INTEGRATE
The UK ENT Trainee Research Network

THE DECODE PROJECT

DEveloping consensus Core Outcomes and Diagnostic criteria for acute otitis Externa

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	An initiative by **INTEGRATE** (The UK ENT Trainee Research Network)
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1 Introduction

Acute otitis externa (AOE) is a common condition managed in both primary and secondary care. Despite the high incidence of AOE in the adult population, it remains poorly defined, and has no widely accepted diagnostic criteria. In addition, there is a lack of objective and standardised outcomes assessed in AOE interventional trials, and this has limited pooling and comparison of research data.

Core outcome sets (COS) are agreed standardised sets of outcomes that represent the minimum that should be measured and reported in all clinical studies of a specific condition. The existence or use of a core outcome set does not imply that outcomes in a particular study should be restricted to those in the relevant core outcome set. Rather, there is an expectation that the core outcomes will be collected and reported, making it easier for the results of studies to be compared, contrasted and combined as appropriate; while researchers continue to explore other outcomes as well. The development of a COS in health care involves working with key stakeholders to prioritise large numbers of outcomes and achieve consensus as to the core set1. Lack of standardised sets of outcomes in the treatment of AOE has been a key obstacle in improving the care of patients with this common and debilitating infection.

1.1 Scope

Adult patients with AOE, undergoing any form of intervention, designed primary for research use in primary or secondary care.

2 Aims

The overall aim of this work is to facilitate future research into AOE in adults.

1. To generate a consensus **definition** for AOE to characterise the disorder (e.g. acute Vs chronic)
2. To define the minimal clinical features (symptoms and/or signs) required to make a **diagnosis** of AOE in research practice
3. To create a **core outcome set** for AOE: an evidence-based consensus set of outcomes that should be reported in the assessment of any intervention for AOE in adults.

3 Methods

1.2 Overview

The development of the COS will be based on recommended methodology from the COMET handbook1. The adopted methodology contains three separate stages. The initial stage includes semi-structured interviews with patients who have recently suffered with AOE. The second stage includes a systematic review of all published literature on AOE. A long list of candidate outcomes will be created from these first two stages. A Delphi questionnaire based on this candidate list will be presented to key AOE stakeholders in an effort to achieve a consensus of core outcomes for AOE. The candidate criteria for the consensus AOE diagnosis will be produced using the same methodology. The methods of each stage are described below in greater detail.

1.3 Patient Public Input

Six interview questions reflecting the above objectives have been developed by the study team (figure 1). Patients will be identified from emergency ENT outpatient clinics in two NHS Trusts representing two neighbouring counties in North West England. Adults with AOE will be asked to participate in semi-structured interviews by an investigator outside the treating team. Selected individuals will be invited to represent a range of patients with the condition (i.e. students, parents, males, females). Individual patient interviews will be conducted following completion of the patient's outpatient management of AOE, once clinical resolution has been determined. The interview will follow patients' scheduled clinic appointment for participant convenience.

All interviews will be conducted by a single investigator (MK), in line with the predetermined questions, with audio recordings of the interviews. The audio recording will be transcribed, and patient age, gender and laterality or bilaterality of otitis externa will be recorded with complete anonymity maintained.

1. How did the ear infection affect you?

2. What were the most difficult aspects of your infection?

3. What were the most difficult aspects of your treatment?

4. How could the impact of the condition be reduced?

5. How could the treatment be improved?

6. Where do you think future research for this condition should be focussed?

Two investigators working independently will extract content from the transcriptions that relates to treatment and disease outcomes, as well as experiences of the care pathway. Outcomes will be grouped according to proposed taxonomy in the COMET handbook1.

1.4 Systematic review of the literature

To ensure broad representation of existing AOE definitions and outcomes, we will search for all studies (excluding case reports) that assess the effectiveness of treatments on adults with acute otitis externa. We will not restrict by comparator or outcome.

A search of the MEDLINE (Ovid 1946 – present) (search strategy in appendix 1) and EMBASE (Ovid 1974 – present) (appendix 2) databases for published studies will be carried out. We will combine subject strategies with adaptations of the search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in the Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2, Box 6.4.b. (Handbook 2009)).

The results will be combined, de-duplicated via Endnote, and uploaded to Rayyan systematic review web app.

Ten researchers will work in pairs to review the abstracts of captured publications. Therefore, each publication will be reviewed twice by two independent reviewers. Reviewers will exclude studies that do not pertain to treatments for adults with otitis externa.

Included studies will be reviewed by two independent researchers who will perform a full text review and extract relevant information on diagnostic information and primary/secondary outcomes reported.

This will be carried out in two phases according to date of publication. The first group of studies to be reviewed will be from beginning of 2011 to end of 2018 (first extraction), accounting for relevant publications over the last 8 years. The second group of studies reviewed will be from beginning of 2008 to end of 2010 (second extraction). We will assess for outcome saturation, representing no new outcomes being identified in the second extraction. If saturation is not reached in the second extraction, we will extend our search strategy to studies in the preceding two years (2005-2007) – third extraction. This process will be repeated until saturation is achieved.

The diagnostic definitions and outcome domains will be extracted from identified studies by a pair of investigators (NM and RM). The extracted outcomes of studies relating to patient reported outcome measures will be added to the domains and new domains will be added if they are not sufficiently described.

Additionally, we will search PsycInfo database (Ovid 1806 – present) for patient reported outcome measures for otitis externa. We will model the search strategy for PsycInfo by adapting the search strategy designed for MEDLINE and Embase. A grey literature search will be undertaken on EMCARE for AOE. Two review authors will independently review the titles and abstracts from the electronic search. Any identified publication will be

reviewed, and questionnaires extracted. Each question will be either given its own outcome or mapped to a pre-existing outcome.

1.5 Preparation of potential core outcome and diagnostic criteria

The long lists of candidate outcome measures extracted from the literature and service-user interviews will be combined, de-duplicated and placed within the taxonomy categories (MS), producing a short list of candidate AOE outcomes for use in the Delphi. Finally, the outcome domains and included outcomes will be reviewed by the steering committee at a consensus meeting to assess suitability of domain name and grouping of outcomes. All diagnostic criteria identified in the literature and interviews will also be collated. These, along with elements of established definitions and criteria from respected organisations will create a list of candidate diagnostic criteria, agreed by the steering committee.

Identified candidate diagnostic criteria will be used as the basis for a consensus definition, formulated by the steering committee after initial stakeholder responses are collated.

1.6 Delphi consensus process:

An online Delphi consensus process will be used to determine the COS and diagnostic criteria for AOE.

Participants

Representatives from the following stakeholder groups will be asked to participate in the Delphi process:

- Adult health service users who have recently suffered with AOE (age >16yrs)
- Consultant Otologists
- Consultant General ENT surgeons
- ENT Registrars
- Junior doctors and specialist nurses in ENT
- General Practitioners with or without a specialist interest
- Microbiologists
- Audiologists

The health service user (HSU) group will not be involved in the development of the diagnostic criteria or AOE definition. 140 HSUs and professionals will be invited to participate, with the number of participants invited from each stakeholder group based on their contact with otitis externa treatment. An approximate 2:1 ratio will be used, with fewer stakeholders from microbiologist and audiologist groups. Factoring in for attrition, we aim for over 100 stakeholders to complete the entire Delphi process, which should provide a meaningful consensus. We will use the INTEGRATE network to identify and invite individuals from the aforementioned stakeholder groups to provide national representation.

Process

Participants will be contacted via email and provided with information about the Delphi Process. This information will emphasise the importance of completing all rounds and allow for a brief introduction to the aims of the project. These will be neutrally phrased to ensure that participants are not influenced by the views of the steering committee.

There will be three rounds of the online questionnaire. The candidate outcomes and diagnostic criteria will be put to stakeholders in an easily accessible online format using Google forms. Participants will be asked to rate their agreement with each outcome on an interval scale of 1-9, where 1 indicates lowest importance and 9 indicates highest importance. There will also be an 'unable to score' option.

After each round, all items will be assessed for consensus. Scores of 1-3 will be interpreted as items of limited importance, 4-6 as items that are important but not critical, and 6-9 as items of critical importance. Consensus to include is defined as 70% or more participants (from all stakeholder groups) scoring as 7 to 9 AND <15% of all participants scoring as 1 to 3. Consensus to exclude is defined as 70% or more participants (from all stakeholder groups) scoring as 1 to 3 AND <15% of all participants scoring as 7 to 9.

Round 1

In round 1, all candidate outcomes, definition and diagnostic criteria will be presented, and as well as rating agreement, there will be the opportunity for participants to comment and suggest additional outcomes and criteria. In addition, the online form will start with a question relating to the time threshold beyond which OE would no longer be defined as acute.

After round 1, only items meeting consensus for inclusion or exclusion *in every stakeholder group* will be removed from further rounds. This ensures that the opinions of minority groups will be presented and taken into consideration by participants from all other stakeholder groups.

Following round 1, a steering committee meeting will review stakeholder ratings for diagnostic criteria and formulate one or more candidate definitions for AOE based on these.

Round 2

In round 2, items not meeting round 1 consensus for inclusion or exclusion in every stakeholder group will be included, along with any further items suggested by participants in round 1. Choices of AOE definitions created by the steering committee, based on the results from round 1 will be presented in round 2.

Participants will see pooled responses for candidate outcomes and diagnostic criteria from each stakeholder group, separated by group, to inform the rating process, which will take the same format as round 1.

After round 2, items meeting consensus *in every stakeholder group* will be removed from further rounds. The candidate definition(s) will be further refined by the steering committee based on stakeholder feedback.

Round 3

In round 3, items not yet meeting consensus in every stakeholder group will be included. Participants will be presented with pooled responses from each stakeholder group, separated by group, to inform their rating, which will take the same format as rounds 1 & 2. The responses for each definition example in round 2 will be presented in round 3 and participants will be free to keep or change their original selection.

After round 3, items meeting consensus when all stakeholder groups are pooled as one will be combined with items meeting consensus in rounds 1 & 2. Items that do not meet consensus to either include or exclude will be scrutinised by the steering committee, who will take a final decision based on factors including how near items are to reaching consensus, and the views of each stakeholder group. All items that meet these criteria for inclusion will be presented as the diagnostic criteria and core outcomes set for AOE. A final definition will be prepared by the steering committee based on the responses in round 3.

4 Problems anticipated

Prevention of attrition during the Delphi process is of key importance. Emphasis will be placed on the importance of completion of the entire process in all correspondence. Participants will only be listed as collaborators on subsequent publications if they complete all three rounds. Efforts will be made to ensure that participants from smaller stakeholder groups do not undergo significant attrition, using reminders as necessary. Recruiting 140 participants initially should keep the final number of complete response above 100.

5 Ethical considerations

None identified.

6 Authorship policy

The authorship policy will follow the format adopted in the INTEGRATE Terms of Reference. The first line author will be listed as INTEGRATE (The UK ENT Trainee Research Network). Contributors to the project will be listed as collaborators with their roles delineated in any subsequent publications or presentations.

For stakeholders involved in the Delphi process, participation in all three stages will be required for recognition.

7 References

1. Williamson PR, Altman DG, Bagley Het al. The COMET Handbook: version 1.0. Trials 2017; 18:280.