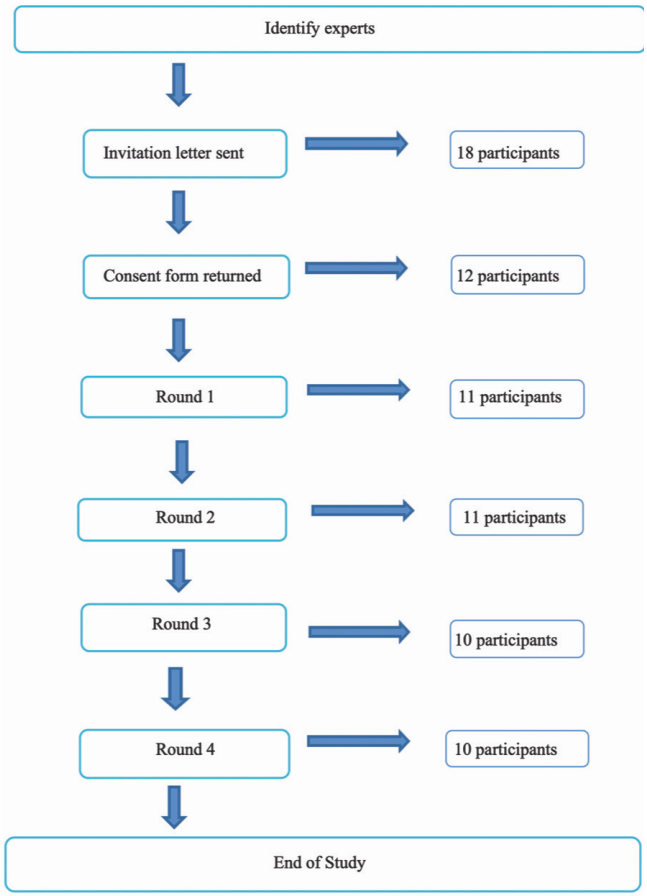
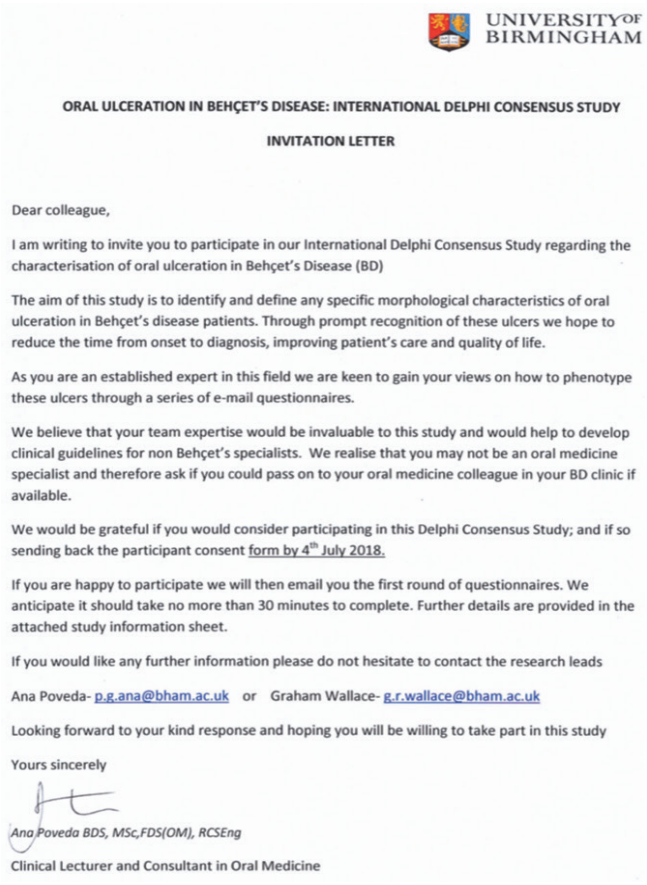


Supplementary Fig. S1. Study plan.



UNIVERSITY OF BIRMINGHAM

ORAL ULCERATION IN BEHÇET'S DISEASE: INTERNATIONAL DELPHI CONSENSUS STUDY

INVITATION LETTER

Dear colleague,

I am writing to invite you to participate in our International Delphi Consensus Study regarding the characterisation of oral ulceration in Behçet's Disease (BD)

The aim of this study is to identify and define any specific morphological characteristics of oral ulceration in Behçet's disease patients. Through prompt recognition of these ulcers we hope to reduce the time from onset to diagnosis, improving patient's care and quality of life.

As you are an established expert in this field we are keen to gain your views on how to phenotype these ulcers through a series of e-mail questionnaires.

We believe that your team expertise would be invaluable to this study and would help to develop clinical guidelines for non Behçet's specialists. We realise that you may not be an oral medicine specialist and therefore ask if you could pass on to your oral medicine colleague in your BD clinic if available.

We would be grateful if you would consider participating in this Delphi Consensus Study; and if so sending back the participant consent form by 4th July 2018.

If you are happy to participate we will then email you the first round of questionnaires. We anticipate it should take no more than 30 minutes to complete. Further details are provided in the attached study information sheet.

If you would like any further information please do not hesitate to contact the research leads

Ana Poveda- p.g.ana@bham.ac.uk or Graham Wallace- g.r.wallace@bham.ac.uk

Looking forward to your kind response and hoping you will be willing to take part in this study

Yours sincerely

Ana Poveda BDS, MSc,FDS(OM), RCSEng

Clinical Lecturer and Consultant in Oral Medicine

Supplementary Fig. S2. Invitation letter and Information Sheet to participants.

UNIVERSITY OF BIRMINGHAM

DELPHI STUDY INFORMATION SHEET

We would like to invite you to take part in a Delphi consensus study. Before you make your decision as to whether you would like to participate in this study or not, we would like to explain why this research is taking place and what it will involve.

What is a Delphi study?

The Delphi method is a widely used and accepted method for seeking consensus among experts within a certain topic. It is based on the principle that forecasts from a structured group of experts are more accurate than those from unstructured groups or individuals. Different methods have been used, but it commonly involves structured questionnaires delivered in rounds, with the outcome converging closer to a consensus after each round. As part of the method, the responses from each round are fed back to the participants who can refine their views following new data until a consensus is reached.

What is the purpose of this study?

Oral ulceration may present in a variety of forms and is a significant manifestation of several systemic conditions, such as Behçet's Disease (BD). Previous studies have alluded to the possibility of a morphologically distinct "Behçet's ulcer": early clinical recognition may aid earlier diagnosis of this rare disease.

We hypothesise that there the characteristics of a Behçet's ulcer are distinct and their definition will allow differentiation from other causes of oral ulceration.

Hence, the purpose of this Delphi study is to characterise those specific clinical features by an international expert panel. Subsequently, we will compile clinical guidance for non- Behçet's experts to aid prompt recognition of such ulcers and raise earlier suspicion of Behçet's disease as a possible differential diagnosis.

Why have I been invited to take part?

As an established expert in this field we are keen to hear your views about which clinical features may be important when phenotyping a Behçet's ulcer.

What will I get out of it?

You will be acknowledged as part the first Behçet's Delphi consensus group and recognised for your expertise and contribution. We will forward you the study report. We may contact you regarding future studies.

What will I be asked to do if I take part?

We are inviting you to participate as a Delphi panel member. The following rounds will be conducted:

Round 1: The international panel of experts will be formed following invitation via email. The initial questionnaire will include forty clinical pictures which will be circulated to the expert panel to identify crucial defining features of the ulcers in patients with BD.

Round 2: A questionnaire defining the clinical characteristics of these ulcers will be created. Participants will rank their agreement with each statement in the questionnaire. The information will be summarised and included in a new version of the questionnaire for the participants to review

Round 3: Participants will then re-rank their agreement with chance to change their score following disclosure of the results. A consensus should be reached

Guidelines for the non- specialist will be formulated to enhance earlier and more accurate diagnosis of BD

Who is organising and funding the research?

The Delphi study is being conducted by:

Miss Ana Poveda, Clinical Lecturer and Honorary Consultant in Oral Medicine

Dr Graham Wallace, Senior Lecturer in Immunity and Infection

Miss Saaeha Rauz, Clinical Senior Lecturer and Consultant Ophthalmologist

At the Institute of Inflammation and Ageing, Centre for Translational Inflammation Research, University of Birmingham

Confidentiality

No personal information will be collected and questionnaire responses will be collated anony-

mously using an identifying number known only to the participant and lead investigator. All the responses received will be strictly confidential, and your identity will not be divulged.

Data Protection Questionnaire responses will be collected online using Jisc online survey® with permission from the University of Birmingham

Research Ethics

This research is taken place in accordance to the University of Birmingham Ethics with reference number ERN_18-0524

What do I do now?

Thank you for reading this information sheet and for considering taking part of this research. Please let us know whether or not you would like to take part by replying to this email. If you wish to participate we would be very grateful if you could also complete the attached consent form.

CONSENT FORM

UNIVERSITY OF BIRMINGHAM

Name of Lead Researcher: Ana Poveda
Name of Supervisors: Saaeha Rauz, Graham Wallace
Participant Identification Number for this project:

1- I confirm that I have read and understand the information sheet explaining the above research project and I have had the opportunity to ask questions about the project. ☐

2- I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without there being any negative consequences. ☐

3- I give permission for my anonymised responses to be used during the Delphi process, and to be accessed by members of the research team. I understand that my name will not be linked with the research materials, and I will not be identifiable during the Delphi survey or in the reports that result from the research. ☐

4- I agree to take part in the above research project. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Lead Researcher	Date	Signature

Completion: Please returned scanned or electronically completed forms via email to: p.g.ana@bham.ac.uk . Alternatively please return hard copies by post to the following address: Dr Ana Poveda, School of Dentistry, Birmingham Dental Hospital. 5 Mill Pool Way, B5 7EG

Further information: Please contact the Lead researcher if you have any further questions. Contact details 00 44 7972278517

Copies: Please retain a copy of the completed consent form for your personal records. An additional copy will be held in a University secure location for the duration of the research study.

Supplementary Fig. S3. Questionnaire information development for each round.

ROUND 1

The Delphi panel of experts had 6 weeks to respond independently the first round of questionnaire, two reminders were sent. The following question was asked under each clinical picture, with a total of 40 questions randomly allocated (10MMP, 10IBD, 10RAS and 10BD) in this first round

> "Do you consider this clinical presentation of oral ulceration to be consistent with the diagnosis of BD?"
>
> a- Yes
> b- No
> c- I don't know

Free text was also available. Participants were prompted to make comments on the free text when the answer "I don't know" was selected.

Fortnightly remainders in order to increase higher response rate were sent via email.

ROUND 2- REMARKING

Re-marking when showing the results

Once the Round 1 was analysed by the author, the results were shown to all the participants who were asked to repeat the questionnaire as part of the iteration process.

The aim of the re-marking of round 1 is not only to show participants the results and give them the opportunity to change their answers if they deemed appropriate but also to reach agreement, as a collective of BD experts, on which are, from the 40 clinical pictures presented, the ones that would be consistent with a possible diagnosis of BD ulcer simply by clinical phenotype only and without any further aid apart from the visual clinical appearance.

Participants had 6 weeks to fill in and return the questionnaire. In order to increase and facilitate participant return rates 2 remainders were sent. 11 participants returned the questionnaire. No drops outs were seen in this round.

To establish if consensus was reached, we set the following criteria: increase in agreement percentages, sensitivity, specificity, positive predictive value, negative predictive value and accuracy per participant and per question as well as decrease in comments made.

The clinical pictures which reached agreement in this round were subsequently selected for Rounds 2 and 3 to explore and define those clinical characteristics that supported the possible diagnosis in Round 1.

ROUND 3

The next round aimed to rank in order of importance those characteristics that would aid defining the ulcers when describing them by clinical phenotype only

In this round, the clinical pictures selected from the participants that had reached minimum of 50% agreement in ROUND 1 with a 'YES' answer (participants agreed that the clinical picture may be consistent with a possible diagnosis of BD ulcer) were shown. All the 'NO' answers were discarded.

17/40 clinical pictures were subsequently selected. The clinical pictures for each question were shown along with the levels of agreement reached in Round 1.

Prior to the start of this round, the Oral Medicine independent expert panel met a second time to agree on the clinical parameters to be used in Round 2 after a literature search carried out by the author: the most frequent clinical characteristics with different nouns and adjectives used to define RAS and BD ulcers found where shown to the panel. The panel ranked initially independently and then collectively; each characteristic/parameter presented in relation to importance when aiming to define a BD ulcer as per their clinical experience. Any parameter below 80% agreement was discarded. An independent observer also ranked the same clinical parameters. 10 parameters as shown in the material and methods section were finally used in both Rounds 2 and 3

Instructions on how to complete the questionnaire were given. Participants had 8 weeks to return their answers. The increase from 6 weeks in Round 1 to 8 weeks in Round 2 was to avoid participation drop out during the summer period. Also, 3 reminders (every 2 weeks) to increase the response rate were sent.

The participants were asked the following question:

> From this image agreed in Round 1 that was considered to be consistent with a diagnosis of BD, what are, in your views, the clinical features that support your decision?

Margin (erythematous *vs*. others)	Shape (round *vs*. others)
Base (homogeneous *vs*. non)	Depth (shallow *vs*. deep)
Colour (yellow *vs*. red)	Location (anterior *vs*. posterior)
Surrounding tissues (hyperplastic/flat)	Size (major/minor/herpetiform)
Aggravating factor (trauma/others)	Number (single *vs*. multiple)
Other comments-free text	

Particip could click as manyants clinical parameters as they wished to inform their decision.
Free texas also allowed for fut wrther comments if participants considered it to be necessary

ROUND 4

Once the round was completed, a third round with Round 2 results in order of importance (in descending order) was circulated to the experts. As the results were shown, participants were then asked to choose at least 5 parameters that they would consider important to describe the clinical picture

2 further questions were asked:

1- Do you agree with the results?
a- Yes
b- No
c- Other (free text)

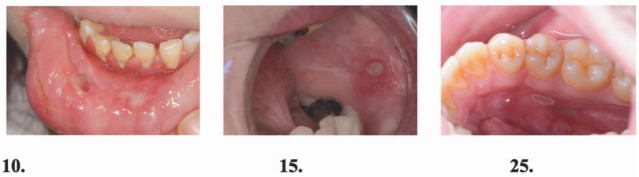
2- Would you consider this clinical picture to differ from a diagnosis of RAS?
a- Yes
b- No

The participants had eight weeks to complete the questionnaire as per the previous round. Two reminders in order to increase the response rate were sent. 10 out of 12 participants who agreed to participate in the study responded to this round. (No drop out from Round 3 to 4)

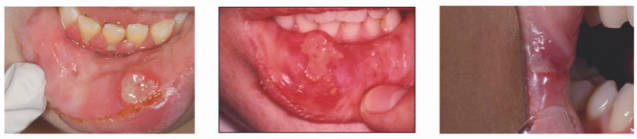
Supplementary Fig. S4.

Round 1 and 2.
Pictures per disease group and number of questions in the questionnaire.
BD ulcers.

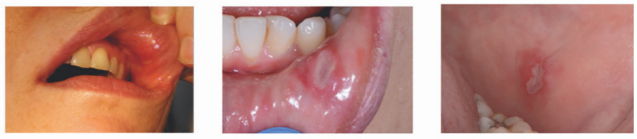
1. 2. 3.



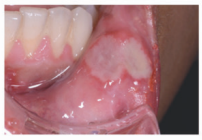
10. 15. 25.



29. 31. 35.



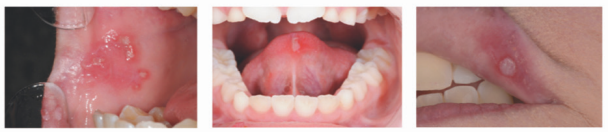
39.



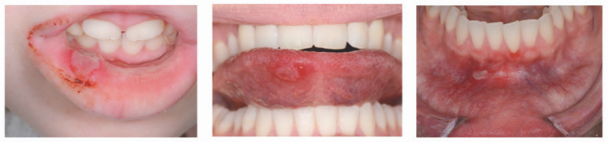
RAS

6. 11. 16.

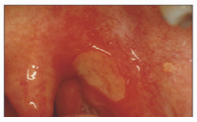
17. 19. 20.



22. 33. 34.

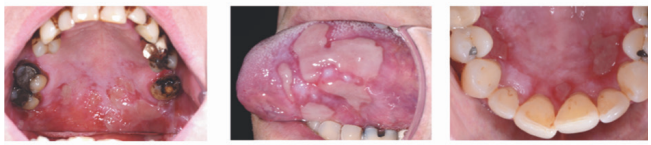


36.

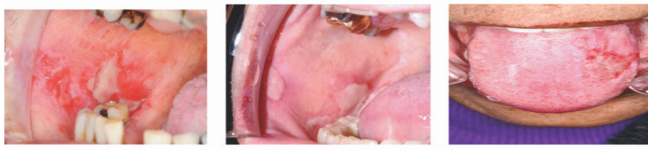


MMP

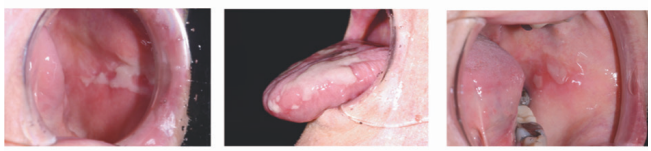
8. 13. 14.



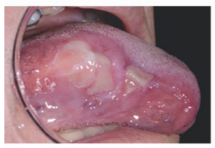
18. 21. 24.



26. 27. 37.

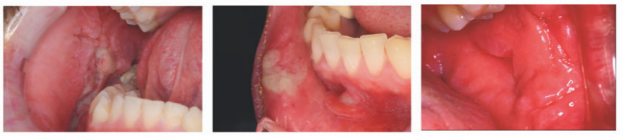


40.

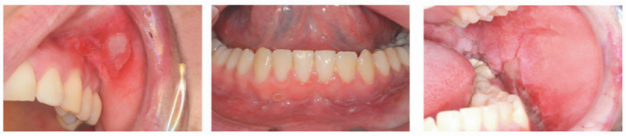


IBD

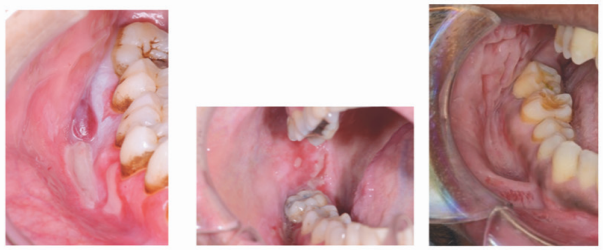
4. 5. 7.



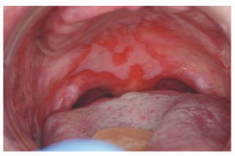
9. 12. 23.



28. 30. 32.



38.



Supplementary Fig. S5.

Round 1.

a-	**Per question**				
Question 1:	*Sensitivity : 0.5*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.5*
Question 2:	*Sensitivity : 0.88*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.88*
Question 3:	*Sensitivity : 0.9*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.9*
Question 4:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 5:	*Sensitivity : 0*	*Specificity: 0.9*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.9*
Question 6:	*Sensitivity : 0*	*Specificity: 0.2*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.2*
Question 7:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 8:	*Sensitivity : 0*	*Specificity: 0.8*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.8*
Question 9:	*Sensitivity : 0*	*Specificity: 0.7*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.7*
Question 10:	*Sensitivity : 0.7*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.7*
Question 11:	*Sensitivity : 0*	*Specificity: 0.2*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.2*
Question 12:	*Sensitivity : 0*	*Specificity: 0.9*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.9*
Question 13:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 14:	*Sensitivity : 0*	*Specificity: 0.66*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.66*
Question 15:	*Sensitivity : 0.5*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.5*
Question 16:	*Sensitivity : 0*	*Specificity: 0.9*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.9*
Question 17:	*Sensitivity : 0*	*Specificity: 0.4*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.4*
Question 18:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 19:	*Sensitivity : 0*	*Specificity 0.2:*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.2*
Question 20:	*Sensitivity : 0*	*Specificity: 0.3*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.3*
Question 21:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 22:	*Sensitivity : 0*	*Specificity: 0.8*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.8*
Question 23:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 24:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 25:	*Sensitivity : 0.66*	*Specificity: 0*	*PPV: 0.66*	*NPV: 0*	*Accuracy: 0.66*
Question 26:	*Sensitivity : 0*	*Specificity:1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 27:	*Sensitivity : 0*	*Specificity:1*	*PPV:0*	*NPV: 1*	*Accuracy: 1*
Question 28:	*Sensitivity : 0*	*Specificity:1*	*PPV:0*	*NPV: 1*	*Accuracy: 1*
Question 29:	*Sensitivity : 1*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 1*
Question 30:	*Sensitivity : 0*	*Specificity:0.7*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.7*
Question 31:	*Sensitivity : 0.77*	*Specificity:0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.77*
Question 32:	*Sensitivity : 0*	*Specificity:1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 33:	*Sensitivity : 0*	*Specificity:0.3*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.3*
Question 34:	*Sensitivity : 0*	*Specificity:0.2*	*PPV:0*	*NPV: 1*	*Accuracy: 0.2*
Question 35:	*Sensitivity : 0.7*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.7*
Question 36:	*Sensitivity : 0*	*Specificity:0.2*	*PPV:0*	*NPV: 1*	*Accuracy: 0.2*
Question 37:	*Sensitivity : 0*	*Specificity:0.6*	*PPV:0*	*NPV: 1*	*Accuracy: 0.6*
Question 38:	*Sensitivity : 0*	*Specificity:1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 39:	*Sensitivity : 0.8*	*Specificity:0*	*PPV:1*	*NPV: 0*	*Accuracy: 0.8*
Question 40:	*Sensitivity : 0*	*Specificity:1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*

Round 1 (Results)

Question 1:	*Sensitivity : 0.45*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.45*
Question 2:	*Sensitivity : 0.90*	*Specificity: 0*	*PPV: 0.90*	*NPV: 0*	*Accuracy: 0.90*
Question 3:	*Sensitivity : 0.82*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.82*
Question 4:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 5:	*Sensitivity : 0*	*Specificity: 0.9*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.90*
Question 6:	*Sensitivity : 0*	*Specificity: 0*	*PPV: 0*	*NPV: 0*	*Accuracy: 0*
Question 7:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 8:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 9:	*Sensitivity : 0*	*Specificity: 0.72*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.72*
Question 10:	*Sensitivity : 1*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 1*
Question 11:	*Sensitivity : 0*	*Specificity: 0*	*PPV: 0*	*NPV:*	*Accuracy: 0*
Question 12:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 13:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 14:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 15:	*Sensitivity : 0.63*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.63*
Question 16:	*Sensitivity : 0*	*Specificity: 0.9*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.9*
Question 17:	*Sensitivity : 0*	*Specificity: 0.36*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.36*
Question 18:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 19:	*Sensitivity : 0*	*Specificity: 0.18*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.18*
Question 20:	*Sensitivity : 0*	*Specificity: 0.09*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.09*
Question 21:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 22:	*Sensitivity : 0*	*Specificity: 0.63*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.63*
Question 23:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 24:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 25:	*Sensitivity : 0.81*	*Specificity: 0*	*PPV: 0.66*	*NPV: 0*	*Accuracy: 0.81*
Question 26:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*

Question 27:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 28:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 29:	*Sensitivity : 1*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 1*
Question 30:	*Sensitivity : 0*	*Specificity: 0.81*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.81*
Question 31:	*Sensitivity : 0.72*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.72*
Question 32:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 33:	*Sensitivity : 0*	*Specificity: 0.36*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.36*
Question 34:	*Sensitivity : 0*	*Specificity: 0.36*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.36*
Question 35:	*Sensitivity : 0.9*	*Specificity: 0*	*PPV: 1*	*NPV: 0*	*Accuracy: 0.9*
Question 36:	*Sensitivity : 0*	*Specificity: 0*	*PPV: 0*	*NPV: 1*	*Accuracy: 0*
Question 37:	*Sensitivity : 0*	*Specificity: 0.72*	*PPV: 0*	*NPV: 1*	*Accuracy: 0.72*
Question 38:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*
Question 39:	*Sensitivity : 0.81*	*Specificity: 0*	*PPV: 0.66*	*NPV: 0*	*Accuracy: 0.81*
Question 40:	*Sensitivity : 0*	*Specificity: 1*	*PPV: 0*	*NPV: 1*	*Accuracy: 1*

b- Per participant

Round 1

Participant 1	*Sensitivity: 0.5*	*Specificity: 0.8*	*PPV: 0.4*	*NPV: 0.85*	*Accuracy: 0.7*
Participant 2	*Sensitivity: 0.7*	*Specificity: 0.83*	*PPV: 0.58*	*NPV: 0.89*	*Accuracy: 0.8*
Participant 3	*Sensitivity: 0.66*	*Specificity: 0.73*	*PPV: 0.42*	*NPV: 0.88*	*Accuracy: 0.7*
Participant 4	*Sensitivity: 0.66*	*Specificity: 0.64*	*PPV: 0.44*	*NPV: 0.81*	*Accuracy: 0.65*
Participant 5	*Sensitivity: 0.64*	*Specificity: 0.80*	*PPV: 0.64*	*NPV: 0.80*	*Accuracy: 0.75*
Participant 6	*Sensitivity: 0.8*	*Specificity: 0.8*	*PPV: 0.57*	*NPV: 0.92*	*Accuracy: 0.8*
Participant 7	*Sensitivity: 0.8*	*Specificity: 0.95*	*PPV: 0.88*	*NPV: 0.90*	*Accuracy: 0.70*
Participant 8	*Sensitivity: 1*	*Specificity: 0.63*	*PPV: 0.47*	*NPV: 1*	*Accuracy: 0.72*
Participant 9	*Sensitivity: 0.66*	*Specificity: 0.67*	*PPV: 0.37*	*NPV: 0.87*	*Accuracy: 0.67*
Participant 10	*Sensitivity: 0.77*	*Specificity: 0.66*	*PPV: 0.41*	*NPV: 0.90*	*Accuracy: 0.67*
Participant 11	*Sensitivity: 0*	*Specificity: 0*	*PPV: 0*	*NPV: 0*	*Accuracy: 0*

Round 1 (Results)

Participant 1	*Sensitivity: 0.5*	*Specificity: 0.8*	*PPV: 0.4*	*NPV: 0.85*	*Accuracy: 0.7*
Participant 2	*Sensitivity: 0.75*	*Specificity: 0.83*	*PPV: 0.64*	*NPV: 0.89*	*Accuracy: 0.8*
Participant 3	*Sensitivity: 0.90*	*Specificity: 0.75*	*PPV: 0.56*	*NPV: 0.95*	*Accuracy: 0.75*
Participant 4	*Sensitivity: 1*	*Specificity: 0.70*	*PPV: 0.52*	*NPV: 1*	*Accuracy: 0.77*
Participant 5	*Sensitivity: 1*	*Specificity: 0.61*	*PPV: 0.42*	*NPV: 1*	*Accuracy: 0.70*
Participant 6	*Sensitivity: 0.7*	*Specificity: 0.8*	*PPV: 0.53*	*NPV: 0.88*	*Accuracy: 0.77*
Participant 7	*Sensitivity: 0.9*	*Specificity: 0.66*	*PPV: 0.47*	*NPV: 0.95*	*Accuracy: 0.72*
Participant 8	*Sensitivity: 0.9*	*Specificity: 0.8*	*PPV: 0.6*	*NPV: 0.96*	*Accuracy: 0.82*
Participant 9	*Sensitivity: 0.2*	*Specificity: 0.83*	*PPV: 0.28*	*NPV: 0.75*	*Accuracy: 0.67*
Participant 10	*Sensitivity: 0.7*	*Specificity: 0.83*	*PPV: 0.58*	*NPV: 0.89*	*Accuracy: 0.80*
Participant 11	*Sensitivity: 1*	*Specificity: 0.6*	*PPV: 0.45*	*NPV: 1*	*Accuracy: 0.7*

Note: Participant 11 left the first-round blank throughout but answered the questions when results from other participants were shown

Supplementary Fig. S5. Comments per Rounds.

Rounds	R1	R2(results)	R3	R4
Number comments	5	1	15	1

Round 1
- ***Q2-*** *I don't know: "May be aphthae due to tooth trauma"*
- ***Q4****- I don't know: "Not clear from the picture what exactly is going on, if this is a single ulcer or multiple that combined over time"*
- ***Q14-*** *I don't know: "Difficult to separate from differentials without more clinical Hx"*
- ***Q25****- I don't know: "???"*
- ***Q31****- I don't know: "May be major aphthae of BD"*

Round 2- Iteration
- ***Q17****- I don't know: "May be herpetic stomatitis"*

Round 3
- ***Q1****. Erythematous halo surrounding ulcer margin*
- ***Q2.*** *Surrounding capillary proliferation is not usual pattern of oral ulcer in BD*
- ***Q3****. Major type*
- ***Q4****. Minor or herpetiform type*
- ***Q7.*** *Major type*
- ***Q8****. Minor type*
- ***Q9.*** *On the ulcer base, linear fissure is not usual pattern of oral ulceration in BD. I didn't think this was a BD ulcer and still don't*
- ***Q10.*** *Minor type*
- ***Q11****. Major type*
- ***Q12****. Major type*
- ***Q13****. Margin is not distinct as like erythematous halo, due to healing state? Major type*
- ***Q14****. I am not sure this ulcer is compatible to BD.*
  It is not clear of erythematous halo, not punched out shape, not clear margin of oral ulcer
  This image shows bullae formation in my view. This is not BD
- ***Q15.*** *There is too much capillary proliferation on surrounding tissues of oral ulcer. Also, base of oral ulcer shows linear fissure*
  This image may be due to a new blister. Suspicious diagnosis
- ***Q16****. We can see scar changes on lower lip showing linear or irregular shape*
  There are multiple plaques on the tongue, multiple erosions on the tooth bottoms and the cicatrix is seen on the lip inside probably due to deep ulceration
  However, linear lacerated ulcer near the BD ulcer makes some confusion for final diagnosis.
- ***Q17.*** *This image may be consistent with a herpetic infection or herpetiform aphthae of BD*

Round 4
- ***Q.16-*** *Old scars on the surrounding tissues*

Supplementary Fig. S6.

Round 3- Parameters shown to Oral Medicine panel following APG literature search

Site: anterior, posterior
Colour of ulcer base: red, yellow, white, grey, brown, black, speckled, non-speckled
Appearance of ulcer base: homogenous, non-homogenous
Shape: round, ragged, oval, linear, ovoid, well defined, non-well defined
Description: major, minor, herpetiform, mixed
Margins: flat, elevated, ragged, enrolled, indented, erythematous, white, well defined, non-well defined
Number: single, multiple
Aggravating factors: trauma (?), fillings
Others: shallow, deep, speckled, non-infective, infective
Free text

Round 3- Parameters agreed by Oral Medicine panel for Rounds 3 and 4

Margin (erythematous *vs*. others)
Shape (round *vs*. others)
Base (homogeneous *vs*. non homogeneous)
Depth (shallow *vs*. deep)
Colour (yellow *vs*. red)
Location (anterior *vs*. posterior)
Surrounding tissues (hyperplastic/flat)
Size (major/minor/herpetiform)
Aggravating factors (trauma/others)

Supplementary Fig. S7.

7 a- Levels of importance of clinical descriptor

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
MARGIN	100%	89%	100%	78%	70.00%	100%	90%	90%	90%	90%	78.00%	90%	90%	67%	88%	55.00%	56.00%
SHAPE	90%	67%	90%	78.00%	60.00%	90%	90%	100%	55%	70%	89.00%	67%	90%	67%	63%	66.70%	67.00%
BASE	80%	56%	60%	66.70%	70%	80%	80%	70%	56%	70%	78.00%	67%	80%	45%	50%	88.90%	45.00%
DEPTH	70%	67%	70%	77.80%	60.00%	60%	60%	60%	44%	50%	67.00%	67%	80%	78%	75%	33.30%	33.00%
COLOUR	60%	89%	80%	78.00%	70.00%	90%	80%	90%	80%	90%	77.80%	90%	70%	45%	50%	33.30%	33.00%
LOCATION	40%	44%	50%	67.00%	70.00%	60%	66%	70%	44%	60%	45.00%	78%	70%	56%	63%	33.00%	11%
SORRROU	30%	22%	40%	22.20%	10.00%	30%	33%	30%	33%	20%	33.00%	56%	30%	22%	13%	56.00%	45.00%
SIZE	20%	44%	50%	66.70%	40.00%	40%	10%	50%	33%	60%	55.60%	56%	60%	45%	63%	22.00%	11.10%
AGRAVAT	10%	0%	0	0%	10%	0%	22%	0%	22%	0%	11%	34%	0%	11%	13%	11.10%	22.00%
NUMBER	10%	0%	40%	22%	10.00%	40%	22%	40%	22%	30%	33.00%	22%	20%	22%	25%	11%	66.70%
OTHERS	20%	20%	10	0%	0%	0%	10%	0%	20%	10%	30%	20%	30%	50%	50%	10.00%	0%

7 b- Would you consider this clinical picture to defer from the diagnosis of RAS?

defer from RAS																BD?	BD?
YES	30%	30%	40%	30%	20%	30%	20%	10%	30%	30%	40%	40%	30%	40%	20%	20%	10%
NO	70%	70%	60%	70%	80%	70%	80%	90%	70%	70%	60%	60%	70%	50%	80%	80%	90%