

# Interpretation of respiratory virus detection in adults hospitalised with acute respiratory infection. Insights from a host response profiling study.

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### Background

Acute Respiratory Infection (ARI) is the commonest reason for antibiotic use but distinguishing bacterial from viral ARI is challenging, leading to antibiotic overuse and AMR. Respiratory viruses detected by PCR in patients with ARI may be causally related, but asymptomatic detection also occurs, especially with rhinoenterovirus, and bacterial co-infection may also occur. Host response profiling may therefore provide insights into the significance of viral detection by PCR.

### Methods

This retrospective study used stored blood samples and data from the FluPOC trial which enrolled adults hospitalised with ARI from 2017-19[1]. Paxgene RNA blood samples were tested using the Triverity (Inflammatix, Sunnyvale, CA, US) test on the Myrna instrument. This host response test measures levels of 29 RNAs to generate separate scores from 0 to 50 indicating the likelihood of bacterial and viral infection (1-10 very low, 11-20 low, 21-30 moderate, 31-40 high, 41-50 very high). Detailed clinical and laboratory data were collected and all patients had multiplex PCR testing for respiratory viruses.

### Findings

169 patients with ARI were tested. 103 (61%) patients had viruses detected by PCR. For the viral positive patients the median (IQR) age was 58 (40-76) years and 45 (44%) were male. Median Charleson co-morbidity index was 4 (4-8) and 77 (75%) had chronic respiratory disease. The median duration of illness prior to presentation was 4 (3-7) days and 152 (90%) received antibiotics during admission. Median Triverity viral score was 30 (18-42) and Bacterial score was 25 (18-35).

Of the 103 patients with viruses detected; 5 (3%) had influenza detected, 9 (5%) had RSV, 22 (13%) had human metapneumovirus (hMPV), 4 (2%) had parainfluenza (PIV), 4 (2%) had adenovirus, 48 (28%) had rhinoenterovirus and 21 (12%) had seasonal coronavirus (HCoV) detected. 94 (91%) of viral detections were with single viruses and 9 (%) were multiple detections, all of which included seasonal human coronavirus (HCoV) with another virus (Rhinoenterovirus x 7, hMPV x 1 and RSV x 1).

Figure 1&2 shows the median Triverity viral and bacterial scores for each patient, according to virus detected. Scores were heterogenous between individual patients and were generally high or low. Median viral scores were highest for Influenza (44) lowest for Rhinoenterovirus (27) and intermediate for the other viruses. The corresponding bacterial scores were also heterogeneous and generally followed the opposite pattern to viral scores.

Heterogeneity of scores was most marked for patients with Rhinoenterovirus (IQR 15-37). Figure 3 shows paired viral and bacterial scores for Rhinoenterovirus positive patients demonstrating an inverse relationship.

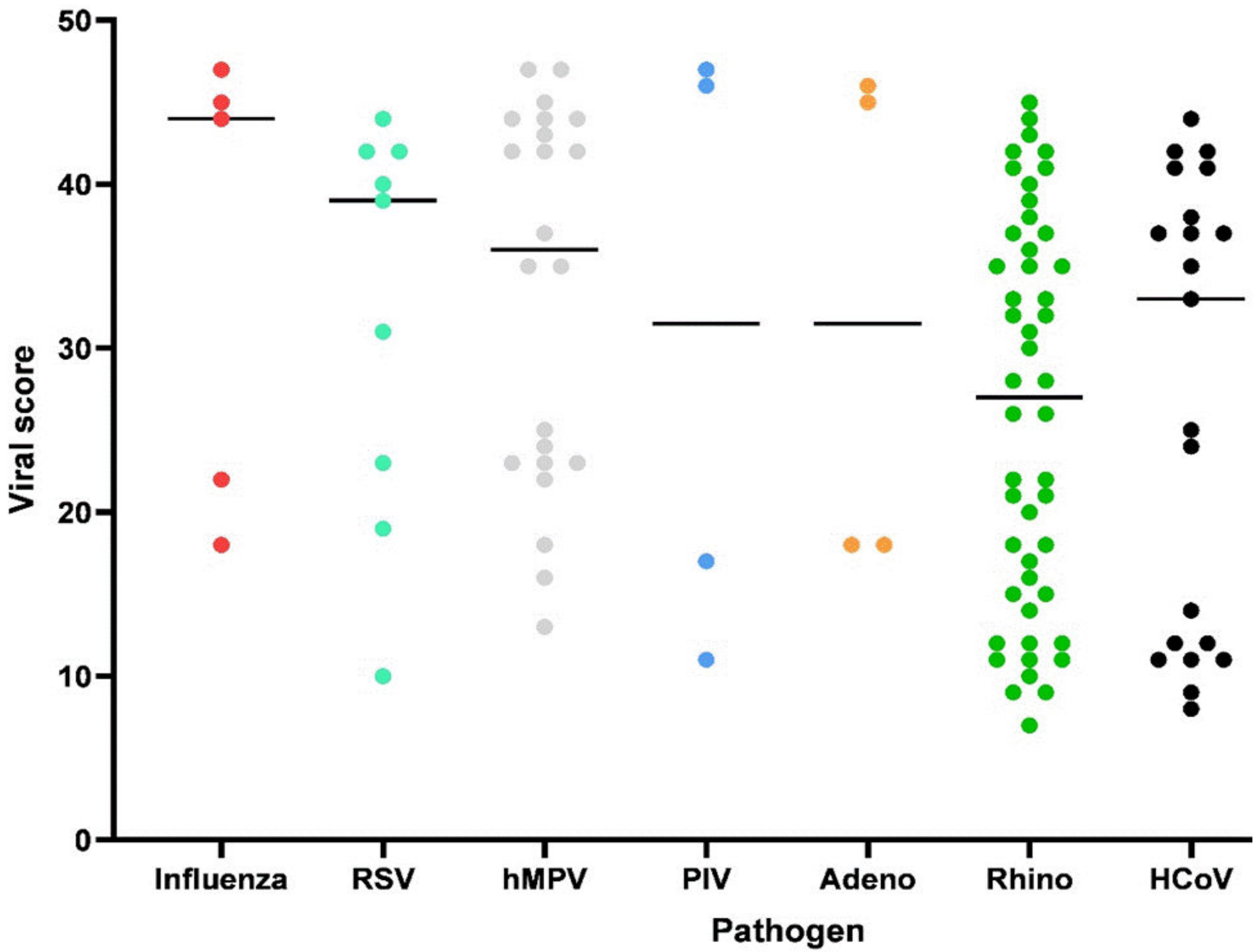


Figure 1: Triverity Viral gene expression scores for patients with ARI by pathogen detected

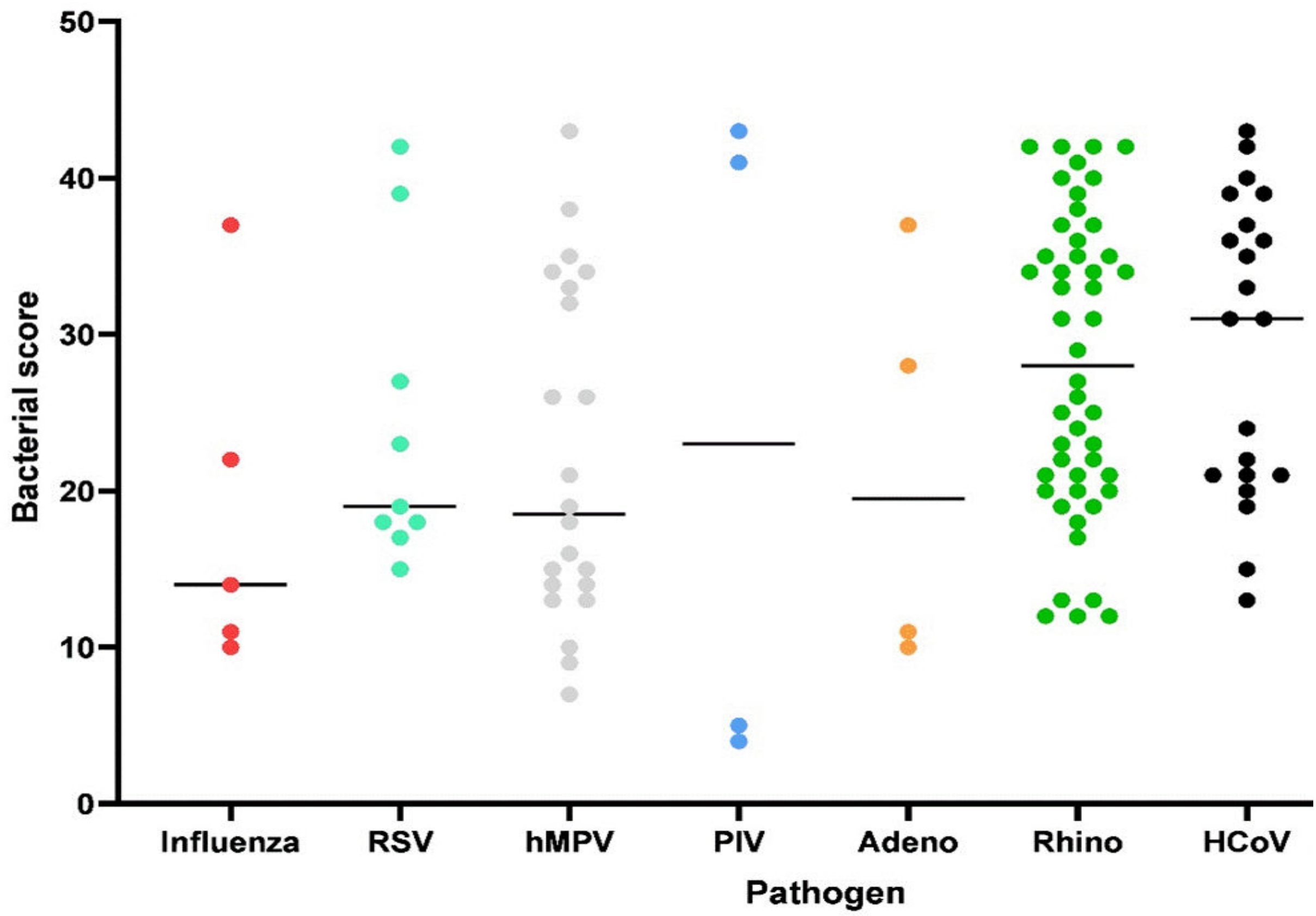


Figure 2: Triverity Bacterial gene expression scores for patients with ARI by pathogen detected

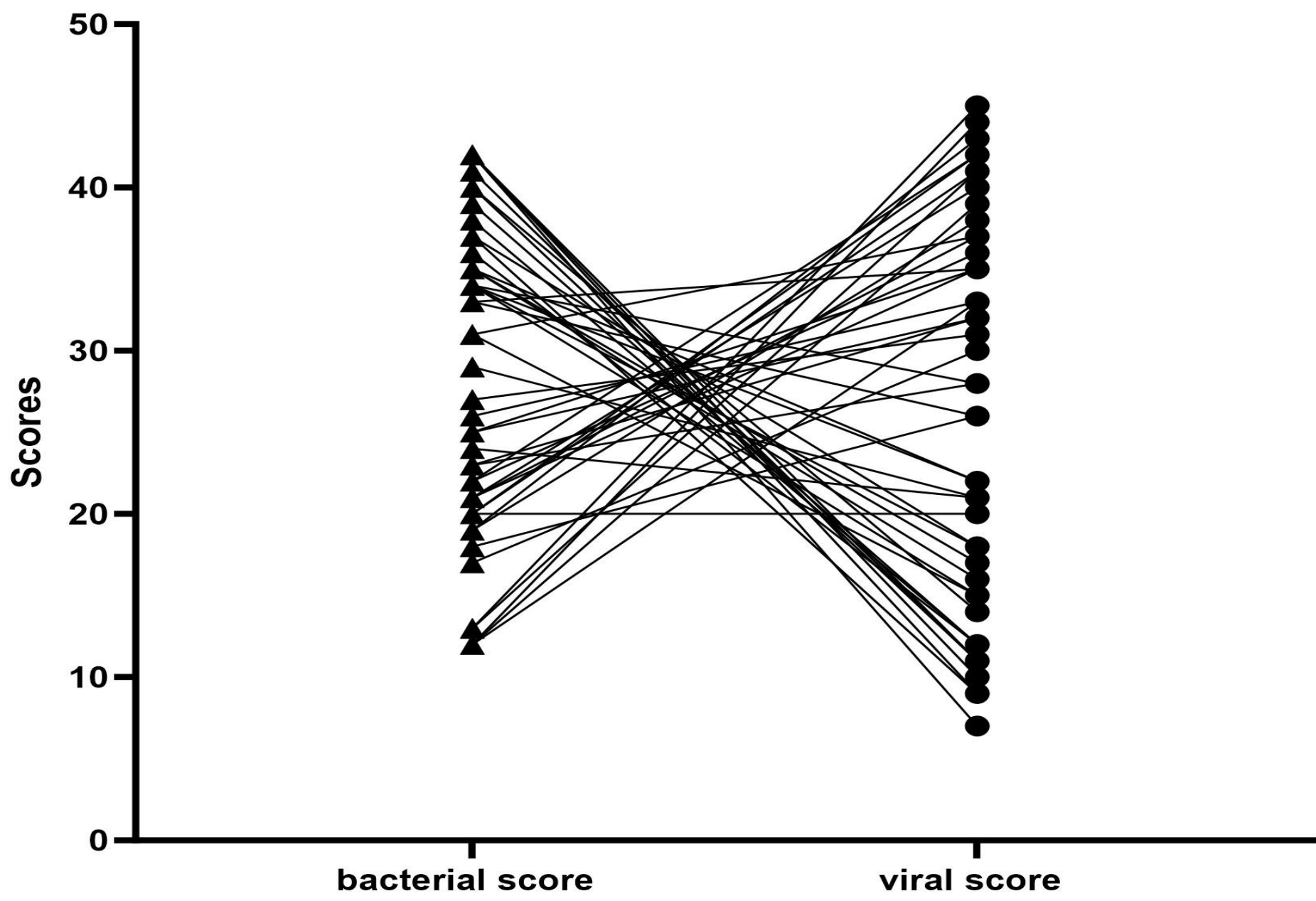


Figure 3: Gene expression (Triverity) viral and bacterial score pairs for each Rhinoenterovirus PCR positive patient

### Conclusions

Host response data from TriVerity testing suggests that aetiology (bacterial or viral) of ARI in adults with respiratory virus detection by PCR is heterogenous, when determined by the presence of bacterial or viral host responses. This was especially true for rhinoenterovirus detection suggesting careful interpretation is required before attributing causality. Combined pathogen PCR with host response testing may aid interpretation and add clinical value.

### References:

[1] Clinical impact of a routine, molecular, point-of-care, test-and-treat strategy for influenza in adults admitted to hospital (FluPOC): a multicentre, open-label, randomised controlled trial. Clark TW et al. Lancet Respir Med. 2021; 9:419-429

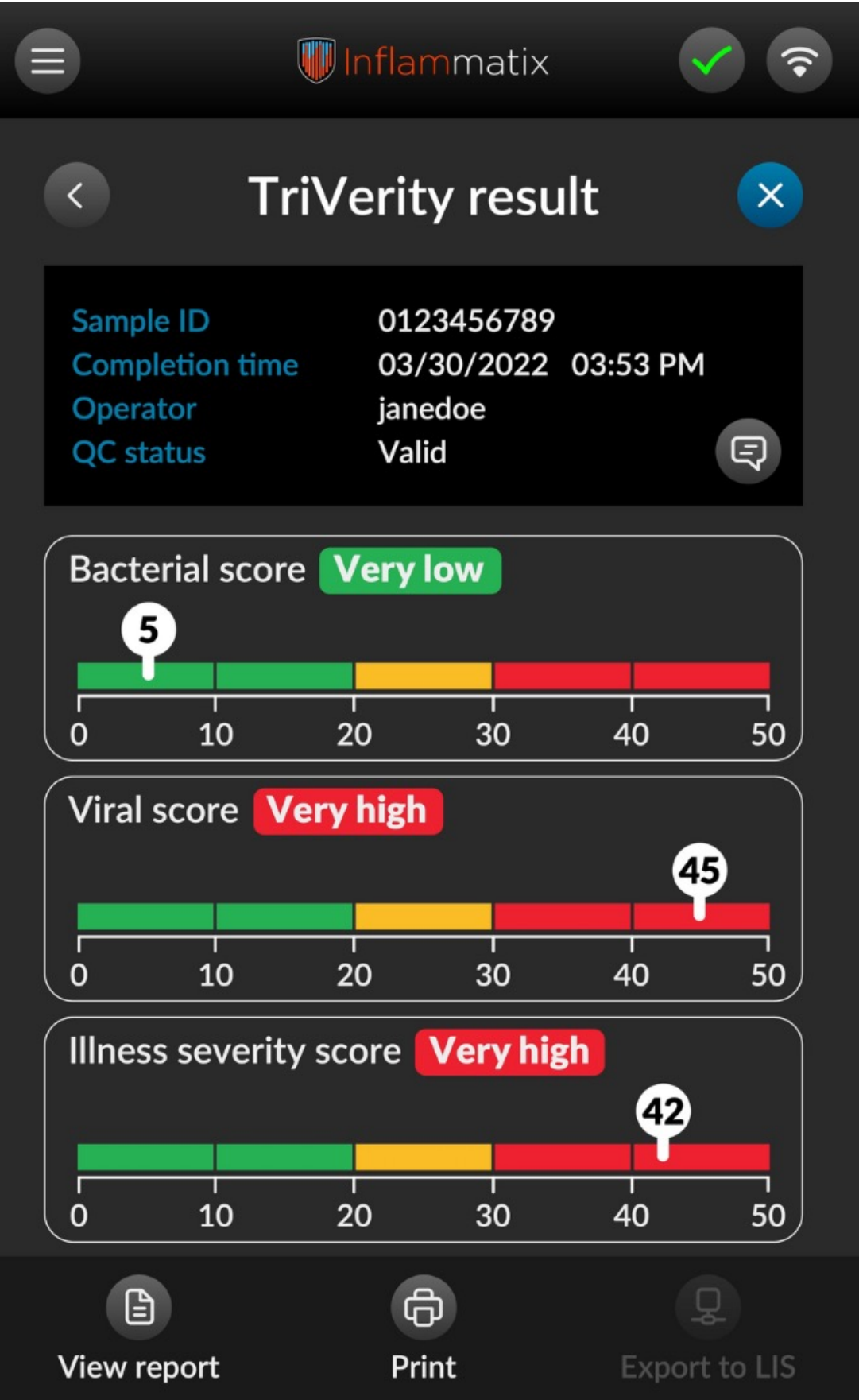


Image 1: Example of Triverity result display (left) and myRNA instrument (above).

Image adapted from: [www.inflammatix.com/triverity/](http://www.inflammatix.com/triverity/)

### Acknowledgements:

The Myrna instrument and TriVerity cartridges were provided by the manufacturer, Inflammatix, who also funded the testing of the PAXgene Blood RNA samples. Inflammatix did not provide any input into the study design, conduct, analysis, or writing of the poster. Blood samples and data for this study are from the FluPOC study, funded by the NIHR (PDF-2016-09-061).