Outcomes from Delphi Round 2: NOE Case Definition

DEFINITE CASE

1a. Symptoms: MAJOR symptoms - necessarily present for all definite cases of NOE:

Consensus	No Consensus
Otalgia AND otorrhoea INCLUDE (86%)	Otalgia OR otorrhoea Otalgia alone Otorrhoea alone

1b. Symptoms: MINOR symptoms - which MAY be present for all definite cases of NOE:

Consensus	No consensus
Night pain – INCLUDE (81%)	Facial pain Trismus Headache Fever

1c. What number of minor symptoms should be present , together with major symptoms, to define a true case:

0 – 35.7%
1 – 25.7%
2 – 22.9%
3 – 14.3%
4 – 1.4%

2. A true case of DEFINITE NOE will have the following clinical signs:

Consensus	No consensus
EAC granulation AND inflammation – INCLUDE (80%) **EAC granulation OR inflammation – INCLUDE (79%)** **No signs – EXCLUDE – 89%**	Inflammation alone Granulation alone

3. A true case of DEFINITE NOE will have the following findings on imaging:

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

Consensus	No consensus
Bone erosion EAC CT – INCLUDE (87%) **Soft tissue EAC CT – INCLUDE (81%)** **Bone erosion AND soft tis EAC – INCLUDE (79%)** **CT soft tis – T1 MR – INCLUDE (81%)** **Normal CT/MR – EXCLUDE (87%)**	Bone erosion OR soft tissue Isolated SBOM from source other than EAC excluded

4a. INVESTIGATION: A true case of DEFINITE NOE will have the following findings on histology:

Consensus	No consensus
Malignancy excluded – INCLUDE (87%) Inflammation confirmed – INCLUDE (83%) Malignancy excluded AND inflammation confirmed – INCLUDE (93%)	Excludes malignancy or confirms inflammation Histo always sent

4b. INVESTIGATION: A true case of DEFINITE NOE will have the following biochemistry/haematology findings:

Consensus	No consensus
	Raised CRP Raised ESR

5. Regarding risk factors for DEFINITE NOE: NO CONSENSUS The patient will be always frail or immunosuppressed (diabetic, steroid therapy, malignancy, biologic therapy, HIV infected etc.)

COMMENTS

- CT alone may lags behind actual bony destruction
- Changes in time are also useful in confirming or refuting definite NOE - e.g. Improvement with treatment on serial imaging
- As a radiologist who has seen many cases of NOE, I believe that even streakiness to the parapharyngeal fat in the appropriate clinical context is sufficient to diagnose NOE and we have had many cases treated as such
- There may be no signs in the ear and the patient has got skull base Osteomyelitis, if the patient had been treated before hand but not adequately.
- minor criteria don't necessarily need to be present, but might be helpful in the absence of definite radiological features eg no bone erosion but soft tissue swelling present, having multiple minor criteria present +/- immunosuppression could be sufficient for a definite diagnosis.
- Certain criteria together make it a DEFINITE NOE. For example a facial palsy AND granulation tissue (even without evidence of bony erosion on CT). We should incorporate that somehow ideally.
- T1 enhanced imaging is an important modality in the diagnosis of NOE

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- Granulation tissue is inflammatory tissue, it is formed in response to inflammation, I don't see how one can have granulation tissue without inflammation in the canal.
- Regarding immunosuppression, advancing age is an important risk factor in itself without necessarily implying frailty.

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PROBABLE CASE

1a. Symptoms: MAJOR symptoms - necessarily present for all probable cases of NOE:

Consensus	No Consensus
Otalgia AND otorrhoea INCLUDE (81%)	Otalgia OR otorrhoea Otalgia alone Otorrhoea alone

1b. Symptoms: MINOR symptoms - which MAY be present for all probable cases of NOE:

Consensus	No consensus
Night pain – INCLUDE (71%)	Facial pain Facial weakness Trismus Headache Fever

1c. What number of minor symptoms should be present , together with major symptoms, to define a probable case:

0 – 22.9%
1 – 32.9%
2 – 30%
3 – 11.4%
4 – 2.9%

2. A case of PROBABLE NOE will have the following clinical signs:

Consensus	No consensus
EAC granulation OR inflammation – INCLUDE (81%) **No signs – EXCLUDE – 81%**	EAC granulation AND inflammation – Inflammation alone Granulation alone

3. A case of PROBABLE NOE will have the following findings on imaging

Consensus	No consensus
Soft tissue swelling of external ear canal will be visible on CT or MRI – INCLUDE - 87%	CT scan excludes bony erosion

4a. INVESTIGATION: A case of PROBABLE NOE will have the following findings on histology

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Consensus	No consensus
Inflammation confirmed – INCLUDE (86%) **Malignancy excluded AND inflammation confirmed – INCLUDE (80%)**	Excludes malignancy or confirms inflammation Histo always sent

4b. INVESTIGATION: A case of PROBABLE NOE will have the following biochemistry/haematology findings:

Consensus	No consensus
CRP MAY be raised – 83% **ESR MAY be raised – 86%**	Raised CRP Raised ESR

5. Regarding risk factors for PROBABLE NOE: NO CONSENSUS The patient will be always frail or immunosuppressed (diabetic, steroid therapy, malignancy, biologic therapy, HIV infected etc.)

COMMENTS

- Bony erosion on CT would confirm NOE in the correct setting but a lack of bone erosion does not exclude it. If there are risk factors, marked soft tissue changes and/or persistent clinical concern I would advocate baseline MRI to assess for bone oedema and serial imaging to assess response to treatment. My concerns would be either missing NOE if we image early in the course but also missing malignancy if we box patients into NOE diagnosis.
- Repeated ear trauma (eg in-ear headphone use) is risk factor in immunocompetent/ non-frail individuals, ear syringing and hearing aid use
- Probable NOE in my mind is the group of patients where the clinical symptoms and signs are compatible but the imaging may not be complete (CT without MRI for example) or unable to tolerate MRI all sequences. They do not need to have an immunosuppression risk factor to meet a case definition.
- I'm not confident that I understand how you will use these answers e.g. Symptoms: MINOR symptoms - which MAY be present for all probable cases of NOE - I don't see how something can be MAY and present in ALL. Also ...A case of PROBABLE NOE will have the following findings on imaging: CT scan excludes bony erosion - you mean WILL -they may because its not perfectly sensitive...?
- the length of duration of symptoms also important
- Also I have disagreed with facial weakness for probably NOE because I think it is more of an indicator of definite NOE!
- Probably diagnosis still shouldn't just be oedema of external canal, should show some evidence of tissue of the external ear and beyond otherwise this is simple otitis externa at that point. Doesn't have to show bone erosion. CRP and ESR May be raised but I don't believe it always has to be, have seen patients with limited raised blood serological marker

SEVERE CASE

1. **Which of the following features present in a definite case of NOE would meet criteria for severe disease?**

Consensus	No consensus
Cerebral venous thrombosis – INCLUDE – 89% **Lower cranial nerve palsy INCLUDE 99%** **Disease spread contralaterally INCLUDE 81%**	Elevated Inflammatory markers (ESR or CRP)

2. **One or a combination of how many of these features in a definite case of NOE should meet criteria for severe disease?**

Consensus	No consensus
1 – INCLUDE – 70%	>1, >2, >3

3. **The following features on MR are suggestive of severe disease (MR as imaging modality reached consensus):**

Consensus	No consensus
Soft tis/fluid collection below skull base - INCLUDE – 70% **Intracranial involvement - INCLUDE– 91%** **Central SBOM – INCLUDE – 88%**	

4. **The following features on CT are suggestive of severe disease (CT as imaging modality reached consensus):**

Consensus	No consensus
Bone erosion of stylomastoid foramen walls – INCLUDE – 73% **Intracranial involvement – INCLUDE – 93%** **Central SBOM – INCLUDE – 91%**	Soft tissue below skull base

COMMENTS

- Facial weakness should be included in the list of features
- Are we delineating between NOE and Skull base osteomyelitis? Whilst they ay be part of the same spectrum, they can appear and act as separate diseases.
- Skull base osteomyelitis is a different disease entity to NOE and should be investigated and managed on its own merits.
- Central skull base without obvious clinical history to support an ear cause I believe is a separate entity to NOE, though in the same family per se.
- I would regard any complication (facial nerve involvement, collection, TMJ involvement/septic arthritis, thrombosis, intracranial spread) as severe, or extensive skull base involvement
- would consider broader terms used for bony erosion on CT as may be variable distributions not just around the SMF e.g. EAC alone, TMJ, extension into mastoid and/or petrous apex

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- I would have thought that severe disease we more of a clinical severity rather than radiological, the neurology and physical impairment being most prominent.
- I am struggling to know without a radiological grading score which of these changes on CT or MRI I would classify as severe versus non severe but definite NOE that is why we need a way of grading the imaging
- for some of the radiology I would rely on specialised radiologist input

RELAPSED CASE

1. **The following SYMPTOMS suggest a relapsed case:**

Consensus	No consensus
Worsening otalgia after improvement after treatment completed – INCLUDE 96% **Worsening otorrhoea after improvement after treatment completed –INCLUDE 71%** **Worsening otalgia AND otorrhoea after improvement after treatment completed –INCLUDE – 77%** **Worsening otalgia OR otorrhoea after improvement after treatment completed –INCLUDE – 74%**	

2. **The following SIGNS suggests a relapsed case**

Consensus	No consensus
Recurrent granulation after resolution and tx completed – INCLUDE – 87% **Recurrent inflammation after resolution and tx completed – INCLUDE – 77%** **Recurrent granulation AND inflammation after resolution and tx completed – INCLUDE – 77%** **Recurrent granulation OR inflammation after resolution and tx completed – INCLUDE – 74%**	

3. **The following IMAGING findings suggest a relapsed case**

Consensus	No consensus
Progression bony erosion or bone marrow oedema after improvement – INCLUDE – 93% **Increased soft tissue after improvement – INCLUDE – 89%** **No role for imagine – EXCLUDE – 82%**	

4. **The following INVESTIGATION results suggest a relapsed case:**

Consensus	No consensus
Rising ESR after treatment completed - - INCLUDE – 70%	Rising CRP after treatment completed

5. Regarding the duration off from treatment prior to diagnosis of relapse (not treatment failure) – NO CONSENSUS: 1 week, 2 weeks, 2 months

COMMENTS

- Variable times commented from 1 week to 3 months based on frequency of imaging
- We find gallium scans are useful for monitoring for treatment response and relapsed disease, or for disease progression. It is the only imaging that gives "real time" data. CT erosive finding are late. MRI oedema takes a long time to resolve. Is there any point in defining the difference between incompletely treated and relapsed disease? if the patient is worsening (at any stage), they need more treatment.
- is there enough evidence to define this between 2 weeks and 2 months post treatment
- unless antibiotic treatment is standardised, the definition for 'relapse' is subject to bias/ Would nee ID guidance on the duration of treatment completion to be able to confidently answer Q5
- Any signs or symptoms after treatment cessation has been agreed should constitute a relapse.
- I think relapse is when the patient 's condition mainly pain/headache deteriorates after a period of being asymptomatic as patient can still be down graded to oral AB and can get a recurrence of symptoms.
- It is technically a "relapse" of that infection. Better to use the term recurrence of NOE instead of relapse? and then define relapse as return of symptoms/signs at any point after Completion of treatment and recurrence as having to have a minimum gap of one month off treatment?
- I don’t think inflammatory markers are reliable markers of active infection but would worry if raised.
- It depends how we define 'cure' or cessation of treatment
- If a patient reaches 2 months post-diagnosis is it another (new) infection?
- increase in time after treatment completed adds to the confidence in the diagnosis of relapse

NON-RESPONSE TO TREATMENT

1. Symptoms

Consensus	No consensus
Worsening otalgia on treatment – INCLUDE 91% **Worsening otorrhoea on treatment – INCLUDE 70%** **Both – INCLUDE 76%** **Either/or – INCLUDE 73%**	

2. Signs

Consensus	No consensus
Worsening granulation on treatment – INCLUDE 70% **Worsening inflammation on treatment – INCLUDE 77%** **Either or – INCLUDE 71%**	Both – IGNORE? – 66%

3. Imaging

Consensus	No consensus
Progression bony erosion whilst on treatment – INCLUDE 77% **Progression bone erosion to other parts skull base except EAC – INCLUDE 84%** **Progression bone marrow oedema/enhancement skull base MR – INCLUDE 77%**	Increased soft tissue

4. Investigations

Consensus	No consensus
	Rising CRP on treatment Rising ESR on treatment Exclusion malignancy on histology

5. Duration on treatment prior to diagnosis of non-response:

Consensus	No consensus
Min 3/7 – EXCLUDE – 79%	5 7 10 14

IMAGING

Imaging in Otitis Externa

Consensus	No consensus
No role in severe/persistent – EXCLUDE – 87% **Imaging in severe/persistent when abx failed – INCLUDE 80%** **Severe pain INCLUDE – 74%** **Night pain INCLUDE – 74%** **Lower CN palsies INCLUDE – 100%** **Immunosuppression – include – 76%**	Imaging is only indicated in severe/persistent OE where there has been failure of antibiotic therapy AND risk factors* (diabetes, Immunocompromise etc) for NOE are present Polyp

Imaging in NOE

Consensus	No consensus
CT 1st line – INCLUDE – 87%	MR 1st line If CT shows swelling of external auditory canal but no bone erosion then MRI should be performed If CT shows no swelling of external auditory canal or bone erosion then MRI should be performed PET-CT should be performed if CT and MRI are normal