OBSTETRICS

The relationship between virtual antenatal care and pregnancy outcomes in a diverse UK inner-city population: a group-based trajectory modeling approach using routine health records

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BACKGROUND: The COVID-19 pandemic resulted in major reconfiguration of maternity services, particularly an increase in virtual antenatal care.
OBJECTIVE: We explored associations between virtual antenatal care trajectories and pregnancy outcomes.
STUDY DESIGN: Pregnancy and birth outcome data were obtained from a multiethnic and socioeconomically deprived UK inner-city population before and during the pandemic (with and without lockdown). Data were collected using a health record data linkage from the Born in South London cohort. Antenatal care was characterized by the number of outpatient contacts during 6 gestational windows: 0 to 14^{+6}, 15 to 20^{+6}, 21 to 27^{+6}, 28 to 32^{+6}, 33 to 36^{+6}, and $\geq$37 weeks' gestation. In each window, the proportion of virtual antenatal care was grouped into quartiles, and group-based trajectory modeling was used to extract virtual antenatal care trajectories. Associations between these trajectories and pregnancy outcomes were explored using adjusted multinominal logistic regression.
RESULTS: The analysis included 34,114 mother-child dyads (October 2018—July 2023). Group-based trajectory modeling suggested 4 trajectories of virtual antenatal care contacts: low and stable virtual care throughout pregnancy (Trajectory 0; n=27,751 pregnancies, 81.3%), high first trimester virtual care (Trajectory 1; n=832, 2.4%), high second trimester virtual care (Trajectory 2; n=2,410, 7.1%), and high third trimester virtual care (Trajectory 3; n=3,121, 9.2%). Following adjustment, compared with the low and stable group (Trajectory 0), high second trimester virtual care was associated with less gestational hypertension (adjusted relative risk ratio, 0.84; 95% confidence interval, 0.74—0.96) and assisted vaginal birth (0.87 [0.76—1.00]), and more premature births (<37 weeks, 1.21 [1.02—1.44]), labor induction (1.13; 1.02—1.25), breech presentation (1.92; 1.02—3.62), and postpartum hemorrhage (1.14; 1.00—1.30). Similarly, compared to the low and stable group (Trajectory 0), high third trimester virtual care had less gestational hypertension (0.84 [0.73, 0.96]), more premature births (<37 weeks; 1.35; 1.16—1.58) and elective (1.54; 1.38—1.72) or emergency (1.21; 1.01—1.34) cesarean sections, and neonatal intensive care admissions (1.28; 1.09—1.50); fewer third-degree/fourth-degree vaginal tears (0.82; 0.75—0.90); and less early infant skin-to-skin contact (0.82; 0.73—0.92) and breastfeeding (0.90; 0.81—0.99).
CONCLUSION: A higher proportion of virtual care contacts in antenatal care in the second or third trimesters was associated with a greater risk of adverse pregnancy outcomes.

Key words: antenatal care, birth outcomes, electronic health records, trajectories, virtual care

Introduction

Before the COVID-19 pandemic in the United Kingdom, maternity care was almost exclusively in-person. At least 7 to 10 routine appointments were offered, depending on parity and multiple pregnancy status.[1] During the pandemic, routine antenatal care was modified, to minimize the risk of infection, with cancellation of many in-person appointments.[2] Virtual technology (ie, remote consultations via video conferencing or by telephone) was used as an alternative, and out-of-office self-monitoring was implemented for some women with conditions such as pregnancy hypertension or gestational diabetes mellitus.[3] To further limit in-person contact, appointments were combined when possible, and limitations were made on the choice of carer and place of birth.[4] Furthermore, public health messaging to maintain social distancing and stay at home may have inadvertently caused some women not to seek care for problems arising during their pregnancy.[5,6] Modifications to staffing arrangements may have also affected antenatal care.[7–9]

A UK national survey of maternity care providers highlighted the extensive impact of the pandemic on maternity services. The majority of units reported fewer antenatal (70%) or postnatal (56%) appointments and unscheduled antenatal presentations (89%), greater use of remote consultation (89%), and temporary suspension of births in midwife-led units or at home (59%). Nearly half of mental healthcare staff

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AJOG AT A Glance

Why was this study conducted?

The COVID-19 pandemic led to increased virtual antenatal care, but the impact of virtual care on pregnancy outcomes remains unclear. This study examines virtual care trajectories and associations with maternal and neonatal outcomes in a multiethnic, urban UK population.

Key findings

For the mother, virtual antenatal care in the second or third trimesters was associated with less gestational hypertension; more preterm birth, labor induction, assisted vaginal birth, breech presentation, cesareans, and postpartum hemorrhage; and fewer third-degree/fourth-degree vaginal tears. For the baby, virtual antenatal care in later pregnancy was associated with lower early skin-to-skin contact and breastfeeding rates, and more frequent neonatal intensive care admission.

What does this add to what is known?

This study provides new insights into associations between different patterns of virtual antenatal care and pregnancy outcomes. The integration of virtual contacts into antenatal care requires careful assessment of potential risks.

reported feeling less able to assess women, some of whom engaged poorly with virtual appointments.[7,10]

While much of the virtual antenatal care adopted during the pandemic (*in lieu* of in-person care) has been reversed postpandemic, some continues. It is important to understand whether or not it is advisable to have ongoing virtual antenatal care or to adopt more virtual care contacts during any future health system shock. A substantial body of experiential literature has described largely negative experiences with virtual care during the pandemic, including those of patients who received virtual care[11,12] and of providers who delivered it.[6,8,9,13–20] The concerns raised were about compromised quality, access, and participation. While some providers acknowledged greater convenience for certain patients, they also reported substantial challenges, including digital exclusion of some women.

In contrast, relatively little is known about the impact of virtual antenatal care on clinical outcomes.[21–23] In Australia, an interrupted time series analysis reported no change in pregnancy outcomes during the widespread use of telehealth in the first 14 months of the pandemic.[24] However, a lack of overall effect may mask opposing changes in different outcomes.[25]

In this analysis of data from a UK inner-city population cohort, we used routine electronic health data, and the method of group-based trajectory modeling, to describe associations between virtual antenatal care and pregnancy outcomes. In contrast to interrupted time series analysis, group-based trajectory modeling incorporates variations in virtual antenatal care exposure over time. We explored these associations before and during the pandemic (with and without lockdowns) to quantify the potential impact on pregnancy outcomes of virtual antenatal care.

Methods

Study design

Data were obtained from the "early Life Cross-Linkage in Research, Born in South London" (eLIXIR-BiSL) routine healthcare data linkage from October 2018 to July 2023. This linkage collects data from 2 National Health Services (NHS) hospitals. The linkage and governance permissions have been described previously[26] (Supplemental File and Supplemental Figure 1).

In the United Kingdom, antenatal care is provided free-of-charge for the ≈550,000 births per year.[27] Women are offered 2 routine ultrasound scans (for gestational age dating and fetal anomaly detection), and a minimum of 7 antenatal care visits for multiparous women and 10 for nulliparous women.[1] Midwives lead the care of low-risk pregnancies, and obstetricians assist in the care of those at higher risk. Gestational diabetes screening is based on clinical risk factors, which prompt formal biochemical testing.[28,29] During pandemic lockdowns, NHS England provided ≈16,000 home blood pressure monitors to support the monitoring of higher-risk pregnancies (eg, 1%–2% of women with chronic hypertension).[30]

Participants

We included all singleton pregnancies, with information on antenatal registration, at least one antenatal appointment after registration, and birth outcomes.

We excluded duplicate records and those without an identification number and records of pregnancies without outpatient antenatal care records. Duplicate records were identified by 2 or more antenatal care registration identification numbers, with estimated delivery dates within 14 days (such as when women were transferred from one of the hospitals to the other); in this instance, the first record was included. Multiple pregnancies were also excluded because antenatal care pathways often differ from singleton pregnancies and birth outcomes for each baby may differ.

Data

Data obtained at antenatal care registration provided information on demographics, past medical and obstetric history, and characteristics of the current pregnancy. Antenatal care was characterized by the total number of outpatient contacts, and the proportion of care delivered by virtual contact, during 6 gestational windows: 0 to 14^{+6}, 15 to 20^{+6}, 21 to 27^{+6}, 28 to 32^{+6}, 33 to 36^{+6}, and $\geq 37^{+0}$ weeks' gestation. An appointment was deemed to have been 'virtual' if: (1) maternal blood pressure,

dipstick proteinuria, and fetal heart rate (after 15 weeks' gestation) were missing from the visit record or (2) appointment notes suggested that it was virtual, by use of 'virtual', 'telephone', or 'call' in the free-text. Otherwise, the appointment was considered to have taken place in-person. The proportion of virtual antenatal care was estimated for each of the 6 gestational windows listed above, and then converted to quartiles: 0% to 25%, 26% to 50%, 51% to 75%, and 76% to 100%; for example, if in a gestational age window, a woman attended 3 appointments from 28 to 32^{+6} weeks and 2 appointments were virtual, then 2/3 (66.6%) were considered to have been virtual and care in that gestational window was coded as the third quartile (51%−75%).

We evaluated key outcomes across pandemic phases, according to the antenatal registration date: prepandemic (October 1, 2018−March 22, 2020), pandemic with lockdowns (March 23, 2020−July 17, 2021), and pandemic without lockdowns (July 18, 2021−July 8, 2023).[31] The outcomes assessed reflect a combination of organizational performance indicators, clinical quality improvement metrics, and national maternity ndicators in the United Kingdom (for further details, see Supplemental Table 3).

Trajectory modeling

It could not be assumed that all participants during the study period experienced the same longitudinal changes in virtual antenatal care, especially given the repeated cycles of pandemic lockdown and easing. Therefore, we used group-based trajectory modeling, a form of latent class analysis, to identify subgroups of individuals with similar trajectories of virtual antenatal care.

To identify the number of trajectories (latent classes) for virtual care which best described the data, we adopted a forward modeling approach using the Guidelines for Reporting on Latent Trajectory Studies[32] checklist (Supplemental Table 4). First, a one-class model was fitted, and then additional classes were added incrementally. Each time a class was added, model adequacy was assessed using the model estimation criteria of: Bayesian Information Criterion, average posterior probability of assignments, the ratio of the odds of a correct classification, group membership, and relative entropy (Supplemental File). Once the model adequacy stopped improving, an additional model was fitted with one extra class, to ensure that the full array of possible models had been tested (Supplemental Table 5).

Statistical analysis

Binary and categorical variables are presented using counts and percentages. The distributions of continuous variables were assessed and summarized by mean and standard deviation or median and interquartile range for normally or non-normally distributed variables, respectively. We used a 'censored normal model' suitable for use with scaled data (ie, virtual antenatal care percentage quartiles).[33] The 6 gestational windows ($0-14^{+6}$, $15-20^{+6}$, $21-27^{+6}$, $28-32^{+6}$, $33-36^{+6}$, and $\geq 37^{+0}$ weeks, as above) were converted to mean gestational age.

Univariable and multivariable multinominal logistic regression analyses were used to assess the associations between the virtual care trajectories and birth outcomes. These associations are presented as adjusted relative risk ratios. To identify confounders for inclusion in multivariable models, direct acyclic graphs were created for birth outcomes (Supplemental Figure 2). The minimal adjustment variables were determined to be index of multiple deprivation, parity, time (months of antenatal registration), gestation, hospital, smoking status, and pandemic epoch.

Pandemic epochs were classified as prepandemic (October 1, 2018−March 22, 2020), first pandemic lockdown (March 23, 2020−June 23, 2020), first lockdown easing (June 24, 2020−November 4, 2020), second pandemic lockdown (November 5, 2020−January 5, 2021), third pandemic lockdown (January 6, 2021−July 17, 2021), and pandemic without lockdown (July 18, 2021−July 8, 2023). Due to the correlation between time and pandemic epoch, only pandemic epoch was retained as a confounder in the final model. An interaction term was included for index of multiple deprivation and ethnicity.

Although body mass index was included in the direct acyclic graph, it was not identified as a necessary confounder. Body mass index data were frequently missing during the pandemic period, likely due to a reduction in in-person appointments where height and weight are typically measured. Given that this analysis focused on relationships during the pandemic, including body mass index could have introduced bias due to nonrandom missingness.

Finally, we modeled the differences between the number of appointments for each trajectory using negative binomial regression (due to overdispersion) and adjusted for parity, registration gestation, and antenatal care type.

Sensitivity analyses

First, we assessed the differences between those women who were included in the analysis vs those excluded; birth and delivery data were compared using chi-squared test or regression for categorical and continuous outcomes, respectively. Second, we truncated the pregnancies included at the beginning and end of the study period, to ensure that the number of births was stable, and to minimize the impact of pregnancies that booked late for antenatal care or delivered very early; the adjusted study period was April 1, 2019 to April 30, 2023. Third, we removed parity as an adjustment variable and stratified the analysis for parity. All analyses were undertaken in Stata (version 18.0).

Results

Following removal of duplicates and multiple pregnancies (n=1012), 58,402 unique pregnancy identification numbers were recorded between October 2018 and July 2023, of which 34,114 were included in the analysis (Supplemental Figure 1). Women excluded from the analysis differed from those included, with regards to a number of registration characteristics and birth outcomes (Supplemental Tables 6 and 7).

At antenatal care registration, mean maternal age was 32.7 years, 17% of pregnancies were affected by obesity (≥30 kg/m^2), median gestational age was 9.7 weeks, 13% of the cohort registered after 16 weeks, and 22.7% had only midwifery-led care (meaning that they were deemed to be low risk) (Table 1). Half of the cohort were from the global majority, of which 42% and 20% were of Black or Asian ethnicity, >60% were from the 2 lowest quintiles of the index of multiple deprivation, and 7% had difficulty understanding English. Just more than half of women were nulliparous and few reported prior drug use (<7%). Of the multiparous women, 31.9%, 1.8%, 8.8%, and 7.9% reported a prior Caesarean, stillbirth, postpartum hemorrhage, and preterm birth, respectively.

The median number of antenatal appointments was 9 (interquartile range, 7−12), with a median of 1 (0−2) received virtually (Table 2). 22.8% of women gave birth prepandemic and 45.6% during pandemic without lockdowns. 2.5% were smoking at delivery and 12.1% developed gestational hypertension. The majority of women (68.5%) had no risk factors at birth, 94.1% of pregnancies ended at term, 22.0% of births were induced, and 46.9% were by unassisted vaginal delivery. Breech delivery was rare (0.3%) and third-degree or fourth-degree vaginal tears were uncommon (1.5%). Postpartum hemorrhage occurred in 10.0% of pregnancies. Stillbirth and neonatal death were rare at 3.9 and 2.3 births per 1000, respectively. 88.3% of newborns had early skin-to-skin contact, 6.9% were small-for-gestational age, and 5.6% were admitted to a neonatal intensive care unit.

Group-based trajectory modeling identified 4 trajectories of virtual antenatal care which best described the data (Supplemental Figure 2, Supplemental Table 4, Supplemental Tables 3 and 4). 81.3% of participants (n=27,751) were in 'Trajectory 0', characterized by low and stable virtual care throughout pregnancy. 2.4% of participants (n=832) were in 'Trajectory 1' and had a high proportion of virtual care during the first trimester. 7.1% of participants (n=2410) were in 'Trajectory 2' and had a high proportion of virtual care during the second trimester. Finally, 9.2% of participants (n=3121) were in 'Trajectory 3' and had a high proportion of virtual care during the third trimester.

Characteristics at registration for antenatal care, stratified by trajectory group

There were many baseline differences between the trajectory groups (Table 1).

- Low and stable virtual care throughout pregnancy (Trajectory 0): These participants were more likely to have registered for antenatal care before the pandemic or during the pandemic without lockdowns, register late for antenatal care, and be <20 years of age.
- High first trimester virtual antenatal care (Trajectory 1): These participants were more likely to register for antenatal care during the pandemic without lockdowns and had more body mass index missingness and fewer late registrations.
- High second trimester virtual antenatal care (Trajectory 2): These participants were most likely to register during the first and second pandemic lockdowns, had the lowest percentage of participants <20 years of age, were more likely to be of White ethnicity, and less likely to have difficulty understanding English.
- High third trimester virtual antenatal care (Trajectory 3): These participants were most likely to register prepandemic, had the highest percentage of midwifery-only care, were more likely to have used recreational drugs in the previous 12 months, were more likely to be nulliparous, and when multiparous, were more likely to have previous postpartum hemorrhage or preterm birth.

Overall, the median number of antenatal visits was similar for the 4 trajectory groups (Table 2). However, following adjustment, the rate of visits was 6% lower for those with high first trimester virtual care (Trajectory 1; incidence rate ratio, 0.94) and 4% higher for those with high third trimester virtual care (Trajectory 3; incidence rate ratio, 1.04), compared to those with low and stable virtual care (Trajectory 0, Table 3).

Adjusted analyses

In adjusted analyses using the low and stable virtual antenatal care throughout pregnancy group (Trajectory 0) as the reference outcome, pregnancy outcomes differed by virtual care trajectory. Similar results were obtained in the unadjusted analyses (Table 3).

- High first trimester virtual care (Trajectory 1): There was no significant difference in pregnancy outcomes.
- High second trimester virtual care (Trajectory 2): These participants were:
  - Less likely to be diagnosed with gestational hypertension (adjusted relative risk ratio, 0.84; 95% confidence interval, 0.74, 0.96);
  - More likely to experience preterm birth <37 weeks, and specifically birth at 24 to 27^{+6} weeks' gestation (1.79 [1.10, 2.93]);
  - More likely to have a baby with a breech presentation (1.92 [1.02, 3.62]);
  - More likely to be induced (1.13 [1.02, 1.25]);
  - Less likely to have an assisted vaginal birth (0.87 [0.76, 1.00]); and
  - More likely to have a postpartum hemorrhage (1.14 [1.00, 1.30]).
- High third trimester virtual care (Trajectory 3): These participants were:
  - Less likely to be diagnosed with gestational hypertension (0.84 [0.73, 0.96]);
  - More likely to deliver preterm (1.35 [1.16, 1.58]) at 28 to 33^{+6} or 34 to 36^{+6} weeks' gestation;
  - More likely to give birth by elective or emergency cesarean section;
  - Less likely to have a third-degree or fourth-degree vaginal tear (0.82 [0.75, 0.90]);
  - Less likely to have early skin-to-skin (0.82 [0.73, 0.92]) with the newborn;

TABLE 1
Maternal registration of antenatal care data, stratified by trajectories obtained using group-based trajectory modeling[a] (n = 34,114)

Baseline characteristics	All (n=34,114)	Trajectory 0 (n=27,751) stable	Trajectory 1 (n=832) high first trimester	Trajectory 2 (n=2410) high second trimester	Trajectory 3 (n=3121) high third trimester
		Mean (standard deviation)/median (interquartile range)/N (%)[b]			
Midwifery only care type	7740 (22.7%)	6244 (22.5%)	194 (23.3%)	539 (22.4%)	763 (24.4%)
Registration appt pandemic time point					
October 1, 2018—March 22, 2020	12,092 (35.4%)	10,806 (38.9%)	117 (14.1%)	270 (11.2%)	899 (28.8%)
March 23, 2020—June 23, 2020	2151 (6.3%)	1384 (5.0%)	107 (12.9%)	294 (12.2%)	366 (11.7%)
June 24, 2020—November 4, 2020	2800 (8.2%)	1867 (6.7%)	54 (6.5%)	316 (13.1%)	563 (18.0%)
November 5, 2020—January 5, 2021	1321 (3.9%)	897 (3.2%)	29 (3.5%)	152 (6.3%)	243 (7.8%)
January 6, 2021—July 17, 2021	4638 (13.6%)	3367 (12.1%)	173 (20.8%)	505 (21.0%)	593 (19.0%)
July 18, 2021—May 4, 2023	11,112 (32.6%)	9430 (34.0%)	352 (42.3%)	873 (36.2%)	457 (14.6%)
Maternal age (y)	32.7 (5.4)	32.7 (5.38)	32.5 (5.40)	33.2 (5.11)	32.9 (5.35)
Age <20 years	412 (1.2%)	356 (1.3%)	9 (1.1%)	14 (0.6%)	33 (1.1%)
BMI at registration (kg/m^2)	24.3 (21.7, 28.2)	24.3 (21.7, 28.3)	24.2 (21.4, 28.2)	24.2 (21.6, 28.3)	24.3 (21.6, 28.1)
Missing	1502 (4.4%)	1038 (3.7%)	144 (17.4%)	144 (6.0%)	176 (5.6%)
Obesity (BMI ≥30.0 kg/m^2)	5873 (17.2%)	4824 (17.4%)	113 (13.6%)	431 (17.9%)	506 (16.2%)
Gestation at registration (wk)	9.7 (8.6, 12.3)	9.9 (8.6, 12.4)	10.6 (8.9, 12.4)	9.6 (8.7, 11.6)	9.1 (8.3, 11.1)
Late registration (at >16 weeks)	4604 (13.5%)	4043 (14.6%)	8 (1.0%)	200 (8.3%)	353 (11.3%)
Ethnicity					
White	17,346 (50.8%)	14,070 (50.7%)	389 (46.8%)	1265 (52.5%)	1622 (52.0%)
Asian or Asian British	3367 (9.9%)	2763 (10.0%)	101 (12.1%)	249 (10.3%)	254 (8.1%)
Black, Caribbean, or African	7082 (20.8%)	5726 (20.6%)	179 (21.5%)	507 (21.0%)	670 (21.5%)
Mixed or multiple ethnic groups	1822 (5.3%)	1501 (5.4%)	55 (6.6%)	137 (5.7%)	129 (4.1%)
Other ethnic group	2314 (6.8%)	1875 (6.8%)	69 (8.3%)	176 (7.3%)	194 (6.2%)
Missing	2183 (6.4%)	1816 (6.5%)	39 (4.7%)	76 (3.2%)	252 (8.1%)
Index of multiple deprivation					
Most deprived	6607 (19.4%)	5395 (19.4%)	174 (20.9%)	447 (18.5%)	591 (18.9%)
2	14,079 (41.3%)	11,566 (41.7%)	342 (41.1%)	987 (41.0%)	1184 (37.9%)
3	8459 (24.8%)	6790 (24.5%)	180 (21.6%)	570 (23.7%)	919 (29.4%)
4	3146 (9.2%)	2523 (9.1%)	82 (9.9%)	253 (10.5%)	288 (9.2%)

(continued)

TABLE 1
Maternal registration of antenatal care data, stratified by trajectories obtained using group-based trajectory modeling[a] (n = 34,114) *(continued)*

Baseline characteristics	All (n=34,114)	Trajectory 0 (n=27,751) stable	Trajectory 1 (n=832) high first trimester	Trajectory 2 (n=2410) high second trimester	Trajectory 3 (n=3121) high third trimester
		Mean (standard deviation)/median (interquartile range)/N (%)[b]			
Least deprived	1273 (3.7%)	1026 (3.7%)	38 (4.6%)	110 (4.6%)	99 (3.2%)
Missing	550 (1.6%)	451 (1.6%)	16 (1.9%)	43 (1.8%)	40 (1.3%)
Difficulty understanding English	2400 (7.0%)	2033 (7.3%)	60 (7.2%)	124 (5.1%)	183 (5.9%)
Drug use					
Current	140 (0.4%)	117 (0.4%)	1 (0.1%)	8 (0.3%)	14 (0.5%)
In previous 12 months	452 (1.3%)	387 (1.4%)	6 (0.7%)	17 (0.7%)	51 (1.6%)
Any previous	2227 (6.5%)	1827 (6.6%)	32 (3.8%)	136 (5.6%)	232 (7.4%)
Nulliparous	18,151 (53.2%)	14,711 (53.0%)	425 (51.1%)	1270 (52.7%)	1745 (55.9%)
Multiparous women only (n=15,963)					
Previous cesarean	5084 (31.9%)	4063 (31.2%)	143 (35.1%)	391 (34.3%)	487 (35.4%)
Previous stillbirth	291 (1.8%)	236 (1.8%)	11 (2.7%)	15 (1.3%)	29 (2.1%)
Previous PPH	1400 (8.8%)	1092 (8.4%)	30 (7.4%)	123 (10.8%)	155 (11.3%)
Previous preterm birth	1211 (7.6%)	951 (7.3%)	32 (7.9%)	101 (8.9%)	127 (9.2%)

BMI, body mass index; *PPH*, postpartum hemorrhage.

[a] Negative binomial regression using offset command; [b] Binary and categorical variables are presented using counts and percentages. Continuous variables are summarized by mean and standard deviation or median and IQR depending on the distribution of the data.

TABLE 2
Birth outcomes, stratified by trajectories obtained using group-based trajectory modeling (n = 34,114)

Birth outcomes	All (n=34,114)	Trajectory 0 (n=27,751) stable	Trajectory 1 (n=832) high first trimester	Trajectory 2 (n=2410) high second trimester	Trajectory 3 (n=3121) high third trimester
		Mean (standard deviation)/N (%)			
N antenatal appointments	9 (7, 12)	9 (7, 12)	9 (7, 12)	10 (8, 12)	10 (7, 13)
Virtual appointments	1 (0, 2)	1 (0, 2)	2 (1, 3)	2 (1, 3)	4 (2, 5)
Delivery time point					
October 1, 2018—March 22, 2020	7770 (22.8%)	7404 (26.7%)	95 (11.4%)	58 (2.4%)	213 (6.8%)
March 23, 2020—June 23, 2020	2058 (6.0%)	1820 (6.6%)	12 (1.4%)	6 (0.2%)	220 (7.0%)
June 24, 2020—November 4, 2020	3064 (9.0%)	2095 (7.5%)	56 (6.7%)	319 (13.2%)	594 (19.0%)
November 5, 2020—January 5, 2021	1252 (3.7%)	823 (3.0%)	46 (5.5%)	166 (6.9%)	217 (7.0%)
January 6, 2021—July 17, 2021	4404 (12.9%)	2961 (10.7%)	102 (12.3%)	503 (20.9%)	838 (26.9%)
July 18, 2021—July 8, 2023	15,566 (45.6%)	12,648 (45.6%)	521 (62.6%)	1358 (56.3%)	1039 (33.3%)
Gestational hypertension[a]	4119 (12.1%)	3425 (12.3%)	132 (15.9%)	283 (11.7%)	279 (9.0%)
Smoker at delivery	857 (2.5%)	679 (2.4%)	23 (2.8%)	64 (2.7%)	91 (2.9%)
Risk factors at birth[b]	10,973 (31.6%)	8799 (31.7%)	226 (27.2%)	769 (31.9%)	999 (32.0%)
Gestation at delivery					
Pre 24 wk	42 (0.1%)	36 (0.1%)	-	6 (0.2%)	-
24^{+0}—27^{+6} wk	153 (0.5%)	116 (0.4%)	5 (0.6%)	20 (0.8%)	12 (0.4%)
28^{+0}—33^{+6} wk	455 (1.3%)	357 (1.3%)	10 (1.2%)	34 (1.4%)	54 (1.7%)
34^{+0}—36^{+6} wk	1344 (3.9%)	1051 (3.8%)	34 (4.1%)	103 (4.3%)	156 (5.0%)
≥37 wk	32,120 (94.1%)	26,191 (94.4%)	783 (94.1%)	2247 (93.2%)	2899 (92.9%)
Induced	7490 (22.0%)	6014 (21.7%)	195 (23.4%)	589 (24.4%)	692 (22.2%)
Mode of delivery					
Vaginal unassisted	15,981 (46.9%)	13,141 (47.4%)	391 (47.0%)	1114 (46.2%)	1335 (42.8%)
Assisted vaginal	5051 (14.8%)	4164 (15.0%)	100 (12.0%)	314 (13.0%)	473 (15.2%)
Elective CS	5547 (16.3%)	4374 (15.8%)	145 (17.4%)	426 (17.7%)	602 (19.3%)
Emergency CS	7535 (22.1%)	6072 (21.9%)	196 (23.6%)	556 (23.1%)	711 (22.8%)
Breech presentation	93 (0.3%)	73 (0.3%)	-	12 (0.5%)	8 (0.3%)
Third-degree/fourth-degree vaginal tear	525 (1.5%)	441 (1.6%)	15 (1.8%)	32 (1.3%)	37 (1.2%)
PPH	3426 (10.0%)	2766 (10.0%)	96 (11.5%)	289 (12.0%)	275 (8.8%)

(continued)

TABLE 2
Birth outcomes, stratified by trajectories obtained using group-based trajectory modeling (n = 34,114) *(continued)*

Birth outcomes	All (n=34,114)	Trajectory 0 (n=27,751) stable	Trajectory 1 (n=832) high first trimester	Trajectory 2 (n=2410) high second trimester	Trajectory 3 (n=3121) high third trimester
		Mean (standard deviation)/N (%)			
5-min Apgar <7	494 (1.5%)	407 (1.5%)	11 (1.3%)	39 (1.6%)	37 (1.2%)
Birth outcome					
Live birth	33,889 (99.3%)	27,567 (99.3%)	826 (99.3%)	2390 (99.2%)	3106 (99.5%)
Stillbirth	138 (0.4%)	109 (0.4%)	3 (0.4%)	12 (0.5%)	14 (0.4%)
Neonatal death	79 (0.2%)	68 (0.2%)	3 (0.4%)	7 (0.3%)	1 (0.0%)
Infant death	8 (0.02%)	7 (0.0%)	-	1 (0.0%)	-
Birth outcome					
Live birth	993/1000	993/1000	993/1000	992/1000	995/1000
Stillbirth	3.93/1000	3.92/1000	3.6/1000	4.98/1000	4.49/1000
Neonatal death	2.31/1000	2.45/1000	3.6/1000	2.90/1000	0.32/1000
Infant death	0.23/1000	0.25/1000	-	0.41/1000	-
Sex (male)	17,438 (51.1%)	14,158 (51.0%)	428 (51.4%)	1278 (53.0%)	1574 (50.4%)
Early skin-to-skin contact	29,914 (88.3%)	24,411 (88.5%)	730 (88.1%)	2108 (88.0%)	2665 (86.3%)
SGA <10th	2350 (6.9%)	1905 (6.9%)	58 (7.0%)	160 (6.6%)	227 (7.3%)
SGA <10th (GA ≥280 d) n=14,081	658 (4.7%)	551 (4.7%)	14 (4.2%)	51 (5.3%)	42 (3.8%)
NICU admission	1929 (5.6%)	1534 (5.5%)	54 (6.5%)	140 (5.8%)	201 (6.4%)
First feed (breast milk)	28,978 (84.9%)	23,654 (85.2%)	744 (89.4%)	2075 (86.1%)	2505 (80.3%)

CS, cesarean section; *GA*, gestational age; *NICU*, neonatal intensive care unit; *PPH*, postpartum hemorrhage; *SGA*, small-for-gestational age.

[a] Gestational hypertension was defined as a systolic blood pressure [BP] ≥140 mmHg or diastolic BP ≥90 mmHg at ≥20 weeks' gestation, in women without prior chronic hypertension; [b] Risk factors at birth were as identified by clinicians in real-time, as conditions that developed antepartum (ie, GDM, high blood pressure [any], proteinuria, or preeclampsia specifically, low iron, reduced fetal movement) or intrapartum (ie, malpresentation, hemorrhage/vaginal blood loss, placenta abruption specifically, infection, meconium, suspicious or pathological fetal heart rate trace or other concerns, uterine rupture, delayed labor, or need for labor augmentation), in addition to chronic hypertension, pregestational diabetes, and GDM if not otherwise included.

TABLE 3
Unadjusted and adjusted associations between the trajectories and birth outcomes in women and their children from the eLIXIR-BiSL cohort

Birth outcomes	Trajectory 0 (n=27,751) stable	Trajectory 1 (n=832) high first trimester	Trajectory 2 (n=2410) high second trimester	Trajectory 3 (n=3121) high third trimester
Unadjusted findings	Incidence rate ratio/relative risk ratio (95% confidence interval)			
Smoker at delivery[a]	Ref	1.10 (0.72, 1.67)	1.06 (0.81, 1.36)	1.18 (0.97, 1.47)
Gestation at delivery				
Before 24^{+0} wk	Ref	-	1.94 (0.82, 4.61)	NA
24^{+0}–27^{+6} wk		1.44 (0.58, 3.54)	**2.00 (1.24, 3.23)**[b]	0.93 (0.52, 1.70)
28^{+0}–33^{+6} wk		0.93 (0.50, 1.58)	1.11 (0.78, 1.58)	**1.37 (1.68, 2.68)**[c]
34^{+0}–36^{+6} wk		1.08 (0.76, 1.53)	1.14 (0.92, 1.40)	**1.34 (1.13, 1.59)**[b]
≥37 wk		Ref	Ref	Ref
Induced	Ref	1.06 (0.94, 1.30)	**1.17 (1.06, 1.29)**[b]	1.03 (0.94, 1.13)
Mode of delivery				
Vaginal unassisted	Ref	Ref	Ref	Ref
Assisted vaginal		0.81 (0.65, 1.00)	0.89 (0.78, 1.01)	**1.12 (1.00, 1.25)**[c]
Elective CS		1.14 (0.92, 1.35)	**1.15 (1.02, 1.29)**[c]	**1.35 (1.22, 1.50)**[d]
Emergency CS		1.08 (0.91, 1.29)	1.08 (0.97, 1.20)	**1.15 (1.05, 1.26)**[b]
Breech		-	**1.89 (1.03, 3.50)**[c]	0.97 (0.47, 2.02)
Third/fourth degree				
Ref	1.10 (0.66, 1.86)	0.81 (0.56, 1.16)	**0.72 (0.51, 1.00)**[c]	
PPH	Ref	1.18 (0.95, 1.46)	**1.23 (1.08, 1.40)**[b]	**0.87 (0.77, 0.99)**[c]
Apgar at 5 min less than 7				
Ref	0.90 (0.49, 1.65)	1.10 (0.79, 1.54)	0.82 (0.58, 1.13)	
Birth outcome				
Live birth	Ref	Ref	Ref	Ref
Stillbirth		0.92 (0.29, 2.90)	1.27 (0.70, 2.30)	1.13 (0.65, 1.99)
Neonatal death		1.47 (0.46, 4.68)	1.19 (0.54, 2.59)	**0.13 (0.02, 0.94)**[c]
Infant death		-	1.65 (0.20, 13.40)	-
Sex (female)	Ref	0.98 (0.87, 1.13)	0.92 (0.85, 1.00)	1.02 (0.95, 1.10)
SGA <10th percentile	Ref	1.01 (0.77, 1.33)	0.97 (0.82, 1.14)	1.06 (0.92, 1.22)
Skin-to-skin (yes)	Ref	0.96 (0.77, 1.18)	0.94 (0.83, 1.08)	**0.82 (0.73, 0.91)**[d]
NICU admission	Ref	1.19 (0.89, 1.57)	1.05 (0.88, 1.26)	**1.18 (1.01, 1.37)**[c]
Gestational hypertension	Ref	**1.33 (1.11, 1.62)**[b]	0.95 (0.83, 1.08)	**0.69 (0.61, 0.79)**[b]
Adjusted findings				
Number of appointments[a]		**0.94 (0.92, 0.97)**[b]	1.00 (0.98, 1.01)	**1.04 (1.03, 1.06)**[b]
Smoker at delivery[e]	Ref	1.30 (0.85, 2.01)	1.18 (0.90, 1.55)	1.19 (0.94, 1.51)
Gestational hypertension	Ref	1.09 (0.90, 1.32)	**0.84 (0.74, 0.96)**[c]	**0.84 (0.73, 0.96)**[c]
Preterm <37 wk		1.02 (0.76, 1.38)	**1.21 (1.02, 1.44)**[c]	**1.35 (1.16, 1.58)**[d]

(continued)

TABLE 3
Unadjusted and adjusted associations between the trajectories and birth outcomes in women and their children from the eLIXIR-BiSL cohort *(continued)*

Birth outcomes	Trajectory 0 (n=27,751) stable	Trajectory 1 (n=832) high first trimester	Trajectory 2 (n=2410) high second trimester	Trajectory 3 (n=3121) high third trimester
Unadjusted findings	Incidence rate ratio/relative risk ratio (95% confidence interval)			
Gestation at delivery				
$<24^{+0}$ wk	Ref	-	-	-
24^{+0}–27^{+6} wk		1.24 (0.50, 3.08)	**1.79 (1.10, 2.93)**[c]	0.94 (0.50, 1.76)
28^{+0}–33^{+6} wk		0.89 (0.47, 1.69)	1.15 (0.80, 1.65)	**1.60 (1.18, 2.18)**[b]
34^{+0}–36^{+6} wk		1.08 (0.76, 1.54)	1.15 (0.93, 1.41)	**1.37 (1.14, 1.65)**[d]
≥37 wk		Ref	Ref	Ref
Induced	Ref	1.06 (0.89, 1.25)	**1.13 (1.02, 1.25)**[c]	1.03 (0.93, 1.13)
Breech presentation		NA	**1.92 (1.02, 3.62)**[c]	1.16 (0.54, 2.50)
Mode of delivery				
Vaginal unassisted	Ref	Ref	Ref	Ref
Assisted vaginal		0.85 (0.67, 1.08)	**0.87 (0.76, 1.00)**[c]	0.94 (0.84, 1.07)
Elective CS		0.99 (0.81, 1.21)	1.06 (0.94, 1.19)	**1.54 (1.38, 1.72)**[d]
Emergency CS		0.98 (0.81, 1.17)	1.00 (0.89, 1.12)	**1.21 (1.01, 1.34)**[b]
Third-degree/fourth-degree vaginal tear	Ref	1.00 (0.86, 1.17)	0.96 (0.88, 1.05)	**0.82 (0.75, 0.90)**[d]
PPH	Ref	1.00 (0.80, 1.24)	**1.14 (1.00, 1.30)**[c]	1.07 (0.93, 1.22)
5-min Apgar <7	Ref	0.83 (0.45, 1.53)	1.05 (0.75, 1.48)	0.90 (0.63, 1.28)
Birth outcome				
Live birth	Ref	Ref	Ref	Ref
Stillbirth		0.87 (0.27, 2.78)	1.20 (0.65, 2.22)	1.11 (0.62, 2.01)
Neonatal death		1.42 (0.44, 4.64)	1.16 (0.52, 2.57)	0.13 (0.02, 0.97)
Sex (female)	Ref	0.98 (0.85, 1.12)	**0.91 (0.84, 0.99)**[c]	1.02 (0.94, 1.10)
SGA <10th percentile	Ref	1.00 (0.76, 1.31)	0.97 (0.81, 1.15)	1.06 (0.91, 1.24)
SGA <10th (GA ≥280 d)	Ref	0.83 (0.49, 1.42)	1.07 (0.79, 1.45)	0.91 (0.65, 1.27)
Early skin-to-skin contact	Ref	0.92 (0.73, 1.14)	0.91 (0.80, 1.04)	**0.82 (0.73, 0.92)**[d]
NICU admission	Ref	1.13 (0.85, 1.50)	1.04 (0.87, 1.24)	**1.28 (1.09, 1.50)**[b]
Breastfeeding	Ref	1.08 (0.86, 1.36)	0.95 (0.83, 1.07)	**0.90 (0.81, 0.99)**[c]

CS, cesarean section; *eLIXIR-BiSL*, early Life Cross-Linkage in Research, Born in South London; *GA*, gestational age; *NA*, not applicable; *NICU*, neonatal intensive care unit; *PPH*, postpartum hemorrhage; *Ref*, reference; *SGA*, small-for-gestational age.

Multinominal logistic was used to assess the relationship between the 4 trajectories and the birth outcomes, the reference group is the stable trajectory (group 0).

Models were adjusted for: parity, registration hospital, registration gestation, pandemic time point, smoking status at registration, and an interaction between index of multiple deprivation and ethnicity.

[a] Modeled using negative binominal regression, adjusted for parity, gestation at registration, and antenatal care type; [b] $P<.01$; [c] $P<.001$; [d] $P<.05$; [e] Not adjusted for smoking status.

- More likely for the newborn to be admitted to the neonatal intensive care unit (1.28 [1.09, 1.50]); and
- Less likely to breastfeed as the first feed (0.90 [0.81, 0.99]).

Sensitivity analyses

The exclusion of those without any antenatal care record appeared justified as these women (n=2174) were at higher risk of adverse outcomes, compared to those included (Supplemental Tables 8 and 9). This was evidenced by higher body mass index or obesity, late registration, and delivery <37 weeks' gestation. Their infants were less likely to be

breastfed and more likely be admitted to neonatal intensive care, be stillborn or to suffer a neonatal death. Inpatient antenatal care was also more prevalent.

In the second analysis, results were truncated to n=29,434 pregnancies, excluding those at the beginning and end of the study period, to minimize the impact of pregnancies that registered late or delivered early (Supplemental Table 10). Nevertheless, outcomes did not differ from the entire cohort (Table 3).

In the third analysis, stratified by parity, most point estimates had the same direction of effect, and the 95% confidence intervals overlapped, with some minor exceptions for nulliparous women with high first trimester virtual care (n=425).

Discussion

In this cohort of more than 34,000 pregnancies from a diverse, South London UK population, 4 distinct trajectories of virtual antenatal care were identified before and during the COVID-19 pandemic, including periods with and without lockdowns. These trajectories were characterized by distinct patterns of virtual care, including high first, second, or third trimester virtual antenatal care. For the majority of pregnancies, virtual antenatal care was low and stable throughout pregnancy. Compared with the low/stable group, a high proportion of virtual care during the second or third trimester was associated with less gestational hypertension and more adverse pregnancy outcomes for mothers (such as cesarean sections and postpartum hemorrhage) and babies (such as neonatal intensive care admission and lower rates of breastfeeding as the first feed). Notably, women who had no antenatal care after a registration appointment, and were excluded from the main analysis, experienced more adverse outcomes, compared with women who were included.

These observations contrast with 2 previous investigations. First, in an Australian study of routinely collected data from more than 27,000 births before and during the pandemic (January 2018 to April 2021),[24] an interrupted time series analysis found no differences in adverse pregnancy outcomes associated with telehealth-integrated antenatal care. These outcomes included preeclampsia, fetal growth restriction, and perinatal mortality. Second, a similar study of more than 12,000 pregnancies in the United States, also including the pandemic period, compared outcomes from May 2019 to October 2020 and found that the implementation of audio-only virtual prenatal visits was not associated with changes in perinatal outcomes.[34] The differences observed between the present findings and the results of these 2 published studies may reflect variations in analytical approaches. While interrupted time series is a valuable method for modeling the impact of an 'interruption' on outcomes over time, a latent class modeling approach, as used in this article, offers greater granularity by identifying distinct patterns of virtual antenatal care use across trimesters. Also, the relationship between time and pregnancy outcomes during the pandemic has been examined using generalized linear models in the eLIXIR-BiSL cohort, with no observed differences in patterns established prior to the pandemic.[35] Viewed together, these results suggest that a trajectory modeling approach (as used in our analysis) may reveal different trajectories of virtual care use and capture variations that were not identified by broader time-based analyses as undertaken in previous publications.

For decision-makers to fully evaluate policies related to the use of virtual antenatal care, evidence on clinical outcomes, costs, and patient experiences is essential. In this analysis, we observed adverse associations between virtual care and adverse pregnancy outcomes when virtual care was incorporated into care in the second or third trimesters of pregnancy. A key consideration is whether these associations reflect a causal-effect relationship of virtual care, or if women with more complex pregnancies are more likely to receive virtual care as part of enhanced monitoring. This study supports the former explanation: compared with the low and stable (predominantly in-person) group, there was no evidence of increased appointment frequency or higher risk factors at birth among women in the high second or third trimester trajectory groups. Furthermore, the lower prevalence of gestational hypertension observed in the high second and third virtual care groups may reflect underdiagnosis, as this is the period when gestational hypertension and preeclampsia are typically diagnosed through repeated blood pressure monitoring, but this is less likely to occur during virtual appointments.

There was no association between virtual antenatal care at registration and adverse pregnancy outcomes. In England, this raises questions about antenatal care that currently focusses on early first trimester registration. Models developed in other counties (eg, Scotland and Canada[36,37]) place greater emphasis on care later in pregnancy, when complications are more likely to arise. Whether England should consider refocusing face-to-face care toward later pregnancy would first require validation of our findings in other cohorts.

In an interrupted time series analysis of data from the same eLIXIR-BiSL cohort, we reported that the pandemic was associated with a temporary reduction in healthcare utilization, with ongoing, rising maternity costs that were unchanged from prepandemic trajectories.[38] However, we found that virtual antenatal care was associated with higher costs, with a 1% increase in virtual care associated with a £7 (£3 to £10) rise in maternity costs.

Experiences with virtual care have been predominantly negative, both among pregnant women[11] and maternity care providers.[8,13–20] A systematic review reported that women often expressed concerns about disrupted care, safety, and limited access to adequate technology. Similarly, studies involving maternity care providers[8,13–20] have described a decline in perceived care quality and raised concerns about digital exclusion of certain population groups.

Nevertheless, others have reported potential benefits of virtual care, including increased convenience and

flexibility,[11] which may be particularly valuable in rural areas, or for those with inflexible commitments such as childcare.[39,40] However, accessing these benefits depends on having mobile data, internet-enabled devices, and a private space to participate in virtual care.[7] A recent review concluded that digital barriers such as these could be addressed by designing virtual care systems that are tailored to users' needs, digital literacy, and available resources.[41]

Interpretation and future implications

We provide evidence that virtual care during the second and third trimesters of pregnancy is associated with poorer clinical outcomes. These findings highlight the need for careful consideration when implementing virtual care as part of routine care during future health system shocks, or in maternity care outside of health crises. Women interested in some component of virtual antenatal care and identified as being at very low risk may benefit from the provision of some virtual care, but this requires discussion. Although virtual care is a valuable tool for improving access, it has the potential to reinforce or amplify existing health disparities, especially for disadvantaged populations. Further investigations are required to clarify outcomes in relation to maternal ethnicity and deprivation, as well as the underlying rationale for virtual appointments, whether provider or patient driven. Structured virtual care could be acceptable and effective in uncomplicated pregnancies; however, digital exclusion, driven by factors such as limited internet access, language barriers, or low digital literacy, may restrict access to and engagement with virtual antenatal care, exacerbating existing health inequities. Future research should explore how flexible care models might better support these women.

Strengths and limitations

This analysis has several strengths; eLIXIR-BiSL is a population-based cohort which incorporates demographic, maternal, and neonatal health records from a multiethnic and socially deprived inner-city population of pregnant women. The granularity of the data enabled modeling of virtual care trajectories, exploration of their associations with pregnancy outcomes, and evaluation of group-based trajectory modeling using several model adequacy criteria.

Limitations to the use of any routinely collected data include missingness and a lack of standardization. Also, we inferred that care was 'virtual' when all of 3 key assessments were missing; this assumption is supported by the overall robustness of NHS care standards. Nevertheless, some in-person visits may have had incomplete documentation, and others may have included partial assessments, leading to possible misclassification which could bias the observed associations.

Some methodological and analytical limitations should be considered in interpretation of the data. Group-based trajectory modeling assumes each trajectory group has a fixed shape (eg, linear or quadratic), and within each trajectory, the slope and intercept are constant for all individuals; violating these assumptions can affect classification accuracy.[42,43] The data may be subject to reverse causation (meaning that early signs of pregnancy complications may have led to the subsequent use of virtual care) or indication bias (whereby patients with certain underlying characteristics or risks were more likely to receive virtual care). Although we attempted to address these sources of bias through sensitivity analyses and adjustment for confounders, the reported associations may still reflect unmeasured or unrecorded risk factors that influenced both virtual care uptake and pregnancy outcomes. Additionally, given the exploratory nature of this study and the broad range of pregnancy outcomes examined, we have not adjusted for multiple testing.

We were unable to adjust for SARS-CoV-2 positivity, due to the low prevalence rate of 0.1% in this cohort, as reported previously in England.[44] The exclusion of multiple pregnancies also limits generalizability of our findings to multiple pregnancies. The cohort included a low proportion of pregnancies receiving midwifery-only care (approximately 23%), limiting the ability to explore relationships between virtual care and outcomes in this group.

Compared to other reports, trajectory modeling offers advantages over interrupted time series in interpreting the influence of virtual care. However, group-based trajectory modeling cannot fully account for other contemporaneous changes to antenatal care introduced during the pandemic. These include managing women with a history of gestational diabetes as although they had current gestational diabetes, the use of fasting/random blood glucose and HbA1c in the diagnosis of gestational diabetes[29] and the adoption of home blood pressure monitoring in high-risk pregnancies.[30] As observed, the absence of routine monitoring of blood pressure may have contributed to adverse outcomes; however, this is also an inherent feature and potential limitation of virtual antenatal care itself.

Conclusion

This study identified distinct patterns of virtual antenatal care use during pregnancy in a diverse UK inner-city population. Virtual care delivered during the second or third trimester was associated with adverse outcomes for both mothers and babies. These associations highlight the need for further research to guide when and how virtual care should be implemented. Caution is advised when replacing in-person care with a virtual alternative, especially during future health system disruptions, but also as part of future service planning. ■

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Data availability: The data accessed by eLIXIR remain within an NHS firewall and governance is provided by the eLIXIR Oversight Committee which reports to relevant information governance clinical leads. Subject to these conditions, data access is encouraged and those interested should contact the eLIXIR Chief Investigator (Professor Lucilla Poston; Lucilla.poston@kcl.ac.uk). Access can also be requested through the HDRUK Innovation Gateway (https://web.www.healthdatagateway.org/dataset/3c780d45-ed7b-4101-9c32-d50512cd9cfe).

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Data linkage

This linkage of maternity and neonatal and maternal mental health records was created in 2018, generating a repository of real-time, pseudonymised, structured data derived from the electronic health record systems of National Health Service (NHS) providers in South London, UK including 2 acute (Guy's and St Thomas' Hospital NHS Foundation Trust and King's College Hospital NHS Foundation Trust), and one mental health (South London and Maudsley NHS Foundation Trust [SLaM]) provider, together with primary care data (Lambeth DataNet for women registered in the London borough of Lambeth). These data include pregnancy records from antenatal registration appointments and assessments to birth and birth outcomes, blood test results, mental health records from secondary and community care, and postnatal information for mothers and babies up to 6 weeks after birth.

Early Life Cross-Linkage in Research data

Clinical data from maternity and neonatal service datasets at the 2 sites Guy's and St Thomas' Hospital NHS Foundation Trust and King's College Hospital NHS Foundation Trust (Badgernet System C.com) are extracted by NHS information and communication technology staff. Following secure transfer to the SLaM Clinical Data Linkage Service (CDLS), antenatal data are linked in the CDLS Trusted Research Environment, using common identifiers, with mental health data (as relevant) from the SLaM Clinical Record Interactive Service system, and with primary care records. Match quality is 98.5% for infants with their mothers' records. Results from all linkages (current and prior) are stored within the CDLS Trusted Research Environment, as are the identifier fields (used to create a 'master patient index') required for data linkage. This process is summarized in Supplemental Figure 1.

NHS patients in the United Kingdom have the opportunity to opt out of all research by advising their general practitioner, and their data are automatically excluded from research downloads at source. Opt-out information and details of the project are also given to each patient entering maternity and neonatal services providing the option of opting out of the program at any time, based on Section 251 approval under the NHS Act 2006 granted by the Health Research Authority Confidentiality Advisory Group to the eLIXIR team for all the standard linkages. Data are available in an identifiable format to only a small number of data-processing staff, in accordance with data sharing contracts between the data provider institutions (Health Research Authority Confidentiality Advisory Group Ref: 18/CAG/0040). Ethical approval for use of clinical data was obtained from the South Central−Oxford C Research Ethics Committee (18/SC/0086, 2018−23; renewal 23/SC/0116, 2023−8).

Adjustment: IMD, registration gestation, registration hospital, parity, pandemic time, and smoking status.

dag {
bb="0,0,1,1″
"Smoking status" [adjusted, pos="0.769,0.169"]
"birth outcomes" [outcome, pos="0.892,0.472"]
"maternal age" [pos="0.240,0.906"]
"registration gestation" [pos="0.474,0.405"]

"registration hospital" [pos="0.075,0.202"]
"virtual care" [exposure, pos="0.099,0.487"]
BMI [pos="0.780,0.611"]
IMD [pos="0.077,0.752"]
comorbidities [pos="0.700,0.818"]
ethnicity [pos="0.174,0.588"]
pandemic [pos="0.273,0.083"]
parity [pos="0.510,0.638"]
time [pos="0.500,0.213"]
"Smoking status" -> "birth outcomes"
"Smoking status" -> "registration gestation"
"Smoking status" -> BMI.
"Smoking status" -> comorbidities [pos="0.653,0.623"]
"maternal age" -> "birth outcomes"
"maternal age" -> "registration gestation"
"maternal age" -> BMI.
"maternal age" -> comorbidities.
"maternal age" -> parity.
"registration gestation" -> "birth outcomes"
"registration gestation" -> "virtual care"
"registration hospital" -> "birth outcomes" [pos="0.487,0.251"]
"registration hospital" -> "virtual care"
"virtual care" -> "birth outcomes"
BMI -> "birth outcomes"
BMI -> comorbidities.
IMD -> "Smoking status" [pos="0.532,0.521"]
IMD -> "birth outcomes"
IMD -> "maternal age"
IMD -> "registration gestation"
IMD -> "registration hospital" [pos="0.003,0.465"]
IMD -> "virtual care"
IMD -> BMI.
IMD -> comorbidities.
IMD -> parity [pos="0.334,0.759"]
IMD <-> ethnicity
comorbidities -> "registration gestation"
ethnicity -> "Smoking status" [pos="0.490,0.259"]
ethnicity -> "birth outcomes"
ethnicity -> "maternal age"
ethnicity -> "registration gestation"
ethnicity -> "registration hospital" [pos="0.231,0.402"]
ethnicity -> BMI
ethnicity -> comorbidities
ethnicity -> parity
pandemic -> "birth outcomes" [pos="0.583,0.028"]
pandemic -> "registration gestation"
pandemic -> "virtual care"
pandemic -> time
parity -> "birth outcomes"
parity -> "registration gestation"
parity -> "virtual care" [pos="0.347,0.559"]
parity -> BMI
parity -> comorbidities
time -> "birth outcomes"
time -> "virtual care" }

Summary of group-based trajectory modelling

Model adequacy

Bayesian Information Criterion (BIC) is calculated for each model and is a likelihood-based statistic, a value closer to zero implies better model fit.[3] The average posterior probability assignment (APPA) was calculated for each participant, with the value representing the average posterior probability of belonging to a class over all individuals assigned to a class. The APPA trajectory mean should be more than 70%.[4] The odds of correct classification for each trajectory should be greater than 5. The odds of correct classification are trajectory specific; it is the ratio of the odds of a correct classification into each trajectory. Each trajectory should hold a group membership of at least 5%.[3] However, this is dependent on sample size; the minimum sample size recommended for latent class modelling is between 300 and 500, but if there is a much larger sample size then group membership can be less than 5%.[5,6] Relative entropy estimates the accuracy (convergence) of classification of individuals into the different latent classes.[7] Entropy values close to 1 indicate greater classification certainty.[3]

Model selection

The objective of model selection is to summarize the distinct features of the data considering parsimony, interpretability, and model adequacy. The BIC value is commonly used to assess the appropriate number of trajectories. However, BIC values may decrease as more classes are added reflecting model overfit.[3] It is therefore advised that the number of trajectories chosen be based on the lowest BIC and satisfactory values for the remaining criteria.

Group-based trajectory modelling

Group-based trajectory modelling (GBTM) is a semi-parametric technique used to identify distinct trajectories. Each individual in the eLIXIR-BiSL cohort had a distinct pattern of vANC during their pregnancy and distinct changes in their pattern over time, GBTM allows for the distribution of individual differences within the data to be clustered. Given that the strength and direction of change can vary for each trajectory, an intercept and slope are generated for each trajectory. GBTM fixes the slope and the intercept equally across individuals within a trajectory. GBTM can handle trajectories in the same model that follow a different pattern/shape (eg, intercept, linear, quadratic, and cubic). As there were 6 gestational epochs, our analysis can accommodate cubic shape trajectories (as these require a minimum of 4 data points). GBTM handles missing data under the 'missing at random' assumption as the model uses maximum likelihood estimation.

When applying GBTM to the data, the intercept, linear, quadratic, and cubic functions of each trajectory can be tested. To ensure model parsimony, nonsignificant cubic and quadratic terms are removed. However, linear parameters can be retained irrespective of significance as long as the BIC is lower than if an intercept parameter was used. This process is repeated until there is no evidence of an improvement in model fit assessed. A summary of the model fit criteria is summarized in Supplemental Table 5. Our analysis was also confirmed using latent class analysis.

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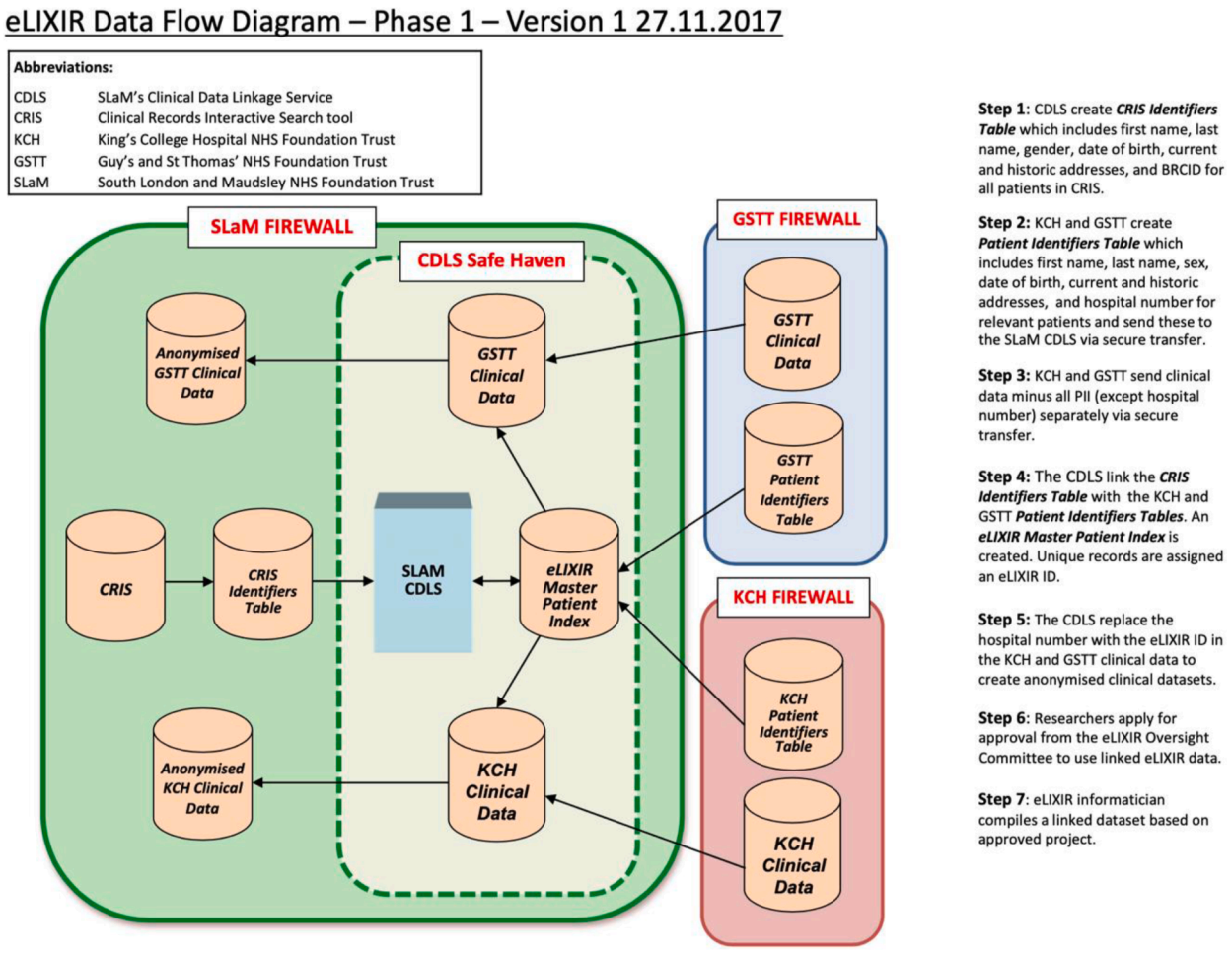
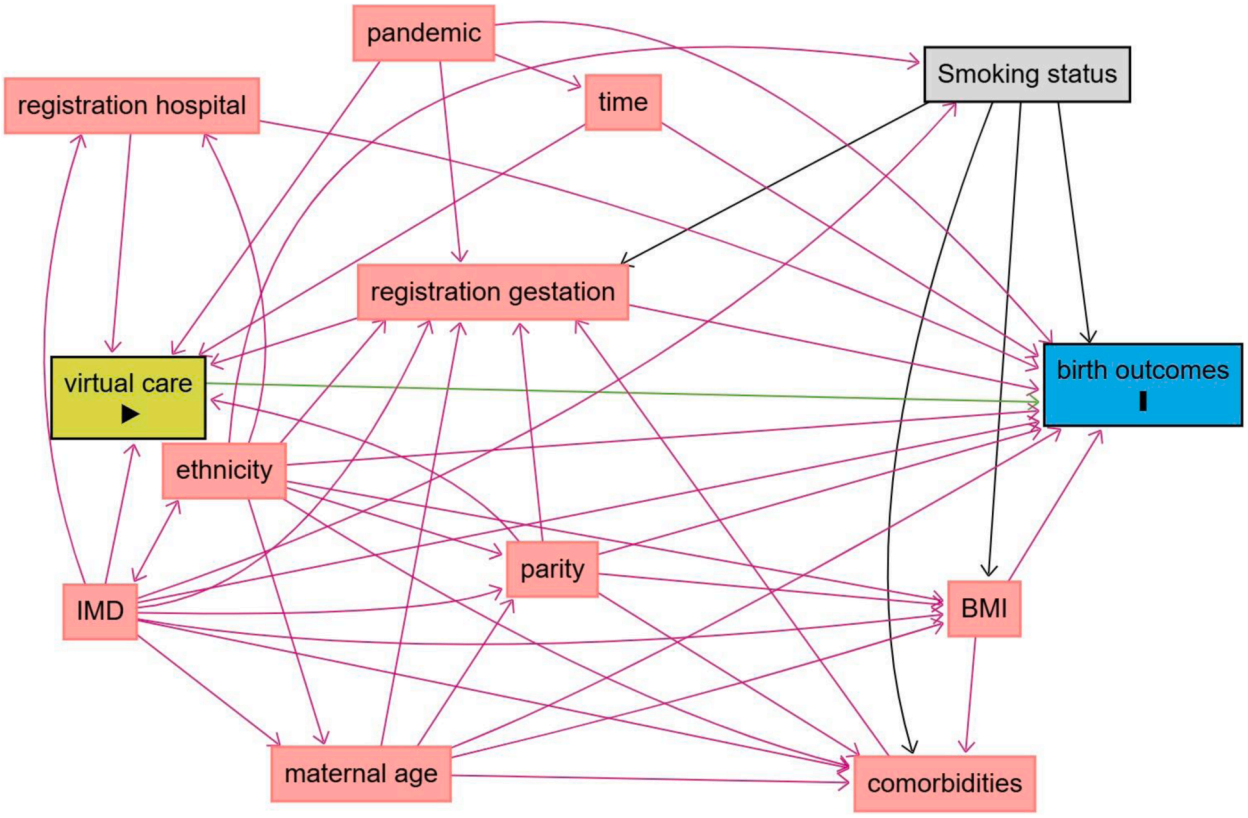
SUPPLEMENTAL FIGURE 1
Data flow diagram for the eLIXIR-BiSL data linkage

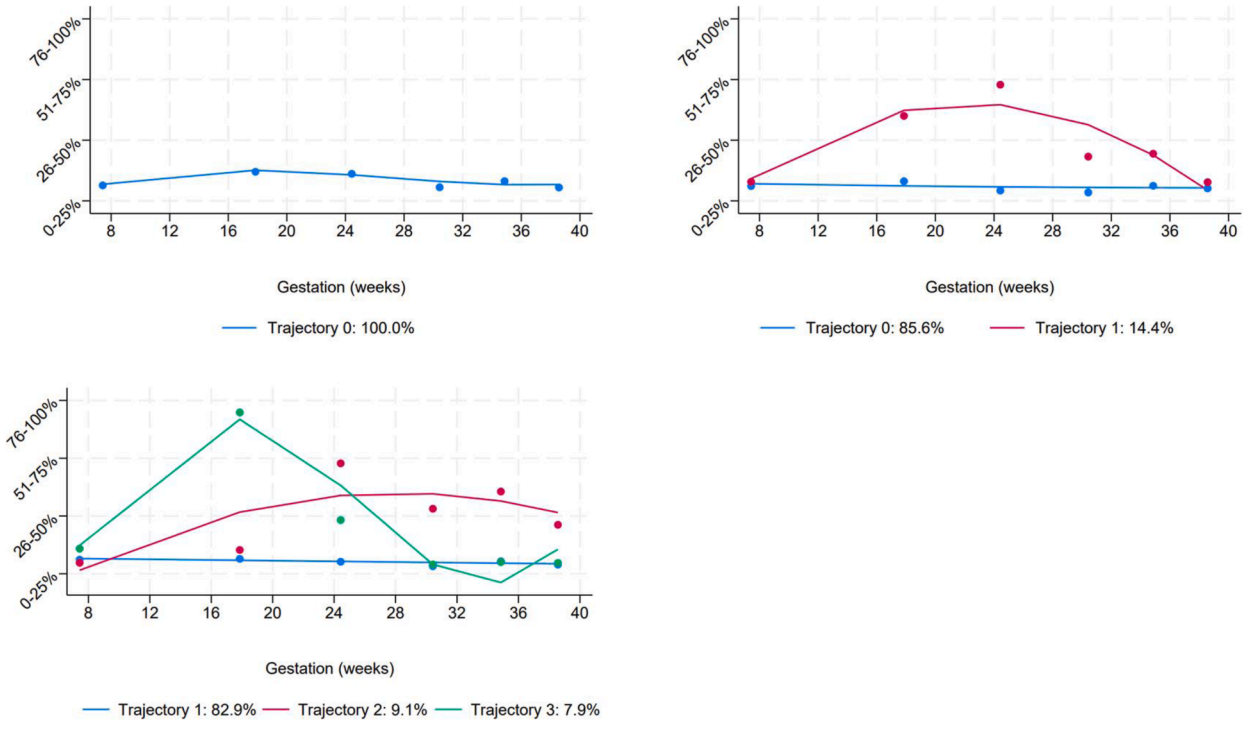


BiSL, born in south london; *CDLS*, clinical data-linkage service; *eLIXIR*, early life cross-linkage in research; *SlaM*, south london and maudsley national health service foundation trust.

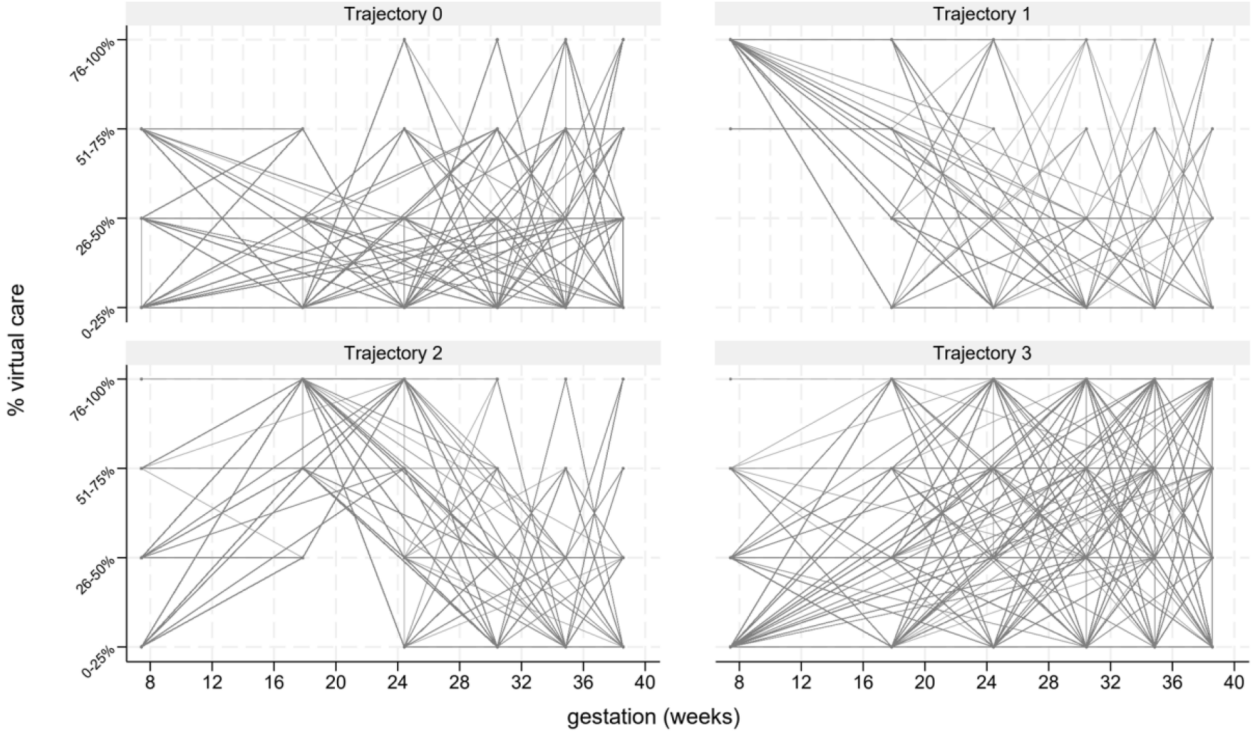
SUPPLEMENTAL FIGURE 2
Direct acyclic graph for virtual care and birth outcomes (co-morbidities are chronic hypertension and pre-gestational diabetes)



SUPPLEMENTAL FIGURE 3
Trajectories for models 1 to 3



SUPPLEMENTAL FIGURE 4
Individual trajectories



SUPPLEMENTAL TABLE 1
The RESILIENT study group

Chief investigator	
Prof. Laura A. Magee	Professor of Women's Health, King's College London
Co-investigators	
Prof. Debra Bick	Professor of Clinical Trials in Maternal Health, University of Warwick
Dr Harriet Boulding	Research Fellow, The Policy Institute, King's College London
Prof. Peter von Dadelszen	Professor of Global Women's Health, King's College London
Dr Kathryn Dalrymple	Lecturer in Nutritional Sciences, King's College London
Ms. Tisha Dasgupta	Research Associate and PhD Candidate, King's College London
Prof. Emma L Duncan	Professor of Clinical Endocrinology, King's College London
Dr Abigail Easter	Reader in Perinatal Mental Health, King's College London
Prof. Julia Fox-Rushby	Professor of Health Economics, King's College London
Ms. Gillian Horgan	Operations Assistant, King's College London
Prof. Asma Khalil	Professor of Obstetrics and Maternal Fetal Medicine, St George's University Hospitals NHS Foundation Trust and Director of Fetal Medicine at Liverpool Women's Hospital NHS Foundation Trust.
Ms. Alice McGreevy	Research Assistant in Health Economics, King's College London
Dr Hiten D. Mistry	Senior Research Fellow, King's College London
Prof. Eugene C. Nelson	Professor of Community and Family Medicine, Dartmouth College
Prof. Lucilla Poston	Professor of Maternal & Fetal Health, King's College London
Mr. Paul Seed	Reader in Medical Statistics, King's College London
Mr. Sergio A. Silverio	Research Fellow in Social Science of Women's Health, King's College London and Lecturer in Medical Psychology & Lifecourse Health, University of Liverpool
Dr Marina Soley-Bori	Lecturer in Health Economics, King's College London
Dr Florence Tydeman	Research Associate in Medical Statistics, King's College London
Ms. Aricca Van Citters	Senior Research Scientist, Dartmouth College
Dr Sara White	Senior Clinical Lecturer in Women's Health & Diabetes, King's College London
Prof. Ingrid Wolfe	Professor of Paediatrics and Child Population Health, King's College London
Prof. Wang Yangzhong	Professor of Statistics in Population Health, King's College London

SUPPLEMENTAL TABLE 2

Members of the early Life Cross-Linkage in Research, Born in South London (eLIXIR-BiSL) partnership

Professor Lucilla poston	eLIXIR-BiSL Principal Investigator, and Professor of maternal & fetal health, Department of women and Children's health, School of life course and population Sciences, King's College London
Professor Laura A Magee	eLIXIR-BiSL Co-Investigator, Professor of Women's Health, Department of Women and Children's Health, School of Life Course and Population Sciences, King's College London
Professor Robert Stewart	eLIXIR-BiSL Co-Investigator Professor of Psychiatric Epidemiology & Clinical Informatics, Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London and NIHR Maudsley Biomedical Research Centre, South London and Maudsley NHS Foundation Trust, London. Consultant Psychiatrist at South London and Maudsley NHS Foundation Trust, London
Professor David Edwards	Chair in Paediatrics & Neonatal Medicine, Department of Perinatal Imaging and Health, King's College London. Neonatal Consultant at Guy's and St. Thomas' NHS Foundation Trust
Professor Mark Ashworth	Professor of Primary Care, Department of Population Health Sciences, School of Life Course and Population Sciences, King's College London
Professor Jane Sandall	Professor of Social Science & Women's Health, Department of Women and Children's Health, School of Life Course and Population Sciences, King's College London
Dr Ingrid Wolfe	Professor of Paediatrics and Child Population Health, Department of Women and Children's Health, School of Life Course and Population Sciences, King's College London and Consultant in Children's Public Health Medicine and Director of the Evelina London Children's Healthcare
Dr Cheryl Gillett	Head of Tissue Banking, Department of Comprehensive Cancer Centre, School of Cancer & Pharmaceutical Sciences, King's College London
Dr Michael Absoud	Paediatric Consultant at Evelina London Children's Healthcare
Dr Lucy Pickard	Consultant Paediatrician, King's College Hospital NHS Foundation Trust
Ms Amanda Grey	Lay member of the eLIXIR Oversight Committee
Ms Sarah Spring	Lay member of the eLIXIR Oversight Committee
Ms Toyin Kazeem	Information Governance Operations Lead, South London and Maudsley NHS Foundation Trust, London
Ms Amelia Jewell	Clinical Data Linkage Service Lead, NIHR Maudsley Biomedical Research Centre, South London and Maudsley NHS Foundation Trust
Mr Matthew Broadbent	CRIS Clinical Informatics Lead, NIHR Maudsley Biomedical Research Centre, South London and Maudsley NHS Foundation Trust, London
Ms Finola Higgins	Research Informatics Programme Manager, Guy's and St Thomas' NHS Foundation Trust

(continued)

SUPPLEMENTAL TABLE 2
Members of the early Life Cross-Linkage in Research, Born in South London (eLIXIR-BiSL) partnership *(continued)*

Mr Leonardo de Jongh	Data Warehouse Manager, Guy's and St. Thomas's Hospital NHS Foundation Trust
Ms Tisha Dasgupta	Research Associate and eLIXIR Coordinator, Department of Women & Children's Health, School of Life Course and Population Sciences, King's College London
Dr Carolyn Gill	School Bioresource Manager, School of Life Course and Population Sciences, King's College London.

SUPPLEMENTAL TABLE 3
Key pregnancy and birth indicators

(i) Organization performance indicators	measured at antenatal registration (ie, maternal age and N<20 years, ethnicity, index of multiple deprivation, complex social factors [eg, difficulty understanding English, or drug use currently, ever, or previously in the last 12 months], body mass index, prior cesarean, prior stillbirth, and gestational age at registration, including late registration >16 weeks, or at birth [interventional birth defined below], and skin-to-skin contact within 1 hour).
(ii) Clinical quality improvement metrics	measured at birth (ie, smoker at delivery, gestational age at birth, preterm birth <37 weeks, mode of birth, third-degree or fourth-degree vaginal tear, 5-minute Apgar <7, and first feed as breastmilk).
(iii) National maternity indicators	(ie, mode of birth, third-degree or fourth-degree vaginal tear, postpartum haemorrhage [PPH, >1L], 5-minute Apgar <7, birthweight <10th centile with birth at ≥40 weeks, and first feed as breastmilk). Additionally, we included: intrapartum risk factors (malpresentation, gestational diabetes, high blood pressure [any], proteinuria, preeclampsia, postpartum hemorrhage/vaginal blood loss, placenta abruption specifically, infection, meconium, suspicious or pathological fetal heart rate or pattern, low iron, uterine rupture, reduced fetal movement, issue with FHR, delayed labour, or need for labour augmentation), gestational hypertension (defined as systolic blood pressure [BP] ≥140mmHg or diastolic BP ≥90mmHg at ≥20 weeks gestation, in women without prior chronic hypertension[1]), stillbirth, small-for-gestational age (SGA, <10th centile) infants,[2] and neonatal intensive care unit admission. Interventional birth was defined as birth by cesarean or operative vaginal delivery (which included mid-cavity forceps without rotation, rotational forceps [including Kiellands], ventouse with rotation, low forceps without rotation, forceps not otherwise specified, and Ventouse without rotation or Ventouse not otherwise specified).

SUPPLEMENTAL TABLE 4
Guidelines for Reporting on Latent Trajectory Studies (GRoLT) checklist

Item 1: Metric of time	Gestational age
Item 2: fixed or varying occasion	6 fixed gestational window; 0—14^{+6} weeks, 15—20^{+6} weeks, 21—27^{+6} weeks, 28—32^{+6} weeks, 33—36^{+6} weeks, and +37 weeks.
Item 3a: missing data mechanism	Missing at random, there were available data at the following timepoints: 0—14^{+6} weeks: 28,967; 15—20^{+6} weeks: 27,003; 21—27^{+6} weeks: 23,142; 28—32^{+6} weeks: 30,237; 33—36^{+6} weeks: 30,876; and +37 weeks: 27,137.
Item 3b: auxiliary variables	Supplemental Tables 6 and 7: reports the demographic differences between those included in the analysis (n=34,114) and those who were excluded (n=24,288 due to missing registration, delivery or antenatal data)
Item 3c: how dealt with missing data	Pregnancies with registration, at least 1 antenatal appointment and delivery data from October 2018 — July 2023 were included in the analysis
Item 4: distribution	Censored normal distribution (as the dependent was scaled)
Item 5: software	Stata 18.0 'traj' command
Item 6a: LGMM vs LCGA	Our findings for the GBTM were compared with the output of a latent class analysis.
Item 6b: across-class variance-covariance matrix	Default
Item 7: functional form	Intercept, linear, quadratic, and cubic.
Item 8: covariates	Covariates were not included in the model to predict trajectory groups
Item 9: random starts	Default
Item 10: model comparison	Average Posterior Probability Assignment, Bayesian Information Criterion, odds of correct classification, entropy, and percentage of participants assigned to each group
Item 11: 1-class solution	Supplemental Table 5
Item 12: sample size per class	Group 1: n=27,751 (81.3%); group 2: n=832 (2.4%); group 3: n=2410 (7.1%); and group 4: n=3121 (9.2%)
Item 13: entropy	0.915 for the final model
Item 14a: plot of final solution	Supplemental Figure 2
Item 14b: plots for each model	Supplemental Figure 3
Item 14c: plots of individual trajectories	Supplemental Figure 4
Item 15: descriptive statistics	Table 1
Item 16: syntax	Example code: traj, var(quartile_*) indep(t_*) model(cnorm) order(2 2 2 3) min(0) max(4)

SUPPLEMENTAL TABLE 5
Trajectory criteria statistics for 1 to 5 trajectories

	BIC	Group membership	APPA	Entropy	OCC
1 class; order (3)	−192606	100%			
2 classes; order (2 2)	−186826	87.2%	0.96	0.82	4.3
		12.8%	0.87		38.8
2 classes; order (1 3)	−184817	91.5%	0.98	0.91	6.8
		8.5%	0.92		127.5
2 classes; order (2 3)	−184717	91.9%	0.98	0.91	6.2
		8.1%	0.93		144.4
3 classes; order (1 2 3)	−178873	84.0%	0.97	0.90	7.0
		8.7%	0.87		64.0
		7.3%	0.93		170.3
3 classes; order (2 1 3)	−179171	85.3%	0.97	0.91	6.6
		6.7%	0.89		97.0
		8.0%	0.94		169.1
3 classes; order (2 2 3)	−179597	89.3%	0.98	0.93	7.3
		2.4%	0.99		15,492.2
		8.2%	0.93		145.8
4 classes; order (1 1 2 3)	−175030	7.4%	0.88	0.92	86.9
		2.6%	0.97		1079.2
		82.3%	0.97		7.5
		7.6%	0.95		204.5
4 classes; order (1 2 2 3)	−172981	7.7%	0.87	0.92	78.5
		82.1%	0.97		7.7
		2.4%	0.99		12,797.1
		7.7%	0.96		245.2
4 classes; order (2 2 2 3)	−172617	2.4%	0.99	0.91	5534.1
		9.2%	0.88		71.0
		81.3%	0.97		7.6
		7.1%	0.95		218.6
4 classes; order (2 2 1 3)	−176703	10.3%	0.87	0.89	54.7
		78.8%	0.95		6.2
		2.7%	0.96		789.1
		8.2%	0.94		145.2
4 classes; order (2 1 2 3)	−176468	14.2%	0.89	0.90	45.1
		79.2%	0.96		7.4
		4.1%	0.91		215.0
		2.5%	0.98		1957.0

(continued)

SUPPLEMENTAL TABLE 5
Trajectory criteria statistics for 1 to 5 trajectories *(continued)*

	BIC	Group membership	APPA	Entropy	OCC
4 classes; order (2 1 3 2)	−182758	3.9%	0.90	0.90	202.7
		0.0%	-		-
		83.7%	0.96		5.3
		12.4%	0.86		42.0
5 classes; order (2 1 2 1 3)	−176573	1.4%	0.77	0.89	209.8
		79.2%	0.96		6.7
		12.1%	0.86		40.0
		4.7%	0.87		127.6
		2.5%	0.98		1661.7
5 classes; order (2 2 2 2 3)	−172638	2.4%	0.99	0.93	5534.1
		0.0%	-		-
		81.4%	0.97		7.6
		9.2%	0.88		71.0
		7.0%	0.95		218.6

APPA, Average Posterior Probability Assignment; *BIC*, Bayesian Information Criteria; *OCC*, odds of correct classification.

SUPPLEMENTAL TABLE 6
Registration characteristics from those included (n = 34,114) vs those not included in the analysis (n = 18,593)

	All women (n=52,707)	Not included n=18,593 (35.3%)	Included n=34,114 (64.7%)	Included vs not included
Maternal age at registration (y)	32.9 (5.4)	33.2 (5.5)	32.7 (5.4)	<0.001
Age>20 years	618 (1.1%)	206 (1.1%)	412 (1.2%)	0.309
BMI at registration (kg/m^2)	24.2 (21.6, 28.2)	24.1 (21.5, 28.0)	24.3 (21.7, 28.2)	<0.001
BMI missing	3211 (6.1%)	1709 (9.2%)	1502 (4.4%)	<0.001
BMI category				
underweight	1274 (2.6%)	440 (2.6%)	834 (2.6%)	<0.001
healthy weight	26,581 (53.7%)	9239 (54.7%)	17,342 (53.2%)	
overweight	12,890 (26.0%)	4328 (25.6%)	8562 (26.3%)	
obesity I	5512 (11.1%)	1872 (11.1%)	3640 (11.2%)	
obesity II	2148 (4.3%)	656 (3.9%)	1492 (4.6%)	
obesity III	1091 (2.2%)	348 (2.1%)	741 (2.3%)	
Gestation at registration (wk)	9.7 (8.6, 12.1)	9.6 (8.4, 12.1)	9.7 (8.6, 12.3)	<0.001
Late registration (>16 wk)	7460 (14.1%)	2856 (15.4%)	4604 (13.5%)	<0.001
Registration timepoint				
October 1, 2018—March 22, 2020	17,940 (34.0%)	5848 (31.5%)	12,092 (35.4%)	<0.001
March 23, 2020—June 23, 2020	3047 (5.8%)	896 (4.8%)	2151 (6.3%)	
June 23, 2020—November 4, 2020	3929 (7.5%)	1129 (6.1%)	2800 (8.2%)	
November 5, 2020—January 5, 2021	1842 (3.5%)	521 (2.8%)	1321 (3.9%)	
January 6, 2021—July 17, 2021	6361 (12.1%)	1723 (9.3%)	4638 (13.6%)	
July 18, 2021—May 4, 2023	19,588 (37.2%)	8476 (45.6%)	11,112 (32.6%)	
IMD score				
1 most deprived	10,069 (19.1%)	3462 (18.6%)	6607 (19.4%)	<0.001
2	21,343 (40.5%)	7264 (39.1%)	14,079 (41.3%)	
3	13,022 (24.7%)	4563 (24.5%)	8459 (24.8%)	
4	5141 (9.8%)	1995 (10.7%)	3146 (9.2%)	
5 least deprived	2221 (4.2%)	948 (5.1%)	1273 (3.7%)	
missing	911 (1.7%)	361 (1.9%)	550 (1.6%)	
Mother's ethnicity				
White	26,892 (51.1%)	9546 (51.3%)	17,346 (50.8%)	<0.001
Asian or Asian British	5103 (9.7%)	1736 (9.3%)	3367 (19.9%)	
Black, Black British, Caribbean, or African	10,148 (19.3%)	3066 (16.5%)	7082 (20.8%)	
Mixed or multiple ethnic groups	2690 (5.1%)	868 (4.7%)	1822 (5.3%)	
Other ethnic group	3479 (6.6%)	1165 (6.3%)	2314 (6.8%)	
missing	4395 (8.3%)	2212 (11.9%)	2183 (6.4%)	
Difficulty understanding English	3575 (6.8%)	1175 (6.3%)	2400 (7.0%)	0.002
Drug use in the previous 12 months	621 (1.2%)	169 (0.9%)	452 (1.3%)	<0.001
Current drug use	204 (0.4%)	64 (0.3%)	140 (0.4%)	0.242
Drug use ever	3474 (6.6%)	1247 (6.7%)	2227 (6.5%)	0.429
Nulliparous	28,836 (54.7%)	10,685 (57.5%)	18,151 (53.2%)	<0.001

(continued)

SUPPLEMENTAL TABLE 6

Registration characteristics from those included (n = 34,114) vs those not included in the analysis (n = 18,593)

(continued)

	All women (n=52,707)	Not included n=18,593 (35.3%)	Included n=34,114 (64.7%)	Included vs not included
Multiparous women only (n=23,871)				
Previous c-section	7554 (31.6%)	2470 (31.2%)	5084 (31.8%)	0.337
Previous PPH	2058 (8.6%)	658 (8.3%)	1400 (8.8%)	0.244
Previous preterm birth	1848 (7.7%)	637 (8.1%)	1211 (7.6%)	0.205
Previous still birth	425 (1.8%)	134 (1.7%)	291 (1.8%)	0.480

BMI, body mass index; *IMD*, index of multiple deprivation; *PPH*, postpartum hemorrhage.

SUPPLEMENTAL TABLE 7
Delivery characteristics from those included (n = 34,114) vs those not included in the analysis (n = 7842)

	All women (n=41,956)	Not included n=7842 (18.7%)	Included n=34,114 (81.3%)	Included vs not included
Smoker at delivery	1153 (3.8%)	296 (3.8%)	857 (3.5%)	<0.001
Intrapartum risk factors	8609 (20.5%)	1512 (19.3%)	7097 (20.8%)	0.003
Delivery timepoint				
October 1, 2018—March 22, 2020	14,352 (34.2%)	6582 (83.9%)	7770 (22.8%)	<0.001
March 23, 2020—June 23, 2020	2151 (5.1%)	93 (1.2%)	2058 (6.0%)	
June 23, 2020—November 4, 2020	3132 (7.5%)	68 (0.9%)	3064 (9.0%)	
November 5, 2020—January 5, 2021	1305 (3.1%)	53 (0.7%)	1252 (3.7%)	
January 6, 2021—July 17, 2021	4614 (11.0%)	210 (2.7%)	4404 (12.9%)	
July 18, 2021—July 8, 2023	16,402 (39.1%)	836 (10.7%)	15,566 (45.9%)	
Age<20 y	522 (1.2%)	112 (1.4%)	410 (1.2%)	0.103
Age at delivery	33.0 (30.0, 36.0)	33.0 (29.0, 36.0)	33.0 (30.0, 36.0)	0.001
Gestation				
≤24 wk	83 (0.2%)	41 (0.5%)	42 (0.1%)	<0.001
24^{+0}—27^{+6} wk	302 (0.7%)	149 (1.9%)	153 (0.4%)	
28^{+0}—33^{+6} wk	673 (1.6%)	218 (2.8%)	455 (1.3%)	
34^{+0}—36^{+6} wk	1749 (4.2%)	405 (5.2%)	1344 (3.9%)	
≥37 wk	39,149 (93.3%)	7029 (89.6%)	32,120 (94.2%)	
Mode of delivery				
Vaginal unassisted	19,893 (47.4%)	3912 (49.9%)	15,981 (46.8%)	<0.001
Assisted vaginal	6229 (14.8%)	1178 (15.0%)	5051 (14.8%)	
Elective CS	6719 (16.0%)	1172 (14.9%)	5547 (16.3%)	
Emergency CS	9115 (21.7%)	1580 (20.1%)	7535 (22.1%)	
First feed: breastmilk	35,259 (84.0%)	6281 (80.1%)	28,978 (84.9%)	<0.001
Apgar <7 at 5 min	687 (1.6%)	193 (2.5%)	494 (1.5%)	<0.001
Induction	8845 (21.1%)	1355 (17.3%)	7490 (22.0%)	<0.001
Third-degree or fourth-degree tear	683 (1.6%)	158 (2.0%)	525 (1.5%)	<0.001
Skin to skin	36,319 (87.3%)	6405 (83.1%)	29,914 (88.3%)	<0.001
NICU	2708 (6.5%)	779 (9.9%)	1929 (5.7%)	<0.001
PPH greater than 1000 mL	4148 (9.9%)	772 (9.2%)	3426 (10.0%)	0.220
Birth outcome				
Livebirth	41,542 (99.0%)	7653 (97.6%)	33,889 (99.3%)	<0.001
Stillbirth	239 (0.6%)	101 (1.3%)	138 (0.4%)	
Neonatal death	163 (0.4%)	84 (1.1%)	79 (0.2%)	
Infant death	12 (0.1%)	4 (0.1%)	8 (0.1%)	
Sex (male)	21,489 (51.2%)	4051 (51.7%)	17,438 (51.1%)	0.356
SGA <10th	2962 (7.1%)	612 (7.8%)	2350 (6.9%)	<0.001

CS, cesarean section; *NICU*, neonatal intensive care unit; *PPH*, postpartum haemorrhage; *SGA*, small for gestational age.

SUPPLEMENTAL TABLE 8

Registration of antenatal care characteristics from those included (n = 34,114) vs those without antenatal data but with delivery data (n = 2147)

	No antenatal data n=2147 (5.9%)	Included in analysis n=34,114 (94.1%)	Included vs not included
Registration appointment virtual	529 (25.7%)	857 (2.5%)	<0.001
Maternal age at registration (y)	32.3 (5.8)	32.7 (5.4)	<0.001
Age>20 y	40 (2%)	412 (1%)	0.008
BMI at registration (kg/m^2)	25.3 (22.3 29.5)	24.3 (21.7 28.2)	<0.001
BMI missing	401 (18.7%)	1502 (4.4%)	<0.001
BMI category			
Underweight	37 (2.1%)	834 (2.6%)	<0.001
Healthy weight	803 (46.0%)	17,342 (53.2%)	
Overweight	505 (28.9%)	8562 (26.3%)	
Obesity I	260 (14.9%)	3640 (11.2%)	
Obesity II	102 (5.8%)	1492 (4.6%)	
Obesity III	39 (2.2%)	741 (2.3%)	
Gestation at registration	23.7 (10.6, 33.9)	9.7 (8.6 12.3)	<0.001
Late registration (>16 wk)	1213 (56.5%)	4604 (16.5%)	<0.001
Registration timepoint			
October 1, 2018—March 22, 2020	1458 (67.8%)	12,092 (35.4%)	<0.001
March 23, 2020—June 23, 2020	42 (2.0%)	2151 (6.3%)	
June 23, 2020—November 4, 2020	70 (3.3%)	2800 (8.2%)	
November 5, 2020—January 5, 2021	21 (1.0%)	1321 (3.9%)	
January 6, 2021—July 17, 2021	117 (5.4%)	4638 (13.6%)	
July 18, 2021—May 4, 2023	439 (20.4%)	11,112 (32.6%)	
IMD score			
1 most deprived	451 (21.0%)	6607 (19.4%)	<0.001
2	784 (36.5%)	14,079 (41.3%)	
3	457 (21.3%)	8459 (24.8%)	
4	225 (10.5%)	3146 (9.2%)	
5 least deprived	142 (6.6%)	1273 (3.7%)	
Missing	88 (4.1%)	550 (1.6%)	
Mother's ethnicity			
White	846 (39.4%)	17,346 (50.8%)	<0.001
Asian or Asian British	155 (7.2%)	3367 (9.9%)	
Black, Black British, Caribbean, or African	341 (15.9%)	7082 (20.8%)	
Mixed or multiple ethnic groups	73 (3.4%)	1822 (5.3%)	
Other ethnic group	187 (8.7%)	2314 (6.8%)	
Missing	545 (25.4%)	2183 (6.4%)	
Difficulty understanding English	151 (7.0%)	2400 (7.0%)	0.997
Current drug use	4 (0.2%)	140 (0.4%)	0.109
Drug use in the previous 12 months	13 (0.6%)	452 (1.3%)	0.004

(continued)

SUPPLEMENTAL TABLE 8

Registration of antenatal care characteristics from those included (n = 34,114) vs those without antenatal data but with delivery data (n = 2147) *(continued)*

	No antenatal data n=2147 (5.9%)	Included in analysis n=34,114 (94.1%)	Included vs not included
Drug use ever	56 (2.6%)	2227 (6.5%)	<0.001
Nulliparous	1037 (48.3%)	18,151 (53.2%)	<0.001
Inpatient antenatal care	915 (42.6%)	857 (2.5%)	<0.001
Multiparous women only (n=17,073)			
Previous c-section	296 (26.7%)	5084 (31.8%)	<0.001
Previous PPH	74 (6.7%)	1400 (8.8%)	0.016
Previous preterm birth	80 (7.2%)	1211 (7.6%)	0.623
Previous still birth	19 (1.7%)	291 (1.8%)	0.788

BMI, body mass index; *IMD*, index of multiple deprivation; *PPH*, postpartum hemorrhage.

SUPPLEMENTAL TABLE 9

Delivery characteristics from those included (n = 34,114) vs those without antenatal data but with registration data (n = 2147)

	No antenatal data n=2147 (5.9%)	Included n=34,114 (94.1%)	Included vs not included
Smoker at delivery	104 (4.8%)	857 (2.5%)	<0.001
Intrapartum risk factors	449 (20.9%)	7097 (20.8%)	0.904
Delivery timepoint			
October 1, 2018—March 22, 2020	1444 (67.3%)	7770 (22.8%)	<0.001
March 23, 2020—June 23, 2020	48 (2.2%)	2058 (6.0%)	
June 23, 2020—November 4, 2020	68 (3.2%)	3064 (9.0%)	
November 5, 2020—January 5, 2021	27 (1.3%)	1252 (3.7%)	
January 6, 2021—July 17, 2021	112 (5.2%)	4404 (12.9%)	
July 18, 2021—July 8, 2023	448 (20.9%)	15,566 (45.6%)	
Age<20 y	49 (2.3%)	410 (1.2%)	<0.001
Age at delivery	33.0 (28.0, 36.0)	33.0 (30.0, 36.0)	<0.001
gestation			
≤24 wk	29 (1.4%)	42 (0.1%)	<0.001
24^{+0}—27^{+6} wk	108 (5.0%)	153 (0.4%)	
28^{+0}—33^{+6} wk	135 (6.3%)	455 (1.3%)	
34^{+0}—36^{+6} wk	171 (8.0%)	1344 (3.9%)	
≥37 wk	1704 (79.4%)	32,120 (94.2%)	
Mode of delivery			
Vaginal unassisted	1068 (49.7%)	15,981 (46.8%)	0.020
Assisted vaginal	284 (13.2%)	5051 (14.8%)	
Elective CS	317 (14.8%)	5547 (16.3%)	
Emergency CS	478 (22.3%)	7535 (22.1%)	
First feed: breastmilk	1517 (70.7%)	28,978 (84.9%)	<0.001
Apgar <7 at 5 min	103 (4.8%)	494 (1.4%)	<0.001
induction	332 (15.5%)	7490 (22.0%)	<0.001
Third-degree or fourth-degree tear	47 (2.2%)	525 (1.5%)	<0.001
Skin to skin	1454 (70.6%)	29,914 (88.3%)	<0.001
NICU	438 (20.4%)	1929 (5.7%)	<0.001
PPH greater than 1000	213 (9.9%)	3426 (10.0%)	0.931
Birth outcome			
Livebirth	2003 (93.3%)	33,889 (99.3%)	<0.001
Stillbirth	75 (3.5%)	138 (0.4%)	
Neonatal death	65 (3.0%)	79 (0.2%)	
Infant death	4 (0.2%)	8 (0.1%)	
Sex (male)	1107 (51.6%)	17,438 (51.1%)	0.661
SGA <10th	207 (9.6%)	2350 (6.9%)	<0.001

Summary of those included in the analysis vs those excluded: Compared to those women included in the analysis, women excluded (n=18,593) with registration of antenatal care data were more likely to be younger, have a higher BMI, register their pregnancy late, or be nulliparous (Supplemental Table 6). Women excluded (n=7842) with delivery data were more likely to be a smoker, have an unassisted vaginal delivery, or have a third-degree or fourth-degree vaginal tear; less likely to be induced or have a cesarean section and the infant was less likely to be offered breastmilk or have skin-to-skin after birth, more likely to be admitted to NICU, be stillborn, or suffer a neonatal death (Supplemental Table 7).

CS, cesarean section; *NICU*, neonatal intensive care unit; *PPH*, postpartum hemorrhage; *SGA*, small-for-gestational age.

SUPPLEMENTAL TABLE 10

Sensitivity analyses showing adjusted associations between the trajectories and birth outcomes in women and their children from the eLIXIR-BiSL

Birth outcomes	Trajectory 0 (n=23,364) Stable	Trajectory 1 (n=751) High first trimester	Trajectory 2 (n=2359) High second trimester	Trajectory 3 (n=2960) High third trimester
Relative risk ratio (95% confidence interval)				
Truncated analysis[a] (n=29,434)				
Smoker at delivery[b]	Ref	1.37 (0.87, 2.16)	1.19 (0.91, 1.56)	1.17 (0.92, 1.50)
Gestational hypertension		1.09 (0.89, 1.33)	**0.86 (0.75, 0.98)[c]**	**0.86 (0.75, 0.99)[c]**
Preterm<37 wk		1.04 (0.77, 1.42)	**1.21 (1.02, 1.44)[c]**	**1.38 (1.17, 1.62)[d]**
Gestation at delivery				
Before 24^{+0} wk	Ref	-	-	-
24^{+0}–27^{+6} wk		1.28 (0.51, 3.20)	**1.76 (1.08, 2.89)[e]**	0.98 (0.52, 1.86)
28^{+0}–33^{+6} wk		0.87 (0.44, 1.71)	1.17 (0.82, 1.69)	**1.75 (1.27, 2.41)[d]**
34^{+0}–36^{+6} wk		1.12 (0.78, 1.62)	1.14 (0.92, 1.41)	**1.38 (1.14, 1.68)[d]**
≥37 wk		Ref	Ref	Ref
Induced	Ref	1.02 (0.86, 1.21)	**1.13 (1.02, 1.25)[e]**	1.06 (0.96, 1.17)
Breech		-	**1.89 (1.00, 3.57)[c]**	1.19 (0.54, 2.59)
Mode of delivery				
Vaginal unassisted	Ref	Ref	Ref	Ref
Assisted vaginal		0.85 (0.67, 1.10)	0.88 (0.76, 1.01)	0.94 (0.83, 1.07)
Elective CS		0.96 (0.78, 1.18)	1.07 (0.95, 1.21)	**1.57 (1.40, 1.75)[d]**
Emergency CS		0.93 (0.77, 1.13)	1.01 (0.90, 1.13)	**1.20 (1.08, 1.34)[d]**
Third/fourth degree	Ref	1.15 (0.65, 2.05)	0.84 (0.58, 1.23)	**0.63 (0.43, 0.93)[c]**
PPH	Ref	0.98 (0.78, 1.24)	**1.14 (1.00, 1.30)[e]**	1.04 (0.90, 1.20)
5-min Apgar<7	Ref	0.73 (0.37, 1.43)	1.03 (0.73, 1.50)	0.93 (0.65, 1.34)
Birth outcome				
Live birth	Ref	Ref	Ref	Ref
Stillbirth		0.95 (0.30, 3.06)	1.22 (0.66, 2.27)	1.09 (0.59, 2.04)
Neonatal death		1.39 (0.42, 4.54)	1.10 (0.49, 2.45)	0.15 (0.02, 1.10)
Sex (female)	Ref	0.98 (0.84, 1.13)	0.92 (0.85, 1.00)	1.00 (0.92, 1.09)
SGA $<10^{th}$ percentile	Ref	1.06 (0.80, 1.41)	0.97 (0.82, 1.15)	1.07 (0.91, 1.25)
Skin-to-skin (yes)	Ref	0.89 (0.71, 1.12)	0.90 (0.78, 1.02)	**0.80 (0.71, 0.91)[d]**
NICU admission	Ref	1.14 (0.85, 1.53)	1.04 (0.86, 1.25)	**1.32 (1.12, 1.57)[e]**
Breastfeeding	Ref	1.04 (0.82, 1.33)	0.94 (0.83, 1.06)	**0.88 (0.79, 0.98)[c]**
Analysis stratified by parity[f]				
Nulliparous women (n=18,151)	**Trajectory 0 (n=14,711) Stable**	**Trajectory 1 (n=425) High first trimester**	**Trajectory 2 (n=1270) High second trimester**	**Trajectory 3 (n=1745) High third trimester**
Smoker at delivery[g]	Ref	**2.02 (1.13, 3.62)[c]**	1.30 (0.85, 1.98)	1.23 (0.84, 1.80)
Gestational hypertension	Ref	1.17 (0.91, 1.49)	**0.76 (0.64, 0.90)[e]**	**0.81 (0.68, 0.96)[c]**
Preterm<37 wk		0.98 (0.64, 1.50)	**1.30 (1.03, 1.63)[c]**	**1.29 (1.04, 1.60)[c]**

(continued)

SUPPLEMENTAL TABLE 10
Sensitivity analyses showing adjusted associations between the trajectories and birth outcomes in women and their children from the eLIXIR-BiSL *(continued)*

Analysis stratified by parity[f]

Nulliparous women (n=18,151)	Trajectory 0 (n=14,711) Stable	Trajectory 1 (n=425) High first trimester	Trajectory 2 (n=1270) High second trimester	Trajectory 3 (n=1745) High third trimester
Gestation at delivery				
<24+0 wk	Ref	-	-	-
24+0–27+6 wk		1.42 (0.43, 4.64)	1.78 (0.92, 3.46)	0.96 (0.44, 2.13)
28+0–33+6 wk		1.04 (0.45, 2.38)	1.37 (0.86, 2.18)	**1.82 (1.21, 2.73)**[e]
34+0–36+6 wk		0.94 (0.56, 1.60)	1.23 (0.93, 1.62)	1.23 (0.95, 1.60)
≥37 wk		Ref	Ref	Ref
Induced	Ref	1.13 (0.91, 1.40)	1.09 (0.96, 1.25)	0.97 (0.86, 1.10)
Breech presentation		-	**3.21 (1.49, 6.96)**[e]	1.09 (0.32, 3.74)
Mode of delivery				
Vaginal unassisted	Ref	Ref	Ref	Ref
Assisted vaginal		0.87 (0.66, 1.14)	0.90 (0.76, 1.05)	0.92 (0.80, 1.07)
Elective CS		1.05 (0.76, 1.44)	0.97 (0.80, 1.18)	**1.60 (1.34, 1.90)**[d]
Emergency CS		1.06 (0.83, 1.34)	1.05 (0.91, 1.21)	**1.17 (1.03, 1.35)**[c]
Third-degree/fourth-degree vaginal tear	Ref	1.29 (0.72, 2.29)	0.84 (0.56, 1.27)	**0.65 (0.44, 0.97)**[c]
PPH	Ref	1.03 (0.78, 1.37)	1.15 (0.97, 1.36)	1.13 (0.95, 1.34)
5-min Apgar<7	Ref	0.74 (0.30, 1.82)	1.00 (0.64, 1.60)	0.90 (0.57, 1.40)
Birth outcome				
Live birth	Ref	Ref	Ref	Ref
Stillbirth		0.52 (0.07, 3.81)	0.84 (0.33, 2.12)	1.12 (0.53, 2.38)
Neonatal death		-	0.34 (0.05, 2.50)	0.23 (0.03, 1.76)
Sex (female)	Ref	1.01 (0.83, 1.23)	0.92 (0.82, 1.03)	0.98 (0.88, 1.09)
SGA <10th percentile	Ref	1.14 (0.82, 1.60)	1.00 (0.81, 1.24)	1.03 (0.85, 1.25)
Early skin-to-skin contact	Ref	**0.74 (0.55, 0.99)**[c]	0.85 (0.71, 1.02)	**0.77 (0.65, 0.90)**[e]
NICU admission	Ref	1.26 (0.87, 1.82)	1.13 (0.90, 1.42)	**1.25 (1.01, 1.54)**[c]
Breastfeeding	Ref	1.25 (0.87, 1.82)	0.94 (0.78, 1.12)	0.95 (0.82, 1.09)

Multiparous women (n=15,963)	Trajectory 0 (n=13,040) Stable	Trajectory 1 (n=407) High first trimester	Trajectory 2 (n=1140) High second trimester	Trajectory 3 (n=1376) High third trimester
Smoker at delivery[g]	Ref	0.91 (0.48, 1.74)	1.11 (0.79, 1.58)	1.20 (0.89, 1.63)
Gestational hypertension	Ref	1.00 (0.73, 1.37)	1.00 (0.82, 1.23)	0.86 (0.69, 1.08)
Preterm<37 wk		1.07 (0.70, 1.62)	1.11 (0.86, 1.44)	**1.41 (1.13, 1.77)**[e]
Gestation at delivery				
<24+0 wk	Ref	-	-	-
24+0–27+6 wk		1.05 (0.25, 4.45)	1.81 (0.87, 3.79)	0.83 (0.29, 2.37)
28+0–33+6 wk		0.73 (0.27, 2.01)	0.90 (0.50, 1.61)	1.36 (0.85, 2.20)
34+0–36+6 wk		1.23 (0.76, 1.98)	1.05 (0.76, 1.44)	**1.54 (1.18, 2.00)**[d]
≥37 wk		Ref	Ref	Ref

(continued)

SUPPLEMENTAL TABLE 10

Sensitivity analyses showing adjusted associations between the trajectories and birth outcomes in women and their children from the eLIXIR-BiSL *(continued)*

Multiparous women (n=15,963)	Trajectory 0 (n=13,040) Stable	Trajectory 1 (n=407) High first trimester	Trajectory 2 (n=1140) High second trimester	Trajectory 3 (n=1376) High third trimester
Induced	Ref	0.96 (0.74, 1.25)	**1.18 (1.01, 1.38)**[c]	1.12 (0.96, 1.30)
Breech presentation		-	0.84 (0.25, 2.78)	1.22 (0.46, 3.24)
Mode of delivery				
Vaginal unassisted	Ref	Ref	Ref	Ref
Assisted vaginal		0.90 (0.55, 1.47)	0.78 (0.57, 1.06)	1.05 (0.81, 1.36)
Elective CS		0.96 (0.74, 1.23)	1.11 (0.96, 1.29)	**1.50 (1.30, 1.73)**[d]
Emergency CS		0.87 (0.64, 1.17)	0.89 (0.74, 1.08)	**1.24 (1.05, 1.47)**[c]
Third-degree/fourth-degree vaginal tear	Ref	0.76 (0.18, 3.15)	0.81 (0.34, 1.89)	0.77 (0.32, 1.81)
PPH	Ref	0.95 (0.67, 1.34)	1.14 (0.93, 1.41)	0.95 (0.75, 1.19)
5-min Apgar<7	Ref	0.95 (0.41, 2.18)	1.09 (0.66, 1.81)	0.77 (0.42, 1.42)
Birth outcome				
Live birth	Ref	Ref	Ref	Ref
Stillbirth		1.32 (0.31, 5.64)	1.69 (0.74, 3.90)	1.09 (0.42, 2.86)
Neonatal death		2.61 (0.75, 9.09)	1.85 (0.74, 4.66)	-
Sex (female)	Ref	0.94 (0.77, 1.15)	0.92 (0.81, 1.04)	1.06 (0.94, 1.18)
SGA $<10^{th}$ percentile	Ref	0.80 (0.49, 1.31)	0.91 (0.68, 1.22)	1.12 (0.87, 1.43)
Early skin-to-skin contact	Ref	1.15 (0.83, 1.60)	0.99 (0.81, 1.20)	0.91 (0.76, 1.08)
NICU admission	Ref	0.98 (0.62, 1.54)	0.94 (0.70, 1.27)	**1.29 (1.00, 1.65)**[c]
Breastfeeding	Ref	0.98 (0.73, 1.31)	0.96 (0.81, 1.14)	0.89 (0.77, 1.03)

Multinominal logistic was used to assess the relationship between the 4 trajectories and the birth outcomes and the reference group is the stable trajectory (group 0). Models were adjusted for: parity, registration hospital, registration gestation, pandemic timepoint, smoking status at registration and an interaction between index of multiple deprivation and ethnicity.

CS, cesarean section; *eLIXIR-BiSL*, early Life Cross Linkage in Research, Born-in-South London; *NICU*, neonatal intensive care unit; *PPH*, postpartum haemorrhage; *SGA*, small-for-gestational-age.

[a] Truncated analysis excluding those outside the timeframe of April 1, 2019 to May 1, 2023 to avoid potential bias by including those with short registration to birth intervals, because of late registration for antenatal care or preterm birth; [b] Modelled using negative binominal regression, adjusted for parity, gestation at registration and antenatal care type; [c] $P<0.05$; [d] $P<0.001$; [e] $P<0.01$; [f] Not adjusted for parity; [g] Not adjusted for smoking status.