Maternal influenza-like illness and neonatal health during the 1918 influenza pandemic in a Swiss city

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Abstract

Exposure to the 1918 influenza pandemic may have been associated with preterm birth (<37 weeks). Other outcomes, such as infant size or weight, have rarely been explored. Using 2,177 historical birth records from Lausanne maternity hospital, we estimated whether *in utero* exposure to maternal influenza-like illness (ILI) during the 1918 pandemic was associated with pregnancy outcomes, and whether associations varied depending on the trimester of ILI during pregnancy or on fetal sex. Generalized linear models and robust linear models were used to analyse the association between ILI and gestational age, stillbirth, and anthropometric measurements, adjusting on covariates. Analyses were stratified by fetal sex. 282 (13%) women developed ILI during pregnancy. ILI exposure was associated with lower anthropometric measurements: low birth weight (<2,500grams (g)) marginally adjusted percentage was 13.3% compared to 6.9% in the unexposed group (difference+6.4% [95%CI 5.5 to 7.2%]). There was strong evidence that third trimester exposure was associated with worse adverse pregnancy outcomes, including with low birth weight (+12.8% [95%CI 11.8 to 13.7%]) and preterm birth rates (+9.4% [95%CI 8.2 to 10.6%]). Maternal ILI may have triggered premature birth. The magnitude of the declines in anthropometric parameters was higher among male fetuses, and they had a higher stillbirth rate. For instance, males exposed during the third trimester had their birth weight lowered by 228.4g [95%CI -391.0 to -65.8g], compared to 126.3g among females [95%CI -256.6 to 4.0g]. Only 41% of infants exposed to first-trimester ILI were males, suggesting a selection against male fetuses through miscarriage. Our findings may not generalize to the entire population of Lausanne, as 34% of births were homebirths at the time.

Introduction

The 1918 influenza pandemic had the unique feature of a high mortality rate among young adults (20-40 years old) (1). Pregnant individuals had a particularly high risk of developing severe symptoms, of being admitted to the hospital and of dying when contracting influenza (2–6); this was also the case during the recent influenza pandemic of 2009, albeit to a lower extent (7–9).

While maternal illness during the pandemic of 2009 was associated with higher rates of stillbirth and low birth weight (LBW, birth weight <2500g) (10), there are limited data on pregnancy outcomes during the 1918 pandemic. A contemporary study from 1919 noted that as many as 50% of 1,350 pregnant women with influenza-like illness (ILI) experienced pregnancy complications, including early pregnancy loss and preterm birth (2). Such events were more frequent if the mother had developed pneumonia (3,5,6,11). Population rates of stillbirth and neonatal mortality spiked during the pandemic in the UK and Japan (12,13), though it is uncertain whether it was due to *in utero* exposure to the virus, to maternal stress in times of crisis, or to the repercussions of the First World War. A short-term decrease in birth weight and placenta weight were reported in Basel, Switzerland in 1918-1919, coinciding with *in utero* exposure to both the pandemic and a food supply crisis towards the end of the First World War (14). Other neonatal anthropometric parameters have rarely been documented during the 1918 pandemic.

We take advantage of high-quality archival birth records from the city of Lausanne, in the Western canton of Vaud, Switzerland. The first pandemic wave reached the country in July 1918, followed by the deadliest wave from October 1918 to March 1919, and another wave in early 1920 (15,16) (see *Figure S1* for a visualization of the pandemic waves in Lausanne and the Canton of Vaud) (17). More historical context on Switzerland, the canton of Vaud and the pandemic are provided at the end of the Supplement. We aim to estimate whether *in utero* exposure to maternal ILI was associated with higher risks of adverse pregnancy outcomes, reporting on infant size (including birth weight and head circumference), as well as preterm birth and stillbirth rates. To our knowledge, this is the first study - apart from contemporary physician reports - examining the influence of maternal ILI during the 1918 pandemic on pregnancy outcomes, while controlling for important covariates. Since the literature is inconclusive on the importance of the trimester during which ILI occurs (18,19), and because symptoms severity might be playing a role (3,5,6,11,20), we account for both the window of exposure during pregnancy and the severity of ILI in our analyses. Furthermore, analyses are stratified by fetal sex, as males may be more vulnerable to adverse *in utero* environment than female fetuses (21–24).

Methods

The birth registers of the University Maternity Hospital of Lausanne from 1905-1924 (25) were transcribed from the Cantonal archives of Vaud (see *Supplementary Methods* for detailed information). Although only data from the pandemic time period are used in the analyses, we describe maternal and infant characteristics during 1905-1924, for comparison. Only

singletons and events clearly qualified as “deliveries” on the maternity form were transcribed. Events qualified as abortions are separately reported on (“miscarriages” section).

The following variables were transcribed (and in some cases, categorized): date of birth, date of last menstrual period, maternal age (years), height (cm), address, gravidity (number of pregnancies regardless of the outcome, categorized as 1, 2, >2), civil status (married or single/missing), occupation, syphilis status, neonatal sex (male or female), living status at birth (stillbirth or livebirth), birth weight (grams, g), head circumference (cm), birth length (cm), placenta weight (g), gestational age (GA) assessed at birth. Based on living status at delivery discharge, early neonatal mortality in the five days following delivery was reported. If there was a discrepancy between GA assessed at birth and GA based on date of last menstruation, or if the latter was missing (*n*=630), we used GA assessed at birth (this process is described in the Supplementary material of a previously published work (26)). From this calculated GA variable, we defined preterm birth (<37 weeks). Based on maternal residential address, a variable “living inside Lausanne” (yes or no/unsure) was defined. From qualitative information in a “general health status” section, we created a categorical morphology variable (obese, thin or neither), and the binary variables goitre and rickets. Maternal occupation was coded using the Historical International Standard of Classification of Occupations (HISCO) database (27,28). HISCO codes were then grouped into 3 classes, with higher class representing higher socio-economic status: 1 for unskilled workers/farm workers, 2 for medium-skilled workers, farmers, and 3 non-manual occupations, higher managers/professionals. Seasonality was categorized based on meteorological season of birth (spring, summer, autumn, winter).

Miscarriages: Events qualified as “abortions” (thought to reflect what would today be considered as miscarriage/early fetal loss - mean GA was 13.7 weeks) between 1909 and 1921 (*n*=920) were transcribed. These years were selected so that enough years surrounding the pandemic were available for comparing miscarriages rates.

Maternal ILI: information on maternal illness was reported in a section called “health status during pregnancy”. It included a description of symptoms and an indication of the date of symptoms onset. The amount of information varied from one case to the other. If the illness happened during the pandemic (based on its course in *Figure S1*, July 1, 1918 to March 31, 1919 or January 1, 1920 to March 31, 1920), the infants were considered as exposed to maternal ILI (*n*=282). Based on approximate date of disease onset, exposure was categorised by trimester: first (months 1-3), second (months 4-6), and third (from month 7 to delivery). Trimester of illness was available for 268 (95%) of the ILI cases. Symptom severity was classified as severe (bronchopneumonia, pneumonia, or bronchitis) or mild and was available for 237 (84%) of the ILI cases. See *Supplementary Methods, Figure S2* and *Table S1* for ILI examples.

Investigated outcomes were birth weight, head circumference, placenta weight, birth length, ponderal index ($100\ x \frac{birth\ weight\ (g)}{birth\ length\text{^}3\ (cm)}$), GA, LBW, preterm birth, stillbirth and early neonatal mortality in the first five days after delivery. Ponderal index has previously been used as an

indicator of intra-uterine growth restriction; it is also associated with perinatal mortality and morbidity (29,30).

Exclusion criteria: From the 13,042 births between 1905 and 1924, we successively excluded homebirths (*n*=52, 0.40%) due to missing information, infants with birth weight <500g or GA <22 weeks (*n*=13, 0.10%), based on modern definition for stillbirth (31), and outliers of birth weight, birth length, placenta weight and head circumference (*n*=11, 0.08%). The final dataset consists of 12,966 births. For the analyses, the dataset was restricted to the pandemic period (*Figure S1*), with infants born after July 1, 1918 and conceived before April 1, 1919, or born after January 1, 1920 and conceived before April 1, 1920 (*n*=2,177).

Statistical analyses: Welch Two Sample t-test and Chi squared test for equality of proportions were performed to report mean and proportion differences, respectively, for continuous and categorical maternal characteristics of ILI-exposed vs. unexposed groups. We fitted robust linear models (RLMs) for the continuous outcomes and generalized linear models (GLMs) with a logit for the binary outcomes. Univariable RLMs and GLMs were built to model the relationship between maternal ILI and birth weight, head circumference, placenta weight, birth length, ponderal index, GA, LBW, preterm birth and early neonatal mortality among livebirths only (*n*=2,085). For the stillbirth outcome model, all births were used (*n*=2,177). Multivariable RLMs and GLMs were built for the outcomes birth weight, head circumference, placenta weight, birth length, ponderal index, GA, LBW and preterm birth, and were adjusted for ILI, seasonality, maternal height, age, gravidity, neonatal sex, morphology, civil status, living inside Lausanne. All models were also fitted using a categorical variable describing the trimester of pregnancy during which maternal ILI occurred, or using a categorical variable describing the severity of symptoms. The cases for which trimester or symptoms of ILI was unknown were excluded from the models. All univariable models were also stratified by fetal sex. However, for the models with ILI trimester of exposure or severity, sex-stratified models were fitted for all continuous outcomes but only for LBW and preterm birth binary outcomes, due to the small number of events. For all models, marginal means, marginal proportions, and their difference and associated 95% confidence intervals (CI) were computed, averaging the covariates as follows: mean value for the continuous covariates, and average over all levels for categorical variables, weighted by the sample frequencies.

Regarding miscarriages, only descriptive statistics were used to compare maternal characteristics and yearly changes.

R version and packages: R version 4.4.3 was used (32). `tidyverse` (33) package was used for data processing and graphics. The function `ggemmeans` from `ggeffects (34)` package was used for computing marginal means/proportions and their difference.

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Results

There was no major change in the maternal and neonatal characteristics during the pandemic years, in comparison to the whole time trend (1905-1924) (*Tables S2-3* and *Figure S3-4).* During the pandemic, most mothers who delivered at the hospital were living outside of Lausanne, were married and multiparous (*Table S4*). As the majority of women were housewives, they belonged to the HISCO class 2, corresponding to medium-skilled workers, based on the historical classification of occupation (27,28). There were 282 (13%) mothers who developed ILI during the pandemic, and they had similar characteristics than those who did not (*Table S5*). The onset of ILI during pregnancy was consistent with the pandemic waves, with a peak of 47 women affected in October 1918 (*Figure S5*).

1. Pregnancy outcomes depending on maternal ILI

Pregnancy outcomes depending on maternal ILI exposure are displayed in **Table 1**. More females (54%) were born to ILI-affected mothers. In univariable models (**Figure 1** and *Table S7*), infants exposed to maternal ILI *in utero* had a lower birth weight (marginal mean difference -107.4g), head circumference (-0.26cm), placenta weight (-35.0g), birth length (-0.34cm) and ponderal index (-0.04), and higher LBW (marginal proportion difference +5.0%) and preterm birth (+3.7%) rates. In univariable models stratified by sex, ILI exposure among males was associated with larger decreases of anthropometric measures than among females, and with a higher rate of stillbirth (+1.6%) (**Figure 1**, *Table S8*) For instance, head circumference was lowered by 0.34cm [95%CI -0.61 to -0.06cm] for males exposed to ILI, but there was limited evidence for females (-0.11cm [95%CI -0.35 to 0.12cm]).In multivariable models, maternal ILI was associated with lower placenta weight (-29.5g [95%CI -53.6 to -5.3g]) and higher risks of LBW (+6.4% [95%CI 5.5 to 7.2%]) and PTB (+2.9% [95%CI 1.8 to 4.0]) (**Figure 1** and *Table S7*). The magnitude of the association between maternal ILI and birth weight and size was smaller than in univariable models, but the direction of the associations was consistent.

[Insert Figure 1 here]

2. Pregnancy trimester of maternal ILI

Less women were affected by ILI in the first (*n*=75) than in the second (*n*=95) and third (*n*=98) trimesters (**Table 2**). There were no major differences between maternal characteristics depending on the trimester of ILI (*Table S9*). Exposure in the third trimester seemed to be associated with lower infant anthropometric measures than exposure earlier in pregnancy (**Table 2**). There were less males born to ILI-affected mothers in the first (41%) than in the second (51%) and third (47%) trimesters. Males exposed in the third trimester had a particularly high stillbirth rate (*n*=6, 13% compared to *n*=45, 5% for the unexposed, *Table S10*), but the number of events was too small to fit models. In univariable models (**Figure 2**, *Table S12*), exposure in the first and third trimesters were associated with lower infant size and weight, but the size of the associations was weaker for first compared to third-trimester exposure. Interestingly, stillbirth risk was doubled when ILI occurred in the third trimester

(9.2% compared to 4.2%, marginal proportion difference +5.0% [95%CI 4.2 to 5.7%]). In multivariable models, all anthropometric parameters (and gestational age) were lowered in the case of third trimester exposure (**Figure 2**, *Table S12*). The proportion of LBW was higher among those exposed in the first trimester (+5.3 [95%CI 4.2 to 6.3%]) than among those unexposed, but the proportion was even higher for third trimester exposure (+12.8% [95%CI 11.8 to 13.7%]). In addition, preterm birth risk increased by 9.4% for third trimester exposure [95%CI 8.2 to 10.6%]) and continuous GA was also lower (-0.5 weeks [95%CI -0.8 to -0.2 weeks]).

In models stratified by sex, males were generally affected by first-trimester *in utero* exposure, while females only had a higher LBW rate compared to unexposed females (**Figure 2**, *Table S13*). Females were affected by third trimester exposure, but generally to a lower extent that males were. For instance, birth weight was lowered by 126.3g [95%CI -256.6; 4.01g] for females and by 229.4g [95%CI -391.0; -65.8g] for males.

[Insert Figure 2 here]

3. Severity of influenza-like ILI

More women developed mild (*n*=137) than severe symptoms (*n*=100, *Table S14*). For forty-five women who developed ILI, symptoms severity was not reported. Mothers who developed severe symptoms were more often multiparous (72%) compared to those who did not have ILI (61%) (*Table S17*). The more the pregnancy was advanced, the more often symptoms were severe: while only 15% of women who had ILI in the first trimester had severe symptoms, 49% of those affected in the third trimester reported severe symptoms (*Table S18*). In multivariable models, anthropometric measures were generally lowered to a bigger extent if the mother had developed severe ILI, but not if she had developed mild symptoms. However, associations were not significant anymore. Still, the rates of LBW and preterm birth were much higher in case of severe ILI (+10.6% [95%C 9.6 to 11.6%] for LBW and +4.7% [95%CI 3.5 to 5.9%] for preterm birth) but not of mild ILI (+0.9% [95%CI -0.1 to 2.0%] for LBW and +1.7 [95%CI 0.5 to 2.9%] for preterm birth) (**Figure S6**, *Table S19*). In univariable GLMs stratified by sex, it was not clear whether mild or severe symptoms were associated with worse pregnancy outcomes depending on fetal sex (**Figure S6**, *Table S20*).

Miscarriages

Yearly numbers of miscarriages peaked in 1918-1919 (*Figure S7A*), though percentages relative to births were also high before 1916 (*Figure S7E*). At the quarterly level, the miscarriage rate was already high before the pandemic (first quarter of 1918, *Figure S7F*). However, among women who miscarried in 1918, 1919 and 1920, 13%, 39% and 58% had ILI during pregnancy, respectively (*Table S21*). Comparing women who had miscarriages to those who delivered, we again see that ILI during pregnancy was more frequent among miscarriage cases (34% compared to 12%, i.e. +22% [95%CI 16 to 28%]), but women who had a miscarriage were also older, and more often single or multiparous (*Table S22)*.

Discussion

Infant health is negatively affected by maternal ILI, especially for third trimester exposure

Most measured anthropometric indicators were lowered by maternal ILI, and this was mainly driven by third trimester exposure. For instance, while birth weight was overall lowered by about 84g by maternal ILI, it was lowered by 194g when ILI occurred in the third trimester. In addition, infants whose mothers developed ILI in the third trimester were born on average 3.4 days earlier, with a preterm birth rate almost three times higher. First trimester exposure was associated with poorer pregnancy outcomes in univariable but not in multivariable models, except for a higher LBW rate (+5%) compared to unexposed infants.

As GA is a strong determinant of fetal growth, being born earlier results in a lower birth weight and size. Thus, our findings of lower infant weight and size are probably - at least partly - mediated by shorter gestation. This is consistent with contemporary studies that reported early pregnancy loss and preterm birth among mothers with ILI (2,3,5,6,11). In the 1919 report carried out by the health authorities of Vaud, physicians frequently reported earlier deliveries, especially when illness occurred close to the term (35). In a study using the same birth records than in the current paper, we reported lower birth weight and head circumference for *in utero* exposure to maternal ILI (26). However, GA was not affected: we believe this is because the timing of ILI was not considered. In addition, the dataset had not been restricted to the pandemic period but to the years 1911-1922, and as a result there were many more unexposed cases than in the current study (*n*=8,131 vs. *n*=1,895). During the 1957-1958 (36) and 2009-2010 (20,37) pandemics as well, there were reports of premature deliveries. In fact, even seasonal influenza may be associated with shorter gestation (38,39). In Denmark, seasonal flu was associated with lower birth weight only when GA was not controlled for (39). We chose not to adjust our models for gestational duration to avoid potential collider bias (see *Supplementary Methods*), but this Danish study supports our hypothesis that ILI-triggered premature delivery is the reason that birth weight is lower.

On the other hand, the association between maternal-ILI and birth weight and size may also have been mediated by a reduction in caloric intake. In a randomized-controlled (RCT) trial, maternal immunization against influenza was associated with a higher mean birth weight (3178g) compared to a placebo (2978g) (40). The authors argue that even a few days of maternal illness, associated with fever and anorexia, could affect fetal weight gain (a fetus gains 20-40g per day in the last weeks of pregnancy (41)). In the present paper, mothers often experienced illness lasting several weeks, thus a last-trimester infection could account for reductions in birth weight of several hundred grams. Another RCT reported that nutritional supplementation of pregnant women was associated with a higher birth weight among male but not among female infants (42). It is thus possible that the decreased caloric intake of mothers with ILI had a worse influence on male infants, which could explain the sex-differences we highlight.

At Lausanne maternity, the proportion of women with ILI was higher among those who had a miscarriage compared to those who delivered. A high rate of miscarriage during the 1918 pandemic has long been assumed to be one of the reasons explaining the decrease in the

number of births in the pandemic aftermaths (43–48). However, selection into fertility and especially deliberate postponement of conceptions during the pandemic may have also played a role, and we cannot conclude on the association between ILI and the risk of miscarriage. Additionally, the miscarriage reports may not be representative of all events, as many can go unnoticed or occur at home without resulting in a hospitalisation.

Timing of maternal ILI

There were less women with ILI in the first (27%) than in the second (34%) and third trimesters (35%). A systematic review concluded that during the 2009-2010 pandemic, more women were infected during the third trimester (47%) than in the first (9%) (7). Seasonal flu was also much more frequent in the third trimester (39). Infection closer to the term may lead to more severe symptoms, and would thus have a higher chance of being noticed. Indeed, we find that most severe cases occurred in the third trimester, with about 50% of women having developed pneumonia or bronchitis. Towards the end of pregnancy, altered immunity and reduced lung capacity increase the risk of severe influenza symptoms (7,49). Recall bias is another explanation, but first-trimester illness may also have been associated with miscarriages, and we selected women whose fetuses "survived" to first-trimester exposure.

Males may be more vulnerable to maternal ILI

The magnitude of the impact of maternal ILI was greater among males than females, with larger reductions in anthropometric weight and size, and a higher risk of stillbirth. Furthermore, mostly males were affected by first-trimester exposure. Less males were born to mothers who experienced ILI in the first trimester compared to mothers who were not affected by influenza (41% vs. 52%). This may signal selection against males: if first trimester ILI led to miscarriage more frequently among males, then the sex ratio male:female at birth would be lower. Unfortunately, fetal sex was rarely reported among the miscarriage events and we cannot challenge this hypothesis. In Japan, the sex ratio at birth was also lower for first trimester exposure to the 1918 pandemic (indirectly measured using influenza deaths rates) (24). There is evidence that the sex ratio at birth decreases following other types of crisis, including natural disasters, economic crises, and terrorist attacks (21,23,50,51).

To conclude, it seems that males remained more vulnerable to influenza during the whole pregnancy, likely through a higher rate of miscarriage for first trimester exposure, while third trimester exposure was associated with lower size and weight measured at birth. Higher rates of miscarriage and stillbirth may have led to survival bias for surviving males at birth, but this appears to have been countered by the scarring influence of maternal ILI.

Limitations

The definition of ILI is based on clinical symptoms reported by the mother, which may be undistinguishable from that of other viruses, potentially leading to a misclassification of exposure. By focusing on illnesses occurring during the pandemic waves, we mitigate this bias and discard cases potentially due to seasonal flu or other diseases. Still, ILI diagnosis is limited

to women seeking care or having more severe symptoms: it is possible that women with an asymptomatic or a mild flu were misclassified as “unexposed to ILI”.

We do not know how representative the women who delivered at the maternity hospital are of all those who gave birth in Lausanne and its surroundings. Although there was only one maternity in the city, it was frequent to deliver at home (52). Based on official statistics, 66% of births occurring in Lausanne happened at the maternity in 1920 (53). In the same year, 10% of mothers delivering at the hospital were single, compared to 5% among homebirths. Paternal occupation indicated that socio-economic status was slightly lower among married mothers delivering at the maternity (data not shown). Still, there have never been restrictions on admission at the maternity (54), with both complicated and uncomplicated deliveries taking place, making us believe that our results may be generalizable. Importantly, influenza seems to have affected all women, independently of socio-demographic characteristics, as reported in another paper (55). Finally, apart from maternal occupation and civil status, we did not have detailed information on the socio-economic status, such as household income.

Implications

The poorer outcomes we report in the case of maternal ILI may have lasting consequences. Being born with a LBW is associated with a higher risk of morbidity in childhood (56), and with increased risks of chronic diseases in adulthood (57–62). Several health economics papers report that early-life exposure to the 1918 influenza pandemic negatively impacted socio-economic attainments and health outcomes later in life (63–67). This was also the case for the pandemic birth cohort in Switzerland, with lower educational attainment and occupational status (68). However, unobserved factors may be associated with both the poor *in utero* environment and long-term outcomes: we can hardly separate the cause of fetal stress from other factors which also generate poor health later in life. In addition, the negative long-term economic effects documented for the 1919 US birth cohort (63) were confounded by a negative socio-economic selection of parents (69).

In conclusion, our results highlight the adverse influence of maternal ILI during an influenza pandemic, based on over two thousand birth records. Our findings suggest that maternal ILI, particularly during the third trimester of pregnancy, may have triggered premature birth. Additional research is needed to conclude on stillbirth and early neonatal mortality, since there were only a few cases in our study sample. The 1918 influenza pandemic was the most severe of the last century, and as influenza pandemics regularly occurred throughout history, they are bound to reoccur in the future. Our findings emphasize the importance of mitigating exposure to influenza during pregnancy through effective preventive measures.

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Data Availability Statement

The data that support the findings of this study and the codes used for the data analysis is publicly available in the following online repository: https://github.com/MathildeLV/maternal_ILI_2025_Le_Vu.

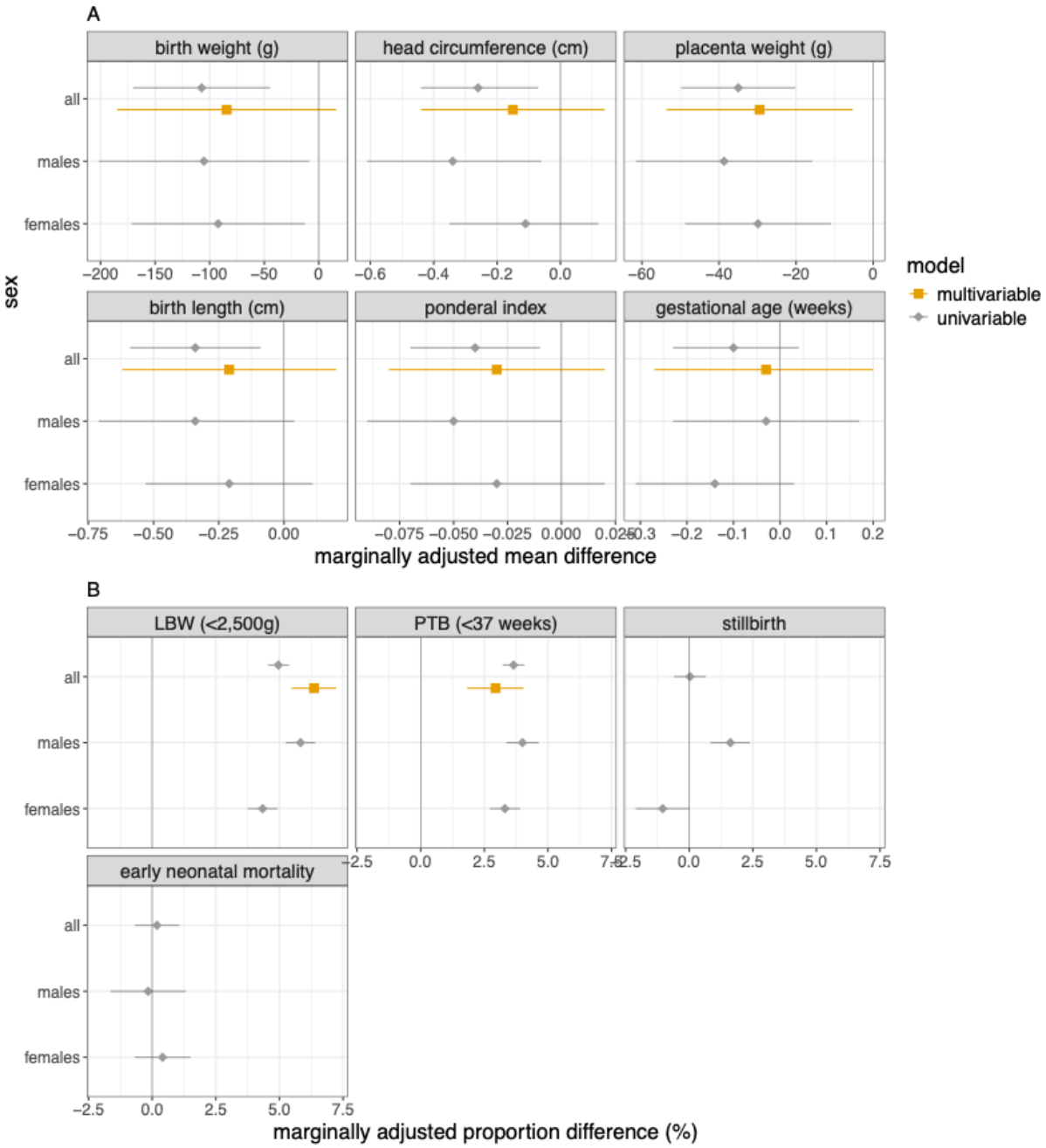

Figure 1: continuous (A) and binary (B) pregnancy outcomes depending on maternal ILI, univariable and multivariable RLMs (continuous outcomes) and GLMs (binary outcomes), all births and stratified by sex. All models are fitted using only livebirths, except for stillbirth outcome. Quantitative results are summarized in *Tables S7-8*. Multivariable models are adjusted for: ILI during pregnancy, maternal age, height and gravidity, sex (except for the sex-stratified models), season, morphology, civil status, living inside Lausanne.

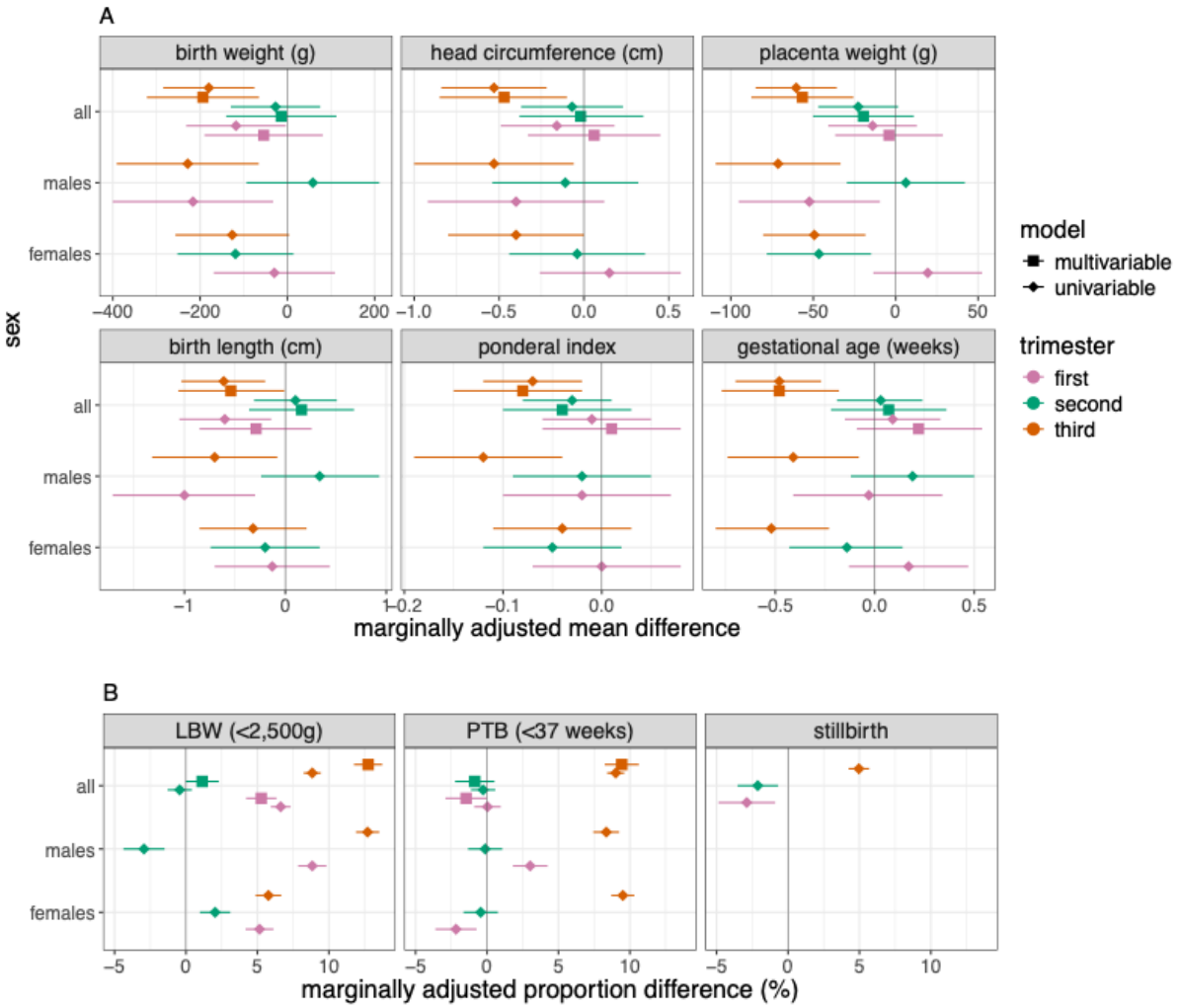

Figure 2: continuous (A) and binary (B) pregnancy outcomes depending on trimester of exposure to maternal ILI, univariable and multivariable RLMs (continuous outcomes) and GLMs (binary outcomes), all births and stratified by sex. All models are fitted using only livebirths, except for stillbirth outcome. The same models are summarized in *Table S12-13*. For each outcome, only one RLM/GLM was fitted, and the exposure variable was a categorical variable (no ILI (reference category), ILI in the first, in the second, or in the third trimester). Note: when the timing of ILI exposure was unknown (*n*=14), cases were not considered.

Supplementary Material to the article:

Maternal influenza-like illness and neonatal health during the 1918 influenza pandemic in a Swiss city

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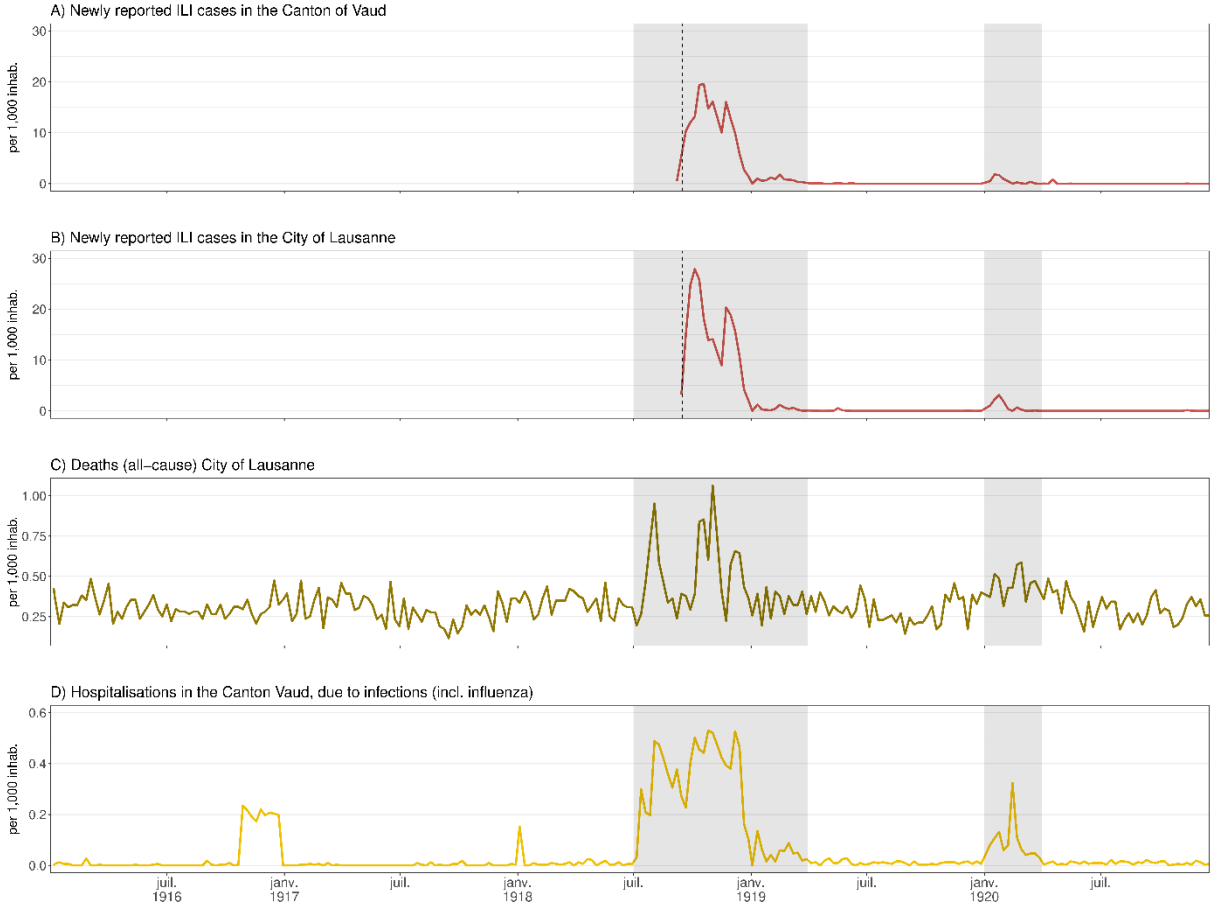
Table of contents

Figure S1: timing of the influenza pandemic in Lausanne and in the canton of Vaud, using data from the Swiss public health weekly reports (1). Influenza-like illness incidence in the Canton of Vaud (**A**) and in the city of Lausanne (**B**); the dashed line indicates the introduction of the cantonal reporting obligation on 24.09.1918. All-cause deaths in the city of Lausanne (**C**); and hospitalisations in the canton of Vaud, due to infections (including influenza) (**D**).



Methods

Database and transcription: in total, 10 investigators transcribed the data. The data analysed in the paper (1918-1920) was transcribed by 7 different persons. Although this might be a limit to the consistency of the transcription, handwritten numbers could easily be read. The variables were manually transcribed with the help of an entry tool designed and coded using R and ShinyApp. The data were stored as a secured SQL database on the server of the University of Zurich. The protocol was approved by the Zurich Ethics Committee (BASEC Number 2021-00628). To limit errors of transcription, quality controls were continuously performed by the research team. In the event that the transcriber was uncertain of a variable (difficult handwriting, seemingly nonsense), the entry was later reviewed by another transcriber and then by the team, until an agreement was reached.

Variables: civil status was categorized into "married" and "single or missing", the latter grouping together "single", "widowed", "divorced" or missing. Syphilis status was based on symptoms or on the Wasserman test (2). Information on early neonatal mortality (first 7 days of life) is missing for mother-child pairs who left the maternity before 7 days post-partum. Hence, we used information concerning the first 5 days after delivery, since virtually all mother-infant pairs stayed for that duration. Based on maternal residential address, a variable "living inside Lausanne" was defined, taking the values "yes", "no", or "unsure". Since Lausanne residence was "unsure" in only 0.42% case, these were pooled with the category "no".

ILI exposure variable: infants *in utero* during the pandemic (based on its course in Lausanne, *Figure S1*, those born after 01/07/1918 and conceived before 01/04/1919, or born after 01/01/1920 and conceived before 01/04/1920), and whose mother had ILI during pregnancy, were considered as exposed to ILI (*n*=299). However, if the timing of the illness indicated that it occurred outside of the pandemic period, these cases were excluded (*n*=17), resulting in a total of *n*=282 infants exposed *in utero.* Regarding the timing of ILI, for women with two ILI episodes, the latter date was used to indicate the trimester of disease onset. Regarding symptoms, they were considered severe if there was a mention of one of the following: bronchopneumonia, pneumonia, or bronchitis. In addition, a few (*n*=4) cases where it was clear the woman had developed severe symptoms were also qualified as such ("pulmonary complications, 3 weeks in bed", "17 days of treatment at the hospital", "very severe influenza with epistaxis", "dry pleurisy"). Examples are given in Figure S2 and Table S1.

Figure S2: Four examples of birth records from the maternity hospital of Lausanne, with a report of maternal ILI during pregnancy. Information on maternal ILI was found in the bottom part "état de santé pendant la grossesse" [health status during pregnancy] and is analysed in the following table. Note: the top of the page which contains demographic information is not shown.

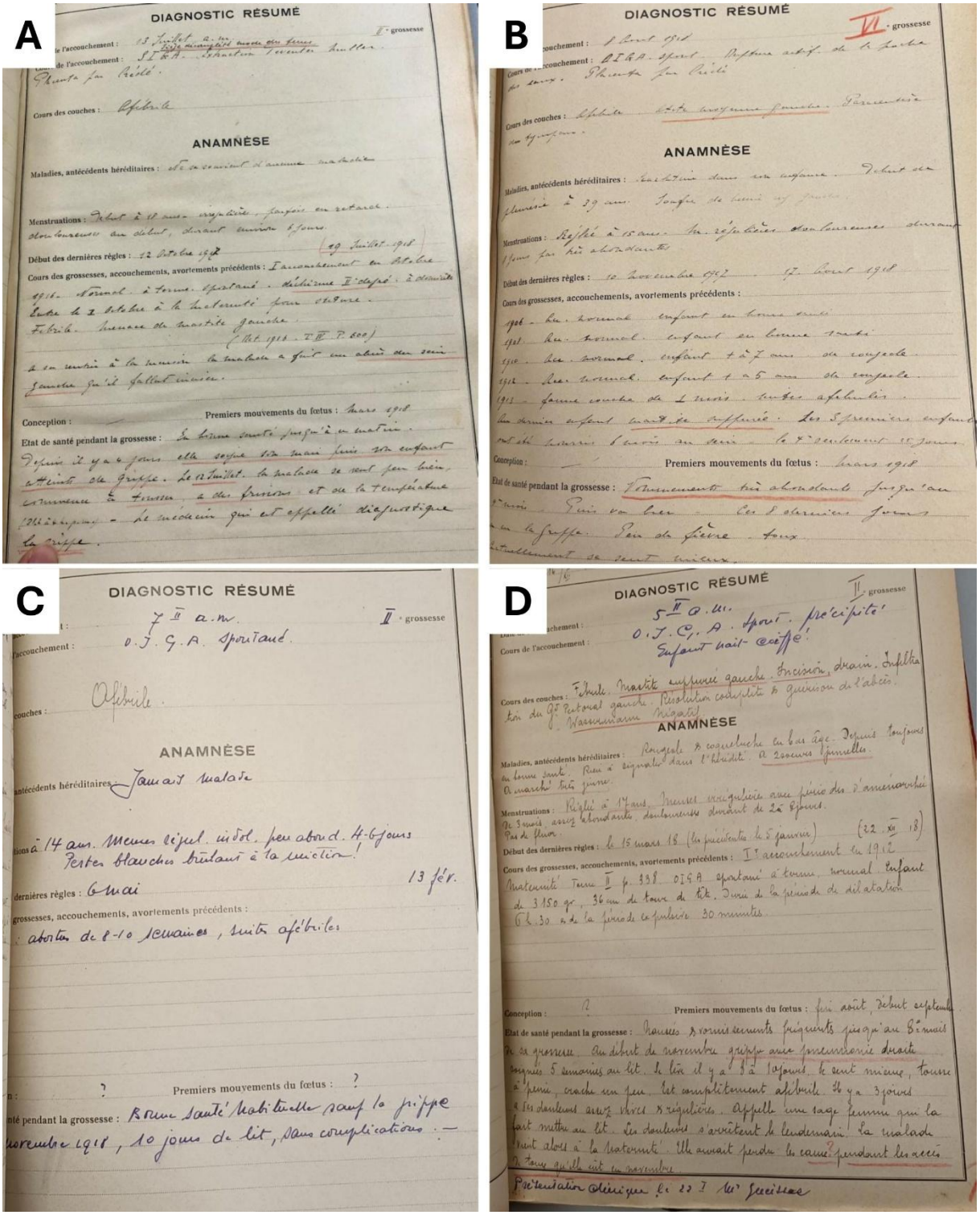


Table S1: Four examples of a report of maternal ILI during pregnancy, corresponding to the previous Figure S2.

	A	B	C	D
French	En bonne santé jusqu'à ce matin. Depuis il y a 4 jours elle soigne son mari puis son enfant atteints de grippe. Le 12 Juillet la malade se sent peu bien, commence à tousser, a des frissons et de la température (38.2 à 4h p.m.) – Le médecin qui est appelé diagnostique la grippe	[…] Les 8 derniers jours a eu la grippe. Peu de fièvre. Toux. Actuellement se sent mieux.	Bonne santé habituelle sauf la grippe novembre 1918, 10 jours de lit, sans complications.	[…] Au début de novembre grippe avec pneumonie droite, soignée 5 semaines au lit. Se lève il y a 8 à 10 jours, se sent mieux, tousse à peine, crache un peu. Est complètement afébrile. […]
English translation	In good health until this morning. Since 4 days she cares for her husband and child who have the flu. On the 12th of July, she does not feel well, starts coughing, shivering and has fever (38.2°C at 4pm). The physician who is called diagnoses the flu.	[…] The last 8 days had the flu. Not much fever. Cough. Feels better now.	Usually in good health except for the flu in November 1918, 10 days of bed, without complications	[…] At the beginning of November, flu with pneumonia on the right side, sick for 5 weeks in bed. She gets up 8-10 days ago and feels better, barely coughs, spits a bit. She is not feverish at all.
Date of delivery	July 13th, 1918	August 8th,1918	February 7th, 1919	February 5th, 1919
Date of last period	October 12th, 1917	November 10th, 1917	May 6th, 1918	March 15th, 1918
Date of ILI	July 12th, 1918	August 1st, 1918	November 1918	November 1918
Trimester of ILI	third	third	third	third
Symptoms category	mild	mild	mild	severe

Exclusion criteria: birth weight, birth length, placenta weight and head circumference which had a sex-*specific Z*-score higher ≥ |7| standard deviations were excluded. This threshold is conservative because outliers are usually excluded at lower cut-offs (3).

Statistical analyses: multivariable RLMs/GLMs were adjusted for variables (ILI, seasonality, maternal height, age and gravidity, neonatal sex), that we expected to be associated with the outcomes, based on the literature. Other potential explanatory variables (morphology, civil status, HISCO class, living inside Lausanne, goitre, rickets) were added using a stepwise algorithm. Based on the lowest Akaike information criterion (AIC), all models were adjusted for ILI, seasonality, maternal height, age, gravidity, neonatal sex, morphology, civil status, living inside Lausanne. GA is an important determinant of birth size (4), but it is also an intermediate variable on the causal path between exposure (disease) and outcome (neonatal size), since GA itself can be affected by maternal ILI and determines the time at which birth

anthropometry is measured. Therefore, adjusting or stratifying for GA in the regression models may induce collider bias (5–7), thus we decided not to adjust our analyses on GA.

Descriptive characteristics of the population

Table S2: Maternal characteristics through the years (1905-1924)

Variable	1905, N = 315[1]	1906, N = 317[1]	1907, N = 340[1]	1908, N = 361[1]	1909, N = 383[1]	1910, N = 360[1]	1911, N = 396[1]	1912, N = 430[1]	1913, N = 423[1]	1914, N = 557[1]	1915, N = 557[1]	1916, N = 576[1]	1917, N = 741[1]	1918, N = 735[1]	1919, N = 795[1]	1920, N = 1,041[1]	1921, N = 1,129[1]	1922, N = 1,146[1]	1923, N = 1,236[1]	1924, N = 1,128[1]
maternal age (years)	27.8 (6.1)	27.6 (6.7)	27.7 (6.7)	27.5 (6.4)	28.2 (6.6)	27.3 (6.4)	28.3 (6.9)	28.5 (6.8)	27.7 (6.8)	27.7 (6.5)	28.2 (6.8)	28.3 (6.4)	28.2 (6.2)	28.4 (6.5)	28.6 (6.2)	28.5 (6.2)	28.3 (6.2)	28.0 (5.9)	28.4 (6.1)	28.6 (6.0)
missing	1	0	0	0	0	0	0	0	0	0	0	1	0	2	2	2	2	0	0	1
height (cm)	155.1 (5.9)	154.3 (6.9)	154.7 (6.6)	155.1 (7.6)	156.0 (6.5)	155.9 (6.4)	155.6 (6.9)	155.7 (6.8)	155.0 (6.1)	154.9 (6.1)	155.5 (6.4)	155.8 (6.8)	155.9 (6.6)	156.0 (6.6)	156.5 (6.1)	156.3 (6.8)	156.4 (6.6)	156.5 (6.4)	156.6 (6.0)	156.7 (5.8)
missing	16	13	7	7	22	9	12	16	24	23	15	8	20	31	36	47	45	38	57	50
civil status																				
married	233 (74%)	208 (66%)	217 (64%)	260 (72%)	277 (72%)	256 (71%)	292 (74%)	324 (75%)	319 (75%)	424 (76%)	445 (80%)	489 (85%)	616 (83%)	619 (84%)	694 (87%)	925 (89%)	1,010 (89%)	1,052 (92%)	1,133 (92%)	1,043 (92%)
single or missing	82 (26%)	109 (34%)	123 (36%)	101 (28%)	106 (28%)	104 (29%)	104 (26%)	106 (25%)	104 (25%)	133 (24%)	112 (20%)	87 (15%)	125 (17%)	116 (16%)	101 (13%)	116 (11%)	119 (11%)	94 (8%)	103 (8%)	85 (8%)
gravidity																				
1	94 (30%)	122 (38%)	119 (35%)	126 (35%)	118 (31%)	131 (36%)	135 (34%)	143 (33%)	158 (37%)	191 (34%)	182 (33%)	186 (32%)	283 (38%)	290 (39%)	284 (36%)	447 (43%)	473 (42%)	430 (38%)	454 (37%)	422 (37%)
2	63 (20%)	65 (21%)	69 (20%)	77 (21%)	81 (21%)	88 (24%)	74 (19%)	92 (21%)	89 (21%)	116 (21%)	137 (25%)	109 (19%)	151 (20%)	143 (19%)	205 (26%)	209 (20%)	247 (22%)	281 (25%)	287 (23%)	257 (23%)
>2	158 (50%)	130 (41%)	152 (45%)	158 (44%)	184 (48%)	141 (39%)	187 (47%)	195 (45%)	176 (42%)	250 (45%)	236 (43%)	281 (49%)	307 (41%)	302 (41%)	306 (38%)	385 (37%)	409 (36%)	435 (38%)	495 (40%)	448 (40%)
missing	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	1
living in Lausanne	158 (50%)	166 (52%)	175 (51%)	179 (50%)	191 (50%)	186 (52%)	203 (51%)	239 (56%)	217 (51%)	287 (52%)	281 (50%)	265 (46%)	344 (46%)	364 (50%)	360 (45%)	454 (44%)	453 (40%)	437 (38%)	446 (36%)	422 (37%)
morphology																				
neither	309 (98%)	297 (94%)	337 (99%)	356 (99%)	381 (99%)	358 (99%)	383 (97%)	405 (94%)	383 (91%)	498 (89%)	487 (87%)	541 (94%)	702 (95%)	699 (95%)	743 (93%)	970 (93%)	1,077 (95%)	1,080 (94%)	1,206 (98%)	1,043 (92%)
obese	1 (0%)	9 (3%)	2 (1%)	4 (1%)	2 (1%)	1 (0%)	5 (1%)	17 (4%)	25 (6%)	33 (6%)	33 (6%)	16 (3%)	11 (1%)	19 (3%)	27 (3%)	44 (4%)	37 (3%)	43 (4%)	22 (2%)	59 (5%)
thin	5 (2%)	11 (3%)	1 (0%)	1 (0%)	0 (0%)	1 (0%)	8 (2%)	8 (2%)	15 (4%)	26 (5%)	37 (7%)	19 (3%)	28 (4%)	17 (2%)	25 (3%)	27 (3%)	15 (1%)	23 (2%)	8 (1%)	26 (2%)
goitre	14 (4%)	33 (10%)	19 (6%)	23 (6%)	42 (11%)	27 (8%)	21 (5%)	26 (6%)	31 (7%)	58 (10%)	97 (17%)	55 (10%)	26 (4%)	20 (3%)	45 (6%)	72 (7%)	98 (9%)	47 (4%)	17 (1%)	7 (1%)
rickets	10 (3%)	43 (14%)	18 (5%)	44 (12%)	15 (4%)	10 (3%)	37 (9%)	57 (13%)	50 (12%)	104 (19%)	125 (22%)	69 (12%)	40 (5%)	44 (6%)	35 (4%)	42 (4%)	30 (3%)	25 (2%)	8 (1%)	15 (1%)
flu during pregnancy and pandemic	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	57 (8%)	155 (19%)	70 (7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
syphilis	5 (2%)	4 (1%)	3 (1%)	5 (1%)	8 (2%)	16 (4%)	7 (2%)	6 (1%)	3 (1%)	8 (1%)	10 (2%)	12 (2%)	6 (1%)	6 (1%)	8 (1%)	13 (1%)	18 (2%)	7 (1%)	15 (1%)	7 (1%)
maternal mortality	2 (1%)	4 (1%)	2 (1%)	4 (1%)	2 (1%)	3 (1%)	2 (1%)	4 (1%)	2 (0%)	9 (2%)	7 (1%)	6 (1%)	2 (0%)	6 (1%)	0 (0%)	4 (0%)	6 (1%)	2 (0%)	7 (1%)	2 (0%)
HISCO class																				
2	218 (69%)	210 (66%)	246 (72%)	276 (76%)	305 (80%)	269 (75%)	291 (73%)	333 (77%)	324 (77%)	434 (78%)	444 (80%)	525 (91%)	640 (86%)	632 (86%)	684 (86%)	894 (86%)	995 (88%)	1,067 (93%)	1,144 (93%)	472 (42%)
1	76 (24%)	90 (28%)	73 (21%)	62 (17%)	58 (15%)	70 (19%)	76 (19%)	70 (16%)	71 (17%)	92 (17%)	84 (15%)	38 (7%)	55 (7%)	47 (6%)	53 (7%)	57 (5%)	60 (5%)	37 (3%)	50 (4%)	59 (5%)
3	4 (1%)	5 (2%)	6 (2%)	11 (3%)	6 (2%)	4 (1%)	6 (2%)	12 (3%)	9 (2%)	14 (3%)	13 (2%)	4 (1%)	12 (2%)	18 (2%)	17 (2%)	15 (1%)	15 (1%)	8 (1%)	7 (1%)	15 (1%)
missing	17 (5%)	12 (4%)	15 (4%)	12 (3%)	14 (4%)	17 (5%)	23 (6%)	15 (3%)	19 (4%)	17 (3%)	16 (3%)	9 (2%)	34 (5%)	38 (5%)	41 (5%)	75 (7%)	59 (5%)	34 (3%)	35 (3%)	582 (52%)
season																				
spring	72 (23%)	106 (33%)	91 (27%)	98 (27%)	100 (26%)	82 (23%)	119 (30%)	119 (28%)	113 (27%)	164 (29%)	169 (30%)	141 (24%)	188 (25%)	206 (28%)	181 (23%)	265 (25%)	300 (27%)	315 (27%)	335 (27%)	307 (27%)
summer	75 (24%)	72 (23%)	92 (27%)	98 (27%)	106 (28%)	103 (29%)	84 (21%)	117 (27%)	107 (25%)	143 (26%)	129 (23%)	153 (27%)	204 (28%)	185 (25%)	187 (24%)	260 (25%)	298 (26%)	301 (26%)	295 (24%)	274 (24%)
autumn	91 (29%)	82 (26%)	69 (20%)	84 (23%)	96 (25%)	88 (24%)	87 (22%)	100 (23%)	110 (26%)	118 (21%)	102 (18%)	137 (24%)	179 (24%)	176 (24%)	241 (30%)	251 (24%)	261 (23%)	267 (23%)	300 (24%)	261 (23%)
winter	77 (24%)	57 (18%)	88 (26%)	81 (22%)	81 (21%)	87 (24%)	106 (27%)	94 (22%)	93 (22%)	132 (24%)	157 (28%)	145 (25%)	170 (23%)	168 (23%)	186 (23%)	265 (25%)	270 (24%)	263 (23%)	306 (25%)	286 (25%)

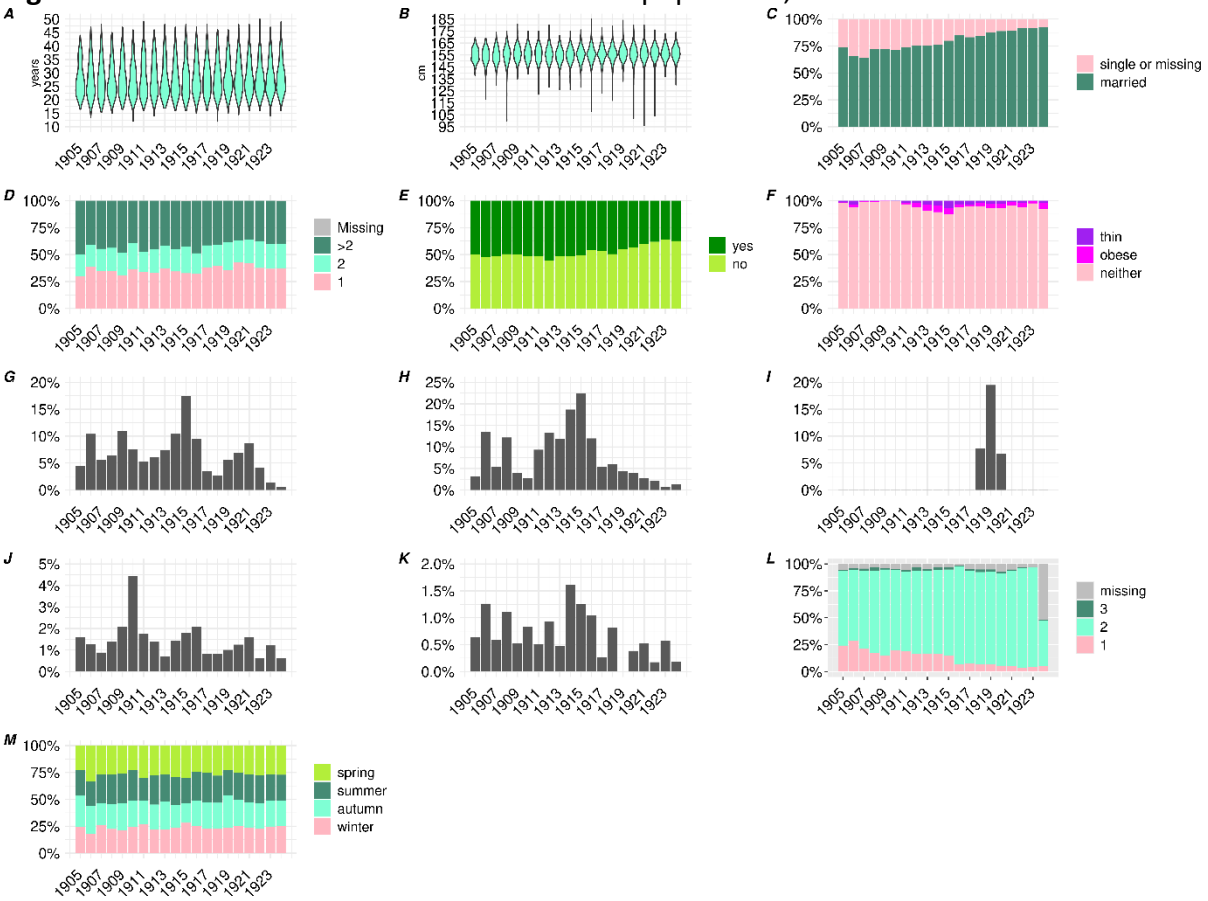
[1]Mean (SD); n (%)

Table S3: Neonatal characteristics through the years (1905-1924)

Variable	**1905**, N = 315[1]	**1906**, N = 317[1]	**1907**, N = 340[1]	**1908**, N = 361[1]	**1909**, N = 383[1]	**1910**, N = 360[1]	**1911**, N = 396[1]	**1912**, N = 430[1]	**1913**, N = 423[1]	**1914**, N = 557[1]	**1915**, N = 557[1]	**1916**, N = 576[1]	**1917**, N = 741[1]	**1918**, N = 735[1]	**1919**, N = 795[1]	**1920**, N = 1,041[1]	**1921**, N = 1,129[1]	**1922**, N = 1,146[1]	**1923**, N = 1,236[1]	**1924**, N = 1,128[1]
birth weight (g)	3,042.9 (602.5)	3,104.3 (571.4)	3,085.9 (560.4)	3,039.4 (562.9)	3,089.7 (604.0)	3,048.7 (601.7)	3,093.5 (607.5)	3,050.7 (580.7)	3,095.5 (600.4)	3,201.5 (572.9)	3,215.2 (554.4)	3,177.6 (549.0)	3,156.0 (547.0)	3,132.1 (567.1)	3,168.7 (588.2)	3,198.9 (567.9)	3,209.5 (540.7)	3,221.9 (503.5)	3,220.3 (544.4)	3,294.0 (520.0)
head circumference (cm)	33.6 (1.7)	33.6 (1.7)	34.0 (1.8)	34.5 (1.7)	34.8 (2.2)	33.9 (2.2)	34.3 (1.8)	34.1 (1.9)	34.0 (2.1)	34.3 (2.0)	34.4 (1.9)	34.5 (1.8)	34.3 (1.7)	34.4 (1.9)	34.4 (1.9)	34.3 (1.8)	34.5 (1.7)	34.5 (1.5)	34.5 (1.8)	34.7 (1.6)
missing	12	11	3	12	9	8	10	5	8	8	5	7	9	12	9	25	12	26	13	9
placenta weight (g)	568.3 (130.6)	553.3 (107.2)	557.5 (130.7)	571.6 (123.2)	575.6 (125.0)	566.1 (122.8)	559.1 (124.4)	544.3 (114.1)	551.2 (122.4)	569.4 (122.2)	558.9 (117.8)	575.9 (124.9)	572.9 (128.3)	570.2 (125.6)	584.2 (119.2)	580.7 (117.0)	590.2 (126.8)	591.1 (118.4)	584.1 (124.8)	579.3 (113.0)
missing	2	3	1	0	3	1	3	4	3	8	6	10	9	17	7	18	25	13	7	5
birth length (cm)	48.9 (3.3)	48.7 (2.6)	48.7 (2.5)	48.5 (2.9)	48.8 (3.2)	48.6 (3.1)	49.2 (3.0)	48.6 (2.8)	49.1 (3.1)	49.4 (2.7)	49.3 (2.8)	49.2 (2.7)	49.1 (2.3)	49.0 (2.9)	49.0 (2.9)	49.0 (2.7)	49.2 (2.5)	49.3 (2.4)	49.3 (2.5)	49.6 (2.2)
missing	2	1	1	1	1	1	1	0	4	1	2	0	5	3	2	3	5	1	2	2
ponderal index	2.6 (0.3)	2.7 (0.3)	2.6 (0.3)	2.7 (0.3)	2.6 (0.3)	2.6 (0.3)	2.6 (0.3)	2.6 (0.3)	2.6 (0.3)	2.6 (0.2)	2.7 (0.3)	2.6 (0.3)	2.7 (0.3)	2.6 (0.3)	2.7 (0.3)	2.7 (0.3)	2.7 (0.3)	2.7 (0.3)	2.7 (0.3)	2.7 (0.2)
missing	2	1	1	1	1	1	1	0	4	1	2	0	5	3	2	3	5	1	2	2
gestational age (weeks)	38.9 (2.4)	39.0 (2.1)	39.1 (2.1)	38.9 (2.3)	38.9 (2.5)	38.7 (2.5)	38.9 (2.3)	38.8 (2.5)	39.0 (2.4)	39.3 (2.2)	39.3 (2.2)	38.9 (2.2)	39.0 (2.0)	39.2 (2.3)	39.1 (2.2)	39.2 (2.1)	39.3 (2.0)	39.5 (1.7)	39.4 (1.8)	39.7 (1.7)
sex																				
Male	155 (49%)	165 (52%)	179 (53%)	177 (49%)	183 (48%)	197 (55%)	199 (51%)	222 (52%)	210 (50%)	293 (53%)	274 (49%)	312 (54%)	388 (52%)	383 (52%)	402 (51%)	537 (52%)	573 (51%)	558 (49%)	658 (53%)	556 (49%)
Female	159 (51%)	152 (48%)	160 (47%)	184 (51%)	200 (52%)	163 (45%)	195 (49%)	208 (48%)	213 (50%)	261 (47%)	282 (51%)	264 (46%)	353 (48%)	352 (48%)	391 (49%)	501 (48%)	546 (49%)	585 (51%)	577 (47%)	570 (51%)
missing	1	0	1	0	0	0	2	0	0	3	1	0	0	0	2	3	10	3	1	2
low birth weight (<2'500g)	44 (14%)	39 (12%)	40 (12%)	46 (13%)	51 (13%)	46 (13%)	50 (13%)	63 (15%)	50 (12%)	51 (9%)	42 (8%)	52 (9%)	60 (8%)	72 (10%)	81 (10%)	87 (8%)	89 (8%)	67 (6%)	92 (7%)	64 (6%)
preterm birth (<37 weeks)	32 (10%)	39 (12%)	38 (11%)	35 (10%)	43 (11%)	42 (12%)	46 (12%)	68 (16%)	41 (10%)	49 (9%)	52 (9%)	83 (14%)	100 (13%)	69 (9%)	68 (9%)	90 (9%)	82 (7%)	70 (6%)	74 (6%)	53 (5%)
stillbirth	20 (6%)	19 (6%)	18 (5%)	21 (6%)	23 (6%)	17 (5%)	21 (5%)	15 (3%)	18 (4%)	20 (4%)	20 (4%)	23 (4%)	25 (3%)	36 (5%)	32 (4%)	42 (4%)	27 (2%)	36 (3%)	47 (4%)	36 (3%)
neonatal mortality d1-5	5 (2%)	12 (4%)	10 (3%)	8 (2%)	18 (5%)	15 (4%)	20 (5%)	19 (4%)	14 (3%)	12 (2%)	12 (2%)	13 (2%)	17 (2%)	14 (2%)	22 (3%)	18 (2%)	26 (2%)	13 (1%)	16 (1%)	21 (2%)
missing	1	1	0	0	3	1	0	0	1	1	0	0	0	2	0	0	2	1	0	0

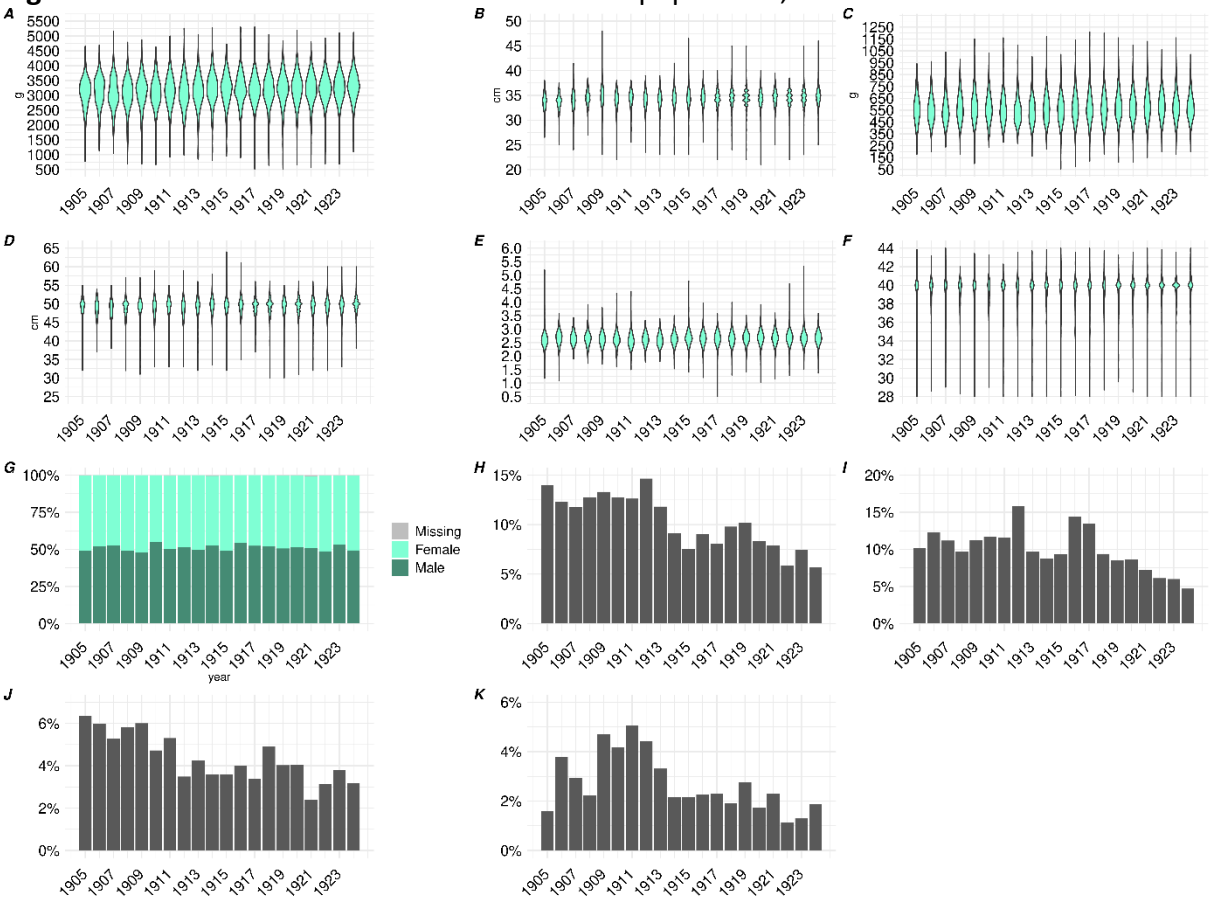
[1]Mean (SD); n (%)

Figure S3: annual maternal characteristics of the population, 1905-1924



Maternal age (**A**), height (**B**), civil status region (**C**), gravidity (**D**), living in the city of Lausanne at the time of delivery (**E**), morphology (**F**), goitre (**G**), rickets (**H**), influenza during pregnancy and during the pandemic (**I**), syphilis diagnosis (**J**), maternal mortality (**K**), HISCO class (**L**), season (**M**)

Figure S4: annual neonatal characteristics of the population, 1905-1924



Birth weight (**A**), head circumference (**B**), placenta weight (**C**), birth length (**D**), ponderal index (**E**), gestational age (**F**), sex (**G**), low birth weight (<2'500g, **H**), preterm birth (<37 weeks, **I**), stillbirth (**J**), early neonatal mortality in the first five days after birth (**K**)

Table S4: Maternal and neonatal characteristics during the pandemic. [1]Mean (SD); n (%).

Maternal characteristics	
Variable	***n* = 2,177**[1]
maternal age (years)	28.5 (6.2)
missing	4
height (cm)	156.4 (6.5)
missing	101
civil status	
married	1,918 (88%)
single or missing	259 (12%)
gravidity	
1	4,788 (37%)
2	2,840 (22%)
>2	5,335 (41%)
living in Lausanne	981 (45%)
morphology	
neither	2,031 (93%)
obese	85 (4%)
thin	61 (3%)
goitre	122 (6%)
rickets	87 (4%)
flu during pregnancy and pandemic	282 (13%)
syphilis	24 (1%)
HISCO class	
2	1,876 (86%)
1	127 (6%)
3	39 (2%)
missing	135 (6%)
season	
spring	446 (20%)
summer	569 (26%)
autumn	666 (31%)
winter	496 (23%)
maternal mortality	10 (0%)

Neonatal characteristics	
Variable	***n* =2,177**[1]
birth weight (g)	3,187.8 (566.9)
head circumference (cm)	34.4 (1.8)
missing	37
placenta weight (g)	581.9 (118.4)
missing	29
birth length (cm)	49.1 (2.7)
missing	6
ponderal index	2.7 (0.3)
missing	6
gestational age (weeks)	39.2 (2.1)
sex	
Male	1,122 (52%)
Female	1,050 (48%)
missing	5
low birth weight (<2'500g)	195 (9%)
preterm birth (<37 weeks)	186 (9%)
stillbirth	92 (4%)
neonatal mortality d1-5	43 (2%)
missing	1

Maternal characteristics and pregnancy outcomes depending on maternal ILI

Table S5: Maternal characteristics depending on influenza during pregnancy (during the pandemic period only). [1]Mean (SD); n (%). [2]Welch Two Sample t-test; Chi squared test for equality of proportions. Note: all categorical variables were treated as binary variables.

Variable	**no** N = 1,895[1]	**yes** N = 282[1]	**Difference**[2]	**95% CI**[2]
maternal age (years)	28.5 (6.2)	28.6 (6.2)	0.07	-0.71, 0.84
missing	4	0		
height (cm)	156.4 (6.5)	156.1 (6.8)	-0.25	-1.1, 0.62
missing	90	11		
civil status: married	1,668 (88%)	250 (89%)	0.63%	-3.6%, 4.8%
gravidity				
1	758 (40%)	104 (37%)	-3.1%	-9.4%, 3.1%
2	413 (22%)	70 (25%)	3.0%	-2.5%, 8.6%
>2	724 (38%)	108 (38%)	0.09%	-6.1%, 6.3%
living in Lausanne	851 (45%)	130 (46%)	1.2%	-5.2%, 7.6%
morphology				
neither	1,770 (93%)	261 (93%)	-0.85%	-4.3%, 2.6%
obese	72 (4%)	13 (5%)	0.81%	-2.0%, 3.6%
thin	53 (3%)	8 (3%)	0.04%	-2.1%, 2.2%
goitre	106 (6%)	16 (6%)	0.08%	-2.9%, 3.1%
rickets	76 (4%)	11 (4%)	-0.11%	-2.6%, 2.4%
syphilis	20 (1%)	4 (1%)	0.36%	-1.3%, 2.0%
maternal mortality	7 (0%)	3 (1%)	0.69%	-0.74%, 2.1%
HISCO class				
2	1,627 (86%)	249 (88%)	2.4%	-1.8%, 6.7%
1	112 (6%)	15 (5%)	-0.59%	-3.6%, 2.4%
3	34 (2%)	5 (2%)	-0.02%	-1.7%, 1.7%
missing	122 (6%)	13 (5%)	-1.8%	-4.7%, 1.1%
season				
spring	344 (18%)	102 (36%)	18%	12%, 24%
summer	502 (26%)	67 (24%)	-2.7%	-8.3%, 2.8%
autumn	628 (33%)	38 (13%)	-20%	-24%, -15%
winter	421 (22%)	75 (27%)	4.4%	-1.3%, 10%

Figure S5: comparison of the timing of maternal ILI in the maternity hospital of Lausanne and the hospital incidence of infectious diseases in the Canton of Vaud. A) incidence of hospitalisations in the Canton of Vaud, due to infections (including influenza) – this is the same figure than *S1.D*, but aggregated at the monthly level. **B) counts and dates of *n*=244 reported influenza-like-illness during pregnancy. C) counts and dates of n=227 reported influenza-like-illness during pregnancy and during the pandemic, based on the waves defined in the Methods section (July 1918-March 1919, January 1920-March 1920).** Note: the exact month was unknown for *n*=55 cases ILI cases and these cases are not displayed on the graphs.

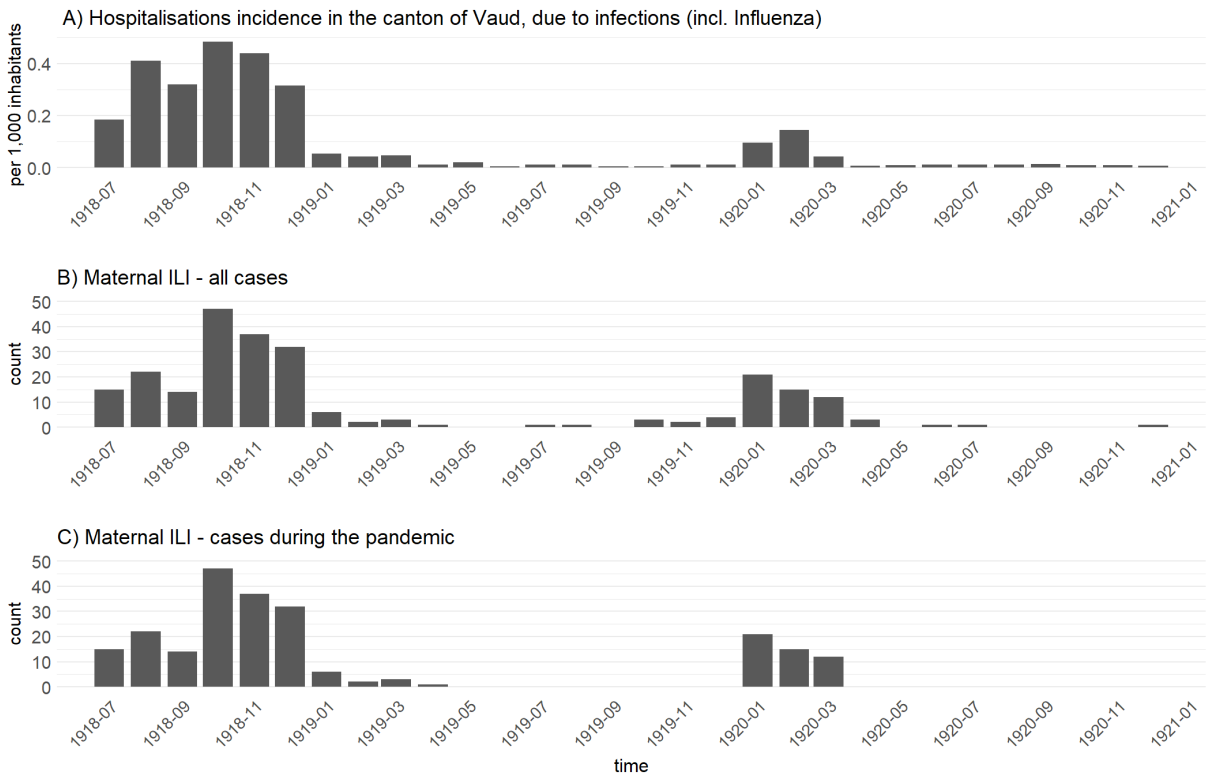


Table S6: pregnancy outcomes depending on maternal ILI (during pregnancy and during the pandemic) **and infant sex.** [1]Mean (SD); n (%).

	All births		Males		Females	
ILI exposure	**no**, N = 1,895[1]	**yes**, N = 282[1]	**no**, N = 992[1]	**yes**, N = 130[1]	**no**, N = 898[1]	**yes**, N = 152[1]
birth weight (g)	3,203.5 (562.4)	3,083.0 (586.7)	3,263.6 (584.8)	3,099.7 (647.8)	3,142.2 (520.0)	3,068.8 (530.7)
head circumference (cm)	34.4 (1.8)	34.1 (1.9)	34.7 (1.8)	34.2 (2.1)	34.1 (1.7)	34.0 (1.8)
missing	32	5	18	3	13	
placenta weight (g)	586.6 (119.2)	550.2 (107.4)	595.7 (124.0)	550.6 (112.4)	576.9 (112.8)	549.9 (103.3)
missing	26	3	15		11	
birth length (cm)	49.1 (2.7)	48.7 (3.0)	49.5 (2.7)	48.8 (3.5)	48.8 (2.5)	48.6 (2.5)
missing	5	1	3		2	
ponderal index	2.7 (0.3)	2.6 (0.3)	2.7 (0.3)	2.6 (0.3)	2.7 (0.3)	2.7 (0.3)
missing	5	1	3		2	
gestational age (weeks)	39.2 (2.1)	39.0 (2.4)	39.3 (2.1)	38.9 (2.7)	39.2 (2.0)	39.1 (2.0)
sex						
Male	992 (52%)	130 (46%)				
missing	5	0				
low birth weight (<2'500g)	157 (8%)	38 (13%)	85 (9%)	21 (16%)	70 (8%)	17 (11%)
preterm birth (<37 weeks)	153 (8%)	33 (12%)	78 (8%)	18 (14%)	73 (8%)	15 (10%)
stillbirth	80 (4%)	12 (4%)	45 (5%)	8 (6%)	33 (4%)	4 (3%)
neonatal mortality d1-5	37 (2%)	6 (2%)	17 (2%)	2 (2%)	20 (2%)	4 (3%)
missing	0	1			0	1

Table S7: pregnancy outcomes depending on maternal ILI, univariable and multivariable RLMs (continuous outcomes) and GLMs (binary outcomes), marginally adjusted means or percentages. Using ggemmeans: it takes the mean value as a reference of continuous covariates (for instance maternal age) and it averages over all levels of the categorical variable, weighted by the sample frequencies). All models are fitted using only livebirths, except for stillbirth outcome. [1]adjusted for: ILI during pregnancy, maternal age, maternal height, gravidity, sex, season, morphology, civil status, Lausanne. Note: both males and females are considered in these analyses.

		univariable			multivariable	
outcome	**Maternal ILI**	**mean**	**Mean difference [95%CI]**	**Maternal ILI**	**mean**	**Mean difference [95%CI]**
birth weight (grams)	no	3249.28 [3226.65, 3271.90]	-107.39 [-170.26, -44,52]	no	3188.21 [3127.30, 3249.13]	-84.43 [-184.74, 15.88]
	yes	3141.88 [3083.23, 3200.54]		yes	3103.78 [3024.09, 3183.47]	
head circumference (cm)	no	34.52 [34.46, 34.59]	-0.26 [-0.44, -0.07]	no	34.35 [34.17, 34.52]	-0.15 [-0.44, 0.14]
	yes	34.26 [34.09, 34.43]		yes	34.19 [33.96, 34.42]	
placenta weight (grams)	no	585.09 [579.73, 590.44]	-34.99 [-49.80, -20.17]	no	576.06 [561.38, 590.74]	-29.46 [-53.61, -5.31]
	yes	550.10 [536.29, 563.91]		yes	546.60 [527.42, 565.78]	
birth length (cm)	no	49.41 [49.32, 49.50]	-0.34 [-0.59, -0.09]	no	49.18 [48.93, 49.43]	-0.21 [-0.62, 0.20]
	yes	49.07 [48.53, 49.31]		yes	48.97 [48.65, 49.30]	
ponderal index	no	2.69 [2.68, 2.70]	-0.04 [-0.07, -0.01]	no	2.66 [2.63, 2.69]	-0.03 [-0.08, 0.02]
	yes	2.65 [2.63, 2.68]		yes	2.63 [2.59, 2.67]	
gestational age (weeks)	no	39.68 [39.63, 39.73]	-0.10 [-0.23, 0.04]	no	39.55 [39.41, 39.69]	-0.03 [-0.27, 0.20]
	yes	39.58 [39.45, 39.71]		yes	39.52 [39.34, 39.70]	
	Maternal ILI	**Percentage [95%CI]**	**Percentage difference [95%CI]**	**Maternal ILI**	**Percentage**	**Percentage difference [95%CI]**
LBW (<2,500g)	no	6.89% [5.81, 8.15]	4.96% [4.55, 5.38]	no	6.91% [4.01, 11.64]	6.36% [5.48, 7.23]
	yes	11.85% [8.51, 16.28]		yes	13.27% [7.31, 22.88]	
PTB (<37 weeks)	no	6.72% [5.66, 7.97]	3.65% [3.22, 4.08]	no	5.89% [2.91, 11.56]	2.94% [1.83, 4.04]
	yes	10.37% [7.26, 14.61]		yes	8.83% [4.07, 18.09]	
Stillbirth	no	4.22% [3.40, 5.23]	0.03% [-0.59, 0.65]			
	yes	4.26% [2.43, 7.34]				
Early neonatal mortality	no	2.04% [1.48, 2.80]	0.19% [-0.68, 1.06]			
	yes	2.23% [1.01, 4.87]				

Table S8: pregnancy outcomes depending on maternal ILI and infant sex, univariable RLMs (continuous outcomes) and GLMs (binary outcomes), marginally adjusted means or percentages. Using ggemmeans: it takes the mean value as a reference of continuous covariates (for instance maternal age) and it averages over all levels of the categorical variable, weighted by the sample frequencies). All models are fitted using only livebirths, except for stillbirth outcome. [1]adjusted for: ILI during pregnancy, maternal age, maternal height, gravidity, season, morphology, civil status, Lausanne.

	females			males		
outcome	**Maternal ILI**	**Mean**	**Mean difference [95%CI]**	**Maternal ILI**	**Mean**	**Mean difference [95%CI]**
birth weight (grams)	no	3184.83 [3154.50, 3215.16]	-92.25 [-171.61, -12.89]	no	3313.01 [3280.44, 3345.57]	-105.25 [-201.67, -8.84]
	yes	3092.59 [3019.25, 3165.92]		yes	3207.75 [3117.01, 3298.49]	
head circumference (cm)	no	34.16 [34.06, 34.25]	-0.11 [-0.35, 0.12]	no	34.87 [34.78, 34.96]	-0.34 [-0.61, -0.06]
	yes	34.04 [33.82, 34.26]		yes	34.53 [34.27, 34.79]	
placenta weight (grams)	no	574.99 [567.72, 582.26]	-29.87 [-48.80, -10.94]	no	595.00 [587.24, 602.76]	-38.69 [-61.59, -15.80]
	yes	545.12 [527.65, 562.60]		yes	556.31 [534.77, 577.85]	
birth length (cm)	no	49.09 [48.96, 49.21]	-0.21 [-0.53, 0.11]	no	49.76 [49.63, 49.88]	-0.34 [-0.71, 0.04]
	yes	48.88 [48.58, 49.17]		yes	49.42 [49.07, 49.77]	
ponderal index	no	2.69 [2.68, 2.71]	-0.03 [-0.07, 0.02]	no	2.69 [2.67, 2.70]	-0.05 [-0.09, 0.00]
	yes	2.67 [2.63, 2.70]		yes	2.64 [2.60, 2.68]	
gestational age (weeks)	no	39.67 [39.61, 39.74]	-0.14 [-0.31, 0.03]	no	39.70 [39.63, 39.77]	-0.03 [-0.23, 0.17]
	yes	39.53 [39.37, 39.69]		yes	39.67 [39.49, 39.86]	
	Maternal ILI	**Mean percentage [95%CI]**	**Percentage difference [95%CI]**	**Maternal ILI**	**Mean percentage**	**Percentage difference [95%CI]**
LBW (<2,500g)	no	6.47% [5.02, 8.32]	4.34% [3.75, 4.92]	no	7.29% [5.79, 9.12]	5.83% [5.25, 6.41]
	yes	10.81% [6.73, 16.92]		yes	13.11% [8.19, 20.34]	
PTB (<37 weeks)	no	6.82% [5.32, 8.70]	3.31% [2.72, 3.91]	no	6.65% [5.23, 8.43]	4.00% [3.37, 4.63]
	yes	10.14% [6.20, 16.13]		yes	10.66% [6.29, 17.49]	
Stillbirth	no	3.67% [2.62, 5.12]	-1.04% [-2.10, 0.01]	no	4.54% [3.40, 6.02]	1.62% [0.84, 2.39]
	yes	2.63% [0.99, 6.80]		yes	6.15% [3.11, 11.82]	
Early neonatal mortality	no	2.31% [1.50, 3.56]	0.41% [-0.68, 1.50]	no	1.80% [1.12, 2.87]	-0.16% [-1.63, 1.32]
	yes	2.72% [1.03, 7.02]		yes	1.64% [0.41, 6.31]	

Maternal characteristics and pregnancy outcomes depending on the trimester of maternal ILI

Table S9: Maternal characteristics depending on trimester of exposure to maternal ILI. diff: difference. [1]Mean (SD); n (%). [2]Welch two sample t-test; Chi squared test for equality of proportions. Notes: the difference compares exposure in each trimester vs. not exposed. All categorical variables were treated as binary variables.

Variable	**no ILI** *n* = 1,895[1]	**first** *n* = 75[1]	**diff**[2]	**95% CI**[2]	**second** *n* = 95[1]	**diff**[2]	**95% CI**[2]	**third** *n* = 98[1]	**diff**[2]	**95% CI**[2]	**unknown** *n* = 14[1]	**diff**[2]	**95% CI**[2]
maternal age (years)	28.5 (6.2)	29.0 (6.7)	0.50	-1.1, 2.1	28.2 (5.9)	-0.32	-1.6, 0.91	28.3 (5.9)	-0.24	-1.5, 0.98	31.0 (6.0)	2.5	-0.95, 6.0
missing	4	0			0			0			0		
height (cm)	156.4 (6.5)	155.8 (6.4)	-0.55	-2.1, 0.99	156.8 (6.5)	0.40	-0.99, 1.8	156.0 (7.3)	-0.41	-1.9, 1.1	154.5 (7.8)	-1.9	-6.4, 2.6
missing	90	3			3			5			0		
civil status: married	1,668 (88%)	63 (84%)	-4.0%	-13, 5.1%	86 (91%)	2.5%	-4.1, 9.1%	89 (91%)	2.8%	-3.6, 9.2%	12 (86%)	-2.3%	-23, 18%
gravidity													
1	758 (40%)	35 (47%)	6.7%	-5.5, 19%	35 (37%)	-3.2%	-14, 7.3%	31 (32%)	-8.4%	-18, 1.6%	3 (21%)	-19%	-44, 6.6%
2	413 (22%)	16 (21%)	-0.46%	-10, 9.5%	25 (26%)	4.5%	-5.1, 14%	26 (27%)	4.7%	-4.7, 14%	3 (21%)	-0.37%	-22, 22%
>2	724 (38%)	24 (32%)	-6.2%	-18, 5.3%	35 (37%)	-1.4%	-12, 9.1%	41 (42%)	3.6%	-6.9, 14%	8 (57%)	19%	-11, 49%
living in Lausanne	851 (45%)	34 (45%)	0.43%	-11, 12%	45 (47%)	2.5%	-8.4, 13%	47 (48%)	3.1%	-7.6, 14%	4 (29%)	-16%	-44, 11%
morphology													
neither	1,770 (93%)	69 (92%)	-1.4%	-8.3, 5.5%	86 (91%)	-2.9%	-9.4, 3.7%	92 (94%)	0.47%	-4.9, 5.8%	14 (100%)	6.6%	1.9, 11%
obese	72 (4%)	4 (5%)	1.5%	-4.3, 7.4%	7 (7%)	3.6%	-2.3, 9.4%	2 (2%)	-1.8%	-5.2, 1.7%	0 (0%)	-3.8%	-8.3, 0.66%
thin	53 (3%)	2 (3%)	-0.13%	-4.0, 3.7%	2 (2%)	-0.69%	-4.2, 2.8%	4 (4%)	1.3%	-3.2, 5.8%	0 (0%)	-2.8%	-6.3, 0.74%
goitre	106 (6%)	2 (3%)	-2.9%	-7.4, 1.6%	6 (6%)	0.72%	-4.8, 6.3%	6 (6%)	0.53%	-4.9, 5.9%	2 (14%)	8.7%	-13, 31%
rickets	76 (4%)	4 (5%)	1.3%	-4.5, 7.2%	3 (3%)	-0.85%	-5.0, 3.3%	3 (3%)	-0.95%	-5.0, 3.1%	1 (7%)	3.1%	-14, 20%
syphilis	20 (1%)	3 (4%)	2.9%	-2.2, 8.1%	1 (1%)	0.00%	-2.1, 2.1%	0 (0%)	-1.1%	-2.1, -0.06%	0 (0%)	-1.1%	-2.6, 0.46%
HISCO class													
2	1,627 (86%)	63 (84%)	-1.9%	-11, 7.3%	86 (91%)	4.7%	-2.0, 11%	86 (88%)	1.9%	-5.3, 9.1%	14 (100%)	14%	9.0, 19%
1	112 (6%)	6 (8%)	2.1%	-4.8, 9.0%	3 (3%)	-2.8%	-7.0, 1.5%	6 (6%)	0.21%	-4.9, 5.3%	0 (0%)	-5.9%	-11, -1.3%
3	34 (2%)	2 (3%)	0.87%	-3.5, 5.3%	2 (2%)	0.31%	-2.9, 3.6%	1 (1%)	-0.77%	-3.4, 1.8%	0 (0%)	-1.8%	-4.2, 0.60%
missing	122 (6%)	4 (5%)	-1.1%	-7.0, 4.8%	4 (4%)	-2.2%	-7.0, 2.5%	5 (5%)	-1.3%	-6.4, 3.7%	0 (0%)	-6.4%	-11, -1.7%
season													
spring	344 (18%)	29 (39%)	21%	8.7, 32%	43 (45%)	27%	16, 38%	23 (23%)	5.3%	-3.8, 14%	7 (50%)	32%	2.0, 62%
summer	502 (26%)	34 (45%)	19%	6.7, 31%	18 (19%)	-7.5%	-16, 1.1%	10 (10%)	-16%	-23, -9.4%	5 (36%)	9.2%	-20, 38%
autumn	628 (33%)	7 (9%)	-24%	-31, -16%	7 (7%)	-26%	-32, -20%	24 (24%)	-8.7%	-18, 0.66%	0 (0%)	-33%	-39, -27%
winter	421 (22%)	5 (7%)	-16%	-22, -8.9%	27 (28%)	6.2%	-3.6, 16%	41 (42%)	20%	9.1, 30%	2 (14%)	-7.9%	-30, 14%

Table S10: pregnancy outcomes depending on trimester of exposure to maternal ILI among males (*n*=1,122). [1]Mean (SD); n (%).

Trimester of exposure	**not exposed**, *n* = 992[1]	**first**, *n*= 31[1]	**second**, *n* = 48[1]	**third**, *n* = 46[1]	**unknown**, *n* = 5[1]
birth weight (g)	3,263.6 (584.8)	3,038.4 (615.6)	3,310.6 (569.2)	2,918.0 (694.5)	3,126.0 (715.9)
head circumference (cm)	34.7 (1.8)	34.1 (2.2)	34.5 (1.9)	33.9 (2.4)	33.6 (1.9)
placenta weight (g)	595.7 (124.0)	545.6 (94.0)	598.5 (108.3)	508.2 (112.1)	512.0 (111.2)
birth length (cm)	49.5 (2.7)	48.2 (3.5)	49.8 (2.7)	48.2 (4.0)	48.6 (2.7)
ponderal index	2.7 (0.3)	2.7 (0.2)	2.6 (0.2)	2.6 (0.3)	2.7 (0.2)
gestational age (weeks)	39.3 (2.1)	39.0 (2.7)	39.5 (2.1)	38.1 (3.2)	39.3 (2.7)
low birth weight (<2'500g)	85 (9%)	5 (16%)	3 (6%)	12 (26%)	1 (20%)
preterm birth (<37 weeks)	78 (8%)	3 (10%)	4 (8%)	10 (22%)	1 (20%)
stillbirth	45 (5%)	0 (0%)	2 (4%)	6 (13%)	0 (0%)
neonatal mortality d1-5	17 (2%)	0 (0%)	0 (0%)	2 (4%)	0 (0%)

Table S11: pregnancy outcomes depending on trimester of exposure to maternal ILI among females. [1]Mean (SD); n (%).

ILI exposure	**not exposed**, *n* = 898[1]	**first**, *n*= 44[1]	**second**, *n* = 47[1]	**third**, *n* = 52[1]	**unknown**, *n* = 9[1]
birth weight (g)	3,142.2 (520.0)	3,104.8 (552.5)	3,087.4 (485.5)	3,014.6 (569.9)	3,107.8 (468.6)
head circumference (cm)	34.1 (1.7)	34.2 (1.6)	34.2 (2.1)	33.7 (1.6)	33.9 (1.5)
placenta weight (g)	576.9 (112.8)	592.8 (113.7)	532.1 (93.6)	533.3 (91.4)	526.7 (117.5)
birth length (cm)	48.8 (2.5)	48.7 (1.8)	48.9 (2.1)	48.3 (3.1)	48.3 (3.2)
ponderal index	2.7 (0.3)	2.7 (0.3)	2.6 (0.3)	2.7 (0.2)	2.8 (0.3)
gestational age (weeks)	39.2 (2.0)	39.6 (1.4)	39.3 (1.4)	38.6 (2.6)	38.9 (2.6)
low birth weight (<2'500g)	70 (8%)	6 (14%)	4 (9%)	6 (12%)	1 (11%)
preterm birth (<37 weeks)	73 (8%)	2 (5%)	3 (6%)	8 (15%)	2 (22%)
stillbirth	33 (4%)	1 (2%)	0 (0%)	3 (6%)	0 (0%)
neonatal mortality d1-5	20 (2%)	0 (0%)	2 (4%)	2 (4%)	0 (0%)

Table S12: pregnancy outcomes depending on trimester of exposure to maternal ILI, univariable and multivariable RLMs (continuous outcomes) and GLMs (binary outcomes), marginally adjusted means or percentages. Using ggemmeans: it takes the mean value as a reference of continuous covariates (for instance maternal age) and it averages over all levels of the categorical variable, weighted by the sample frequencies). All models are fitted using only livebirths, except for stillbirth outcome. [1]adjusted for: ILI during pregnancy, maternal age, maternal height, gravidity, sex, season, morphology, civil status, Lausanne. Notes: both males and females are considered in these analyses. When the timing of ILI exposure was unknown (*n*=14), cases were not considered. For each outcome, only one RLM/GLM was fitted, and the exposure variable was a categorical variable (no ILI (reference category), ILI in the first, second or third trimester).

	univariable			multivariable		
outcome	**Maternal ILI**	**mean**	**Mean difference [95%CI]**	**Maternal ILI**	**mean**	**Mean difference [95%CI]**
birth weight (grams)	no	3249.28 [3226.68, 3271.87]		no	3186.95 [3126.32, 3247.59]	
	T1	3131.59 [3019.68, 3243.49]	-117.69 [-231.85, -3.52]	T1	3132.62 [3011.54, 3253.69]	-54.34 [-189.75, 81.07]
	T2	3222.10 [3122.28, 3321.92]	-27.18 [-129.53, 75.17]	T2	3173.00 [3062.08, 3283.93]	-13.95 [-140.37, 112.47]
	T3	3069.26 [2967.22, 3171.30]	-180.01 [-284.53, -75.50]	T3	2993.45 [2880.32, 3106.58]	-193.50 [-321.86, -65.15]
head circumference (cm)	no	34.52 [34.46, 34.59]		no	34.34 [34.17, 34.52]	
	T1	34.36 [34.04, 34.69]	-0.16 [-0.49, 0.18]	T1	34.40 [34.05, 34.75]	0.06 [-0.33, 0.45]
	T2	34.45 [34.16, 34.74]	-0.07 [-0.37, 0.23]	T2	34.33 [34.00, 34.65]	-0.02 [-0.38, 0.35]
	T3	33.99 [33.69, 34.30]	-0.53 [-0.84, -0.22]	T3	33.87 [33.54, 34.20]	-0.47 [-0.85, -0.10]
placenta weight (grams)	no	585.10 [579.75, 590.46]		no	575.26 [560.60, 589.91]	
	T1	571.08 [544.75, 597.40]	-14.03 [-40.89, 12.84]	T1	571.20 [542.04, 600.37]	-4.06 [-36.69, 28.58]
	T2	562.39 [538.78, 586.00]	-22.72 [-46.93, 1.50]	T2	555.68 [528.85, 582.50]	-19.58 [-50.15, 10.99]
	T3	524.75 [500.75, 548.76]	-60.35 [-84.95, -35.75]	T3	518.67 [491.41, 545.93]	-56.59 [-87.54, -25.64]
birth length (cm)	no	49.41 [49.32, 49.50]		no	49.18 [48.93, 49.43]	
	T1	48.8 [48.37, 49.26]	-0.60 [-1.05, -0.14]	T1	48.88 [48.39, 49.38]	-0.29 [-0.85, 0.26]
	T2	49.51 [49.11, 49.91]	0.10 [-0.31, 0.51]	T2	49.34 [48.88,49.80]	0.16 [-0.36, 0.68]
	T3	48.80 [48.39, 49.21]	-0.61 [-1.03, -0.20]	T3	48.64 [48.18, 49.11]	-0.54 [-1.06, -0.01]
ponderal index	no	2.69 [2.68, 2.70]		no	2.66 [2.63, 2.69]	
	T1	2.68 [2.63, 2.74]	-0.01 [-0.06, 0.05]	T1	2.68 [2.62, 2.74]	0.01 [-0.06, 0.08]
	T2	2.65 [2.61, 2.70]	-0.03 [-0.08, 0.01]	T2	2.63 [2.57, 2.68]	-0.04 [-0.10, 0.03]
	T3	2.62 [2.57, 2.66]	-0.07 [-0.12, -0.02]	T3	2.58 [2.52, 2.64]	-0.08 [-0.15, -0.02]
gestational age (weeks)	no	39.66 [39.62, 39.71]		no	39.55 [39.41, 39.69]	
	T1	39.76 [39.52, 39.99]	0.09 [-0.15, 0.33]	T1	39.77 [39.49, 40.05]	0.22 [-0.09, 0.54]
	T2	39.69 [39.48, 39.90]	0.03 [-0.19, 0.24]	T2	39.62 [39.36, 39.87]	0.07 [-0.22, 0.36]
	T3	39.18 [38.97, 39.39]	-0.48 [-0.70, -0.27]	T3	39.07 [38.81, 39.33]	-0.48 [-0.77, -0.18]
	Maternal ILI	**Percentage [95%CI]**	**Percentage difference [95%CI]**	**Maternal ILI**	**Percentage [95%CI]**	**Percentage difference [95%CI]**
LBW (<2,500g)	no	6.89% [5.81, 8.15]		no	7.00% [4.07, 11.78]	
	T1	13.51% [7.43, 23.33]	6.63% [5.94, 7.32]	T1	12.26% [5.41, 25.48]	5.27% [4.21, 6.33]
	T2	6.45% [2.93, 13.62]	-0.44% [-1.28, 0.41]	T2	8.14% [3.16, 19.39]	1.14% [-0.01, 2.30]
	T3	15.73% [9.54, 24.83]	8.84% [8.24, 9.44]	T3	19.75% [9.87, 35.61]	12.75% [11.76, 13.74]
PTB (<37 weeks)	no	6.72% [5.66, 7.97]		no	5.96% [2.94, 11.69]	
	T1	6.76% [2.84,15.23]	0.03% [-0.89, 0.96]	T1	4.50% [1.34, 14.02]	-1.46% [-2.91, -0.02]
	T2	6.45% [2.93, 13.62]	-0.27% [-1.12, 0.58]	T2	5.10% |1.65, 14.67]	-0.86% [-2.23, 0.52]
	T3	15.73% [9.54, 24.83]	9.01% [8.41, 9.61]	T3	15.39% [6.67, 31.66]	9.43% [8.24, 10.62]
stillbirth	no	4.22% [3.40, 5.23]				
	T1	1.33% [0.19, 8.85]	-2.89% [-4.87, -0.90]			
	T2	2.11% [0.53, 8.03]	-2.12% [-3.53, -0.70]			
	T3	9.18% [4.85, 16.72]	4.96% (4.24, 5.68]			

Table S13: pregnancy outcomes depending on trimester of exposure to maternal ILI and infant sex, univariable and multivariable RLMs (continuous outcomes) and GLMs (binary outcomes), marginally adjusted means or percentages. Using ggemmeans: it takes the mean value as a reference of continuous covariates (for instance maternal age) and it averages over all levels of the categorical variable, weighted by the sample frequencies). All models are fitted using only livebirths, except for stillbirth outcome. [1]adjusted for: ILI during pregnancy, maternal age, maternal height, gravidity, season, morphology, civil status, Lausanne. Note: when the timing of ILI exposure was unknown (*n*=14), cases were not considered. For each outcome, only one RLM/GLM was fitted, and the exposure variable was a categorical variable (no ILI (reference category), ILI in the first, second or third trimester).

	females			males		
outcome	**Maternal ILI**	**Mean**	**Mean difference [95%CI]**	**Maternal ILI**	**Mean**	**Mean difference [95%CI]**
birth weight (grams)	no	3184.83 [3154.66, 3215.00]		no	3313.03 [3280.30, 3345.76]	
	T1	3154.93 [3019.60, 3290.26]	-29.90 [-168.56, 108.75]	T1	3096.71 [2915.80, 3277.62]	-216.32 [-400.17, -32.46]
	T2	3065.88 [2936.44, 3195.32]	-118.95 [-251.87, 13.96]	T2	3371.39 [3222.88, 3519.91]	58.37 [-93.72, 210.45]
	T3	3058.52 [2931.75, 3185.30]	-126.31 [-256.63, 4.01]	T3	3084.68 [2925.41, 3243.94]	-228.35 [-390.95, -65.75]
head circumference (cm)	no	34.16 [34.06, 34.25]		no	34.87 [34.78, 34.96]	
	T1	34.31 [33.90, 34.72]	0.15 [-0.26, 0.57]	T1	34.47 [33.96, 34.98]	-0.40 [-0.92, 0.12]
	T2	34.12 [33.73, 34.51]	-0.04 [-0.44, 0.36]	T2	34.76 [34.34, 35.19]	-0.11 [-0.54, 0.32]
	T3	33.76 [33.37, 34.14]	-0.40 [-0.80, 0.00]	T3	34.34 [33.88, 34.80]	-0.53 [-1.00, -0.06]
placenta weight (grams)	no	574.99 [567.77, 582.22]		no	594.87 [587.19, 602.56]	
	T1	594.43 [562.22, 626.65]	19.44 [-13.57, 52.46]	T1	542.49 [500.37, 584.61]	-52.38 [-95.20, -9.57]
	T2	528.42 [497.61, 559.23]	-46.57 [-78.22, -14.92]	T2	601.03 [566.07, 635.98]	6.15 [-29.64, 41.94]
	T3	525.62 [495.44, 555.80]	-49.37 [-80.40, -18.34]	T3	523.55 [486.47, 560.63]	-71.32 [-109.19, -33.45]
birth length (cm)	no	49.09 [48.96, 49.21]		no	49.76 [49.63, 49.88]	
	T1	48.95 [48.40, 49.51]	-0.13 [-0.70, 0.44]	T1	48.75 [48.06, 49.44]	-1.00 [-1.71, -0.30]
	T2	48.89 [48.36, 49.41]	-0.20 [-0.74, 0.34]	T2	50.10 [49.53, 50.67]	0.34 [-0.24, 0.93]
	T3	48.76 [48.25, 49.28]	-0.32 [-0.85, 0.21]	T3	49.06 [48.45, 49.67]	-0.70 [-1.32, -0.08]
ponderal index	no	2.69 [2.68, 2.71]		no	2.69 [2.67, 2.70]	
	T1	2.69 [2.62, 2.77]	0.00 [-0.07, 0.08]	T1	2.67 [2.59, 2.75]	-0.02 [-0.10, 0.07]
	T2	2.64 [2.57, 2.71]	-0.05 [-0.12, 0.02]	T2	2.67 [2.60, 2.73]	-0.02 [-0.09, 0.05]
	T3	2.65 [2.59, 2.72]	-0.04 [-0.11, 0.03]	T3	2.57 [2.50, 2.64]	-0.12 [-0.19, -0.04]
gestational age (weeks)	no	39.67 [39.61, 39.74]		no	39.70 [39.63, 39.77]	
	T1	39.84 [39.55, 40.14]	0.17 [-0.13, 0.47]	T1	39.67 [39.30, 40.04]	-0.03 [-0.41, 0.34]
	T2	39.53 [39.25, 39.81]	-0.14 [-0.43, 0.14]	T2	39.89 [39.58, 40.19]	0.19 [-0.12, 0.50]
	T3	39.16 [38.88, 39.43]	-0.52 [-0.80, -0.23]	T3	39.29 [38.96, 39.61]	-0.41 [-0.74, -0.08]
	Maternal ILI	**Mean percentage [95%CI]**	**Percentage difference [95%CI]**	**Maternal ILI**	**Mean percentage [95%CI]**	**Percentage difference [95%CI]**
LBW (<2,500g)	no	6.47% [5.02, 8.32]		no	7.29% [5.79, 9.12]	
	T1	11.63% [4.92, 25.05]	5.15% [4.18, 6.12]	T1	16.13% [6.88, 33.37]	8.84% [7.85, 9.83]
	T2	8.51% [3.23, 20.58]	2.04% [0.98, 3.10]	T2	4.35% [1.09, 15.79]	-2.94% [-4.38, -1.50]
	T3	12.24% [5.61, 24.69]	5.77% [4.87, 6.67]	T3	20.00% [10.33, 35.17]	12.71% [11.90, 13.53]
PTB (<37 weeks)	no	6.82% [5.32, 8.70]		no	6.65% [5.23, 8.43]	
	T1	4.65% [1.17, 16.78]	-2.17% [-3.61, -0.73]	T1	9.68% [3.15, 26.06]	3.02% [1.81, 4.24]
	T2	6.38% [2.07, 18.00]	-0.44% [-1.64, 0.76]	T2	6.52% [2.12, 18.36]	-0.13% [-1.33, 1.07]
	T3	16.33% [8.38, 29.39]	9.51% [8.70, 10.31]	T3	15.00% [6.90, 29.59]	8.35% [7.44, 9.25]

Maternal characteristics and pregnancy outcomes depending on the severity of maternal ILI

Table S14: pregnancy outcomes depending on the severity of ILI symptoms. The same tables separated for males and females are in *Tables S15-16*. CI: confidence interval [1]Mean (SD); n (%).

ILI exposure	not exposed	mild symptoms	severe symptoms	unknown symptoms
	n = 1,895[1]	*n* = 137[1]	*n* = 100[1]	*n* = 45[1]
birth weight (g)	3,203.5 (562.4)	3,092.4 (527.5)	3,089.0 (648.2)	3,041.1 (624.8)
head circumference (cm)	34.4 (1.8)	34.1 (1.7)	34.2 (2.3)	33.9 (1.9)
placenta weight (g)	586.6 (119.2)	550.7 (111.9)	552.5 (102.9)	543.8 (105.2)
birth length (cm)	49.1 (2.7)	48.8 (2.7)	48.8 (3.3)	48.2 (3.0)
ponderal index	2.7 (0.3)	2.6 (0.3)	2.6 (0.3)	2.7 (0.3)
gestational age (weeks)	39.2 (2.1)	39.2 (2.0)	38.8 (2.7)	38.9 (2.6)
sex	992 (52%)	59 (43%)	53 (53%)	18 (40%)
low birth weight (<2'500g)	157 (8%)	13 (9%)	17 (17%)	8 (18%)
preterm birth (<37 weeks)	153 (8%)	15 (11%)	14 (14%)	4 (9%)
stillbirth	80 (4%)	5 (4%)	7 (7%)	0 (0%)
neonatal mortality d1-5	37 (2%)	1 (1%)	4 (4%)	1 (2%)

Table S15: pregnancy outcomes depending on the severity of ILI symptoms among males (*n*=1,112). [1]Mean (SD); n (%).

ILI exposure	not infected	mild	severe	missing
Variable	*n* = 992[1]	*n* = 59[1]	*n* = 53[1]	*n* = 18[1]
birth weight (g)	3,263.6 (584.8)	3,123.1 (603.9)	3,115.3 (687.7)	2,977.2 (688.8)
head circumference (cm)	34.7 (1.8)	34.2 (2.1)	34.3 (2.1)	33.7 (2.4)
placenta weight (g)	595.7 (124.0)	**547.7 (117.7)**	556.0 (110.0)	544.4 (107.1)
birth length (cm)	49.5 (2.7)	49.0 (3.3)	48.9 (3.6)	48.0 (3.4)
ponderal index	2.7 (0.3)	2.6 (0.2)	2.6 (0.3)	2.6 (0.3)
gestational age (weeks)	39.3 (2.1)	39.0 (2.3)	39.3 (2.1)	0.8
low birth weight (<2'500g)	85 (9%)	7 (12%)	**10 (19%)**	4 (22%)
preterm birth (<37 weeks)	78 (8%)	8 (14%)	8 (15%)	2 (11%)
stillbirth	45 (5%)	2 (3%)	**6 (11%)**	0 (0%)
neonatal mortality d1-5	17 (2%)	1 (2%)	1 (2%)	0 (0%)

Table S16: pregnancy outcomes depending on the severity of ILI symptoms among females (*n*=1,050). [1]Mean (SD); n (%).

ILI exposure	not infected	mild	severe	missing
Variable	*n* = 898[1]	*n* = 78[1]	*n* = 47[1]	*n* = 27[1]
birth weight (g)	3,142.2 (520.0)	3,069.2 (464.3)	3,059.4 (606.6)	2,977.2 (688.8)
head circumference (cm)	34.1 (1.7)	34.0 (1.4)	34.2 (2.4)	33.7 (2.4)
placenta weight (g)	576.9 (112.8)	552.9 (108.1)	548.6 (95.2)	544.4 (107.1)
birth length (cm)	48.8 (2.5)	48.7 (2.2)	48.6 (2.8)	48.0 (3.4)
ponderal index	2.7 (0.3)	2.7 (0.3)	2.6 (0.2)	2.6 (0.3)
gestational age (weeks)	39.2 (2.0)	39.3 (1.7)	**38.8 (2.3)**	39.1 (2.3)
low birth weight (<2'500g)	70 (8%)	6 (8%)	7 (15%)	4 (22%)
preterm birth (<37 weeks)	73 (8%)	7 (9%)	6 (13%)	2 (11%)
stillbirth	33 (4%)	3 (4%)	1 (2%)	0 (0%)
neonatal mortality d1-5	20 (2%)	0 (0%)	3 (7%)	0 (0%)

Table S17: Maternal characteristics depending on the severity of ILI symptoms. diff: difference. [1]Mean (SD); n (%). [2]Welch two-sample t-test; Chi squared test for equality of proportions. Notes: the difference compares symptoms severity vs. not exposed. All categorical variables were treated as binary variables.

Variable	no ILI	mild	diff[2]	95% CI[2]	severe	diff[2]	95% CI[2]	unknown	diff[2]	95% CI[2]
	n = 1,895[1]	*n* = 137[1]			*n* = 100[1]			*n* = 45[1]		
maternal age (years)	28.5 (6.2)	29.4 (6.3)	0.90	-0.21, 2.0	27.7 (5.6)	-0.79	-1.9, 0.36	27.9 (6.5)	-0.56	-2.5, 1.4
missing	4	0			0			0		
height (cm)	156.4 (6.5)	156.1 (6.9)	-0.31	-1.5, 0.91	155.5 (6.9)	-0.85	-2.3, 0.57	157.8 (6.4)	1.4	-0.70, 3.4
missing	90	4			3			4		
civil status: married	1,668 (88%)	118 (86%)	-1.9%	-8.3, 4.5%	91 (91%)	3.0%	-3.3, 9.3%	41 (91%)	3.1%	-6.5, 13%
gravidity										
1	758 (40%)	53 (39%)	-1.3%	-10, 7.5%	28 (28%)	-12%	-22, -2.4%	23 (51%)	11%	-4.8, 27%
2	413 (22%)	31 (23%)	0.83%	-6.8, 8.5%	32 (32%)	10%	0.35, 20%	7 (16%)	-6.2%	-18, 5.7%
>2	724 (38%)	53 (39%)	0.48%	-8.4, 9.3%	40 (40%)	1.8%	-8.6, 12%	15 (33%)	-4.9%	-20, 10%
living in Lausanne	851 (45%)	62 (45%)	0.35%	-8.6, 9.3%	42 (42%)	-2.9%	-13, 7.5%	26 (58%)	13%	-2.9, 29%
morphology										
neither	1,770 (93%)	128 (93%)	0.03%	-4.3, 4.4%	91 (91%)	-2.4%	-8.6, 3.8%	42 (93%)	-0.07%	-7.5, 7.4%
obese	72 (4%)	5 (4%)	-0.15%	-3.6, 3.3%	6 (6%)	2.2%	-3.1, 7.5%	2 (4%)	0.64%	-6.1, 7.4%
thin	53 (3%)	4 (3%)	0.12%	-2.9, 3.2%	3 (3%)	0.20%	-3.4, 3.8%	1 (2%)	-0.57%	-5.5, 4.4%
goitre	106 (6%)	9 (7%)	0.98%	-3.7, 5.6%	6 (6%)	0.41%	-4.8, 5.6%	1 (2%)	-3.4%	-8.9, 2.2%
rickets	76 (4%)	4 (3%)	-1.1%	-4.4, 2.3%	6 (6%)	2.0%	-3.3, 7.3%	1 (2%)	-1.8%	-7.3, 3.7%
syphilis	20 (1%)	3 (2%)	1.1%	-1.8, 4.0%	0 (0%)	-1.1%	-2.0, -0.07%	1 (2%)	1.2%	-4.3, 6.6%
HISCO class										
2	1,627 (86%)	123 (90%)	3.9%	-1.8, 9.6%	90 (90%)	4.1%	-2.5, 11%	36 (80%)	-5.9%	-19, 7.1%
1	112 (6%)	6 (4%)	-1.5%	-5.5, 2.4%	5 (5%)	-0.91%	-5.8, 4.0%	4 (9%)	3.0%	-6.5, 12%
3	34 (2%)	2 (1%)	-0.33%	-2.8, 2.1%	1 (1%)	-0.79%	-3.4, 1.8%	2 (4%)	2.7%	-4.5, 9.8%
missing	122 (6%)	6 (4%)	-2.1%	-6.1, 1.9%	4 (4%)	-2.4%	-7.0, 2.1%	3 (7%)	0.23%	-7.4, 7.8%
season										
spring	344 (18%)	64 (47%)	29%	20, 37%	31 (31%)	13%	3.1, 23%	7 (16%)	-2.6%	-14, 9.3%
summer	502 (26%)	29 (21%)	-5.3%	-13, 2.2%	18 (18%)	-8.5%	-17, -0.18%	20 (44%)	18%	2.2, 34%
autumn	628 (33%)	11 (8%)	-25%	-31, -20%	14 (14%)	-19%	-27, -11%	13 (29%)	-4.3%	-19, 10%
winter	421 (22%)	33 (24%)	1.9%	-5.9, 9.7%	37 (37%)	15%	4.6, 25%	5 (11%)	-11%	-22, -0.60%

Table S18: maternal ILI depending on trimester of illness and symptoms severity

	trimester of ILI			
symptoms severity	first	second	third	unknown
mild	49 (65,3%)	50 (52,6%)	32 (32,7%)	6 (42,9%)
severe	11 (14,7%)	35 (36,8%)	48 (49,0%)	6 (42,9%)
unknown	15 (20,0%)	10 (10,5%)	18 (18,4%)	2 (14,3%)
total	75 (100%)	95 (100%)	98 (100%)	14 (100%)

Figure S6: continuous (A) and binary (B) pregnancy outcomes depending on the severity of ILI symptoms, univariable and multivariable RLMs (continuous outcomes) GLMs (binary outcomes), all births and stratified by sex. All models are fitted using only livebirths, except for stillbirth outcome. The same models are summarized in *Table S19-20*. For each outcome, only one RLM/GLM was fitted, and the exposure variable was a categorical variable (no ILI (reference category), ILI with mild symptoms, ILI with severe symptoms). Note: when the severity of ILI was unknown (*n*=45), cases were not considered.

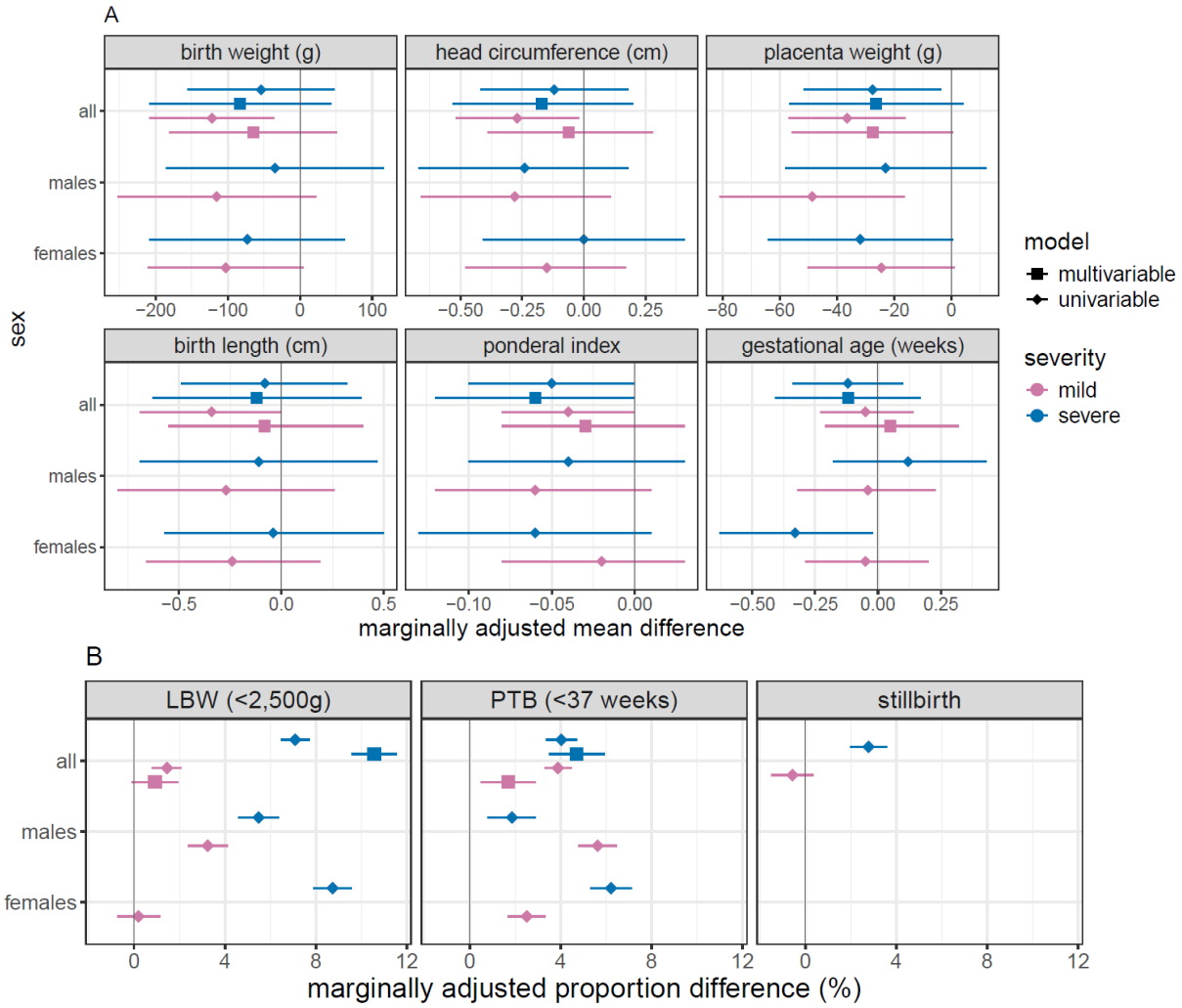


Table S19: pregnancy outcomes depending on the severity of ILI symptoms, univariable and multivariable RLMs (continuous outcomes) and GLMs (binary outcomes), marginally adjusted means or percentages. Using ggemmeans: it takes the mean value as a reference of continuous covariates (for instance maternal age) and it averages over all levels of the categorical variable, weighted by the sample frequencies). All models are fitted using only livebirths, except for stillbirth outcome. [1]adjusted for: ILI during pregnancy, maternal age, maternal height, gravidity, sex, season, morphology, civil status, Lausanne. Notes: both males and females are considered in these analyses. When the severity of ILI symptoms was unknown (*n*=45), cases were not considered. For each outcome, only one RLM/GLM was fitted, and the exposure variable was a categorical variable (no ILI (reference category), ILI with mild symptoms, ILI with severe symptoms).

	univariable			multivariable		
outcome	**Maternal ILI**	**mean**	**Mean difference [95%CI]**	**Maternal ILI**	**mean**	**Mean difference [95%CI]**
birth weight (grams)	no	3249.28 [3226.79, 3271.76]		no	3181.50 [3120.50, 3242.50]	
	mild	3127.38 [3044.01, 3210.75]	-121.89 [-208.24, -35.54]	mild	3116.70 [3018.09, 3215.31]	-64.80 [-180.75, 51.16]
	severe	3195.45 [3096.12, 3294.77]	-53.83 [-155.67, 48.01]	severe	3098.79 [2988.97, 3208.62]	-82.70 [-208.34, 42.93]
head circumference (cm)	no	34.52 [34.46, 34.59]		no	34.33 [34.16, 34.51]	
	mild	34.25 [34.01, 34.50]	-0.27 [-0.52, -0.02]	mild	34.27 [33.99, 34.56]	-0.06 [-0.39, 0.28]
	severe	34.40 [34.11, 34.70]	-0.12 [-0.42, 0.18]	severe	34.17 [33.85, 34.49]	-0.17 [-0.53, 0.20]
placenta weight (grams)	no	585.09 [579.74, 590.44]		no	574.60 [559.79, 589.41]	
	mild	548.67 [528.90, 568.43]	-36.42 [-56.90, -15.94]	mild	547.13 [523.20, 571.06]	-27.47 [-55.61, 0.67]
	severe	557.61 [534.15, 581.07]	-27.47 [-51.54, -3.41]	severe	548.36 [521.78, 574.94]	-26.24 [-56.67, 4.19]
birth length (cm)	no	49.41 [49.32, 49.50]		no	49.15 [48.90, 49.40]	
	mild	49.07 [48.73, 49.40]	-0.34 [-0.69, 0.00]	mild	49.07 [48.67, 49.47]	-0.08 [-0.55, 0.40]
	severe	49.33 [48.93, 49.72]	-0.08 [-0.49, 0.32]	severe	49.03 [48.58, 49.48]	-0.12 [-0.63, 0.39]
ponderal index	no	2.69 [2.68, 2.70]		no	2.66 [2.63, 2.69]	
	mild	2.65 [2.61, 2.69]	-0.04 [-0.08, 0.00]	mild	2.64 [2.59, 2.68]	-0.03 [-0.08, 0.03]
	severe	2.64 [2.59, 2.69]	-0.05 [-0.10, 0.00]	severe	2.60 [2.55, 2.66]	-0.06 [-0.12, 0.00]
gestational age (weeks)	no	39.67 [39.62, 39.71]		no	39.55 [39.40, 39.69]	
	mild	39.62 [39.44, 39.79]	-0.05 [-0.23, 0.14]	mild	39.60 [39.37, 39.83]	0.05 [-0.21, 0.32]
	severe	39.55 [39.33, 39.76]	-0.12 [-0.34, 0.10]	severe	39.42 [39.17, 39.68]	-0.12 [-0.41, 0.17]
	Maternal ILI	**Percentage [95%CI]**	**Percentage difference [95%CI]**	**Maternal ILI**	**Percentage [95%CI]**	**Percentage difference [95%CI]**
LBW (<2,500g)	no	6.89% [5.81, 8.15]		no	7.38% [4.30, 12.38]	
	mild	8.33% [4.67, 14.42]	1.45% [0.80, 2.09]	mild	8.30% [3.69, 17.59]	0.92% [-0.11, 1.95]
	severe	13.98% [8.29, 22.60]	7.09% [6.48, 7.71]	severe	17.95% [8.87, 32.97]	10.57% [9.58, 11.56]
PTB (<37 weeks)	no	6.72% [5.66, 7.97]		no	5.97% [2.95, 11.72]	
	mild	10.61% [6.38,17.11]	3.88% [3.30, 4.47]	mild	7.68% [3.13, 17.62]	1.70% [0.50, 2.90]
	severe	10.75% [5.88, 18.84]	4.03% [3.35, 4.71]	severe	10.68% [4.31, 24.11]	4.71% [3.48, 5.93]
stillbirth	no	4.22% [3.40, 5.23]		no		
	mild	3.65% [1.53, 8.47]	-0.57% [-1.49, 0.35]	mild		
	severe	7.00% [3.37, 13.96]	2.78% [1.98, 3.58]	severe		

Table S20: pregnancy outcomes depending on the severity of ILI symptoms and infant sex, univariable and multivariable RLMs (continuous outcomes) and GLMs (binary outcomes), marginally adjusted means or percentages. Using ggemmeans: it takes the mean value as a reference of continuous covariates (for instance maternal age) and it averages over all levels of the categorical variable, weighted by the sample frequencies). All models are fitted using only livebirths, except for stillbirth outcome. [1]adjusted for: ILI during pregnancy, maternal age, maternal height, gravidity, season, morphology, civil status, Lausanne. Notes: when the severity of ILI symptoms was unknown (*n*=45), cases were not considered. For each outcome, only one RLM/GLM was fitted, and the exposure variable was a categorical variable (no ILI (reference category), ILI with mild symptoms, ILI with severe symptoms).

	females			**males**		
outcome	**Maternal ILI**	**Mean**	**Mean difference [95%CI]**	**Maternal ILI**	**Mean**	**Mean difference [95%CI]**
birth weight (grams)	no	3184.68 [3154.33, 3215.02]		no	3313.02 [3280.28, 3345.76]	
	mild	3081.90 [2978.85, 3184.95]	-102.78 [-210.20, 4.65]	mild	3197.67 [3064.22, 3331.12]	-115.36 [-252.76, 22.05]
	severe	3111.75 [2980.17, 3243.33]	-72.92 [-207.96, 62.11]	severe	3278.44 [3131.48, 3425.40]	-34.58 [-185.15, 115.98]
head circumference (cm)	no	34.16 [34.06, 34.25]		no	34.87 [34.78, 34.96]	
	mild	34.00 [33.69, 34.31]	-0.15 [-0.48, 0.17]	mild	34.59 [34.22, 34.97]	-0.28 [-0.66, 0.11]
	severe	34.16 [33.76, 34.55]	0.00 [-0.41, 0.41]	severe	34.63 [34.21, 35.04]	-0.24 [-0.67, 0.18]
placenta weight (grams)	no	574.99 [567.69, 582.30]			594.87 [587.18, 602.57]	
	mild	550.56 [525.90, 575.22]	-24.43 [-50.16, 1.29]	mild	546.25 [514.86, 577.64]	-48.62 [-80.94, -16.31]
	severe	543.19 [511.70, 574.68]	-31.80 [-64.13, 0.53]	severe	571.91 [537.65, 606.17]	-22.96 [-58.08, 12.15]
birth length (cm)	no	49.09 [48.96, 49.21]		no	49.76 [49.63, 49.88]	
	mild	48.85 [48.44, 49.26]	-0.24 [-0.66, 0.19]	mild	49.49 [48.97, 50.00]	-0.27 [-0.80,0.26]
	severe	49.05 [48.53, 49.57]	-0.04 [-0.57, 0.50]	severe	49.65 [49.08, 50.21]	-0.11 [-0.69, 0.47]
ponderal index	no	2.69 [2.68, 2.71]		no	2.69 [2.67, 2.70]	
	mild	2.67 [2.62, 2.72]	-0.02 [-0.08, 0.03]	mild	2.63 [2.57, 2.69]	-0.06 [-0.12, 0.01]
	severe	2.63 [2.56, 2.70]	-0.06 [-0.13, 0.01]	severe	2.65 [2.58, 2.72]	-0.04 [-0.10, 0.03]
gestational age (weeks)	no	39.65 [39.58, 39.72]		no	39.70 [39.63, 39.77]	
	mild	39.60 [39.37, 39.83]	-0.05 [-0.29, 0.20]	mild	39.66 [39.39, 39.93]	-0.04 [-0.32, 0.23]
	severe	39.32 [39.02, 39.62]	-0.33 [-0.63, -0.02]	severe	39.82 [39.52, 40.12]	0.12 [-0.18, 0.43]
	Maternal ILI	**Mean percentage [95%CI]**	**Percentage difference [95%CI]**	**Maternal ILI**	**Mean percentage [95%CI]**	**Percentage difference [95%CI]**
LBW (<2,500g)	no	6.47% [5.02, 8.32]		no	7.29% [5.79, 9.12]	
	mild	6.67% [2.80, 15.04]	0.19% [-0.75, 1.14]	mild	10.53% [4.81, 21.52]	3.24% [2.36, 4.12]
	severe	15.22% [7.43, 28.64]	8.74% [7.89, 9.59]	severe	12.77% [5.85, 25.63]	5.48% [4.59, 6.37]
PTB (<37 weeks)	no	6.82% [5.32, 8.70]		no	6.65% [5.23, 8.43]	
	mild	9.33% [4.51, 18.31]	2.51% [1.69, 3.33]	mild	12.28% [5.97, 23.59]	5.63% [4.80, 6.46]
	severe	13.04% [5.98, 26.13]	6.22% [5.32, 7.12]	severe	8.51% [3.23, 20.58]	1.86% [0.80, 2.91]

Miscarriages

Figure S7: yearly and quarterly miscarriage and birth counts between 1909 and 1921, and percentage of miscarriages relative to births.

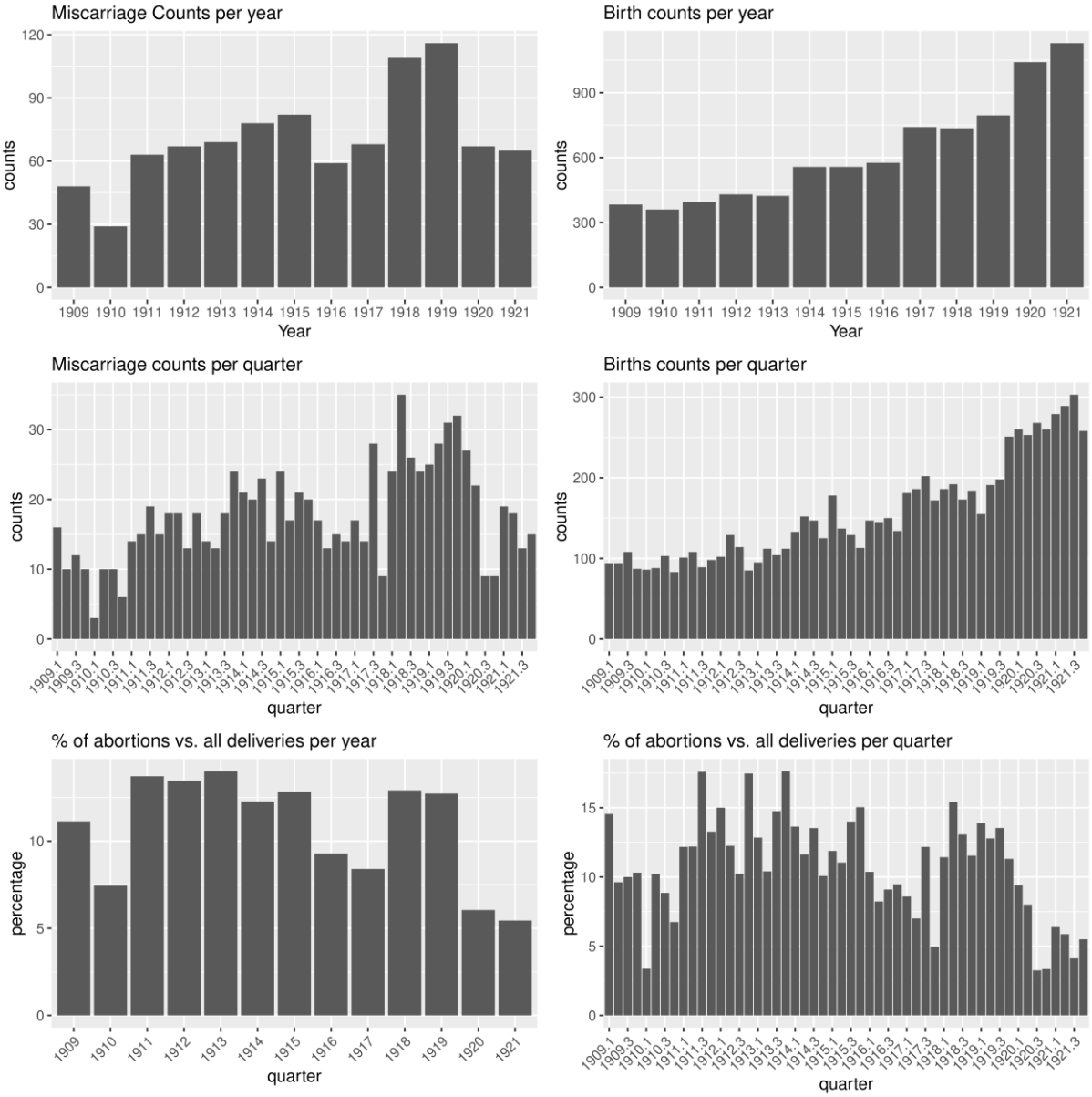


Table S21: maternal characteristics of those who had a miscarriage, by year (1909-1920).

Variable	**1909**, N = 48[1]	**1910**, N = 29[1]	**1911**, N = 63[1]	**1912**, N = 67[1]	**1913**, N = 69[1]	**1914**, N = 78[1]	**1915**, N = 82[1]	**1916**, N = 59[1]	**1917**, N = 68[1]	**1918**, N = 109[1]	**1919**, N = 116[1]	**1920**, N = 67[1]	**1921**, N = 65[1]
maternal age (years)	32.2 (6.8)	31.1 (6.8)	31.1 (7.2)	29.8 (5.4)	31.6 (6.2)	30.2 (6.5)	29.8 (5.6)	29.7 (6.6)	30.3 (5.9)	30.6 (6.9)	30.7 (6.5)	31.6 (7.4)	29.6 (6.8)
missing	0	0	0	0	0	0	0	0	1	0	0	0	0
civil status													
married	41 (85%)	25 (86%)	48 (76%)	58 (87%)	56 (81%)	68 (87%)	68 (83%)	45 (76%)	55 (81%)	85 (78%)	90 (78%)	54 (81%)	53 (82%)
single or missing	7 (15%)	4 (14%)	15 (24%)	9 (13%)	13 (19%)	10 (13%)	14 (17%)	14 (24%)	13 (19%)	24 (22%)	26 (22%)	13 (19%)	12 (18%)
living in Lausanne	30 (63%)	17 (59%)	37 (59%)	58 (87%)	44 (64%)	51 (65%)	49 (60%)	37 (63%)	39 (57%)	62 (57%)	63 (54%)	32 (48%)	39 (60%)
gravidity													
1	6 (13%)	2 (7%)	8 (13%)	11 (16%)	10 (14%)	8 (10%)	12 (15%)	10 (17%)	10 (15%)	19 (17%)	21 (18%)	13 (19%)	10 (15%)
2	2 (4%)	5 (17%)	8 (13%)	9 (13%)	11 (16%)	11 (14%)	11 (13%)	9 (15%)	10 (15%)	23 (21%)	27 (23%)	16 (24%)	9 (14%)
>2	39 (83%)	22 (76%)	46 (74%)	47 (70%)	48 (70%)	58 (75%)	59 (72%)	40 (68%)	48 (71%)	67 (61%)	68 (59%)	38 (57%)	46 (71%)
missing	1	0	1	0	0	1	0	0	0	0	0	0	0
HISCO class													
1	9 (19%)	6 (21%)	9 (14%)	6 (9%)	8 (12%)	9 (12%)	8 (10%)	8 (14%)	8 (12%)	9 (8%)	8 (7%)	5 (7%)	5 (8%)
2	34 (71%)	22 (76%)	50 (79%)	59 (88%)	55 (80%)	61 (78%)	65 (79%)	46 (78%)	52 (76%)	87 (80%)	96 (83%)	53 (79%)	55 (85%)
3	0 (0%)	1 (3%)	1 (2%)	0 (0%)	2 (3%)	1 (1%)	5 (6%)	2 (3%)	5 (7%)	3 (3%)	3 (3%)	2 (3%)	1 (2%)
missing	5 (10%)	0 (0%)	3 (5%)	2 (3%)	4 (6%)	7 (9%)	4 (5%)	3 (5%)	3 (4%)	10 (9%)	9 (8%)	7 (10%)	4 (6%)
gestational age (weeks)	13.4 (4.8)	13.8 (5.5)	13.8 (6.4)	12.9 (5.5)	13.7 (6.7)	15.0 (6.3)	15.0 (6.2)	12.9 (5.7)	13.0 (4.9)	12.5 (6.7)	13.3 (6.0)	14.4 (6.4)	14.6 (7.9)
missing	27	10	17	20	15	23	13	7	11	21	37	27	16
syphilis	0 (0%)	1 (3%)	2 (3%)	1 (1%)	1 (1%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)	4 (4%)	1 (1%)	4 (6%)	2 (3%)
flu during pregnancy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	**14 (13%)**	**45 (39%)**	**39 (58%)**	0 (0%)

Table S22: maternal characteristics and gestational age for miscarriages compared to births between 1918 and 1920. CI: confidence interval. [1]Mean (SD); n (%). [2]Welch two-sample t-test; Chi squared test for equality of proportions.

Variable	**no** N = 2,571[1]	**yes** N = 292[1]	**Difference**[2]	**95% CI**[2]
maternal age (years)	28.5 (6.3)	30.9 (6.9)	2.4	1.5, 3.2
missing	6	0		
civil status: married	2,238 (87%)	229 (78%)	-8.6%	-14%, -3.5%
gravidity				
1	1,021 (40%)	53 (18%)	-22%	-27%, -17%
2	557 (22%)	66 (23%)	0.94%	-4.3%, 6.2%
>2	993 (39%)	173 (59%)	21%	14%, 27%
Living in Lausanne	975 (59%)	157 (54%)	-4.9%	-11%, 1.5%
gestational age (weeks)	39.9 (2.9)	13.2 (6.4)	-27	-28, -26
missing	140	85		
Syphilis	27 (1%)	9 (3%)	2.0%	-0.18%, 4.2%
flu during pregnancy	299 (12%)	98 (34%)	22%	16%, 28%
HISCO class				
2	2,210 (86%)	236 (81%)	-5.1%	-10%, -0.24%
1	157 (6%)	22 (8%)	1.4%	-1.9%, 4.8%
3	50 (2%)	8 (3%)	0.79%	-1.3%, 2.9%
missing	154 (6%)	26 (9%)	2.9%	-0.67%, 6.5%

Historical context

Socio-economic context

From 1870, Swiss living standards markedly improved, interrupted only by the two World Wars (8). By the First World War, Switzerland was one of the three richest countries (among Western Europe and the USA), in terms of GDP per capita. Although Switzerland was not directly involved in the conflict, the country still suffered a long-lasting economic crisis (8). Nonetheless, in the majority of the period under study (1900s-1920s), Switzerland can be considered a high-income country. Infant mortality rates drastically declined between 1870 and the 1920s, at the national level and also in Lausanne, thanks to sanitation and modernisation of the water supply ((9). The number of inhabitants in the Canton of Vaud was 317,457 in 1910 and 317,498 in 1920 ((10). In the city of Lausanne, it was 64,446 in 1910 and 68,533 in 1920 (10).

The maternity hospital in Lausanne

In 1890, the Hospital of Lausanne became a university hospital, and it was the only one in the city. No restrictions were put into place at admission (11). A new and larger building was built in 1916. As a result, an increasing proportion of births took place at the hospital.

The 1918-20 influenza pandemic in Switzerland, the canton of Vaud and in the city of Lausanne

The first pandemic wave hit the country in July 1918, while the second and deadliest one spread from October 1918 until March 1919. A third and milder wave took place between January and March 1920. More than half of the Swiss population was infected by influenza, and about 25,000 died of it in the first pandemic year alone (12).

In the early 20th century, there were 25 federal member states in Switzerland, the so-called cantons. The city of Lausanne is located in the canton of Vaud; compared with the other Swiss cantons, the canton of Vaud was moderately affected by the pandemic and followed the wave pattern of Switzerland. It was estimated that 2,221 people died of the influenza, i.e. 0.70% of the population (13,14). Half of them were men and 32% were aged 20-40 years old (13,14). Compared to other Swiss cantons, the canton of Vaud introduced the mandatory reporting of influenza relatively late, on September 24th 1918, i.e. after the summer wave (15,16). The Swiss Army was demobilized in November 1918 and a general strike followed, assumed to have caused the strong wave in the end of 1918 (17). In Lausanne, during the first month of the pandemic (July 1918), there were already 101 deaths due to the flu. In comparison, the 1889 pandemic made only 2 victims in the first month (17).

After the first two waves of the pandemic in mid-1919, the health authorities of the canton of Vaud carried out a review of the pandemic (17). This was done within the framework of a detailed survey to all physicians in the canton. A hundred and eighteen physicians responded to the 15 questions about the course of the pandemic and the disease. These questionnaires were processed into a report. It was estimated that around 55% (*n* = 175,000) of the cantonal population had been infected (17). There is a whole section on influenza among pregnant women: most doctors agreed that the flu was more dangerous for pregnant women, with higher frequencies of pulmonary complications. Early pregnancy loss and preterm birth was also noted. Dr Gilliard from Chateau d'Oex observed three cases in which both the mother

and infant died. In Lausanne, Dr Zbinden observed frequent miscarriages and preterm births, while Prof Démiéville stated that flu among pregnant women was “extremely severe”. Dr Perrin, in Avenche reported 50% cases of miscarriages among pregnant women with influenza. In general, if the infection occurred close to the term of pregnancy, consequences were more severe for the mother and the child.

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