

# hCG levels can decline pre- or post-onset of bleeding in early pregnancy loss

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## Introduction

- Non-progressive rise in human chorionic gonadotrophin (hCG) followed by decline is indicative of early pregnancy loss
- Decline of hCG has been observed to occur before bleeding, but the proportion of losses identifiable prior to bleeding has not been established
- It is also not known whether the temporal relationship between bleeding and hCG decline relates to timing of loss or peak levels of hCG achieved
- UK clinical practice is to conduct home pregnancy tests after pregnancy loss to check the loss is complete, but rate of hCG decline is not well characterised
- This analysis examined changes in daily urinary hCG levels in relation to onset of bleeding

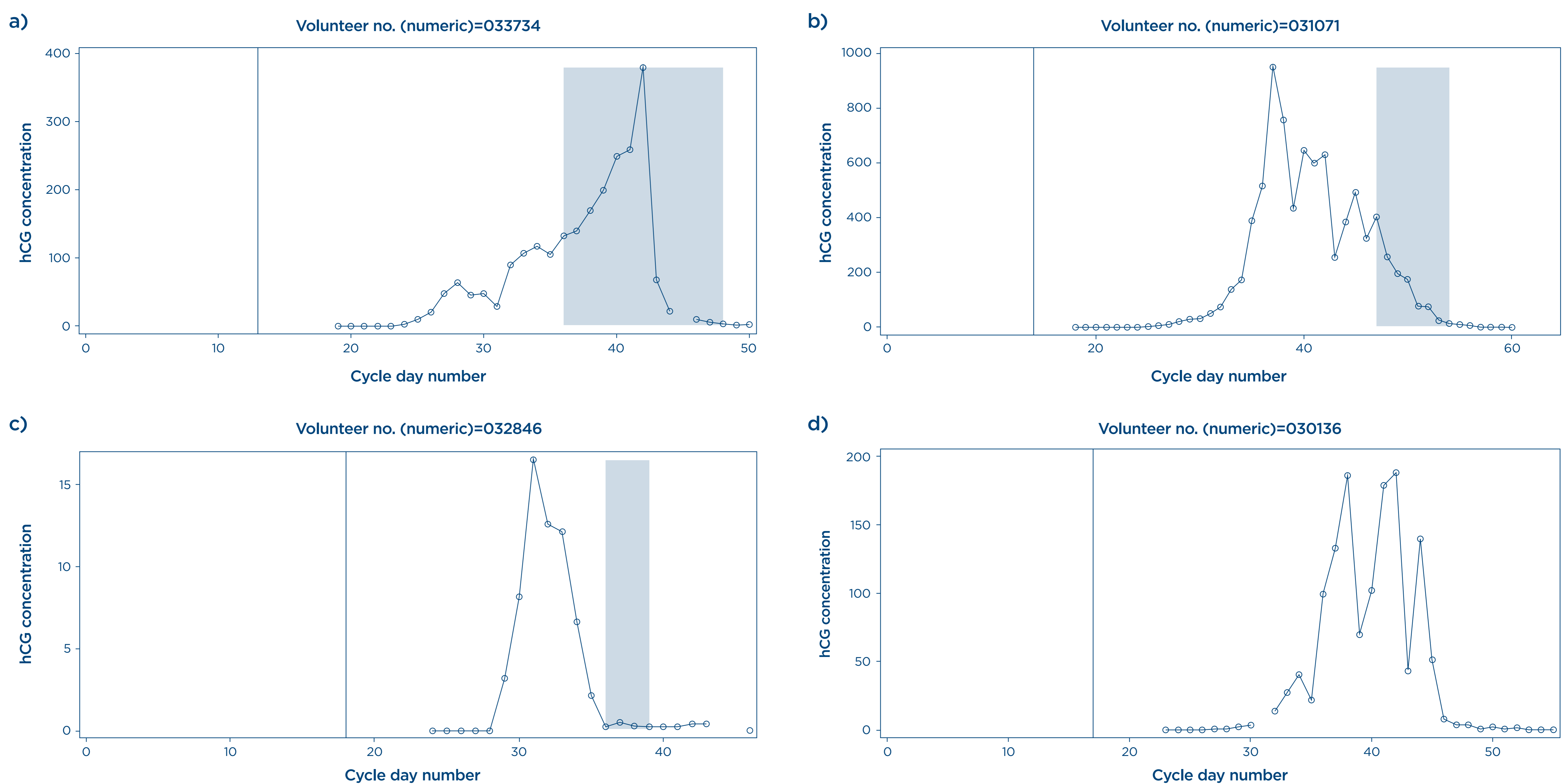
## Methods

- Home-based observational cohort study following women pre-conception to early pregnancy (NCT01577147)
- Volunteers seeking to conceive naturally (>18 years old) were recruited via online advertisements from across the UK
- Volunteers collected daily urine samples for one entire menstrual cycle and completed daily diaries detailing menses/bleed information for around 30 days following Expected Period (EP) if they became pregnant
- Of 348 pregnancies, 54 were reported as miscarriages at 12-week follow-up
- The luteinising hormone surge was determined for each conception cycle (AutoDELFIATM) to calculate day of EP (15 days post-ovulation), with one volunteer excluded due to insufficient samples
- Of the remaining 53 pregnancies, all provided daily urine samples to examine hCG levels (AutoDELFIATM)

## Results

- Of 53 volunteers who reported early loss, only 40 recorded that they experienced bleeding during the study period
- Most volunteers with bleeding had hCG decline during the study period (n=38). Examples of hCG decline are shown in Figure 1
- Median day for peak hCG was 3 days after expected period (range -4 to 25 days)
- Median peak hCG concentration was 29.24 mIU/mL (range 4-7557mIU/ml)
- On average, onset of bleeding occurred 3 days after hCG peak level, but ranged widely from 14 days before hCG peak to 10 days afterwards
- Median time for hCG levels to decline to <1 mIU/mL (baseline) from peak was 5.5 days (range 2-23 days)
- Time to decline was highly correlated with peak hCG concentration (p=<0.0001)
- Time for hCG to decline to baseline from onset of bleeding was also variable. Median was 2 days after bleeding started, but hCG levels could return to baseline as early as 25 days before onset of bleeding and up to 13 days after onset
- Median days of bleeding was 5 days (range 1-14 days) and correlated with peak hCG concentration (p=0.0148) and day of peak hCG concentration (p=0.0054)

Figure 1: Examples of urinary hCG trajectories in early pregnancy loss. Blue bars indicate days on which the volunteer reported bleeding, with day of ovulation marked by a line. a) bleeding before hCG reaches peak levels, b) bleeding during hCG decline, c) bleeding after hCG returned to baseline, d) no bleeding reported



## Conclusions

- Tracking of urinary hCG revealed a decline in hCG levels prior to symptoms in many women, enabling early detection of miscarriage
- Bleeding duration was also related to hCG profile
- Given the heterogeneity in time of decline of hCG level, several measurements may be needed to check loss is complete
- Therefore, hCG tracking could provide useful clinical information or assist in setting women's expectations in early pregnancy

## Declaration of interest

Authors are employees of SPD Development Company Ltd, a wholly owned subsidiary of SPD Swiss Precision Diagnostics GmbH, the manufacturer of Clearblue pregnancy and fertility tests. The study was funded by SPD Development Company Ltd.