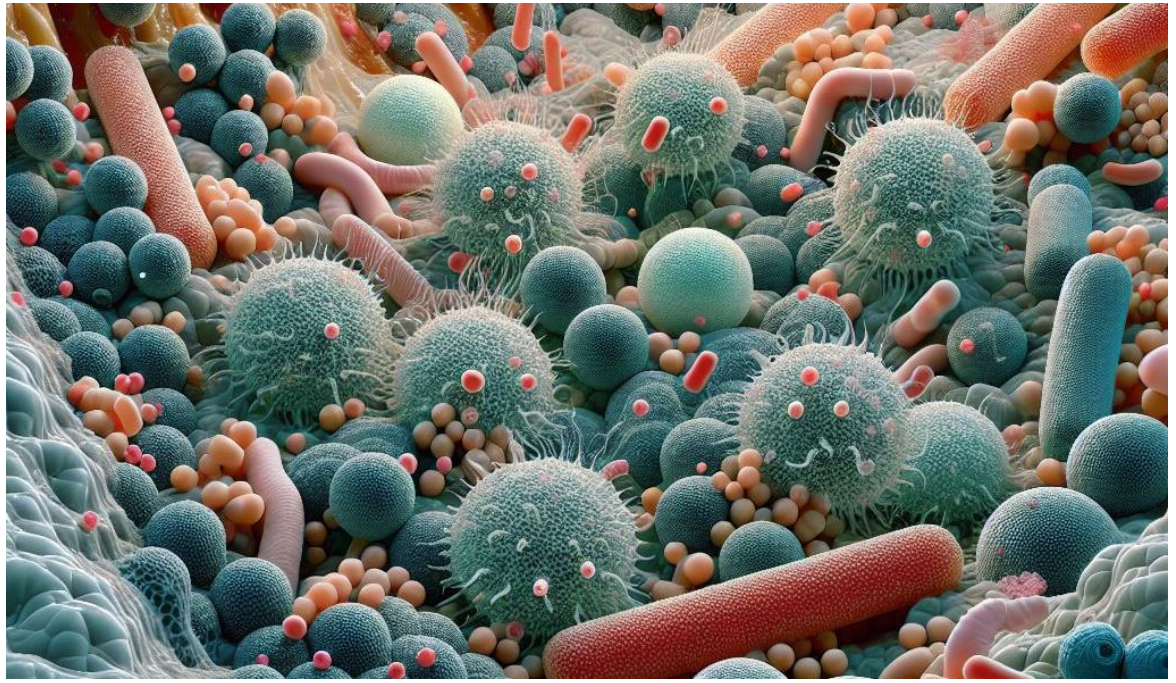


The microbiology of noma: insights from a pilot deep shotgun metagenomic project of patients presenting at the Noma Children's Hospital, Sokoto, Nigeria

Dr Stuart Ainsworth, University of Liverpool, UK

Stuart.ainsworth@liverpool.ac.uk

Ethics

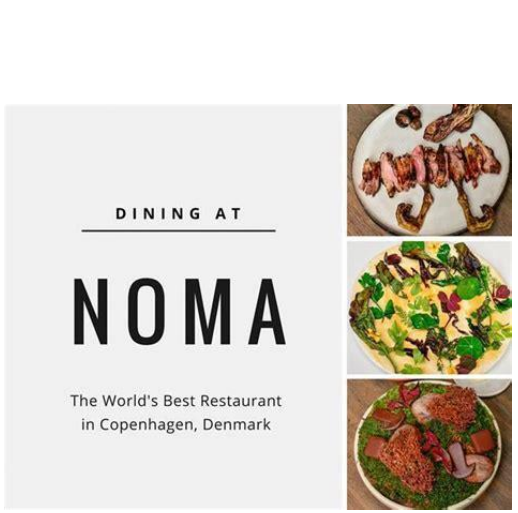
This study was approved by the MSF Ethics Review Board (ERB), the Liverpool School of Tropical Medicine ERB, the Nigerian Federal ERB, the Usman Danfodiyo University Teaching Hospital Health Research and Ethics Committee, and the Sokoto Ministry of Health Ethics Department.

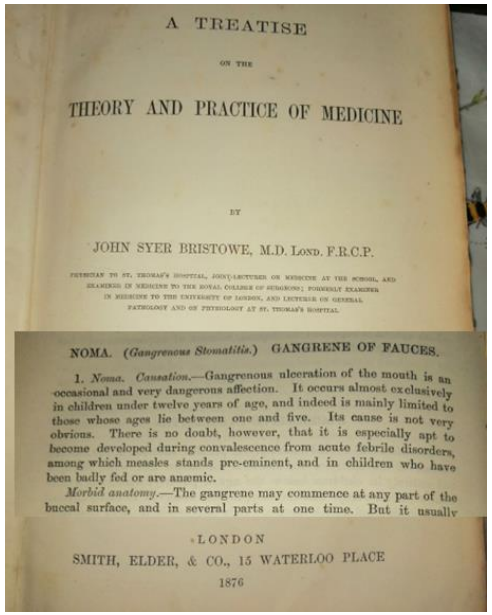
Conflict of Interest:

The author has declared no conflict of interest.

What is noma?

- Rapidly progressive oral-facial gangrene
  - Children aged 2-12 years
  - Chronic malnutrition
  - Abject poverty
- Common throughout Europe &USA up to the end of the 19th – ample recorded medical evidence
  - All but disappeared in the 20th century
  - Disappeared from consciousness as well.




A TREATISE
ON THE
THEORY AND PRACTICE OF MEDICINE
BY
JOHN SYER BRISTOWE, M.D. Lond. F.R.C.P.
NOMA. (*Gangrenous Stomatitis.*) GANGRENE OF FAUCES.
1. *Noma. Causation.*—Gangrenous ulceration of the mouth is an occasional and very dangerous affection. It occurs almost exclusively in children under twelve years of age, and indeed is mainly limited to those whose ages lie between one and five. Its cause is not very obvious. There is no doubt, however, that it is especially apt to become developed during convalescence from acute febrile disorders, among which measles stands pre-eminent, and in children who have been badly fed or are anæmic.
Morbid anatomy.—The gangrene may commence at any part of the buccal surface, and in several parts at one time. But it usually
LONDON
SMITH, ELDER, & CO., 15 WATERLOO PLACE
1876

Today – Noma is still prevalent in many LMICs

- estimate of global incidence is 30,000–40,000/year
- mortality rate of approximately 85%

Photo: Claire Jeantet - Fabrice Catérini / Inediz

What causes noma?

- We simply don't know.
- It's bacterial
- Likely polymicrobial
- Many organisms suspected

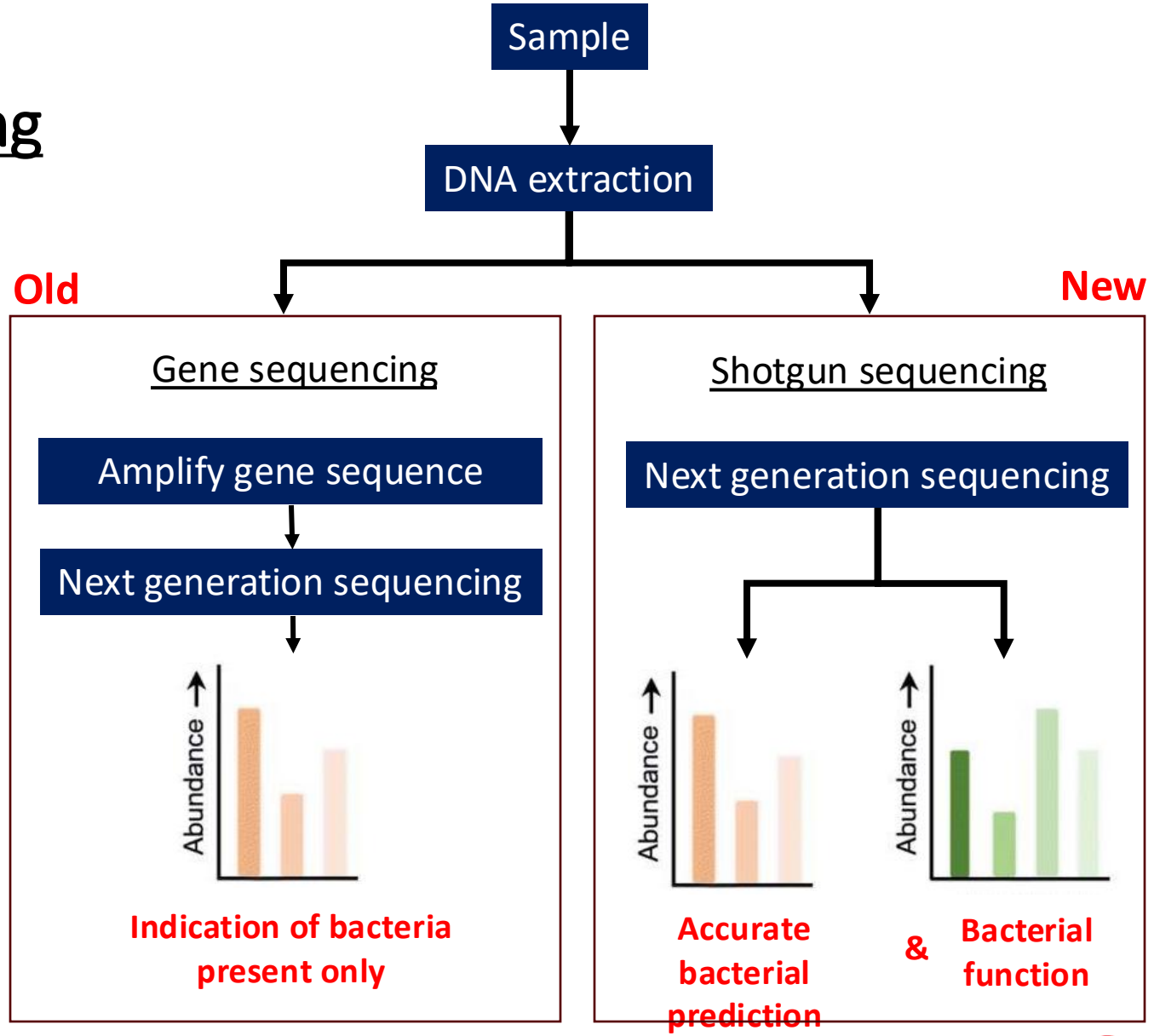
Previous attempts to define causative agents have ultimately failed

- Difficult to grow
  - Some oral bacteria do not grow well in laboratory conditions
- Metagenomic gene sequencing (16s rRNA)
  - Doesn't provide an accurate picture

MEDECINS SANS FRONTIERES

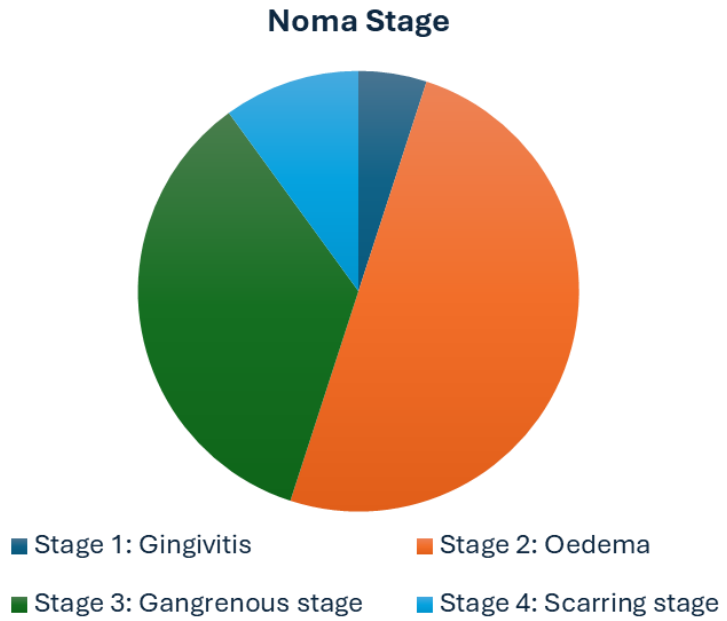
This study used an improved technique: **shotgun sequencing metagenomics**

- The shotgun technique sequences **everything**
- **Much more accurate description of bacteria present**
- **Much more data rich**
- Cheap: £70/sample!



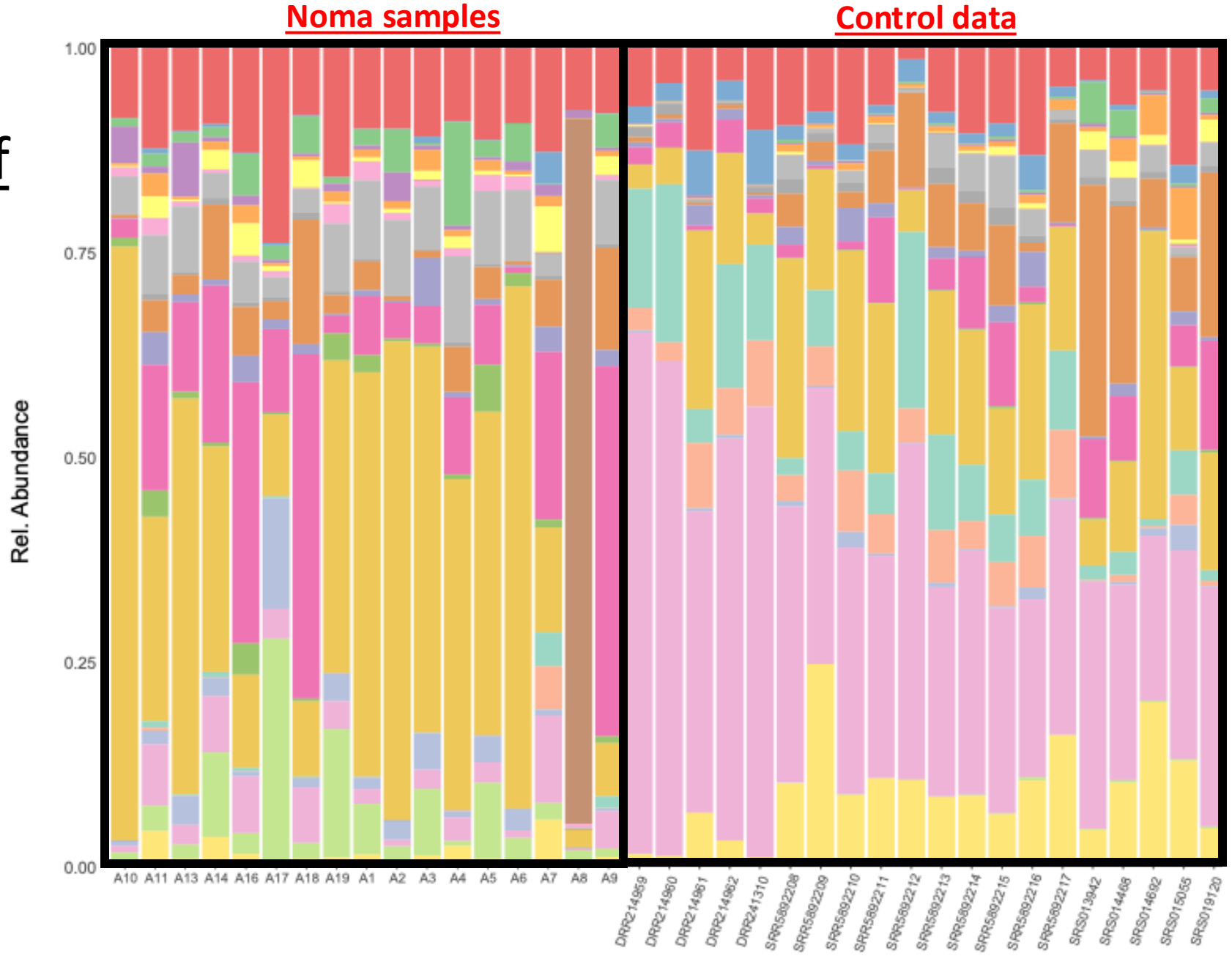
Study setting & sampling

- Noma Children's Hospital, Sokoto, Nigeria
- October 2023 to February 2024
- **53** patients presented
- **20** patients with Noma enrolled
  - Sokoto state (**n=10**), Zamfara (**n=6**) and Kebbi (**n=4**)
- Saliva sample taken on admission
- Control data obtained from existing studies of healthy individuals (**n = 20**)



What are the main differences between saliva microbiomes of noma patients and healthy controls?

- Increased presence of *Treponema*
- Depletion of ***Streptococcus***



What can the data tell us?

We ran three, independent, predictive tests based on the data

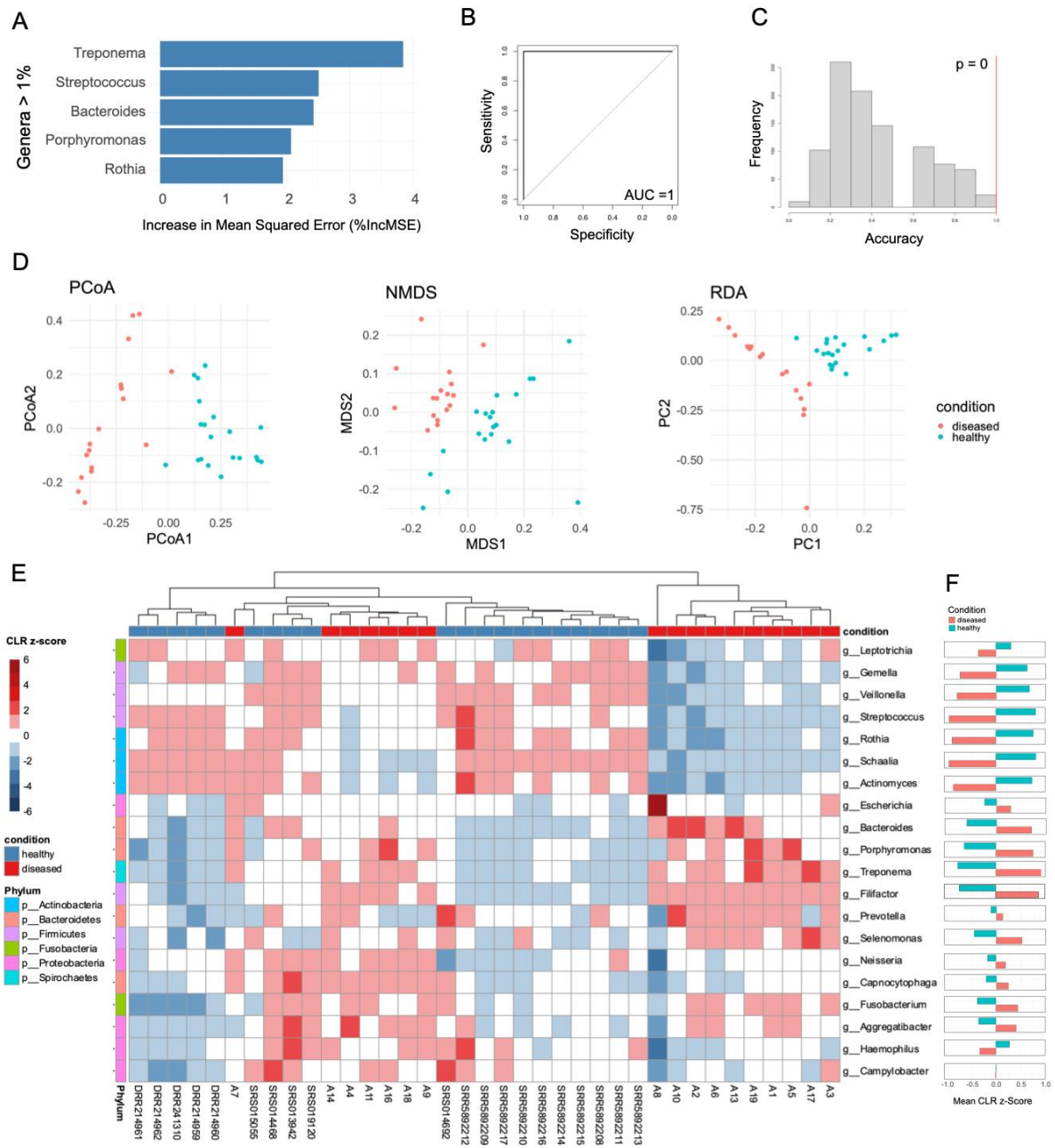
Question – what species are the predictive signatures of noma?

All produce the same prediction:

That the **Presence/enrichment of**
Treponema, Bacteroides, Porphyrmonas

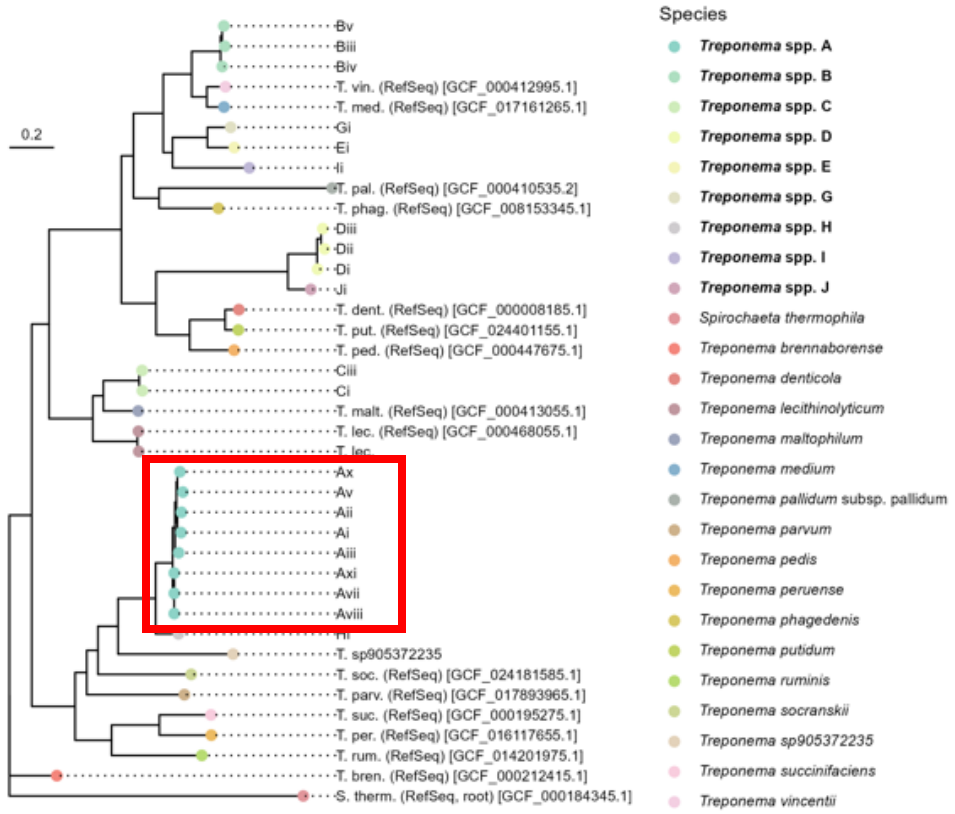
& the **depletion of**
Streptococcus, Rothia

<u>are predictive of noma</u>

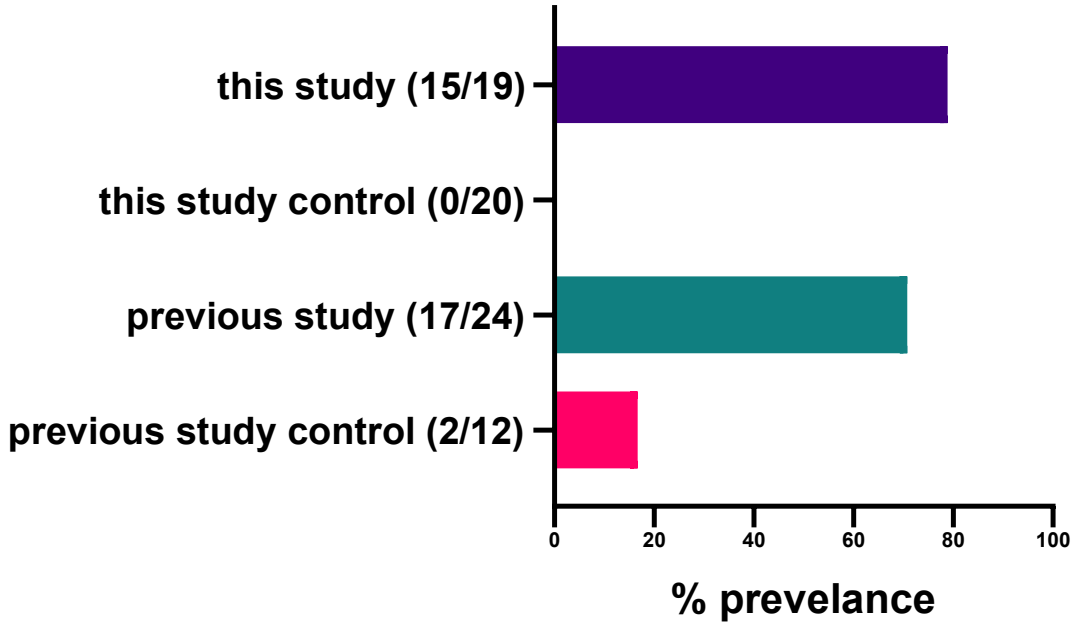


Suspect novel noma causing bacteria?

Multiple genomes of a new-to-science species of *Treponema* recovered in the noma samples



Re-analysing previous gene sequencing studies also found the presence of this novel *Treponema*



Detection of the first bacterial species that is only associated with noma disease

What does this all mean?

Identification of a possible specific contributing agent of noma:

- Enables development of possible diagnostics
- Enables development of targeted interventions
- Enables development of specific prevention

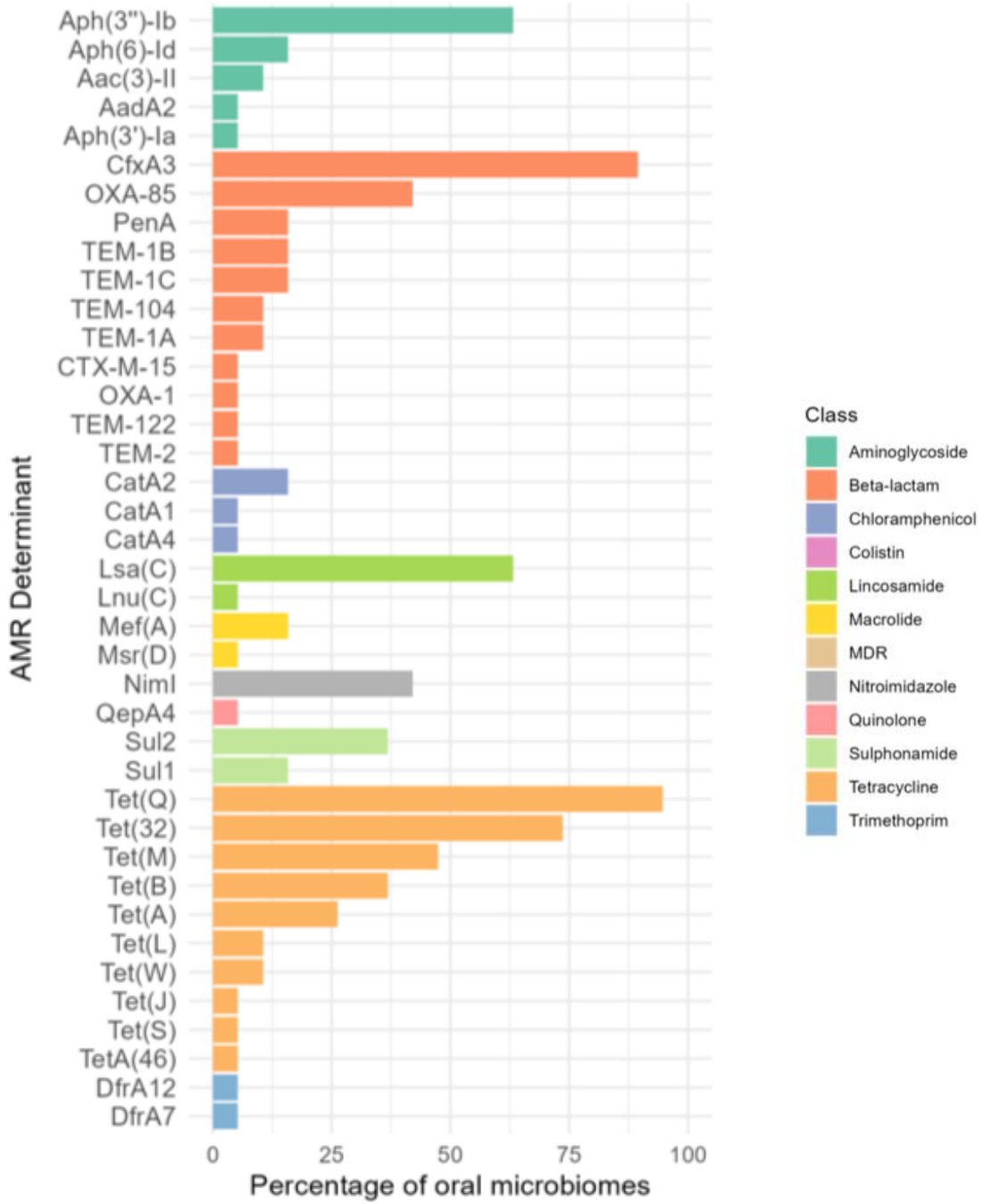
Next questions

- Do we get the same results in other locations with noma?
- Can we isolate and grow the new species of Treponema?
- Can we prevent the depletion of healthy bacteria (*Streptococcus*) to prevent noma?

Finally……

Shotgun sequencing can be used to monitor antimicrobial resistance

Resistance to the three antibiotics used to treat noma (co-amoxiclav, metronidazole and aminoglycoside) were all present in multiple patients



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