Evaluate Vantage

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# Europe approves a Covid-19 crystal ball

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## Memed claims that its newly CE-marked test can predict Covid-19 severity.

A test that promises to predict which Covid-19 patients will go on to have severe disease has today become available in Europe. Made by the tiny private Israeli company Memed, the Covid-19 Severity assay measures a combination of biomarkers in a patient's blood, assigning a score the company says correlates with the chances of the condition worsening.

Clinical data on the product are indeed impressive at first glance. But there are reasons to suspect that the assay might not work quite so well in the real world, and questions over the level of demand for such a test remain.

Memed's test can be run in 15 minutes on the company's Memed Key platform. It measures levels of tumour necrosis factor-related apoptosis inducing ligand (Trail), interferon gamma-inducible protein-10 (IP-10) and C-reactive protein (CRP).

Trail levels increase in viral infection but are believed to fall in severe viral infections, which could make this a particularly useful biomarker for severe cases. In Covid-19 specifically, low Trail levels are associated with inability to clear the virus and increased disease severity. IP-10 has been implicated in lung injury in severe viral infection, and CRP is a marker of inflammation.

### Predicting survival

Trial data published as a preprint at the start of July give an idea of what the test might be able to achieve. The study recruited 394 eligible Covid-19 patients between March and November 2020 at the emergency departments, wards and intensive care units of six sites in Israel, Germany, and the US. All had PCR-confirmed Covid-19.

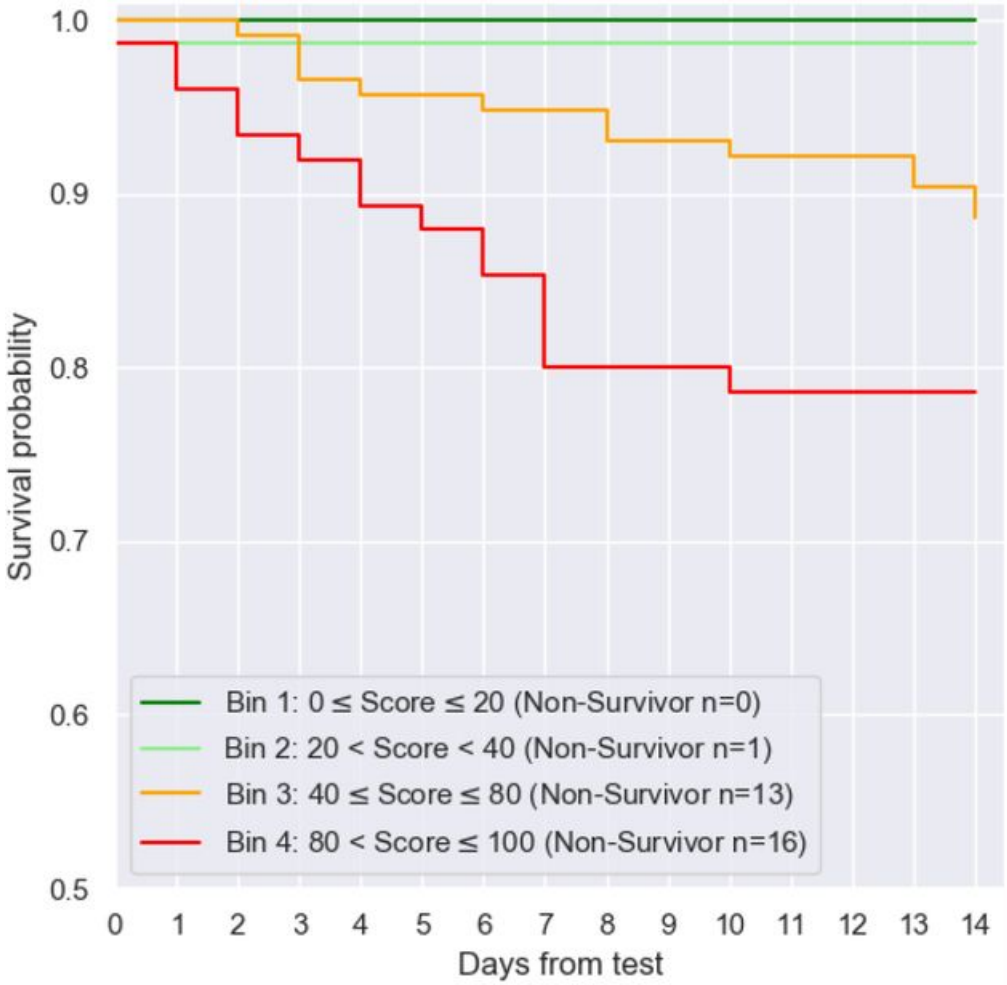
Based on these results, patients were assigned a score from 0-100, and using this, were stratified into four categories or bins. The likelihood of severe outcome – defined as ICU admission, non-invasive or invasive ventilation, or death – increased significantly ($p<0.001$) with higher scores.

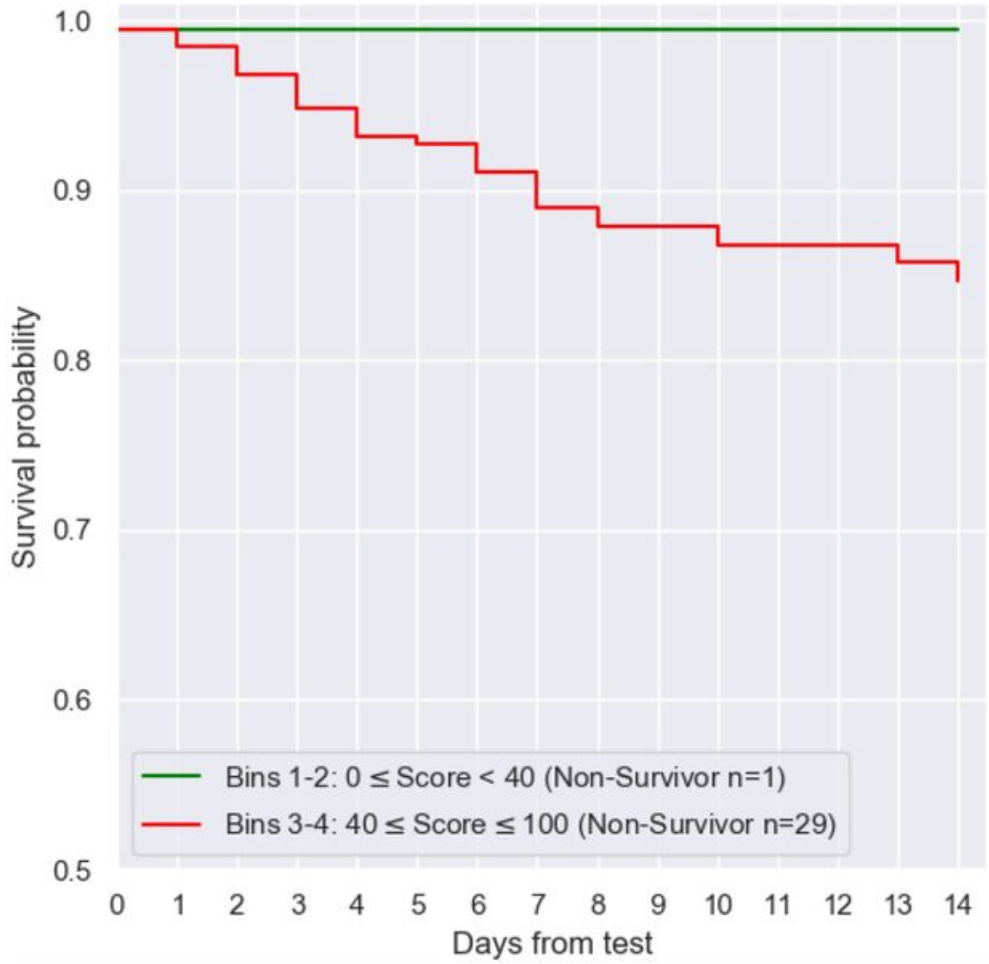
| Distribution of patients across score bins | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Bin** | **Score** | **n Total** | **% Patients** | **n Severe** | **n Non-Severe** | **% Severe (PPV)** | **% Non-Severe (NPV)** |
| 4 | 80-100 | 75 | 19.0 | 54 | 21 | 72.0 | 28.0 |
| 3 | 40-80 | 116 | 29.4 | 46 | 70 | 39.7 | 60.3 |
| 2 | 20-40 | 79 | 20.1 | 10 | 69 | 12.7 | 87.3 |
| 1 | 0-20 | 124 | 31.5 | 3 | 121 | 2.4 | 97.6 |
| | **Total** | **394** | **100** | **113** | **281** | | |

*PPV = positive predictive value; NPV = negative predictive value. Source: Medrxiv preprint.*

The signature produced by Memed's test also differentiated patients who further deteriorated after having a severe outcome from those who improved (p=0.004).

14-day survival distribution was significantly different between patients scoring less than 40, in bins 1 and 2, and those scoring 40 and above, in bins 3 and 4, with a p value of 0.001.




Kaplan-Meier survival estimates for signature score bins. Source: Medrxiv preprint.

All this points to a test that could be hugely useful in hospitals, not least because it might allow patients to be discharged if they are predicted to have a mild infection.

But there are reasons for caution, most obviously that the study has not yet been peer reviewed. Moreover, the trial was retrospective: some of the patients enrolled in the trial had already been admitted into the ICU, and had thus already met one of the criteria for severe disease.

Lastly, the study was conducted in the spring, summer and autumn of 2020, before the emergence of Delta and other new coronavirus variants. Newer variants might produce slightly different biomarker signatures, rendering the test less accurate.