Background
The clinically appropriate range for oxygen saturation in preterm infants is unknown. Previous studies have shown that infants had reduced rates of retinopathy of prematurity when lower targets of oxygen saturation were used.

Methods
In three international randomized, controlled trials, we evaluated the effects of targeting an oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, on disability-free survival at 2 years in infants born before 28 weeks’ gestation. Halfway through the trials, the oximeter-calibration algorithm was revised. Recruitment was stopped early when an interim analysis showed an increased rate of death at 36 weeks in the group with a lower oxygen saturation. We analyzed pooled data from patients and now report hospital-discharge outcomes.

Results
A total of 2448 infants were recruited. Among the 1187 infants whose treatment used the revised oximeter-calibration algorithm, the rate of death was significantly higher in the lower-target group than in the higher-target group (23.1% vs. 15.9%; relative risk in the lower-target group, 1.45; 95% confidence interval [CI], 1.15 to 1.84; P = 0.002). There was heterogeneity for mortality between the original algorithm and the revised algorithm (P = 0.006) but not for other outcomes. In all 2448 infants, those in the lower-target group for oxygen saturation had a reduced rate of retinopathy of prematurity (10.6% vs. 13.5%; relative risk, 0.79; 95% CI, 0.63 to 1.00; P = 0.045) and an increased rate of necrotizing enterocolitis (10.4% vs. 8.0%; relative risk, 1.31; 95% CI, 1.02 to 1.68; P = 0.04). There were no significant between group differences in rates of other outcomes or adverse events.

Conclusions
Targeting an oxygen saturation below 90% with the use of current oximeters in extremely preterm infants was associated with an increased risk of death.