Introduction:
Oxylipins are oxidative breakdown products of cell membrane fatty acids. Animal models have demonstrated that various vasoactive oxylipin pathways may be implicated in septic shock pathophysiology but these have been poorly studied in humans.

Methods:
Oxylipin profiling was performed on serum samples collected on enrolment to the VANISH (Vasopressin vs. Norepinephrine as Initial Therapy in Septic Shock) trial. Samples were analysed with liquid chromatography-mass spectrometry. Patients were followed up until 28 days.

Results:
Samples were collected from 154 of 409 (37.7%) patients on inclusion to the trial and 39 (25.3%) had died by 28 days. Non-survivors were found to have higher levels of a number of oxylipins including: 14,15-dihydroxyeicosatrienoic acid (DHET) (p<0.01), 11,12-DHET (p=0.03), 15(S)-hydroxyeicosatetraenoic acid (p=0.02), 14-hydroxyoctadecapentaenoic acid (p=0.04) but lower levels of the precursor eicosapentaenoic acid (p=0.012). When corrected for multiple comparisons with the Benjamini-Hochberg test, only 14,15-DHET remained significant (p=0.025).

Although there was a difference in median 14,15-DHET levels between survivors and non-survivors, many values were below the level of detection (n=84/154 (54.5%)). As such, we also analysed 14-15-DHET as a binary variable (Figure). Patients with detectable 14,15-DHET were more likely to die (HR 2.4 [95% CI 1.2-4.6], p<0.01) and have a higher median lactate (p =0.01) and total SOFA score (p<0.01) than those patients where baseline 14,15-DHET was undetectable.

Conclusion:
Our study suggests the oxylipin 14,15-DHET may be associated with septic shock severity and 28-day mortality. These results are consistent with the known vasodilatory actions of this class of oxylipin. More work is needed to confirm its exact role in septic shock and whether this pathway is amenable to therapeutic intervention.
Survival curve for patients with vs without detectable levels of the oxylipin 14,15-DHET. Followed up until 28 days.