Can we measure Antimicrobial Resistance (AMR) better with "Quantitative Estimation of Population AMR" (QEPA)?

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Introduction

Antimicrobial Resistance (AMR) in humans is of substantial public health concern. In human & veterinary medicine it is desirable to target usage of antimicrobials so as to minimise the development & transfer of resistance whilst retaining the desired clinical outcomes. For example it would be useful to deploy the best metrics of AMR for predicting clinical outcomes following administration of antimicrobials.

Conventionally, testing for AMR is based on selection of a single bacterial isolate which is exposed to an antimicrobial of fixed concentration giving us a binary outcome.

Quantitative Estimation of Population AMR (QEPA) is novel and provides a more informative set of metrics and may therefore be an important part of our armoury when measuring AMR.

Methods

Standard lab practices can provide us bacterial counts representing several low confidence estimates of bacterial density in the absence and presence of an antimicrobial.

Bayesian analysis allow us to combine even relatively uninformative data to give robust estimates of: a) total bacterial density; b) proportion of bacteria within a population that are resistant; c) credible intervals around both these point estimates.

A validation experiment tested this combination of lab+stats on samples that were constructed artificially to have different proportions of bacteria resistant. They were "constructed" by mixing a purely resistant culture with a purely sensitive culture in different ratios.

Results

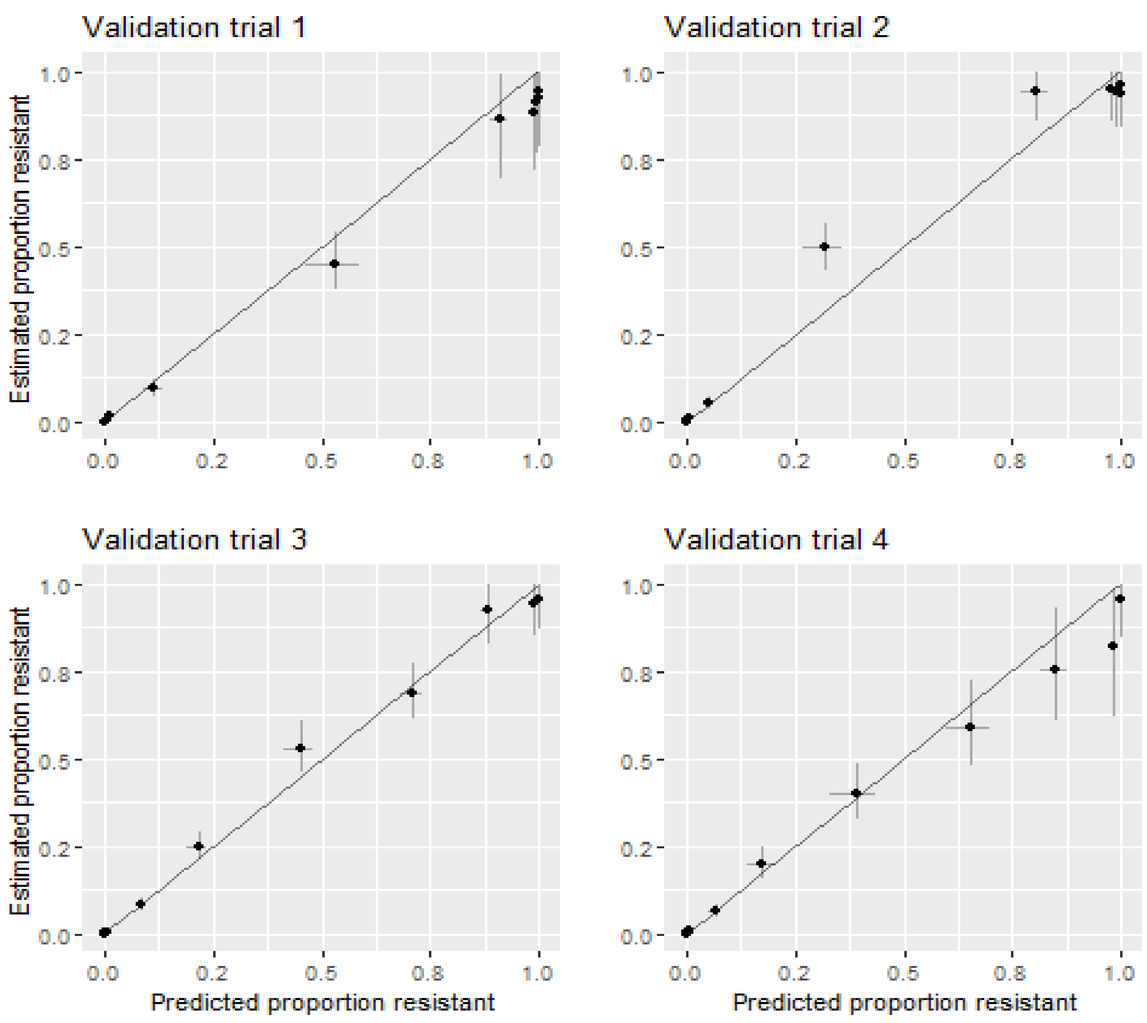

Fig. 1. Results from the four validation trials. The whiskers represent 95% credible intervals around each point estimate. The x-axis is the proportion of bacteria resistant that we expected to have based on the particular mix of two pure cultures (i.e. one resistant & one sensitive). The y-axis gives the proportion of bacteria resistant as estimated using QEPA. The solid line y=x is the line near which we'd expect most points to lie if the method was working as desired. The level of agreement is high.

Conclusion

- The estimates from QEPA closely match the expected values, therefore validating the method (Fig. 1)
- QEPA gives a lot more information about a sample than the typical method of a binary classification of a single bacterial isolate.
- It will be valuable to assess whether any of the direct metrics or derived metrics from QEPA are better than conventional methods for example in predicting clinical outcomes
- The information provided by QEPA can be used to fit models to explain the different levels of AMR and their associated variables.
- There are some limitations:
  - QEPA is purely phenotypic but can be used to relate genotypic measures to the level of phenotypic AMR
  - A population of bacteria can be characterised quantitatively with an even more informative suite of metrics (but with greater effort)

QEPA in practice

- We have deployed QEPA in two pilot studies (cross-sectional & cohort). Both involved sampling from the faeces of dairy calves.
  - We found a strong "group effect" – i.e. there was a big difference in proportion of bacteria resistant, between the two studies.
  - We found measurable differences in the level of AMR from separate samples obtained from a single animal at a single time point.
  - We found a high level of consistency in the proportion of bacteria resistant in samples from different animals in the same group and over a two-week period.
  - We observed that QEPA was able to distinguish quantitatively in the AMR between samples that would very likely have appeared identical using conventional methodsWe are now embarking on a series of studies to estimate important parameters such as the rate at which AMR decreases following the removal of antimicrobials from an animal group.

Fig. 2 Sampling in a cold, Feb 2020, just a few weeks before such work was prohibited, due to the arrival of a zoonotic virus in humans.

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