NOE DELPHI ROUND 5

Setting the Foundations

Thank you so much for your Round 4 replies and very helpful comments. The response rate was 75% (61/81), with 59% of these replies from ENT, 31% from Infection and 10% from Radiology specialists.

We have consensus (>70% respondents agreeing or strongly agreeing) for all of the statements included in the Round 4 questionnaire. However, some very useful points were raised, which will help to improve these definitions and their utility moving forward. For this reason, we have modified the definitions and would like to re-confirm consensus before they are finalised. Once we have your agreement, we will circulate a manuscript which will form the basis of a proposal for adoption by ENT, Infection and Radiology bodies in the UK.

When considering these definitions, we would like to emphasise the following aims:

1. They can be implemented in all centres across the UK, from a small DGH to a tertiary referral centre.
2. They aim to be highly specific (i.e. describe a typical 'definite' case of NOE and minimise the chances of misclassifying another condition), but do not necessarily describe **all** potential presentations of NOE.
3. They are for guidance only and are not prescriptive in terms of practice.
4. They allow standardised description of cases which will facilitate recruitment to clinical trials and comparison of cases across different cohorts.
5. This is the start of an iterative process. The lack of quality data is making it difficult to propose clear recommendations for some definitions. As more information becomes available these definitions will be revisited and revised.

We have been using a Delphi method in order to achieve these aims. A Delphi method is a group of facilitation techniques which employs an iterative multistage process, designed to transform opinion into a group consensus. It is a flexible approach which was developed in order to systematically synthesise expert opinion. Currently there are no universally accepted criteria for using this technique, but it has the following features: anonymity, iteration with controlled feedback from one round to the next, aggregation of group responses and expert input until consensus has been achieved.

We have highlighted the changes to the definitions from Round 4 in red. Where necessary, a brief explanation of the change(s) is given. We have included 4 questions in the same format as previously.

Thank you again for your contribution.

Monique Andersson	Pablo Martinez-Devesa	Martin Williams	Emma Stapleton	Pieter Pretorius
Infection	ENT Surgeon	Infection	ENT Surgeon	Neuroradiologist
Oxford	Oxford	Bristol	Manchester	Oxford

I. DEFINITE CASE OF NECROTSING OTITIS EXTERNA (NOE)

Discussion following Round 4:

i) Imaging: Some respondents highlighted that radiological changes suggestive of NOE may be detected by CT and/or MRI and that some centres use both modalities in the early investigation of these cases. For this reason, both modalities will be included in the definition of a definite case of NOE. There is a caveat however, namely that MRI is essentially a more sensitive modality than CT to detect early changes which might be ascribed to this diagnosis. Changes like bone marrow oedema of the temporal bone or other features may be visible on MRI when bony erosion is not yet discernible on CT. Further studies are planned to understand what changes are associated with NOE on MRI, how this compares with findings on CT and whether this difference impacts the management and outcome of NOE. We are proposing a pragmatic approach to dealing with this discrepancy until we have more data.

ii) Histology: Many respondents commented that samples are not routinely sent for histological analysis and so histology excluding malignancy should not be required to make the diagnosis of a definite case of NOE.

QUESTION 1.

A definite case of NOE is an invasive infection of the external ear canal which has the following characteristics:

- Otalgia and otorrhoea OR otalgia and a history of otorrhoea

AND

- Granulation OR inflammation of the external auditory canal

AND

- Histological exclusion of malignancy in cases where this is suspected

AND

- Radiological features consistent with NOE

(This refers to EITHER CT imaging findings of bony erosion of the external auditory canal, together with soft tissue inflammation of the external auditory canal **OR** MRI with changes consistent with NOE, for example bone marrow oedema of the temporal bone with soft tissue inflammation of the external auditory canal).

Strongly disagree Disagree Uncertain Agree Strongly Agree

Hodgson SH, *et al. BMJ Open* 2023; 13:e061349. doi: 10.1136/bmjopen-2022-061349

Comment: _____

II. DEFINING SEVERE NOE

Discussion following Round 4:

i) **Nomenclature: Some participants commented that the term 'severe' used in medicine is commonly used to describe severity of symptoms rather than complexity of disease. Indeed patients with severe NOE e.g. cranial nerve palsy may have mild pain. The term 'severe' has therefore been changed to 'complex'**

ii) **Anatomical spread: Temporomandibular joint (TMJ) involvement is commonly seen in complex disease and has been added to the common sites of disease extension from the EAC.**

iii) **The term 'phlegmon' has been changed to 'soft tissue oedema or inflammation or fluid collection'**

QUESTION 2.

A case of NOE may be classified as 'complex' if any of the following are present:

- Facial nerve palsy or other lower cranial nerve palsy
- Cerebral venous thrombosis seen on MRI or contrast enhanced CT
- Extensive bone involvement as demonstrated by any of the following;
  - CT showing bone erosion in other skull base locations in addition to the external ear canal wall, e.g: around stylomastoid foramen, clivus, petrous apex, temporomandibular joint.
  - MRI showing bone marrow oedema extending to central skull-base.
  - CT or MRI showing extensive soft tissue oedema or inflammation or fluid collection below the skull base.
- Intracranial spread of the disease (dural thickening, extradural or subdural empyema, cerebral/cerebellar abscess)

Strongly disagree Disagree Uncertain Agree Strongly Agree

Comment: _____

III. DEFINING 'POSSIBLE NOE'

Discussion following Round 4:

i) **'Possible NOE' describes a case that does not meet the criteria for a definite case of NOE, but where a high degree of clinical suspicion exists. Having this category was strongly supported at Round 3. These cases may represent atypical presentations or**

may represent severe OE/early NOE. A number of participants suggested that the definition of possible NOE should include reference to the absence of radiological changes typical of a definite case of NOE, since this is a key part of the investigation of these cases.

QUESTION 3.

Possible NOE is a severe infection of the external ear canal which does not show bony erosion of the external auditory canal on CT scan OR does not show changes consistent with NOE on MRI if this is performed (for example bone marrow oedema of the temporal bone) AND which has the following characteristics:

Otalgia and otorrhoea OR otalgia and a history of otorrhoea

AND Granulation OR inflammation of the external auditory canal

AND any of the following features
- immunodeficiency
- night pain
- raised inflammatory markers (ESR/CRP) in absence of other plausible cause
- failure to respond to >2 weeks of topical anti-infectives and aural care

Strongly disagree Disagree Uncertain Agree Strongly Agree

Comment_____

IV. DEFINING 'RELAPSED NOE'

Consensus was reached in Round 4 that a case of NOE is considered treated and cured if a patient has no pain nor otorrhoea for a minimum period of 3 months after completing antibiotic therapy.

Relapse is recurrence of disease after the patient has been treated and cured i.e. at least three months after stopping antibiotic therapy.

Discussion following Round 4:

i) Symptoms: Whilst relapse may present with EAC symptoms, patients may also present with no EAC signs or symptoms, but with progression of base of skull osteomyelitis or other deep-seated complications. The definition of relapse has therefore been modified to reflect this.

ii) Follow up Scanning: It was noted that the definition of relapse included the need for progression of radiological changes after demonstration of radiological improvement. Since it is not routine for many centres to perform follow-up imaging

Hodgson SH, *et al. BMJ Open* 2023; 13:e061349. doi: 10.1136/bmjopen-2022-061349

after resolution, the definition includes the terms 'unchanged or progression'.

iii) **Modality: Centres differ in their choice of modality to investigate relapse and so the definition now includes changes on CT and/or MRI.**

QUESTION 4.

A relapsed case of NOE is a serious, invasive infection which occurs **after the initial infection was considered to be treated and cured** and is characterised by:

Recurrence of local disease
- Recurrent otalgia OR recurrent otorrhoea
  AND
- Recurrent granulation OR inflammation
  AND
- Unchanged or progression of bony erosion of the external auditory canal on CT OR unchanged or progression of MRI changes such as bone marrow oedema of the temporal bone and soft tissue changes of the external auditory canal.

AND/OR

Development or recurrence of complex disease

- Development or worsening of a lower cranial nerve palsy, base of skull osteomyelitis or development or worsening of other intracranial complication deemed a consequence of NOE and supported by radiological imaging.

Strongly disagree Disagree Uncertain Agree Strongly Agree

Comment_____

Any additional final comments about the 'NOE: Setting the foundations' process/any specific issues_____

_____

Thank you for your contribution.

We plan to circulate the first draft of the manuscript detailing the process and outcome of this project in the next 6-8 weeks for your further input.

Hodgson SH, *et al. BMJ Open* 2023; 13:e061349. doi: 10.1136/bmjopen-2022-061349