syringing successes and failures	**Product better**	**Scores equal**	**Control better**
Cerumol (24 ears)	15	5	4
Olive oil (25 ears)	10	6	9
Waxsol (26 ears)	11	6	9
TP (24 ears)	7	7	10
Dioctyl capsules (25 ears)	8	5	12

No. of ears in which very forceful syringing failed	Test ears	Control ears
Cerumol (24 ears)	1	5
Olive oil (25 ears)	2	4
Waxsol (26 ears)	3	5
TP (24 ears)	5	3
Dioctyl capsules (25 ears)	5	2

Appearance of wax removed by syringing	Percentage of lumps	Percentage partially broken up	Percentage completely broken up
Oil-based solvents:			
Cerumol (24 ears)	46	37	17
Olive oil (25 ears)	40	44	16
TP (24 ears)	42	25	33
Dioctyl capsules (25 ears)	36	44	20
Water-based solvents:			
Waxsol (26 ears)	15	46	39
Sodium bicarbonate (124 ears)	33	43	24

Comments: Frequency of otitis externa (redness of the external meatus): total of 12 ears (4%); in 3 ears it was bilateral and probably not due to the study; of the remaining 6 ears, 3 ears had received sodium bicarbonate, 2 Waxsol and 1 TP.

Methodological comments

Allocation to treatment groups: Sodium bicarbonate was used in one ear and another product in the other ear. Products were given code letters and were allocated at random to patients by an assistant. The ear in which the product was used was similarly randomised

Blinding: Except for TP, the surgeon performing the syringing was neither aware of which drops a patient received, nor which was the test ear. For TP, the surgeon knew it had been used but not in which ear

Comparability of treatment groups: No comparison made of participants baseline characteristics, although each patient had a test ear and a comparator ear to try and minimise differences

Method of data analysis: Scores, difference in scores, mean rank and Wilcoxon one-sample ranking test used

Sample size/power calculation: Not stated

Attrition/dropout: Of 142 participants originally identified, 18 failed to complete the trial due to procedure errors and 3 died, leaving 124 participants

General comments

Generalisability: Unknown

Outcome measures: Ease of syringing was compared for each preparation against sodium bicarbonate, with the difference between test and control ear calculated and tested for significance using the Wilcoxon one-sample ranking test. Differences in scores between test and control ears were ranked over all products. The sum of ranks and the mean rank for each product were compared with each other. Frequency of syringing and appearance of wax were other outcomes. Limited information is provided as concerns the definitions of outcome measures

Intercentre variability: Syringing techniques were standardised and undertaken by one operator

Conflict of interests: None stated

RCT, randomised controlled trial; TP, triethanolamine polypeptide.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Inadequate
2. Was the treatment allocation concealed?	Inadequate
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Unknown
5. Were outcome assessors blinded to the treatment allocation?	Inadequate
6. Was the care-provider blinded?	Inadequate
7. Was the patient blinded?	Inadequate
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Inadequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Pothier and colleagues[56]

Extracted by: AC		Checked by: PH	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Pothier and colleagues[56] *Year*: 2006 *Country*: UK *Study design*: RCT (unblinded) *Number of centres*: One *Setting*: Otolaryngology outpatient clinic *Funding*: None reported	1. *Intervention*: endoscopic de-waxing using a Karl–Storz 4-mm 0° otoendoscope and portable light-emitting diode light source 2. *Control*: Microscopic de-waxing using a Zeiss OPMI microscope with a Toynbee aural speculum *Duration of treatment*: Treated and assessed on initial visit, unless cerumenolytics used and then unspecified delay *Other interventions used*: Wax was removed with a Jobson–Horne probe or a wax hook (91%) or crocodile forceps or Zoellner Sucker (9%)	*Number of participants*: $n = 100$ *Intervention*: $n = 50$ *Control*: $n = 50$ *Sample attrition/dropout*: No dropouts. *Inclusion criteria for study entry*: Patients requiring removal of earwax from the ear canal to allow full view of the TM with a history of earwax *Exclusion criteria for study entry*: People with active or previous external or middle ear pathology [i.e. mastoid cavities, active ear infections or any abnormality of TM (perforation or retraction)]	*Primary outcomes*: Levels of pain and discomfort for patient, ease of de-waxing, time taken to de-wax *Secondary outcomes*: see above *Method of assessing outcomes*: Assessed by patient questionnaire (VAS) and through assessment by endoscopist *Length of follow-up*: Treated and assessed on initial visit, unless cerumenolytics used and then unspecified delay

Baseline characteristics of participants

	Endoscopic ($n = 50$)	**Microscopic ($n = 50$)**	***p*-value**
Mean age (SD, range) years	57.2 (16.86, 16–87)	58.3 (17.3, 18–91)	Not stated
Male–female ratio (%)	60:40	62:38	Not stated
Mean % wax obscuring TM	72.0	65.5	Not stated
Number (%) of patients with TM completely obscured	20 (40)	26 (52)	0.69

Results

Primary outcomes

	Endoscopic ($n = 50$)	**Microscopic ($n = 50$)**	***p*-value**
Discomfort – median score on VAS (0–100)	5	25	0.002
Pain – median score on VAS (0–100)	3.5	10	0.075
Difficulty in de-waxing – median score on VAS (0–100)	9	20	0.005
Time taken to perform de-waxing (minutes)	1.8	3.3	0.001

Comments: No complications were reported during de-waxing, however, one patient from each group sustained minor bleeding from ear canals. Five patients from the endoscope group required conversion to microscope (three successfully de-waxed, two sent home with cerumenolytics before finishing de-waxing) and two microscope patients converted to endoscope (one successfully de-waxed, one sent home with cerumenolytics).

Methodological comments

Allocation to treatment groups: Opaque envelopes with single proforma with group marked

Blinding: Blindly selected at random by patient. Endoscopist performing procedure informed patient of allocation

Comparability of treatment groups: Study identified that patient groups were similar at baseline in terms of age, sex and proportion of TM obscured

Method of data analysis: Data on discomfort, pain and difficulty were analysed using Mann–Whitney *U*-test and data on time taken used an unpaired *t*-test to compare means. ITT analysis was used

Sample size/power calculation: Sample of 50 participants would provide power of 90% to detect a mean difference of 10 points assuming a standard deviation of 15, using a two-group test, at 5% significance

Attrition/dropout: No patients dropped out

General comments

Generalisability: Patients from an otolaryngology outpatient clinic with a previous history of earwax, 60% male, mean age 57–58 years old

Outcome measures: Levels of pain (0 = no pain; 100 = very painful) and discomfort (0 = no discomfort; 100 = very uncomfortable) were recorded by the patients using a visual analogue score sheet. Clinician assessed on a VAS the ease of de-waxing, the percentage of TM obscured by wax prior to randomisation and the time taken to de-wax. VASs have not been formally validated

Intercentre variability: Not applicable

Conflict of interests: None stated. Karl Storz loaned otoendoscopes and GVR Products loaned portable light sources

ITT, intention to treat; RCT, randomised controlled trial; SD, standard deviation; TM, tympanic membrane; VAS, visual analogue scale.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Partial
2. Was the treatment allocation concealed?	Inadequate
3. Were the groups similar at baseline in terms of prognostic factors?	Reported
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Inadequate
6. Was the care-provider blinded?	Inadequate
7. Was the patient blinded?	Inadequate
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Adequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Saloranta and colleagues[58]

Extracted by: EL		Checked by: AC	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Saloranta and colleagues[58] *Year*: 2005 *Country*: Finland *Study design*: RCT *Number of centres*: Two *Setting*: Secondary care and community home for people with learning difficulties *Funding*: None reported	1. Skin oil Ceridal lipolotion* emollient, 2 ml, self administered except in those with learning difficulties 2. No treatment *Duration of treatment*: Once a week for 12 months. Patients kept a diary of their treatment *Other interventions used*: Patients all had removal of the impacted earwax prior to randomisation, unclear by what method *Contains paraffinum liquidum, cyclomethicone and *Buxus chinensis*, Stiefel Laboratories (Ireland) Ltd	*Number of participants*: 39 Ceridal: *n* = 20 (13 analysed, 16 ears) Control: *n* = 19 (18 analysed, 29 ears) *Sample attrition/dropout*: Numbers analysed were: Ceridal: 13 (1 death mother, 1 decrepitude, 2 lost to follow-up, 1 death, 2 excluded due to cholesteatoma) Control: 18 (1 death) *Inclusion criteria for study entry*: History of impacted cerumen, with symptoms like impaired hearing or sensation of blocked ear canal more often than once per year and earwax completely obstructing the ear canal at the point of inclusion *Exclusion criteria for study entry*: None noted	*Primary outcomes*: (Not defined as primary or secondary.) Recurrence of cerumen impaction, AEs *Secondary outcomes*: see above *Method of assessing outcomes*: No details *Length of follow-up*: 12 months (visits also at 3 months and at a point of recurrence)

Baseline characteristics of participants (reported for those analysed not those recruited)

	Ceridal (*n* = 13)	**Control (*n* = 18)**	***p*-value**
M/F	7/6	8/10	
Mean age (range), years	34 (4–52)	44 (1–74)	
Learning difficulties	9	10	
No treated ears	16	29	

Results

Primary outcomes

	Ceridal (*n* = 13)	**Control (*n* = 18)**	***p*-value**
Recurrence	3 (23%)	11 (61%)	$p < 0.05$
Recurrence in treated ears	3/16 (19%)	15/29 (52%)	$p < 0.05$

Comments: There was also a trend in the timing of recurrent impaction; 73% of the control ears recurred within 3 months compared with 40% in the Ceridal group.

Secondary outcomes

	Ceridal (*n* = 13)	**Control (*n* = 18)**	***p*-value**
AEs	0	0	

Comments:

Methodological comments

Allocation to treatment groups: After removal of impacted cerumen, patients were randomised. Randomisation was undertaken for the whole study in advance by a co-worker. Forty envelopes were consecutively numbered – half of them randomly containing the treatment code and half of them the control code. This was carried out after extraction of the impacted earwax

Blinding: No blinding evident, participants were seen and evaluated by one of the authors

Comparability of treatment groups: No statistical analysis or comment from authors, mean age appears to be lower in the Ceridal group

Method of data analysis: Differences between groups tested by Fisher's exact test

Sample size/power calculation: Not reported, however this is reported to be a pilot study

Attrition/dropout: Numbers and reasons given

General comments

Generalisability: Large proportion of participants had learning difficulties

Outcome measures: Unknown how valid or objective the outcome measures were

Intercentre variability: None noted

Conflict of interests: None noted

AEs, adverse events; F, female; M, male; RCT, randomised controlled trial.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Inadequate
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Unknown
7. Was the patient blinded?	Unknown
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Appendix 5

Data extraction forms: self-care and other care settings

Harris[64]

Extracted by: PH		**Checked by: EL**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Harris[64] *Year*: 1968 *Country*: Ireland *Study design*: RCT *Number of centres*: One *Setting*: Primary care *Funding*: TP and bulb syringes supplied by HR Napp Ltd	1. *Intervention*: TP (enough ear drops to fill the ear and left in overnight) plus self-syringing with warm water the morning after 2. *Control*: None, self-syringing with warm water in the morning only *Duration of treatment*: 12–24 hours *Other interventions used*: self-syringing with a maximum of 12 squirts of warm water using a 2 fl oz, soft rubber bulb, rat-tailed syringe the morning after the treatment, followed by auroscopic examination in the evening. If self-syringing was unsuccessful syringing was repeated at the surgery after the examination.	*Number of participants*: 45 *TP*: 24 *Control*: 21 *Sample attrition/dropout*: No dropouts *Inclusion criteria for study entry*: All participants attending surgery and complaining of symptoms directly attributable to ceruminosis *Exclusion criteria for study entry*: Underlying systemic disease, perforated TM, chronic otitis externa or middle ear disease	*Outcomes*: (Not stated as primary or secondary) Wax clearance Meati clearance Colour cerumen Symptoms AEs *Method of assessing outcomes*: auroscopic examination *Length of follow-up*: 1 day

Baseline characteristics of participants

Comments: majority of participants had earwax in both ears, but no breakdown provided.

Ceruminosis symptoms across both groups	**Partially obscured TM (*n* = 17)**	**Completely obscured TM (*n* = 28)**
Impaired hearing	8	28
Tinnitus	9	10
Vertigo	3	5
Irritation	2	2
Pain	2	1

Cerumen colour (n = 45) across both groups

	Partial obstruction	**Total obstruction**
Yellow, *n* = 6	3	3
Brown, *n* = 13	0	13
Black, *n* = 12	0	12

Comments: Baseline degree of obstruction reported (see results below).

Results

Outcomes

	TP ($n=24$)	Control ($n=21$)	*p*-value
Completely cleared	18	1[a]	$p<0.005$ ($\chi^2=19.862$)
Partially or not cleared	6[b]	20[c]	

Comments:

Six TP participants had softened wax cleared at surgery with gentle syringing after examination. Nineteen participants in the control group had wax cleared with normal syringing after examination at the surgery.

a Meatus cleared.
b Partial clearance.
c Not cleared.

	TP ($n=24$)		Control ($n=21$)		
	State of meati				
	Obscured completely	Obscured partially	Obscured completely	Obscured partially	*p*-value
Before treatment					Within group comparison, before and after
	14	10	14	7	
After treatment					TP > 0.05 (not significant)
Meati cleared	8	10	0	1	($\chi^2=3.657$)
Meati not cleared	6	0	14	6	Control: not significant

Comments: The colour of wax had no effect on clearance or by treatment in either group (*p*-value not provided).

AEs	1[a]	0

Comments:

a Participant suffered erythema around the external auditory meatus, most likely due to TP. Resolved within 48 hours of treatment with topical corticosteroid cream. Some TP participants noted brownish liquid on pillow, presumed to be liquefied cerumen; no other details reported.

Methodological comments

Allocation to treatment groups: States randomly assigned, no further details

Blinding: Blinding not reported

Comparability of treatment groups: Unknown, no details reported

Method of data analysis: Chi-squared test for small numbers with Yates' correction was calculated (fourfold table)

Sample size/power calculation: None reported

Attrition/dropout: None

General comments

Generalisability: UK Primary Care practice population during 1968, suffering from ceruminosis predominantly in both ears

Outcome measures: Unclear how valid, objective, or consistently applied the outcome measures used were

Intercentre variability: N/A

Conflict of interests: TP and bulb syringes supplied by HR Napp Ltd

AEs, adverse events; N/A, not applicable; RCT, randomised controlled trial; TM, tympanic membrane; TP, triethanolamine polypeptide.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Unknown
4. Were the eligibility criteria specified?	Partial
5. Were outcome assessors blinded to the treatment allocation?	Unknown
6. Was the care-provider blinded?	Unknown
7. Was the patient blinded?	Unknown
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Coppin and colleagues[63]

Extracted by: AC		Checked by: PH	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Coppin and colleagues[63] *Year*: 2008 *Country*: UK *Study design*: RCT *Number of centres*: Seven primary care practices *Setting*: Primary care *Funding*: Royal College of General Practitioners Science Foundation Board and UK Department of Health Support for Science Fund	1. *Intervention*: Ear drops (sodium bicarbonate) for ≥ 2 days (unless drops already used), bulb syringe (25 ml) and instructions for self-treatment 2. *Control*: Ear drops (sodium bicarbonate) for ≥ 2 days (unless drops already used), irrigation by GP or practice nurse *Duration of treatment*: 1–2 weeks *Other interventions used*: none stated	*Number of participants*: $n = 237$ *Intervention*: $n = 118$ *Control*: $n = 119$ *Sample attrition/dropout*: Due to main outcome not documented. *Intervention*: $n = 14$ *Control*: $n = 17$ *Inclusion criteria for study entry*: Adults consulting a GP or practice nurse with symptoms of occluding earwax (itching, sensation of blockage, reduced hearing) consenting to inclusion in study *Exclusion criteria for study entry*: None stated	*Primary outcomes*: Reported symptoms and wax clearance *Secondary outcomes*: Further treatment required and acceptability of treatment *Method of assessing outcomes*: Practice nurse ($n = 230$) or GP ($n = 7$) undertook initial assessment and practice nurses undertook all follow-up assessments. Other outcomes were assessed by patient questionnaire *Length of follow-up*: 1–2 weeks for comparison of interventions; within 6 weeks for assessment of further treatment, adverse effects, rates and reasons for non-participation or non-compliance
Baseline characteristics of participants			
	Bulb ($n = 118$)	**Irrigation ($n = 119$)**	***p*-value**
Mean symptom score[a] at baseline ($n = 205$)	2.37 (SD 1.44)	2.41 (SD 0.90)	Not stated
Right ear completely obstructed with wax, *n* (%)	73/116 (63)	72/116 (62)	Not stated
Left ear completely obstructed with wax, *n* (%)	78/116 (67)	79/114 (69)	Not stated
Male–female ratio (%)	66:34	63:37	Not stated
Mean (SD) age, years	57 (14)	55 (16)	Not stated
Results			
Primary outcomes			
	Bulb ($n = 118$)	**Irrigation ($n = 119$)**	**Difference between groups (95% CI); *p*-value**
Mean (SD) change in symptom score from baseline	–0.81 (1.44)	–1.26 (1.15)	–0.45 (–0.11 to –0.79); $p = 0.01$ (0.02)[b]
Treatment discomfort (slight or more), *n* (%)	43/110 (39)	35/108 (32)	7% (–6% to 19%); $p = 0.30$
Treatment dizziness (slight or more), *n* (%)	14/110 (13)	14/108 (13)	0% (–9% to 9%); $p = 0.96$
Use same treatment again, *n* (%) (agreed slightly or more)	82/110 (75)	106/106 (100)	25% (17% to 25%); $p < 0.001$
Wax clearance (obstruction score 0 or 1), *n* (%)	50/104 (48)	64/102 (63)	15% (1% to 28%); $p = 0.03$
Comments: a Symptoms score: 0 = no symptom to 6 = severe. b Kruskal–Wallis test.			

Secondary outcomes

	Bulb (*n* = 118)	Irrigation (*n* = 119)	Difference between groups (95% CI); *p*-value
Treatment convenient (agreed slightly or more), *n* (%)	84/110 (76)	95/105 (90)	14% (4% to 24%); $p < 0.01$
Satisfied with treatment, *n* (%) (agreed slightly or more)	78/110 (71)	105/106 (99)	28% (19% to 29%); $p < 0.001$
Requires no further clearance (based on normal clinical practice), *n* (%)	51/100 (51)	66/95 (69)	18% (5% to 32%); $p < 0.01$
Infection, *n* (%)	1/97 (1)	1/93 (1)	0% (–3% to 3%); $p = 1.00$[a]
Perforation, *n* (%)	1/97 (1)	1/94 (1)	0% (–3% to 3%); $p = 1.00$[a]
Signs of trauma, *n* (%)	1/97 (1)	1/94 (1)	0% (–3% to 3%); $p = 1.00$[a]

Adverse events: 1 patient in the irrigation group had bilateral otitis externa and 2 patients had perforation (1 old scarring TM and 1 pre-existing cholesteatoma)

Comments:

a Fisher's exact test used.

Methodological comments

Allocation to treatment groups: Using sealed envelopes randomised using random number tables by person not involved data collection or recruitment

Blinding: Patients received an envelope questionnaire and a box containing either ear drops, a bulb syringe and instructions or ear drops and a roll of card of similar weight to bulb and instructions on other treatment. Process was audited to assess whether recruitment was selective and confounded. Assessment of wax clearance could not be blinded

Comparability of treatment groups: Baseline data on age, sex and ear obstruction were similar between groups

Method of data analysis: States that ITT analysis using analysis of covariance and Kruskal-Wallis test for continuous outcomes and chi-squared test or Fisher's exact test for dichotomous variables. Although it states ITT analysis was undertaken, denominators appear to vary with outcomes. Clustering was assessed and found not to affect outcomes

Sample size/power calculation: Observed wax clearance was used for sample size calculation ($\alpha = 0.05$ and power 80%) assuming clearance of wax by bulb of 75% and syringe 90% it was estimated that 100 patients per group and 236 in total if there was a loss to follow-up of 15%

Attrition/dropout: Of the 434 patients invited, 69 declined/excluded, 237 randomised, a further 128 not randomised had notes searched. Of 237 randomised, 206 were followed up and 31 were lost to follow-up due to main outcome not documented (14 people from the intervention and 17 from the control group). Nurses monitored follow-up and noted all patients allocated to bulbs used them

General comments

Generalisability: Participants were from 7 primary care practices in Hampshire (UK), with over 60% male and a mean age between 55 and 57 years

Outcome measures: Overall symptoms and acceptability of treatment were assessed using questions (7-point scale) validated in pilot study. Wax obstruction was measured by a practice nurse using previously described 4-point score (0 = no or minimal wax with TM fully visible; 1 = minor amount of wax with TM essentially visible; 2 = moderate amount of wax with TM partially obscured; 3 = complete occlusion of TM. (Note 0 and 1 were combined to form clinically clear)

Intercentre variability: Not reported

Conflict of interests: None stated

CI, confidence interval; ITT, intention to treat; RCT, randomised controlled trial; SD, standard deviation; TM, tympanic membrane.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Adequate
2. Was the treatment allocation concealed?	Adequate
3. Were the groups similar at baseline in terms of prognostic factors?	Reported
4. Were the eligibility criteria specified?	Unknown
5. Were outcome assessors blinded to the treatment allocation?	Inadequate
6. Was the care-provider blinded?	Not applicable
7. Was the patient blinded?	Not applicable
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Adequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Partial

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Roland and colleagues[62]

Extracted by: EL		**PH**	
Reference and design	**Intervention**	**Participants**	**Outcome measures**
Author: Roland and colleagues[62] *Year*: 2004 *Country*: USA *Study design*: RCT *Number of centres*: One *Setting*: Corporate research clinic *Funding*: Funded by Alcon Research Ltd	1. Cerumenex ear drops* 2. Murine ear drops** 3. Placebo*** *Duration of treatment*: Each treatment consisted of up to two 15-minute applications of treatment/placebo *Other interventions used*: Ear drops were followed by a standardised irrigation procedure using a WaterPik Oral Jet Irrigator. Irrigation consisted of 50 ml of lukewarm water. If cerumen was cleared after a single application and irrigation, the second application was not conducted *10% triethanolamine polypeptide oleate condensate, Purdue Frederick Company **6.5% carbamide peroxide, Abbott Laboratories ***BBS sterile irrigating solution (saline containing 0.64% sodium chloride and physiological concentrations of multiple electrolytes), Alcon Laboratories	*Number of participants*: 230 screened, 74 qualified for enrolment: 1, $n = 24$; 2, $n = 26$; 3, $n = 24$ *Sample attrition/dropout*: None reported *Inclusion criteria for study entry*: Volunteers from company employees who had excessive or impacted cerumen. Required to be ≥ 18 years with mild, moderate, or complete cerumen occlusion, as measured against a previously established 4-point scale (see outcomes for details) *Exclusion criteria for study entry*: Ear anomalies, diabetes, allergies to study medications, were pregnant or nursing or had instilled anything other than water in their ear in the previous 72 hours	*Primary outcomes*: Post-treatment level of occlusion *Secondary outcomes*: Otological signs and symptoms *Method of assessing outcomes*: Assessed by 'qualified specialist' For degree of occlusion a scale of 0–3 used as follows: • 0 = no occlusion, no effective impairment of TM visualisation due to cerumen • 1 = mild occlusion • 2 = moderate occlusion • 3 = complete occlusion Unclear how valid and reliable this test is Adverse events *Length of follow-up*: Immediate

Baseline characteristics of participants

	All ($n = 74$)	***p*-value**
Mean age, years (range)	45 (22–66)	
Mild occlusions	10	
Moderate occlusions	26	
Complete occlusions	38	
Gender, M/F (M/F ratio)	51 : 23 (2.2 : 1)	

Results

Primary outcomes

	Cerumenex ($n = 24$)	**Murine ($n = 26$)**	**Placebo ($n = 24$)**	***p*-value**
No occlusion	7(29.2%)	4 (15.4%)	10 (41.7%)	Cerumenex vs placebo; $p = 0.37$
Mild, moderate or complete occlusion	17 (71%)	22 (85%)	14 (58%)	Murine vs placebo; $p = 0.06$
Comments: Statistical analysis of Cerumenex vs placebo was by chi-squared test, but analysis of Murine vs placebo was by Fisher's exact test.				
Change from baseline in occlusion (estimated from figure)	Resolved: 30% Improved: 8% No change/worse: 62%	Resolved: 16% Improved: 7% No change/worse: 77%	Resolved: 42% Improved: 22% No change/worse: 38%	Not tested

Secondary outcomes

	Cerumenex (*n* = 24)	Murine (*n* = 26)	Placebo (*n* = 24)	*p*-value
AEs related:				
Ear pruritis	1 (4%)	2 (8%)	0	
Ear discomfort	0	0	1 (4%)	
Contact dermatitis	1 (4%)	0	0	
AEs not related:				
Vertigo	1 (4%)	0	0	

Comments: Number of applications – overall 90.5% required 2 applications, 9.5% had successful treatment outcome after 1 application and irrigation [Cerumenex: 2 (8%), Murine: 3 (12%), placebo: 2 (8%)]. Of those with a single application there were no differences between the interventions (*p*-value not reported).

Methodological comments

Allocation to treatment groups: States randomly assigned, no further details

Blinding: States observer- and participant-blind study. The outcome assessors and the participant were masked from treatment allocation by storing test articles out of view and administration was by clinic staff who did not perform the clinical assessments

Comparability of treatment groups: States no statistically significant differences between demographic characteristics (age and gender) or between baseline degree of occlusion were observed between groups. No data reported, however, between groups

Method of data analysis: Summary statistics (mean ± SD) calculated and either a chi-squared test or a *t*-test used

Sample size/power calculation: No power calculations were undertaken as 'planned as a descriptive study'

Attrition/dropout: None reported

General comments

Generalisability: American volunteer participants between ages 22 and 66 years employed by the study sponsor (self-selection bias), so may not be representative of the total population in terms of being likely to have earwax problems

Outcome measures: Unclear how valid or reliable the outcome measure is. Authors acknowledge that the distinction between mild and moderate occlusion is somewhat subjective

Intercentre variability: Not applicable

Conflict of interests: Funded by a private research company, unclear whether the company has any relation to the treatments compared. Drs Roland and Gross served as paid consultants for Alcon Research Ltd

AEs, adverse events; F, female; M, male; RCT, randomised controlled trial; SD, standard deviation.

Quality criteria for assessment of RCTs (NHS CRD)

Item	Judgement[a]
1. Was the assignment to the treatment groups really random?	Unknown
2. Was the treatment allocation concealed?	Unknown
3. Were the groups similar at baseline in terms of prognostic factors?	Inadequate
4. Were the eligibility criteria specified?	Adequate
5. Were outcome assessors blinded to the treatment allocation?	Adequate
6. Was the care-provider blinded?	Partial
7. Was the patient blinded?	Adequate
8. Were the point estimates and measure of variability presented for the primary outcome measure?	Adequate
9. Did the analyses include an ITT analysis?	Inadequate
10. Were withdrawals and dropouts completely described?	Adequate

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Hinchcliffe[61]

Extracted by: PH **Checked by: EL**

Reference and design	Intervention	Participants	Outcome measures
Author: Hinchcliffe[61] *Year*: 1955 *Country*: UK *Study design*: CCT *Number of centres*: One *Setting*: Military *Funding*: Not reported	1. Sodium bicarbonate BPC: 5 drops 2. Cerumol: 5 drops 3. Hydrogen peroxide BPC: 5 drops 4. Olive oil BP: 5 drops 5. Control: No treatment *Duration of treatment*: half hour *Other interventions used*: Syringing with warm tap water	*Number of readings*: *n* = 185, 37 ears per group *Sample attrition/dropout*: N/A *Inclusion criteria for study entry*: Air Force personnel with obscured TM, hard wax in the meatus in one or both ears *Exclusion criteria for study entry*: None reported	*Outcomes*: No. of occasions wax meatus was not cleared within specified time (see below) No. of cases with symptoms of discomfort *Method of assessing outcomes*: The treatment was considered a failure if more than 5 minutes of syringing was needed to clear the wax *AEs*: Tingling or symptoms of irritation were noted before the ear/s was syringed *Length of follow-up*: Immediate

Baseline characteristics of participants

	Sodium bicarbonate (ears = 37)	Cerumol (ears = 37)	Hydrogen peroxide (ears = 37)	Olive oil (ears = 37)	Control (ears = 37)	*p*-value
None reported						

Results

Outcomes

	Sodium bicarbonate (ears = 37)	Cerumol (ears = 37)	Hydrogen peroxide (ears = 37)	Olive oil (ears = 37)	Control (ears = 37)	*p*-value
No. of occasions meatus not cleared	6	7	4	2	9	See comment field
No. of AEs	4	22	6	4	0	

Comments: It is stated that only olive oil was significantly better than no treatment at all, but no further data is reported to support this. It is also reported that symptoms of discomfort for Cerumol occurred significantly more often than any other preparation, but again no further data is reported to support this.

Methodological comments

Allocation to treatment groups: The four treatment bottles were used in alphabetical order, with each fifth participant left untreated as a control

Blinding: Treatments were contained in bottles labelled A, B, C and D, with no distinguishing marks. The doctor syringing the ears was not informed of which treatment if any had been used. Initial otoscopic examination carried out by a alternate doctor

Comparability of treatment groups: Not reported

Method of data analysis: Chi-squared test for small numbers was used

Sample size/power calculation: None reported

Attrition/dropout: None reported

General comments

Generalisability: Adult entrants to the Royal Air Force in the 1950s, found to have hard wax obscuring the meatus on entrant examination

Outcome measures: Unclear how valid, objective or consistently applied the outcome measure was

Intercentre variability: N/A

Conflict of interests: Not reported

AEs, adverse events; BP, British Pharmaceutical grade; BPC, British Pharmaceutical Codex; CCT; controlled clinical trial; N/A, not applicable; TM, tympanic membrane.

Quality criteria for assessment of controlled clinical studies

Item	Judgement[a]
1. Were the groups similar at baseline in terms of prognostic factors?	Unknown
2. Were the eligibility criteria specified?	Adequate
3. Were outcome assessors blinded to the treatment allocation?	Partial
4. Were the point estimates and measure of variability presented for the primary outcome measure?	Inadequate
5. Did the analyses include an ITT analysis?	Inadequate
6. Were withdrawals and dropouts completely described?	Unknown
7. Were participants likely to be representative of the intended population?	Unknown

ITT, intention to treat.
a Adequate, inadequate, partial, reported, unknown.

Appendix 6
Excluded studies

Reasons for study exclusion	Number of studies
Intervention	3
Population	0
Outcomes	0
Study design	16
Total number of excluded studies	19

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Appendix 7

Variables included in the probabilistic sensitivity analyses

Table 40 lists variables included in probabilistic sensitivity analyses (PSA), distributions and parameters of distributions used.

TABLE 40 *Variables included in PSA, distributions and parameters of the distribution*

Variable	Distribution	Parameters
Probability of spontaneous earwax removal (no treatment)	Beta	Alpha = 40.5, beta = 769.5
Probability of successful earwax removal with the use of softeners only	Beta	Alpha = 33.9, beta = 135.8
Probability of successful earwax removal with self-syringing	Beta	Alpha = 21.7, beta = 23.5
Probability of successful earwax removal with syringing administered by nurse at primary care	Beta	Alpha = 15.6, beta = 9.6
Proportion of TM cases in the total number of SAEs	Beta	Alpha = 28.3, beta = 57.4
Probability of SAE associated with both active treatments	Beta	Alpha = 15.4, beta = 25,578.9
Hospital admission for either myringoplasty or treatment of a serious infection	Beta	Alpha = 40.5, beta = 769.5
Probability of partial permanent hearing loss if myringoplasty is only partially successful	Beta	Alpha = 31.8, beta = 95.3
Disutility associated with the loss of hearing	Gamma	Alpha = 3600, lambda = 600,000
Cost of GP referral to OTL	Gamma	Alpha = 96.04, lambda = 0.703589744
Cost of self-syringing	Gamma	Alpha = 96.04, lambda = 16.03338898
Cost of nurse visit	Gamma	Alpha = 96.04, lambda =10.79101124
Cost of earwax removal without SAE at primary care	Gamma	Alpha = 96.04, lambda = 2.653038674
Cost of assessment and referral primary care associated with SAE	Gamma	Alpha = 96.04, lambda = 0.558696917
Cost of secondary care treatment of serious infection	Gamma	Alpha = 96.04, lambda = 0.250234497
Cost of secondary care treatment of TM	Gamma	Alpha = 96.04, lambda = 0.133019391
Cost of hospital admission for serious infection treatment	Gamma	Alpha = 96.04, lambda = 0.045733333
Cost of hospital admission for TM	Gamma	Alpha = 96.04, lambda = 0.067113906
Cost of softeners	Gamma	Alpha = 96.04, lambda = 131.5616438
Cost of de-waxing	Gamma	Alpha = 96.04, lambda = 0.562624487

OTL, otolaryngologist; SAE(s), serious adverse event(s); TM, tympanic membrane.

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Feedback

The HTA programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

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ISSN 1366-5278