Objective:
Continuous glucose monitors (CGMs) are increasingly used in research settings to examine glucose metabolism in newborn babies. Accuracy of these devices depends on calibration blood glucose (BG) measurements entered into the CGM device. The potential impact of variations in timing and accuracy of reference calibration measurements on CGM device output were assessed.

Method:
Clinical CGM data from 50 neonates (total duration ~228 days) and blood-gas analyzer reference BG measurements were used. Normally distributed (SD 2%, 5% or 10%) random errors were added to reference BG concentrations, and random timing lags up to +25 minutes simulated delays in registering calibration BG with the CGM. The CGM trace was recalculated 1,000x in a Monte Carlo analysis using the randomly modified calibration measurements. Uncertainty in each CGM measurement was defined as the range (mmol/L) of that measurement over the 1,000 runs.

Result:
Considering only reference BG measurement error, the median CGM uncertainty across the cohort varied from 0.5mmol/L for SD 2% to 2.4mmol/L for SD 10%. Considering only timing lags the uncertainty was < 0.18mmol/L 75% of time, but reached 3mmol/L or more, depending on local rate of change of glucose. Combining both BG measurement error and timing lag effectively added these uncertainties.

Conclusion:
Reference BG measurement error causes an almost uniform uncertainty band around the CGM trace, with level of uncertainty depending upon the reference sensor accuracy. The effect of timing lags is highly dependent on the local rate of change of glucose, with high rates of change causing very large uncertainties. Clinically, timing lags should be minimized for highly variable situations (e.g. brittle diabetics or post-prandial measurements) to reduce uncertainty.