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INFERENTIAL AND DESCRIPTIVE EPIDEMIOLOGICAL RESEARCH BASED ON THE TAUFFER-CSÁKÁNY OBSTETRIC DATABASE

PhD thesis

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List of Abbreviations

CI:	Confidence Interval
CRL:	Crown-lump lenght
CSO:	Central Statistical Office
ICD:	International Classification of Diseases
GDM:	gestational diabetes mellitus
LGA:	large for gestational age
OR:	Odds Ratio
PIC:	perinatal intensive care unit
SGA:	small for gestational age
WHO:	World Health Organization

1 Introduction

Population-based medical surveys are the cornerstone of high quality data on current status and changes of the characteristics of the population as well as the development of national treatment protocols. This general statement also holds for the field of obstetrics and gynaecology. Vilmos Tauffer pioneered in the collection of nationwide obstetric data after realizing the high rate of obstetrical complications in Hungary. His first assessment was published in 1891 that included obstetrical data of altogether 12,300 villages.(1,2) According to his estimates, the annual number of maternal deaths was approximately 3,000 in Hungary and he opined that this vast number is partly due to the lack of education and financing of midwifes who lead the most deliveries. As a ministerial commissioner he issued a memorandum entitled Obstetric Regulation ("Szülészeti Rendtartás") to all village, district, and city medical officers in 1928 that forms the basis of the nationwide obstetric database. At the time, the primary aim of the data collection was to reduce the frequency of septic complications of delivery. He himself checked and analysed the data for irregularities and outliers. He published a report on the implementation of the Obstetric Regulation in 1932. However, the quality of the data was not officially approved valid for the whole country until after his death in 1935.(2)

The paper-based data collection received a major revamp at the end of the 1980s, when Dr György M. Csákány became responsible for the modernization of the Hungarian Tauffer statistics database. He envisioned and developed digital data recording techniques while working at the National Institute of Obstetrics and Gynaecology in 1989. Countrywide data collection was started under the leadership of the National Institute of Obstetrics and Gynecology (OSZNI) in 1994. Doctor Csákány coordinated data collection and analysis until his death in 2022. His purpose was to collect data on all deliveries after 20 weeks of gestation, thus risk factors of maternal and fetal complications can be investigated, as well as protocols developed to their prevention and also the effect of these protocols and other interventions tested at the national level. In many of his works, Csákány praises the importance and significance of data provision.(3–9) Currently data can be accesses online through the General Directorate of National Hospitals.(3)

Similar obstetric databases exist in many countries around the world, such as the Netherlands (10), Australia (11) and Norway that also aim to reduce obstetrical and perinatological complications in order to improve care.(12) Registry data provide an important addition to the evidence-based recommendations based on randomized trials analysed by the Cochrane Pregnancy and Childbirth Group (the first of the Cochrane groups).(13–15)

The overarching aim of our analyses was to provide evidence for the clinical utility of the obstetrical data stored in the Tauffer database. To this end, we investigated risk factors for obstetrical complications as well as temporal trends in newborn birth weights. Given the fact that the prevalence of both pregestational (16,17) and gestational (18) diabetes is increasing, our first analysis (not covered in the current thesis due to word count restrictions) evaluated the temporal changes in the frequency of deliveries complicated diabetes.(19)

1.1 Importance and risk factors of term breech presentation

The prevalence of pregnancies with breech presentation is surprisingly similar, involving 3-4% of foetuses globally by the time of labour (20–23). While there is uncertainty regarding the exact aetiology of breech presentation, several risk factors are well-described in the literature, such as older maternal age, primiparity, lower fetal weight, lower gestational age at delivery, maternal hip deformities, and oligohydramnion.(22–24).

It is also known that pregnancies with breech presentation are associated with an increased risk of congenital disorders (such as, fetal hydrocephalus),(22) and small for gestational age pregnancies (birth weight <10th percentile).(25) Although premature foetuses show an increased fetal mortality with breech presentation,(26) usual risk factors of perinatal mortality (such as Apgar values, and the need for intensive care) as well as perinatal morbidity are not increased in deliveries with breech presentation compared to those with cephalic presentation.(27)

1.2 The importance of national birth weight percentile charts

Birthweight is one of the first markers of a newborn's general condition, which is closely related to newborn morbidity and mortality. Abnormal birthweight increases perinatal mortality compared to normal birthweight (28). The estimated risk of the neonatal condition can be further improved by adjusting birthweight to gestational age, the so-called birth weight percentile. Its calculation may help estimating and thus reducing the risk of perinatal complications, morbidity, and mortality. It is well established that foetuses on the extremes of birth weight percentile (≥90th percentile or ≤10th percentile) have increased perinatal morbidity and mortality compared to those within the normal weight range.(29)

Hungarian birth weights were first analysed by Tivadar Kézmárszky, then director of the Budapest Obstetrics Clinic, in 1873.(30) Subsequently, Béla Kontsek reported on the detailed anthropometric measurements of 1,000 newborns delivered in Debrecen at the beginning of the 20th century. This analysis is particularly important as in addition to using birth measurements to judge physical development and nutrition, it is the first to analyse birth measurement in relation to parity, parental age, maternal height, and also social conditions in Hungary.(31)

The implementation of the first international birth weight standards is attributed to Lubchenco.(32) A few years later, together with Battaglia, they set up the birth weight groups that take into account gestational age and is still used in clinical practice: normal birth weight (Appropriate for Gestational Age [AGA]: birth weight between the 10th and 90th percentile) and low birth weight (Small for Gestational Age [SGA]: birth weight <10th percentile) and large birth weight (Large for Gestational Age [LGA]: >90th percentile).(33) Soon after the original publication, several percentile tables were published of newborn weight percentiles in Hungary.(34–38) An early analysis of the renewed nationwide Tauffer database was published by Csákány et al. in 1998.(5)

The analysis of Zoltán Papp et al should be highlighted among these publications that reports on weight percentile charts for Eastern Hungary (39), providing the basis for a later comparative work.(40)

The regular and multi-year processing of the national birth data based on the registry of the Central Statistical Office was performed by Kálmán Joubert. Together with prominent obstetricians and neonatologists, he advocated fort the assessment of newborn status based not only on birthweight but weight percentile relative to gestational age as well. (38,41,42) Birth weight percentile charts (stratified by gestational week and gender) require regular updates, as birth weights show significant temporal trends over the last decades parallel to increases in maternal age and maternal weight.(43,44)

1.3 Birth weight trends in the late 20th and early 21st century

Available evidence suggests that both low and high birth weights of term infants are major negative determinants of newborn survival,(45) while large infants are also more prone to injuries related to traumatic deliveries.(46) Similarly, there is some evidence for the association between both small and large for gestational age and the risk of an adverse cardiometabolic risk profile in childhood and common chronic diseases (such as cardiometabolic, neurological, immunological, gastrointestinal, and malignant disorders) in adulthood.(47–49)

Given the strong association between birth weight and later chronic diseases, even small temporal changes in the distribution of term newborns' birth weights could be of utmost public health importance. Indeed, an upward birth weight trend was observed in several high income countries and regions (such as the United States (US),(50) Canada,(50,51) the United Kingdom (UK),(52,53) Norway,(54) Sweden,(55) Denmark,(56) France,(57) Australia,(58) Croatia,(59) Poland,(60) and the Faroese Island(61)) at the end of the last century. In contrast, a reverse trend was found in Japan(62,63) and the increase appeared to reverse in the US,(64–69) China,(70,71) Portugal,(72) Norway,(73,74) and Germany(75) after the 1990s. In a previous analysis of the Hungarian Tauffer database we observed a similarly increasing birth weight trend of term infants between 1996 and 2010, followed by a slight decrease until 2015, however we did not look for potential explanations of this phenomenon.(76) To the best of our knowledge, there is no whole population-based analysis on birth weight trends from Hungary although results from a tertiary care centre in Szeged show an increasing birth weight trend between 1989 and 2009.(77)

While birth weight changes are well described in the literature, potential explanatory factors are much less known, and these factors only partly explain the slope of the birth weight trajectories. Most studies suggest that the increasing trends are associated with older maternal age,(52,53,56–58,63,77) increasing maternal body mass index (BMI),(55–58) and height,(59,63) longer gestations,(54,56,57,61,63) decreases in smoking,(58) decreasing parity,(57,59,61) changes in ethnicity,(53) and socioeconomic factors,(53,59) while the decreases could be related to decreases in the length of gestation,(62–64,67,68,72) induction of labour,(50,64,66–68) and early term caesarean sections,(50,64,66,68) increases in primiparity,(62,63) and decreased fetal growth.(65,68)

2 Objectives

2.1 Risk factors and consequences of term breech presentation

While the literature suggests that several maternal and fetal abnormalities are associated with an elevated risk of breech presentation (22), it is not clear whether breech presentation per se could have an effect on pregnancy outcomes.

Thus, we assumed that pregnancies with breech presentation are not different from pregnancies with cephalic presentation except for the presentation abnormality. To test this hypothesis, we (1) sought predictors of breech presentation and (2) evaluated the association between breech presentation and delivery and fetal outcomes in term pregnancies using registry data for all deliveries in Hungary between 1996 and 2011.

2.2 Updating the Hungarian birth weight percentiles

The aim of our second study was to create percentile standards characterizing the current Hungarian population (2011-2015) based on the Tauffer database. In addition, we analysed the change in birth weights from 1996 to 2015, considering the last 5 years as a reference. Our null hypothesis was that birth weights have not changed in the last twenty years and our investigation aimed at disproving this.

2.3 Birth weight trends and their explanatory factors

The purpose of the birth weight trend analysis was to (1) extend our previous birth weight trend analysis until 2018 and (2) to investigate potential maternal and fetal variables (including common pathologies) that could drive these changes using data from the Hungarian Tauffer registry of all pregnancies.

3 Methods

3.1 Setting and study design

For the investigation of all 3 major aims, we utilise the Tauffer database, which includes data from the compulsory report of each delivery in Hungary. The nationwide Hungarian obstetrics database ("Obstetrics Regulation") was initiated by Vilmos Tauffer in the early 1930's. After each parturition (24 to 43 weeks of gestation), the attending physician has to fill in a standardized report form. The Tauffer database used to be managed by the National Institute of Obstetrics and Gynaecology until 2010 when it was succeeded by the National Institute for Quality and Organisational Development in Healthcare and Medicines (ref. 76/2004 ESzCsM, Decree on the Determination, Collection, Analysis of Health-related Unidentifiable data; Ministry of Health Social and Family Affairs, Hungary). To comply with privacy regulations the database contains anonymised records, which means repeated deliveries to the same woman cannot be identified.(78,79) Data are made available by the National Institute for Quality- and Organizational Development in Healthcare and Medicines after permissions has been obtained. The current analyses use only unidentifiable information collected according to Hungarian law in agreement with European ethical directives. Thus, no ethical approval or individual consent was required for this analysis.

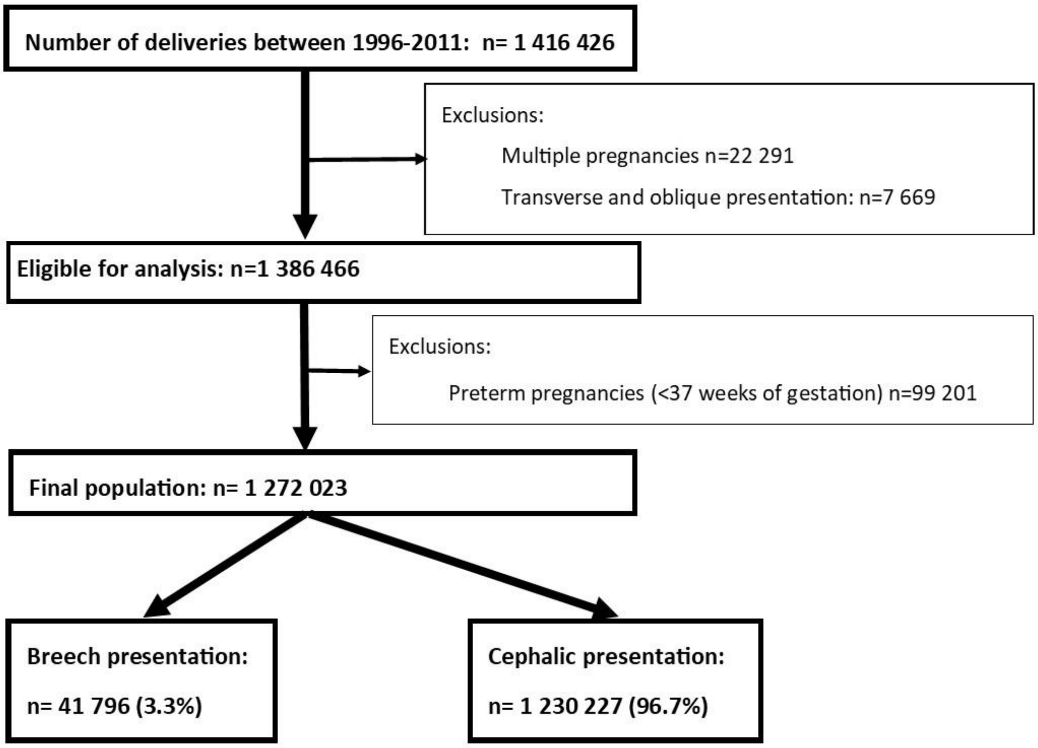
The Tauffer database has a good coverage of pregnancies recorded by the Hungarian Central Statistical Office: For the period between 1996 and 2011, the Tauffer database contains 1,416,426 live births (91.5%) off the total 1,547,755 live births, for the period between 1996-2015, it contains 92.46% of all live births.(19,80)

3.2 Patients

3.2.1 Risk factors and consequences of term breech presentation

For the present analysis we excluded multiple pregnancies (n=22,291), as these are characterised by an increased risk of non-cephalic presentation and premature birth. Pregnancies and deliveries with transverse and oblique presentation (n=7,669) were also excluded. As our preliminary analysis suggested that breech delivery was strongly associated with gestational age at delivery, we also excluded preterm pregnancies (<37 weeks of gestation, n=99,201) leading to a final sample of 1,272,023 singleton term pregnancies and deliveries over the 16-year study period. Of these pregnancies 1,230,227 (96.7%) were cephalic presentations and 41,796 (3.3%) breech presentations. **(Figure 1)**

Figure 1



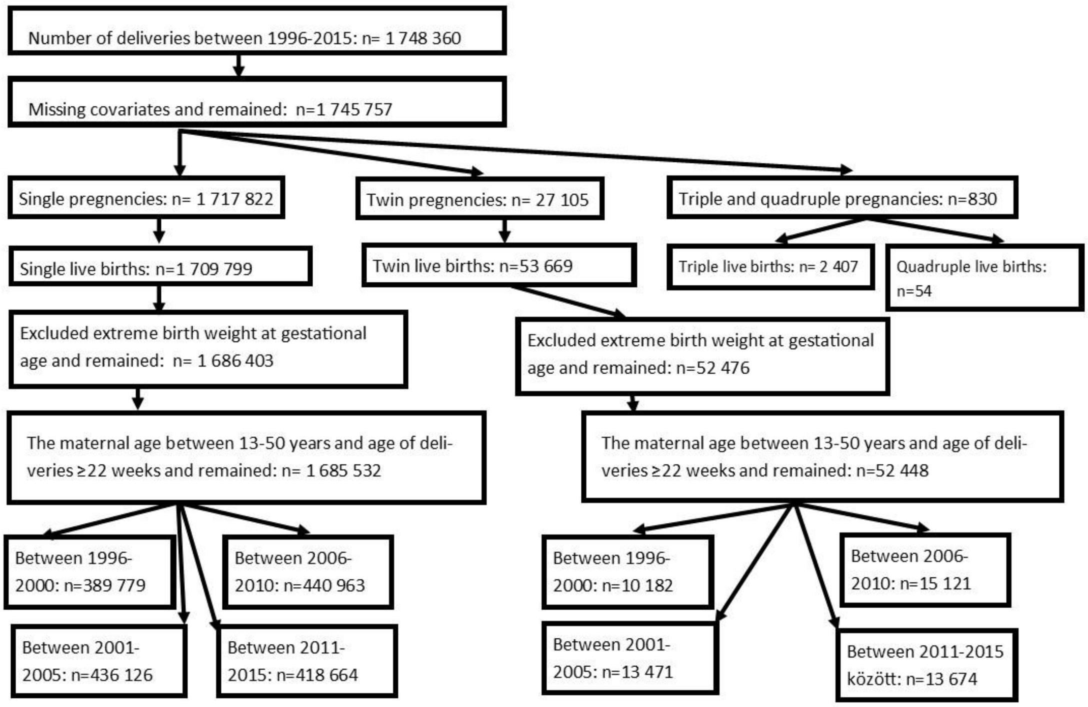
Flow-chart for the selection of study participants.

3.2.2 Updating the Hungarian birth weight percentiles

The Tauffer database includes 1,748,360 births for the period between 1996 and 2015. After deleting cases without data of either birthweight or newborn sex, 1,745,757 deliveries remained. The database contains data of 1,717,822 births from single pregnancies (1,709,799 foetuses born alive – 96.82%), of 27,105 twin pregnancies (53,669 foetuses born alive – 3.04%), of 816 triple pregnancies (2,407 foetuses born alive – 0.14%), and of 14 quadruple pregnancies (54 foetuses born alive – 0.003%). **(Figure 2)**

Given that weight percentiles are reported for each sex and gestational week of delivery separately, we excluded cases with any missing data on these variables. We further excluded newborns with extreme birth weights defined as a sex and gestational age specific birth weight outside the median ± 2 x interquartile range (IQR). After these exclusions, the final analytical sample included 1,685,532 single and 52,448 twin live births. For the development of the percentile charts, we used the most recent data (representing the period between 2011 and 2015 – 418,664 singleton and 13,674 twin foetuses).

Figure 2

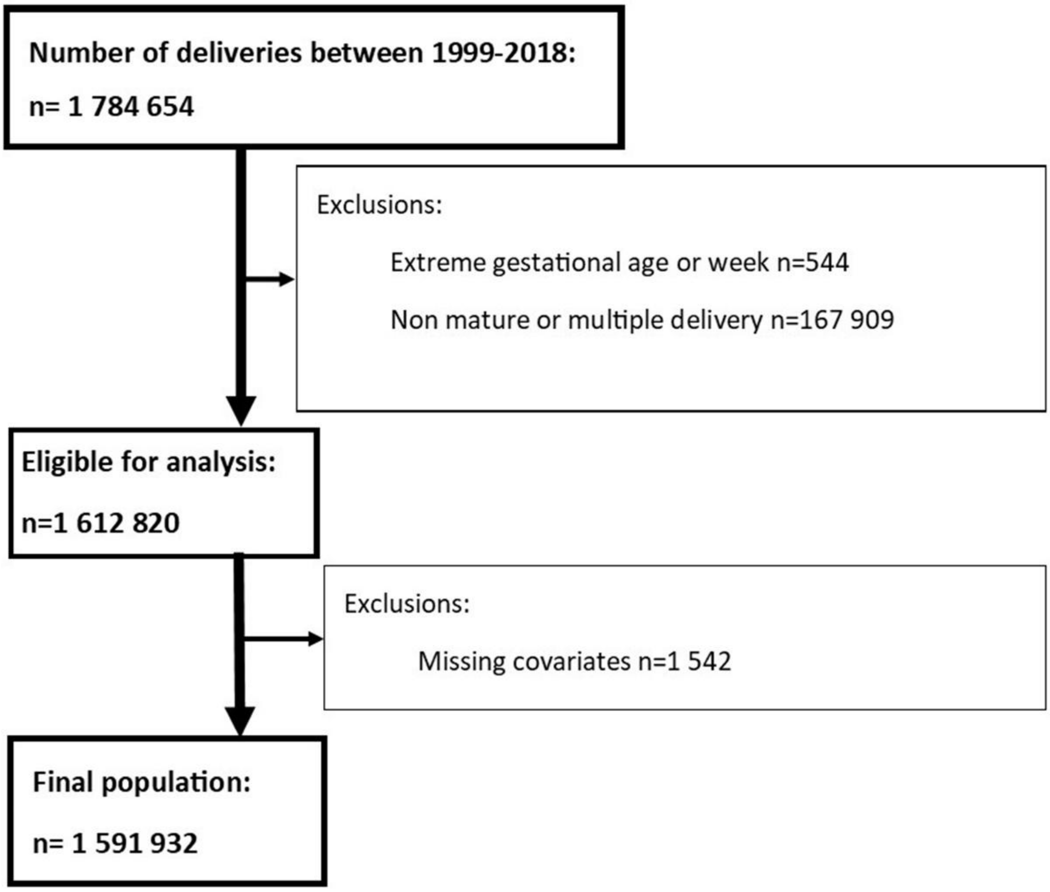


Flow-chart for the selection of study participants.

3.2.3 Birth weight trends and their explanatory factors

Of the 1,784,654 deliveries between 1999 and 2018, we excluded non-term deliveries (<37 or >41 weeks of gestation), stillbirths, and multiple deliveries leaving 1,612,820 records eligible for analysis. We further excluded records with missing birth weights and covariates, as well as those with extreme (likely erroneously recorded) birth weights leading to a final analytical sample of 1,591,932 (98.7% of those eligible) deliveries. (**Figure 3**)

Figure 3



Flow-chart for the selection of study participants.

3.3 Covariates

Maternal age was calculated as the difference between the date of delivery and the date of the mother's birth in years. Furthermore, we created a categorical variable of age for the interaction analysis to investigate whether changes in birthweight differentially affected mothers of younger, usual or advanced ages (<25 years, 25-34 years, and ≥35 years).

Maternal medical history was recorded by the treating physician at the time of delivery, and it included the *number of previous live births* and *stillbirths*, *the number of living children* (parity), as well as *prior spontaneous and induced abortions* (all categorized as 0, 1, >1). Otherwise the 3-level variable describing *birth presentation* (cephalic/breech/oblique) was recorded too that was used to define our variable of interest (cephalic versus breech presentation).

It was also collected data on known diseases/pathologies before the investigated pregnancy from the hospital discharge reports based on the following ICD-10 codes: *pregestational hypertension* – O10*-O11* and I10*-I15*, *pregestational diabetes* – O240-O243 and E10*-E14* (81).

As regards to the present pregnancy, data were extracted from hospital discharge reports on the *method of conception* (spontaneous, hormone induced, or in vitro fertilisation). We also collected data on known diseases/pathologies during the investigated pregnancy based on the following ICD-10 codes: *gestational hypertension* and *eclampsia* – O13*-O16*, *gestational diabetes* – O244 and O249, *oligohydramnion* – O41*, and *placenta praevia* O44* (81). As clinicians tend to consistently record only central placenta praevia that causes severe bleeding during pregnancy, for further analysis we used ICD-10 code O441.

Newborn *sex* and *birth weight* were extracted from discharge reports (compulsory fields in the database). Newborn sex is based on the phenotype at birth. Birth weights were analysed as continuous variables and were also expressed as *sex and gestational age specific percentiles* using national standard charts (42). Small for gestational age (*SGA*) was defined as a birth weight below the 10^{th} percentile and large for gestational age (*LGA*) as a birth weight above the 90^{th} percentile.

Date of delivery –we used year of each delivery as the major covariate of interest in our analyses.

Gestational age at delivery (a mandatory field in the database) was based on the woman's last normal menstrual period if it coincided within 1 week of the date determined by crown-rump length determined by ultrasound done between 10 and 13 weeks of gestation, otherwise we used the ultrasound estimates (82,83).

Obstetrical interventions include data on the initiation of labour (spontaneous / induced) as well as the mode of delivery that was coded as vaginal or caesarean section.

3.4 Outcomes

3.4.1 Risk factors and consequences of term breech presentation

We extracted the following *maternal delivery outcomes*: initiation of labour (spontaneous or induced), membrane rupture (premature spontaneous membrane rupture before start of uterine contractions or induced membrane rupture before or during uterine contractions), the mode of delivery (vaginal or Caesarean section), and the possible interventions during parturition (manual control of the uterine cavity, hysterectomy, sterilisation).

As regards to *fetal outcome indicators*, we assessed 5-minute Apgar values, postnatal status (no transfer to perinatal intensive care [PIC], transfer to PIC, stillbirth, or perinatal mortality), and recorded fetal diseases and congenital disorders. Stillbirth was defined as fetal intrauterine death after 24 weeks of gestation. Perinatal mortality included intrauterine deaths and deaths after delivery up to 168 hours.

Most outcome variables in the database are compulsory (e.g. gestational week of delivery, Apgar value, mode of membrane rupture, applied anaesthesia, fetal mortality before or during delivery or need for PIC treatment). For these variables misclassification is thought to be less likely compared with covariates.

Due to the large number of outcomes potentially related to breech presentation, we created two combined outcome variables: (1) Caesarean section or interventions during parturition (manual control of the uterine cavity, hysterectomy, sterilisation) was considered an adverse delivery related outcome. (2) The presence of either an Apgar value ≤7, need for PIC treatment, intrauterine death or perinatal mortality were taken as signs of pathological fetal outcome.

3.4.2 Updating the Hungarian birth weight percentiles and Analysis of birth weight trends and their explanatory factors

The outcome for both analysis was birth weight.

3.5 Statistical analysis

3.5.1 Risk factors and consequences of term breech presentation

Potential risk factors (categorical variables) for breech presentation (vs. cephalic presentation) were investigated using logistic regression and chi square tests with breech presentation as the dependent variable and individual risk factors as the independent variables. For continuous variables independent samples t-tests were performed.

To determine independent predictors of breech presentation, all parameters that were univariately associated ($p<0.1$) with breech presentation were included in a multivariable logistic regression model with breech (vs. cephalic) presentation as the dependent variable. The final model was selected using the stepwise forward method.

To investigate the association between breech presentation and delivery and/or fetal outcomes we compared outcomes between breech and cephalic presentations using chi-square tests, logistic regressions, and t-tests as appropriate. The independent association between breech presentation and any given outcome was analysed by multi-variable logistic regression, where the dependent was the given outcome, the independent variable was the mode of presentation, and adjustments were made for all independent predictors of breech presentation.

All analyses were done using SPSS 20.0 statistical package. Two-sided p values of <0.05 were considered statistically significant.

3.5.2 Updating the Hungarian birth weight percentiles

The fetal birth weights of the investigated period (between 2011 and 2015) were given in the form of mean, standard deviation and 95% confidence interval (95% CI) or median and 5, 10, 25, 75, 90 and 95 percentiles in tables and graphs per gestational week. Due to the small number of cases in weeks 22 and 43, weeks 22 and 23weeks as well as weeks 42 and 43 were analysed together. We used a similar approach for the analysis of the double twins, where we combined data from weeks 22 and 23, as well as weeks 40 and 41 (there were no twins in weeks 42 or 43).

For the analysis of temporal trends, we compared data to the reference period (the 5-year period between 2011 and 2015). Thus, we compared the birth weights of the periods 1996-2000, 2001-2005, and 2006-2010 to the reference period. For each gestational week, we built general linear models stratified by gender with birth weight as the outcome and the individual 5-year periods, as independent variables. In addition to the average birth weights, its standard errors (SE), and the p values for heterogeneity across the periods are also presented. IBM SPSS version 20.0 was used for data analysis, a two-sided p<0.05 was considered statistically significant.

3.5.3 Birth weight trends and their explanatory factors

First, we visually investigated the time trends of birth weights by newborn sex using loess curves. We found an increasing trend from 1999 with peak birth weights in 2008 followed by a decreasing trend until the end of the observation period. To improve the interpretation of models describing birth weight trends, we modelled the period with increasing (1999-2008) and decreasing trends (2008-2018) separately.

For descriptive purposes, we selected deliveries in 1999 (lowest birth weight from the first period), 2008 (peak birth weight), and 2018 (lowest birth weight in the second period). For the comparison of different variables in the selected years, chi2-tests for categorical variables and one-way analysis of variance (ANOVA) for continuous variables were used.

Then we modelled birth weight with multiple linear regression using calendar year and newborn sex as predictors (*Model 0*). In subsequent models we serially adjusted for other important predictors of birth weight. *Model 1* was further adjusted for gestational age at delivery, *Model 2* for maternal age, and *Model 3* for other important determinants (parity, delivery induction, and mode of delivery). For these models date of delivery was centred at 2008, maternal age at 29 years, and gestational age at 39 weeks. In separate linear regression models, we investigated whether the inclusion of quadratic or cubic terms of gestational age at delivery and maternal age would improve the prediction of birth weight. Based on these models, we used the linear and quadratic terms to adjust for the effect of maternal age, and the linear, quadratic, and cubic terms for the effect of age at delivery.

Finally, we looked for interactions between calendar year and selected parameters in separate models by adding a calendar year by the given variable interaction to *Model 3*. For this analysis, maternal age was categorized (<25 years, 25-34 years, and ≥35 years). We decided to use this parameterization, so the interactions would be easier to interpret for the non-specialist readers. Finally, we calculated estimated marginal means from the interaction models for all those variables where a potential interaction was likely (p-value for interaction <0.10) and showed them graphically with their respective 95% confidence intervals (CI).

All analyses were done using Statistical Package for the Social Sciences (SPSS 25.0) software. Two-tailed P values of <0.05 were considered statistically significant.

4 Results

4.1 Risk factors and consequences of term breech presentation

Of all pregnancies included in the analyses, 1,230,227 (96.7%) were of cephalic and 41,796 (3.3%) of breech presentation.

4.1.1 Predictors of breech presentation

We found that women with breech presentation were significantly older (by 0.67 years, 95%CI 0.62-0.72). Breech presentation was clearly related to fetal sex, with female fetuses having a 25% increased risk of breech presentation (95%CI 1.23-1.27). The risk of breech presentation was higher in primiparas compared to women with prior deliveries (OR 0.62, 95%CI 0.61-0.64 for secundiparity, OR 0.65, 95%CI 0.63-0.67 for multiparity). There was a dose-response relationship between the risk of breech presentation and the number of prior stillbirth (OR 1.12, 95%CI 0.98-1.27 for women with one stillbirth, OR 1.34, 95%CI 0.91-1.99 for women with multiple stillbirths), and the number of prior spontaneous abortions (OR 1.09, 95%CI 1.06-1.13 one abortion, OR 1.36, 95%CI 1.29-1.44 multiple abortions). (**Table 1** and **Table 2**)

Both hormone treatment and assisted reproduction predisposed to a pregnancy with breech presentation compared to spontaneous conception (OR 1.56, 95%CI 1.27-1.91 for hormone treatment, OR 1.83, 95%CI 1.66-2.01 for assisted reproduction). All investigated maternal morbidities increased the risk of breech presentation: pregestational diabetes by 31% (95%CI 1.03-1.65), gestational diabetes by 13% (95%CI 1.04-1.22), gestational and pregestational hypertension including preeclampsia by 48% (95%CI 1.32-1.66), and oligohydramnion by 128% (95%CI 1.91-2.73). Factors related to the fetus also had an important effect on the risk of breech presentation: fetal developmental abnormalities increased the risk by 65% (95%CI 1.56-1.75), small for gestational age by 61%, (95%CI 1.53-1.69), while large for gestational age decreased the risk by 23% (95%CI 0.74-0.79). Mean birth weight was lower in the breech presentation group (by 123g, 95%CI 118-127g). Furthermore, newborns with breech presentation had a lower gestational age at delivery (by 0.3 weeks, 95%CI 0.25-0.27). (**Table 1** and **Table 2**)

In a multiple logistic regression investigation of independent effects, all factors that were related to breech presentation in the univariate analyses remained significant with similar effect sizes, except gestational and pregestational diabetes and large for gestational age. (**Table 2**)

Table 1

	Cephalic presentation	**Breech presentation**	**P**
n	1,230,152 (96.7)	41,794 (3.3)	
Maternal age (years)	27.5±5.4	28.0±5.4	<0.0001
Maternal age			<0.0001
<25 years	446,416 (97.2)	12,960 (2.8)	
25-35 years	693,059 (96.5)	25,083 (3.5)	
>35 years	90,677 (96.0)	3,751 (4.0)	
Parity			<0.0001
nulliparity	540,487 (95.9)	22,845 (4.1)	
primiparity	396,901 (97.4)	10,742 (2.6)	
second or multiparity	254,733 (97.3)	6,978 (2.7)	
Prior stillbirths			0.082
none	1,138,984 (96.7)	38,682 (3.3)	
one	6,461 (96.3)	245 (3.7)	
more than one	571 (95.6)	26 (4.4)	
Prior postnatal deaths			0.59
none	1,139,650 (96.7)	38,732 (3.3)	
one	5,731 (96.5)	208 (3.5)	
more than one	588 (97.0)	18 (3.0)	
Prior spontaneous abortions			<0.0001
none	993,149 (96.8)	33,151 (3.5)	
one	130,728 (96.5)	4,772 (3.5)	
more than one	32,488 (95.7)	1,477 (4.3)	
Prior induced abortions			0.49
none	945,073 (96.7)	32,081 (3.3)	

one	156,493 (96.7)	5,389 (3.3)	
more than one	59,882 (96.7)	2,071 (3.3)	
Conception			<0.0001
spontaneous	1,220,981 (96.7)	41,242 (3.3)	
hormone treatment	1,864 (95.0)	98 (5.0)	
assisted reproduction	7,382 (94.2)	456 (5.8)	
Pregestational diabetes	1,644 (95.7)	73 (4.3)	0.025
Gestational diabetes	17,488 (96.3)	688 (3.7)	0.003
Hypertension and preeclampsia	6,136 (95.2)	307 (4.8)	<0.0001
Severe oligohydramnion	1,653 (92.8)	128 (7.2)	<0.0001
Female fetus	592,480 (96.4)	22,407 (3.6)	<0.0001
Placenta preavia with severe bleeding	330 (97.1)	10 (2.9)	0.88
Gestational age at delivery (weeks)	39.2±1.1	39.0±1.1	<0.0001
Fetal weight (g)	3,360±473	3,237±486	<0.0001
SGA (<10th percentile)	28,929 (94.9)	1,557 (5.1)	<0.0001
LGA (>90th percentile)	147,880 (97.4)	3,966 (2.6)	<0.0001
Developmental abnormality	21,274 (94.7)	1,181 (5.3)	<0.0001

Characteristics of women with cephalic and breech presentation.

n (row %) for categorical parameters, mean ± the standard deviation for continuous parameters.
Independent samples t-test for continuous variables, logistic regression / chi square test categorical variables.
SGA: small for gestational age fetus; LGA: large for gestational age fetus.

Table 2

Variables	Unadjusted odds ratios (95%CI)	Multiple adjusted odds ratios (95%CI)*
Maternal age (years)	1.02 (1.02 to 1.03)	1.04 (1.04 to 1.04)
Parity		
nulliparity	1 (ref)	1 (ref)
primiparity	0.62 (0.61 to 0.64)	0.57 (0.56 to 0.59)
secundi- or multiparity	0.65 (0.63 to 0.67)	0.50 (0.48 to 0.51)
Prior stillbirths		
none	1 (ref)	1 (ref)
one	1.12 (0.98 to 1.27)	1.26 (1.11 to 1.44)
two or more	1.34 (0.91 to 1.99)	1.28 (0.86 to 1.92)
Prior spontaneous abortions		
none	1 (ref)	1 (ref)
one	1.09 (1.06 to 1.13)	1.13 (1.09 to 1.17)
more than one	1.36 (1.29 to 1.44)	1.35 (1.27 to 1.43)
Conception		
spontaneous	1 (ref)	1 (ref)
hormone treatment	1.56 (1.27 to 1.91)	1.20 (0.97 to 1.49)
assisted reproduction	1.83 (1.66 to 2.01)	1.19 (1.08 to 1.31)
Hypertension and preeclampsia	1.48 (1.32 to 1.66)	1.15 (1.02 to 1.29)
Severe oligohydramnion	2.28 (1.91 to 2.73)	1.79 (1.49 to 2.15)
Female fetus	1.25 (1.23 to 1.27)	1.20 (1.18 to 1.23)
Gestational age at delivery (week)	0.82 (0.81 to 0.82)	0.85 (0.84 to 0.86)
Fetal weight (g)	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.00)
SGA (<10th percentile)	1.61 (1.53 to 1.69)	1.11 (1.04 to 1.18)
Developmental abnormality	1.65 (1.56 to 1.75)	1.64 (1.55 to 1.75)

Predictors of breech presentation.

Logisitc regression with breech presentation as the dependent variable.
* Mutually adjusted multiple logistic regression with stepwise forward selection. Other variables available for the model: gestational and pregestational diabetes, large for gestational age.
SGA: small for gestational age fetus; LGA: large for gestational age fetus.

4.1.2 Consequences of breech presentation

Non-spontaneous labour initiation was more frequent in breech presentation (OR 4.09, 95%CI 4.00-4.18). Premature membrane ruptures (OR 1.07, 95%CI 1.05-1.09), Caesarean sections (OR 12.8, 95%CI 12.5-13.0), and other interventions (including sterilisation, hysterectomy or manual control of the uterine cavity (OR 1.30, 95%CI 1.27-1.34) were also more frequent. (**Table 3**)

Newborns in the breech presentation group had a 48% increased risk of a low 5-minute Apgar score (≤7; 95%CI 1.38-1.59). They also had an almost 40% increased risk of requiring perinatal intensive care after birth (OR 1.38, 95%CI 1.32-1.46) as well as increased odds of intrauterine and perinatal mortality (OR 1.58, 95%CI 1.29-1.94, OR 1.67, 95%CI 1.42-1.98). (**Table 3**)

As the last step of our analysis, we investigated whether maternal and fetal outcome indicators were independently related to breech presentation first in unadjusted models with breech presentation as the sole predictor and then taking into account all the covariates of breech presentation described in **Table 2**. All delivery outcomes were strongly related to breech presentation with no major attenuation of the effect size after multiple adjustments, except for premature membrane rupture which changed from a weak positive to a weak negative association. The overall combined pathological delivery outcome was almost 12 times more frequent for breech compared to cephalic presentation both in the adjusted and unadjusted models. There was an elevated risk of all fetal pathologies in breech pregnancies. Risk of the combined fetal pathological outcome was increased by 39% (95%CI 1.33-1.45) in the unadjusted model in breech compared to cephalic pregnancies. This risk was substantially attenuated after multiple adjustment to 18% (95%CI 1.13-1.24). (**Table 3**)

Table 3

	Cephalic presentation	Breech presentation	Odds Ratio (95%CI)	Multiple adjusted Odds Ratio (95%CI)*
n	1,230,152 (96.7)	41,794 (3.3)		
Non-spontaneous labour initiation	168,532 (91.2)	16,338 (8.8)	4.09 (4.00 to 4.18)	4.19 (4.11 to 4.29)
Premature membrane rupture	373,941 (96.5)	13,442 (3.5)	1.07 (1.05 to 1.09)	0.94 (0.92 to 96)
Caesarean section	263,213 (88.8)	33,302 (11.2)	12.8 (12.5 to 13.0)	16.1 (15.6 to 16.5)
Other intervention	154,518 (95.9)	6,648 (4.1)	1.30 (1.27 to 1.34)	1.34 (1.30 to 1.37)
Combined delivery outcome	373,065 (91.5)	34,558 (8.5)	11.7 (11.3 to 12.0)	11.8 (11.4 to 12.1)
Low 5-minute Apgar score (≤7)	20,148 (94.8)	1,112 (5.2)	1.48 (1.38 to 1.59)	1.30 (1.21 to 1.39)
PIC treatment	39,814 (95.5)	1,872 (4.5)	1.38 (1.32 to 1.46)	1.17 (1.12 to 1.23)
Intrauterine death	1,969 (94.6)	112 (5.4)	1.58 (1.29 to 1.94)	1.25 (1.02 to 1.54)
Perinatal mortality	2,768 (94.4)	163 (5.6)	1.67 (1.42 to 1.98)	1.30 (1.10 to 1.54)
Combined fetal outcome	57,915 (95.4)	2,764 (4.6)	1.39 (1.33 to 1.45)	1.18 (1.13 to 1.24)

Delivery related and fetal outcomes in pregnancies with cephalic and breech presentation.

n (row %) for categorical parameters, mean ± the standard deviation for continuous parameters. Odds ratios based on logistic regression analysis.
Combined delivery outcome: caesarian section or other intervention (manual control of the uterine cavity, hysterectomy, sterilisation).
Combined fetal outcome: Apgar value ≤7, need for PIC treatment, intrauterine or perinatal mortality. PIC: perinatal intensive care.
* Adjusted for potential predictors of breech presentation: maternal age, parity, prior stillbirth, spontaneous abortions, mode of conception, hypertension/preecclampsia, severe olygohydramnion, female sex, gestational age at delivery, fetal weight, small for gestational age, and developmental abnormality.

4.2 Updating the Hungarian birth weight percentiles

4.2.1 Birth weight percentiles of singleton newborns

There is a clear difference in birth weight between singleton boys and girls within each investigated gestational age. **(Table 4, Table 5, Figure 4,** and **Figure 5)**. The mean birth weight of boys is higher compared to girls. The birth weight trajectories shows an exponential increase over gestational age. The curve is steeper for boys, and somewhat shallower for girls: the boys' median birth weight increases from 555g to 3650g, while the girls' median increases from 525g to 3518g. Beginning at week 40 of gestation, the birth weights' increase slows down, and after week 41 it becomes stable; and even decreases slightly at the lowest percentiles.

Table 4

Gestational age (weeks)	N	Mean	95% CI	SD	5th percentile	10th percentile	25th percentile	50th percentile	75th percentile	90th percentile	95th percentile
22-23	70	553	531-574	90	400	435	490	555	600	660	700
24	169	659	640-678	124	480	490	580	650	745	800	860
25	155	762	741-783	134	490	600	660	780	870	920	970
26	226	869	848-890	158	590	640	770	895	970	1030	1140
27	233	996	971-1021	195	670	740	880	980	1130	1250	1330
28	267	1156	1129-1184	225	770	830	990	1190	1300	1440	1490
29	286	1285	1257-1314	244	900	970	1110	1300	1450	1600	1690
30	404	1475	1447-1502	282	980	1060	1300	1480	1685	1820	1930
31	541	1652	1625-1680	321	1100	1220	1450	1690	1870	1990	2180
32	843	1850	1828-1873	334	1300	1400	1620	1870	2040	2270	2400
33	1058	2090	2068-2111	353	1470	1600	1880	2100	2330	2490	2670
34	1857	2314	2297-2331	371	1690	1830	2080	2300	2550	2800	2940
35	3083	2548	2534-2562	390	1900	2000	2300	2550	2800	3040	3190
36	7073	2762	2752-2771	396	2100	2250	2490	2750	3000	3280	3440
37	17264	3026	3020-3032	406	2350	2500	2750	3020	3300	3550	3710
38	41131	3249	3245-3253	407	2600	2730	2970	3250	3520	3790	3950
39	65591	3423	3420-3426	410	2750	2900	3150	3400	3700	3960	4110
40	59888	3555	3552-3558	420	2870	3000	3260	3550	3840	4100	4270
41	16317	3669	3663-3676	422	3000	3140	3390	3650	3950	4220	4400

Birth weight percentiles of singleton male newborns in Hungary in 2011-2015

N –number of cases, 95% CI – 95% confidence interval, SD – standard deviation.
Birth weights are given in grams.

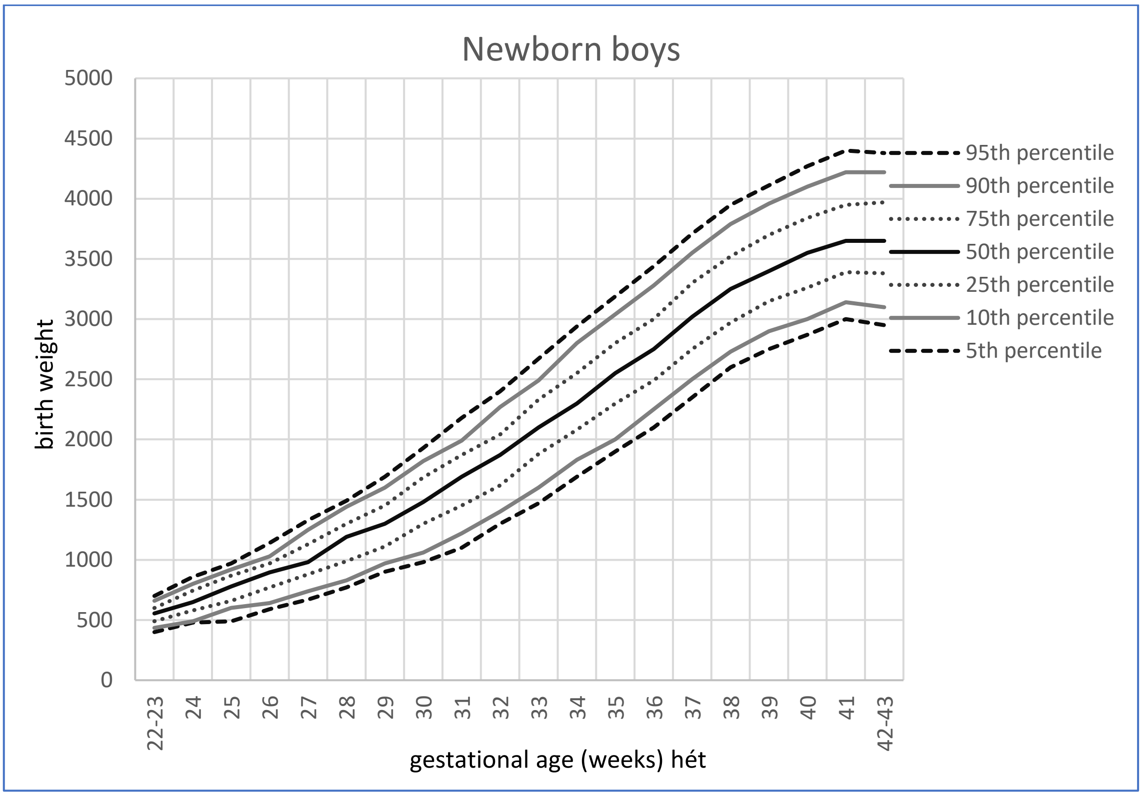
Table 5

Gestational age (weeks)	N	Mean	95% CI	SD	5th percentile	10th percentile	25th percentile	50th percentile	75th percentile	90th percentile	95th percentile
22-23	76	533	513-554	90	380	420	480	525	600	640	660
24	116	605	585-625	109	430	450	535	610	680	735	790
25	155	712	691-733	134	490	510	600	730	800	880	900
26	209	793	770-816	171	490	540	690	800	940	980	1000
27	169	945	918-973	182	660	700	800	970	1030	1200	1260
28	242	1096	1066-1127	240	715	790	930	1105	1280	1400	1460
29	255	1240	1208-1273	261	750	910	1050	1280	1400	1490	1620
30	312	1377	1345-1408	282	920	980	1199	1380	1555	1760	1890
31	410	1538	1510-1566	291	990	1175	1330	1490	1750	1925	1980
32	690	1765	1742-1789	310	1240	1340	1550	1775	1970	2170	2300
33	872	1978	1955-2001	345	1370	1480	1800	1980	2200	2420	2550
34	1505	2207	2188-2225	368	1570	1710	1970	2220	2450	2680	2820
35	2564	2435	2420-2450	390	1800	1950	2198	2450	2700	2930	3090
36	5859	2658	2649-2668	386	1990	2160	2400	2650	2920	3150	3300
37	14937	2903	2897-2909	399	2250	2400	2640	2900	3150	3430	3600
38	37339	3115	3111-3119	396	2470	2600	2850	3100	3380	3640	3800
39	62438	3277	3274-3281	392	2650	2780	3000	3270	3550	3800	3950
40	57805	3399	3396-3403	402	2750	2900	3120	3400	3670	3920	4100
41	15304	3502	3495-3508	405	2850	3000	3220	3500	3773	4040	4200
42-43	458	3523	3482-3563	438	2800	3000	3200	3518	3830	4100	4250

Birth weight percentiles of singleton female newborns in Hungary in 2011-2015.

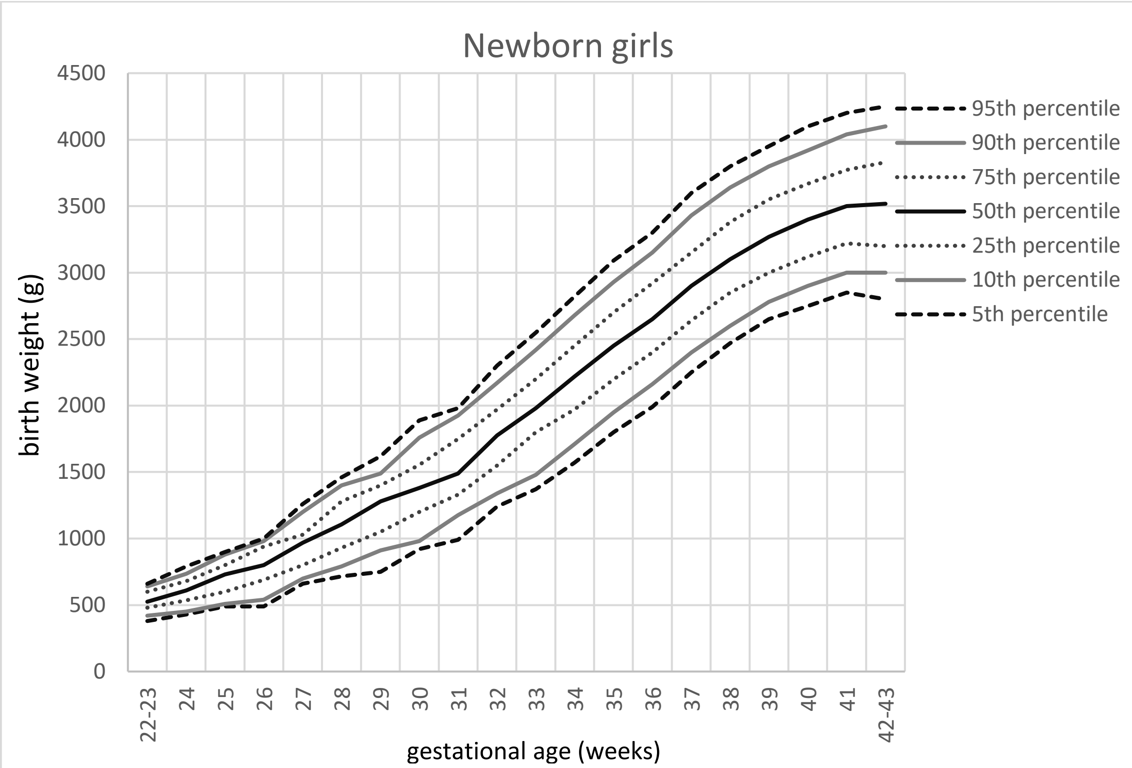
N –number of cases , 95% CI – 95% confidence interval, SD – standard deviation. Birth weights are given in grams.

Figure 4



Reference charts of birth weight percentiles of singleton male newborns in Hungary in 2011-2015.

Figure 5



Reference charts of birth weight percentiles of singleton female newborns in Hungary in 2011-2015.

4.2.2 Birth weight percentiles of newborns from twin pregnancies

The birth weight curve for twin pregnancies, starts at almost the same weight as for single pregnancies (median 550g for boys, 490g for girls), but increases less steeply (and more linearly) and reaches a lower zenith (median 2928g for boys, 2775g for girls) and the curve its shape is more linear. (**Table 6**, **Table 7**, **Figure 6**, and **Figure 7**). Birth weights increase continuously until 38 weeks of gestation, and after that, there is even a small decrease along the 95th percentile for boys and the 90th percentile for girls. The shape of the curves for twins is less smooth compared to singleton pregnancies, mainly related to the limited statistical power due to the smaller number of cases.

Table 6

Gestational age (week)	N	Mean	95% CI	SD	5th percentile	10th percentile	25th percentile	50th percentile	75th percentile	90th percentile	95th percentile
22-23	35	548	522-574	76	400	430	500	550	600	650	670
24	53	652	623-682	106	450	480	600	666	720	770	850
25	39	772	825-818	144	560	600	690	750	830	990	1110
26	49	856	817-895	135	640	650	800	880	970	990	1000
27	61	938	910-967	110	780	800	870	930	980	1100	1170
28	84	1120	1077-1163	199	800	830	978	1140	1278	1375	1440
29	118	1271	1230-1312	224	870	950	1150	1300	1420	1530	1645
30	125	1444	1401-1487	243	990	1150	1300	1450	1580	1740	1900
31	168	1669	1630-1707	252	1310	1350	1490	1650	1828	1990	2140
32	276	1820	1785-1855	297	1340	1450	1630	1830	1980	2200	2360
33	393	1935	1907-1962	278	1420	1560	1780	1950	2130	2290	2360
34	526	2128	2101-2155	318	1560	1720	1940	2130	2360	2490	2650
35	710	2330	2306-2353	322	1780	1910	2100	2330	2560	2750	2850
36	1146	2495	2476-2514	332	1950	2050	2270	2480	2730	2930	3050
37	1495	2667	2650-2684	338	2100	2240	2450	2650	2900	3100	3220
38	1080	2774	2752-2795	358	2145	2300	2550	2795	3010	3225	3360
39	371	2848	2806-2890	412	2150	2330	2600	2850	3115	3360	3500
40-41	46	2942	2840-3045	345	2410	2600	2700	2928	3130	3400	3430

Birth weight percentiles of male newborns from twin pregnancies in Hungary between in 2011-2015.

N –number of cases , 95% CI – 95% confidence interval, SD – standard deviation.
Birth weights are given in grams.

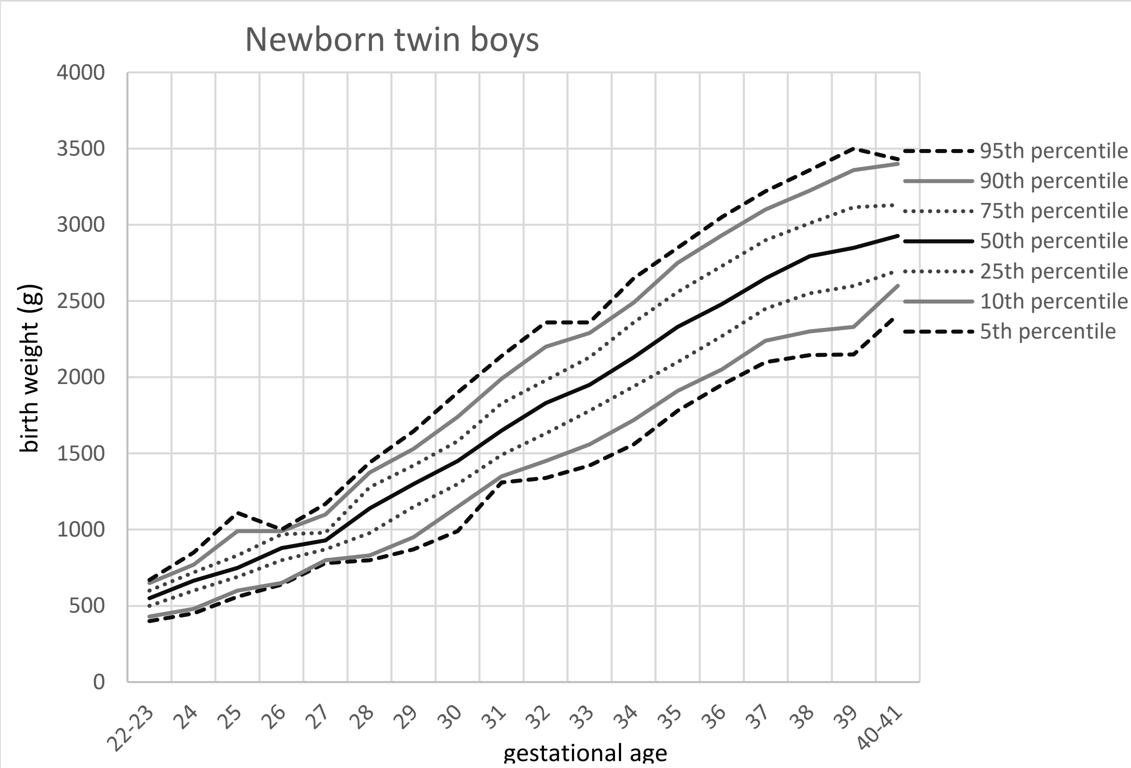
Table 7

Gestational age (week)	N	Mean	95% CI	SD	5th percentile	10th percentile	25th percentile	50th percentile	75th percentile	90th percentile	95th percentile
22-23	23	489	462-517	64	400	400	450	490	550	570	570
24	51	632	604-659	98	470	490	550	650	710	750	780
25	34	695	653-737	120	450	490	650	700	760	850	870
26	53	786	750-821	129	580	610	700	780	885	960	980
27	49	931	896-965	121	720	760	880	940	980	1140	1180
28	79	1061	1028-1095	150	790	900	950	1060	1160	1280	1320
29	98	1219	1173-1264	227	800	970	990	1240	1360	1455	1600
30	104	1361	1320-1401	206	980	1100	1255	1395	1490	1620	1680
31	175	1524	1487-1561	248	1100	1190	1380	1490	1690	1820	1910
32	284	1711	1682-1741	254	1320	1400	1520	1705	1855	1990	2130
33	367	1866	1836-1895	280	1380	1480	1700	1892	2050	2200	2300
34	545	2041	2016-2067	305	1490	1650	1850	1990	2250	2450	2550
35	807	2204	2182-2225	309	1680	1825	1980	2220	2400	2600	2700
36	1169	2394	2375-2412	320	1840	1980	2200	2400	2600	2800	2900
37	1475	2557	2539-2574	337	1990	2120	2330	2550	2790	3000	3140
38	1183	2683	2663-2703	353	2070	2220	2450	2700	2900	3120	3250
39	349	2716	2675-2756	385	2030	2210	2450	2700	2980	3230	3350
40-41	54	2810	2713-2908	356	2250	2400	2600	2775	3000	3200	3400

Birth weight percentiles of female newborns from twin pregnancies in Hungary between in 2011-2015

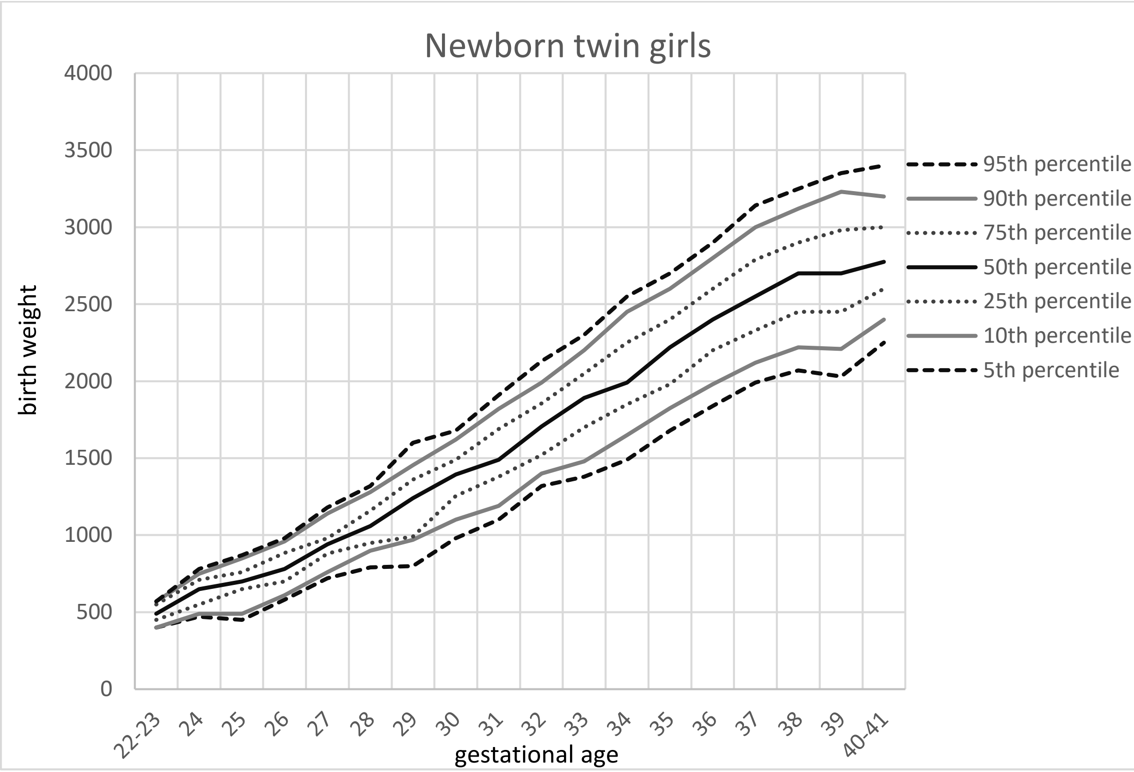
N –number of cases , 95% CI – 95% confidence interval, SD – standard deviation.
Birth weights are given in grams.

Figure 6



Reference charts of birth weight percentiles of male newborns from twin pregnancies in Hungary in 2011-2015.

Figure 7



Reference charts of birth weight percentiles of female newborns from twin pregnancies in Hungary in 2011-2015.

4.2.3 Temporal trends of mean birth weights between 1996 and 2015

When examining the temporal trends in birth weights (between 1996 and 2015), we compared mean birth weights in the following five-year periods: 1996-2000, 2001-2005, and 2006-2010 to the reference period of 2011-2015 (**Table 8** and **Table 9**).

We found statistically significant heterogeneity in birth weights of boys in gestational weeks 30and those between 33 and 41 weeks over the 20-year examination period. For gestational weeks 37, 38, and 39, the birth weights in all periods differed from those in the reference period: birth weights were lower in 1996-2000 and in 2001-2005 compared to the reference period, while birth weights were higher in 2006-2010. Based on all of this, it appears that mean birth weights increased until 2010 followed by a decrease. For example, birth weights increased from 3214g to 3267g and then decreased to 3249g at gestational week 38. (**Table 8 and Figure 8**)

For girls, we found statistically significant heterogeneity in birth weights in gestational weeks 24, 26, 28, and between 35 and 43 during 20-year examination period. For gestational weeks 36 to 38, measured birth weights differed in all time periods from those in the reference period with a similar pattern to that found in girls (e.g. at 38week s of gestation, birth weights increased from 3080g to 3128g between 1996 and 2010, then slightly decreased to 3115g in 2011-2015) (**Table 9 and Figure 8**)

Table 8

	1996-2000			2001-2005			2006-2010			2011-2015 (ref.)	P
Gestational age (weeks)	**mean**	**difference vs ref.**	**SE**	**mean**	**–difference vs ref.**	**SE**	**mean**	**–difference vs ref.**	**SE**	**mean**	
22-23	580	-27.4	19.6	578	-25.5	17.3	553	0.2	18.1	553	ns
24	677	-18.5	13.9	669	-9.7	12.9	663	-4.2	13.4	659	ns
25	757	4.9	15.7	755	7.3	14.9	753	9.4	15.8	762	ns
26	868	0.6	15.1	878	-8.5	15.2	883	-14.2	15.7	869	ns
27	1018	-22.3	17.8	1001	-5.1	16.6	1000	-4.2	17.5	996	ns
28	1153	3.2	19.4	1124	32.7	19.1	1136	20.8	19.6	1156	ns
29	1301	-16.1	20.6	1312	-26.4	19.4	1274	11.1	19.9	1285	ns
30	1481	-6.5	19.7	1447	27.3	19.7	1433	42.2*	20.0	1475	0.04
31	1649	3.3	19.5	1660	-7.8	18.7	1678	-25.3	19.3	1652	ns
32	1845	5.0	16.2	1855	-4.6	15.9	1856	-5.3	15.9	1850	ns
33	2054	35.6*	15.4	2059	30.3*	14.9	2093	-3.5	15.1	2090	0.01
34	2274	39.2*	12.9	2287	26.5*	12.3	2314	-0.8	12.2	2314	0.002
35	2471	76.8*	10.5	2509	38.7*	10.2	2539	8.5	10.0	2548	<0.0001
36	2720	41.2*	7.0	2748	13.5*	6.9	2774	-12.5	6.7	2762	<0.0001
37	2988	38.9*	4.5	3013	13.7*	4.4	3041	-14.4*	4.4	3026	<0.0001
38	3214	34.3*	3.0	3237	11.5*	2.9	3267	-18.1*	2.9	3249	<0.0001
39	3388	35.0*	2.4	3414	9.3*	2.3	3432	-9.2*	2.3	3423	<0.0001
40	3518	37.1*	2.4	3545	10.5*	2.4	3558	-3.4	2.4	3555	<0.0001
41	3621	48.1*	4.5	3648	20.7*	4.5	3671	-1.5	4.5	3669	<0.0001
42-43	3675	-9.6	22.1	3698	-32.8	23.1	3695	-30.4	23.9	3665	ns

Mean birth weights (and difference compared to the reference period) of male newborns in 4 consecutive 5-year periods between 1996-2015.

mean –mean birth weight (g)
ref. – reference period (2011-2015)
SE –standard error of the difference
If the difference is positive the birth weight in a given period is higher than the reference period.
If the difference is negative the birth weight in a given period is lower than the reference period.
p- p for heterogeneity. This indicates whether a significant difference exists between any two of the four periods
* - the statistically significant difference between the marked 5-year period and the reference period (p<0.05).

Table 9

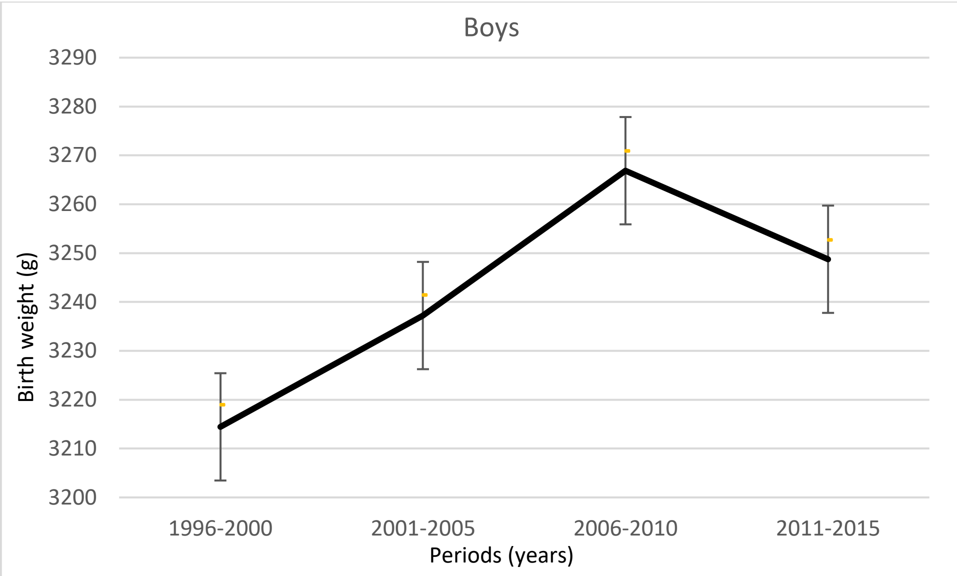
	1996-2000			2001-2005			2006-2010			2011-2015 (ref.)	P
Gestational age (week)	**mean**	**difference vs ref.**	**SE**	**mean**	**difference vs ref.**	**SE**	**mean**	**difference vs ref.**	**SE**	**mean (ref.)**	
22-23	550	-16.7	16.4	529	4.2	16.2	523	10.2	17.1	533	ns
24	650	-44.8*	14.9	623	-17.5	14.1	622	-16.6	13.8	605	0.03
25	720	-8.1	15.9	715	-2.9	15.4	748	-36.1*	15.2	712	ns
26	851	57.6*	17.0	839	-45.6*	16.5	814	-21.0	16.7	793	0.003
27	930	14.9	20.0	930	14.9	19.2	948	-2.6	19.4	945	ns
28	1111	-14.4	20.9	1076	20.3	21.1	1055	41.5	21.3	1096	0.04
29	1194	45.9*	23.3	1235	5.8	23.2	1226	14.4	23.2	1240	ns
30	1419	-42.7	23.3	1399	-22.4	22.8	1375	1.6	23.1	1377	ns
31	1578	-39.6	21.4	1548	-9.6	20.7	1554	-16.2	21.1	1538	ns
32	1767	-1.4	17.2	1782	-16.5	17.3	1787	-21.2	17.7	1765	ns
33	1995	-17.1	17.3	1980	-1.9	16.9	1986	-7.9	17.1	1978	ns
34	2183	23.6	13.7	2201	6.2	16.2	2209	-2.6	13.0	2207	ns
35	2379	56.4*	11.3	2415	20.1	10.8	2431	4.4	10.8	2435	<0.0001
36	2617	41.0*	7.3	2653	5.3	7.1	2676	-17.3*	7.0	2658	<0.0001
37	2874	28.6*	4.8	2904	-0.8	4.7	2928	-25.3*	4.6	2903	<0.0001
38	3080	35.4*	3.1	3106	9.8*	3.0	3128	-12.5*	3.0	3115	<0.0001
39	3245	32.7*	2.4	3277	0	2.3	3289	-11.7*	2.3	3277	<0.0001
40	3366	33.2*	2.4	3396	2.9	2.3	3411	-12.0*	2.3	3399	<0.0001
41	3462	40.2*	4.4	3486	16.1*	4.4	3510	-7.6	4.4	3502	<0.0001
42-43	3513	9.8	23.4	3513	9.8	23.4	3555	-32.6	24.2	3523	0.04

Mean birth weights (and difference compared to the reference period) of female newborns in 4 consecutive 5-year periods between 1996-2015.

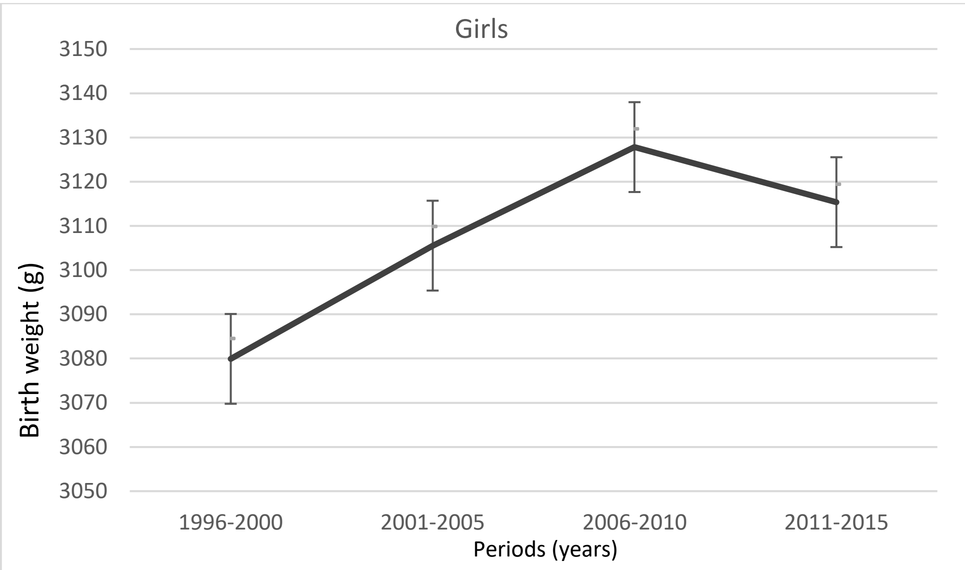
mean –mean birth weight (g)
ref. – reference period (2011-2015)
SE –standard error of the difference
If the difference is positive the birth weight in a given period is higher than the reference period.
If the difference is negative the birth weight in a given period is lower than the reference period.
p- p for heterogeneity. This indicates whether a significant difference exists between any two of the four periods
* - statistically significant difference between the marked 5-year period and the reference period ($p<0.05$).

Figure 8

A



B



Changes of mean birth weights for newborn boys (A) and girls (B) delivered at 38 weeks of gestation from singleton pregnancies by 5-year periods between 1996 and 2015.

Error bars indicate 95% confidence intervals.
Birth weights are given in grams.

In the case of twin pregnancies, the above described temporal changes are not entirely clear. Although the heterogeneity of birth weights can be verified in gestational weeks between 35and 38, their direction is not always consistent. (**Table 10** and **Table 11**)

Table 10

	1996-2000			2001-2005			2006-2010			2011-2015 (ref.)	P
Gestational age (week)	mean	difference vs ref.	SE	mean	difference vs ref.	SE	mean	differenc e vs ref.	SE	mean	
22-23	494	54.5*	24.2	512	36.1	20.3	541	7.3	22.1	548	ns
24	647	5.8	28.8	668	-16.0	22.3	635	17.7	21.8	652	ns
25	745	26.3	38.0	743	28.4	37.0	769	2.3	35.3	772	ns
26	870	-14.0	28.1	883	-26.4	27.1	856	0.3	25.9	856	ns
27	951	-12.4	26.1	920	18.2	23.1	959	-20.7	20.8	938	ns
28	1125	-5.1	28.5	1160	-39.7	29.7	1163	-42.8	29.3	1120	ns
29	1228	42.3	35.6	1262	8.9	30.4	1253	17.2	28.9	1271	ns
30	1380	63.8	33.0	1399	44.5	31.3	1438	6.2	28.9	1444	ns.
31	1571	97.7*	28.5	1646	22.7	26.7	1616	52.6*	25.5	1669	0.005
32	1760	59.9*	28.3	1792	28.4	26.5	1764	55.7*	25.4	1820	ns
33	1873	61.2*	24.1	1905	29.5	20.8	1967	-32.9	20.3	1935	0.001
34	2137	-8.6	23.3	2101	26.6	21.0	2150	-21.7	19.7	2128	ns.
35	2272	57.6*	20.2	2288	41.5*	18.2	2332	-2.1	17.1	2330	0.002
36	2455	39.6*	16.2	2491	3.8	14.4	2493	2.0	14.1	2495	0.059
37	2619	47.5*	14.6	2669	-1.5	13.3	2674	-6.8	12.8	2667	0.001
38	2762	11.8	16.4	2783	-9.3	15.2	2808	-34.1*	15.3	2774	0.02
39	2882	-34.0	27.6	2890	-41.5	27.8	2859	-10.2	28.3	2848	ns.
40-41	2984	-41.3	72.9	3027	-84.5	74.2	2906	36.4	75.8	2942	ns.

Mean birth weights (and difference compared to the reference period) of male newborns from twin pregnancies in 4 consecutive 5-year periods between 1996-2015.

mean –mean birth weight (g)
ref. – reference period (2011-2015)
SE –standard error of the difference
If the difference is positive the birth weight in a given period is higher than the reference period.
If the difference is negative the birth weight in a given period is lower than the reference period.
p- p for heterogeneity. This indicates whether a significant difference exists between any two of the four periods
* - statistically significant difference between the marked 5-year period and the reference period ($p<0.05$).

Table 11

	1996-2000			2001-2005			2006-2010			2011-2015 (ref.)	P
Gestational age (week)	mean	difference vs ref.	SE	mean	difference vs ref.	SE	mean	difference vs ref.	SE	mean (ref.)	
22-23	479	9.7	22.7	476	13.2	20.2	503	-14.3	20.0	489	ns
24	601	30.9	28.7	608	23.3	23.7	612	20.1	20.7	632	ns.
25	710	-14.9	29.8	639	55.9*	26.9	681	13.7	28.4	695	0.04
26	780	5.5	28.6	789	-2.8	28.0	777	8.8	25.1	786	ns.
27	961	-29.8	28.3	912	19.2	26.2	936	-5.6	23.3	931	ns.
28	968	92.6*	29.8	1033	27.9	27.8	1055	6.1	25.7	1061	0.01
29	1166	53.3	35.8	1145	74.0*	31.6	1211	7.6	30.2	1219	ns.
30	1373	-12.3	30.9	1350	11.2	31.3	1411	-50.1	29.8	1361	ns.
31	1469	54.8	31.3	1505	18.5	27.5	1540	-16.7	26.7	1524	ns.
32	1704	7.8	26.5	1671	40.7	25.1	1710	1.4	23.4	1711	ns.
33	1851	15.0	24.7	1876	-9.2	21.8	1897	-30.5	20.1	1866	ns.
34	1997	44.4*	21.2	2010	31.9	19.8	2044	-2.5	18.5	2041	0.057
35	2198	5.6	18.5	2170	33.9*	16.1	2232	-28.1	15.4	2204	0.002
36	2341	53.2*	15.4	2375	19.2	13.7	2384	1.0	13.2	2394	0.005
37	2510	46.5*	13.9	2549	7.6	12.9	2546	10.6	12.4	2557	0.007
38	2643	40.1*	15.5	2653	30.0*	14.4	2684	-1.4	14.2	2683	0.008
39	2737	-20.8	25.8	2773	-57.0*	25.6	2768	-52.0*	26.0	2716	ns.
40-41	2859	-48.5	62.3	2802	8.4	62.8	2850	-39.4	64.4	2810	ns.

Mean birth weights (and difference compared to the reference period) of female newborns from twin pregnancies in 4 consecutive 5-year periods between 1996-2015.

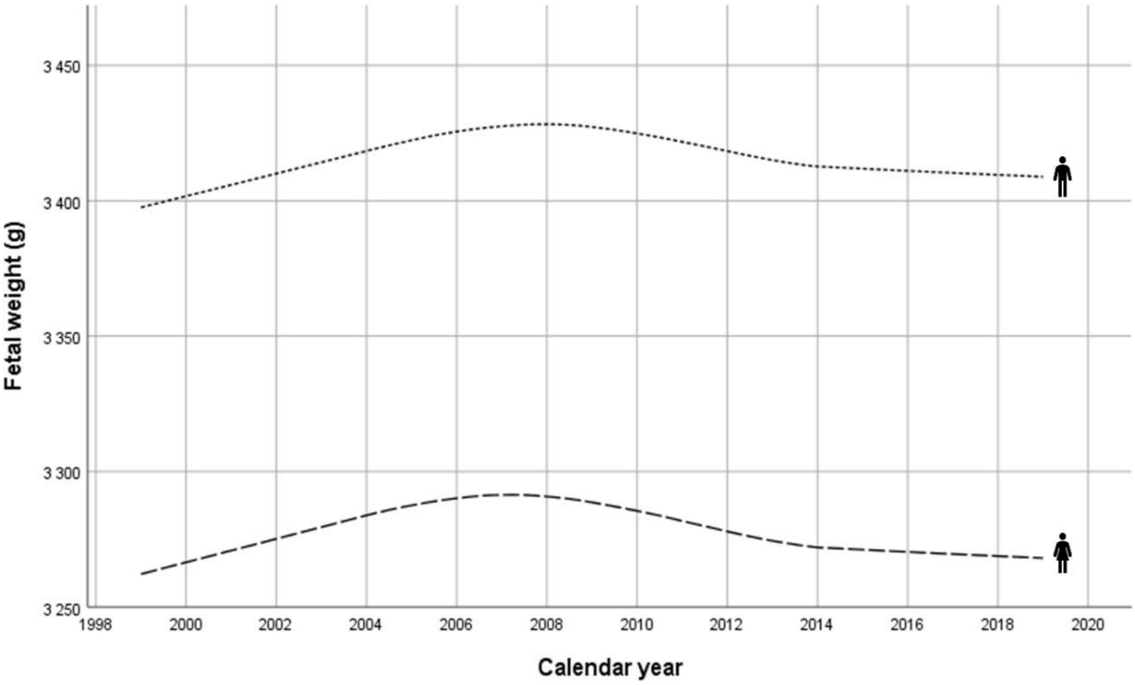
mean –mean birth weight (g)
ref. – reference period (2011-2015)
SE –standard error of the difference
If the difference is positive the birth weight in a given period is higher than the reference period.
If the difference is negative the birth weight in a given period is lower than the reference period.
p – p for heterogeneity. This indicates whether a significant difference exists between any two of the four periods
* - statistically significant difference between the marked 5-year period and the reference period ($p<0.05$).

4.3 Birth weight trends and their explanatory factors

4.3.1 Loess curves of birth weight over time

Mean birth weight increased almost linearly in both sexes by approximately 30g in 1999-2008, followed by a faster decrease in 2008-2013 and a shallower decrease thereafter reaching a value within 10g of the baseline in 1999. (**Figure 9**)

Figure 9



Temporal changes of mean birth weight by newborn sex in Hungary between 1999 and 2018.

Loess curves.

4.3.2 Fetal, maternal, and delivery related characteristics of pregnancies in *1999, 2008, and 2018*

While there was no change in the sex distribution of newborns with around 51-52% boys, all other parameters showed significant increasing or decreasing trends over the three selected years. Median birth weights were 3250/3400g (girl/boy) in 1999, then increased to 3300/3440g in 2008 and decreased to 3260/3400g in 2018. (**Table 12**)

Maternal age increased from 26.2 years in 1999 to 29.6 in 2008 and further to 30.5 in 2018. The proportion of older mothers (≥30 years of age) continuously increased from 24 to 53%. The proportion of primiparas increased from 46.4 to 49.6% while the frequency of multiparity decreased. (**Table 12**)

Mean gestational age at delivery decreased by >1 day between 1999 and 2018. The proportion of both induced deliveries and Caesarean sections more than doubled from 12.7 to 26.2% and 17.6 to 39.7%, respectively. (**Table 12**)

Table 12

		1999	2008	2018	P-value
Fetal parameters					
Sex	n (%)				NS
	boys	38167 (51.8)	43855 (51.8)	40488 (51.4)	
	girls	35523 (48.2)	40732 (48.2)	38282 (48.6)	
Median birth weight	g				
	boys	3400 (3100;3700)	3440 (3130;3750)	3400 (3100;3700)	<0.0001
	girls	3250 (2980;3550)	3300 (3000;3600)	3260 (3000;3550)	<0.0001
Maternal parameters					
Age	year	26.2 (23.0;29.8)	29.6 (25.9;32.9)	30.5 (26.1;34.6)	<0.0001
Age	n (%)				<0.0001
	<20 years	6087 (8.3)	5263 (6.2)	4625 (5.9)	
	20-24.9 years	23940 (32.6)	12691 (15.0)	11378 (14.5)	
	25-29.9 years	25854 (35.2)	26991 (32.0)	20708 (26.3)	
	30-34.9 years	12819 (17.4)	28718 (34.0)	23752 (30.2)	
	35-39.9 years	3916 (5.3)	9179 (10.9)	14038 (17.9)	
	≥40 years	915 (1.2)	1574 (1.9)	4117 (5.2)	
Parity	n (%)				<0.0001
	primiparous	34215 (46.4)	40556 (47.9)	39077 (49.6)	
	multiparous	39475 (53.6)	44031 (52.1)	39693 (50.4)	
Delivery-related parameters					
Time of delivery	week	39.4 (38.5;40.1)	39.2 (38.4;40.0)	39.1 (38.3;39.9)	<0.0001
Mode of delivery	n (%)				<0.0001
	vaginal	60740 (82.4)	60320 (71.3)	47224 (60.3)	
	caesarean section	12950 (17.6)	24267 (28.7)	31108 (39.7)	
Induced delivery	n (%)				<0.0001
	no	64348 (87.3)	71002 (83.9)	58103 (73.8)	
	yes	9342 (12.7)	13585 (16.1)	20667 (26.2)	

Characteristics of singleton live births in Hungary in three selected years (1999, 2008, and 2018).

Results are given as n (%) or median (IQR).
IQR: interquartile range
P-values are given for χ^2-tests for categorical variables, and one-way ANOVA for continuous variables.

4.3.3 The role of fetal, maternal, and delivery related variables in the temporal changes of newborn birth weights

According to *Model 0*, birth weight significantly increased by 4.1g/year in boys and girls in 1999-2008, while decreased by 2.5g/year in 2008-2018. (**Table 13**)

When we adjusted for gestational age at delivery (including linear, quadratic and cubic terms; *Model 1*) the rate of increase in the first period became even more pronounced (5.4 g/year). During the second period, similar adjustment for gestational age at delivery substantially decreased the rate of decline from 2.5 to 1.4g/year. (**Table 13**)

Further adjustment for maternal age (including linear and quadratic terms; *Model 2*) halved the rate of increase in birth weight from 5.4 to 2.4g/year. During the second period, adjustment for maternal age somewhat increased the estimate of yearly change in birth weight. (**Table 13**)

Our final model (further adjusted for parity, induced deliveries, and caesarean sections; *Model 3*) showed similar estimates to the ones in *Model 2*. (**Table 13**)

Table 13

	1999-2008				2008-2018			
Model 0	**Beta**	**SE**	**95% CI**	**P-value**	**Beta**	**SE**	**95% CI**	**P-value**
Intercept	3300	0.98	3298-3302	<0.0001	3291	1.06	3289-3293	<0.0001
Calendar year (year)	4.14	0.17	3.80-4.47	<0.0001	-2.48	0.15	-2.77-(-2.19)	<0.0001
Boy	136.1	0.99	134.1-138.0	<0.0001	140.4	0.94	138.6-142.3	<0.0001
Model 1								
Intercept	3297	1.00	3295-3299	<0.0001	3288	1.06	3286-3290	<0.0001
Calendar year (year)	5.41	0.16	5.10-5.73	<0.0001	-1.42	0.14	-1.68-(-1.15)	<0.0001
Boy	141.5	0.92	139.7-143.3	<0.0001	144.8	0.87	143.1-146.5	<0.0001
Week of delivery (week)	145.0	0.89	143.3-146.8	<0.0001	144.8	0.85	143.2-146.5	<0.0001
(week of delivery)^2	-19.85	0.34	-20.51-(-19.18)	<0.0001	-18.46	0.33	-19.10-(-17.82)	<0.0001
(week of delivery)^3	1.78	0.28	1.22-2.33	<0.0001	2.50	0.27	1.97-3.04	<0.0001
Model 2								
Intercept	3319	1.04	3317-3321	<0.0001	3304	1.08	3301-3306	<0.0001
Calendar year (year)	2.36	0.16	2.05-2.68	<0.0001	-1.81	0.14	-2.08-(-1.55)	<0.0001
Boy	141.2	0.91	139.4-143.0	<0.0001	144.9	0.86	143.2-146.6	<0.0001
Week of delivery (week)	143.3	0.42	141.6-145.1	<0.0001	145.3	0.83	143.7-147.0	<0.0001
(week of delivery)^2	-18.91	0.33	-19.57-(-18.25)	<0.0001	-17.14	0.32	-17.77-(-16.51)	<0.0001
(week of delivery)^3	1.80	0.28	1.25-2.34	<0.0001	1.95	0.27	1.42-2.48	<0.0001
Maternal age (year)	9.41	0.09	9.30-9.65	<0.0001	11.64	0.07	11.50-11.79	<0.0001
(maternal age)^2	-0.91	0.01	-0.94-(-0.89)	<0.0001	-0.71	0.01	-0.73-(-0.69)	<0.0001
Model 3								
Intercept	3296	1.21	3294-3298	<0.0001	3274	1.22	3271-3276	<0.0001
Calendar year (year)	2.62	0.16	2.30-2.93	<0.0001	-1.82	0.14	-2.09-(-1.56)	<0.0001
Boy	141.0	0.91	139.3-142.8	<0.0001	144.8	0.86	143.1-146.5	<0.0001
Week of delivery (week)	144.2	0.88	142.5-146.0	<0.0001	148.0	0.84	146.4-149.6	<0.0001
(week of delivery)^2	-18.62	0.34	-19.28-(-17.97)	<0.0001	-16.49	0.32	-16.13-(-15.86)	<0.0001
(week of delivery)^3	1.81	0.28	1.26-2.36	<0.0001	1.68	0.27	1.15-2.21	<0.0001
Maternal age (year)	8.30	0.09	8.12-8.48	<0.0001	10.43	0.08	10.28-10.59	<0.0001
(maternal age)^2	-0.90	0.01	-0.92-(-0.88)	<0.0001	-0.71	0.01	-0.73-(-0.69)	<0.0001
Multiparous	35.97	0.96	34.09-37.85	<0.0001	47.81	0.90	46.04-49.57	<0.0001
Induced delivery	0.25	1.49	-2.67-3.17	NS	10.52	1.27	8.04-10.01	<0.0001
Caesarean section.	13.99	1.25	11.54-16.43	<0.0001	11.57	1.08	9.45-13.69	<0.0001

Hierarchical linear regression predicting birth weight (grams) of term newborns for the period 1999-2008 and 2008-2018.

SE: standard error; CI: confidence interval
For these models date of delivery was centred at 2008, maternal age at 29 years, and gestational

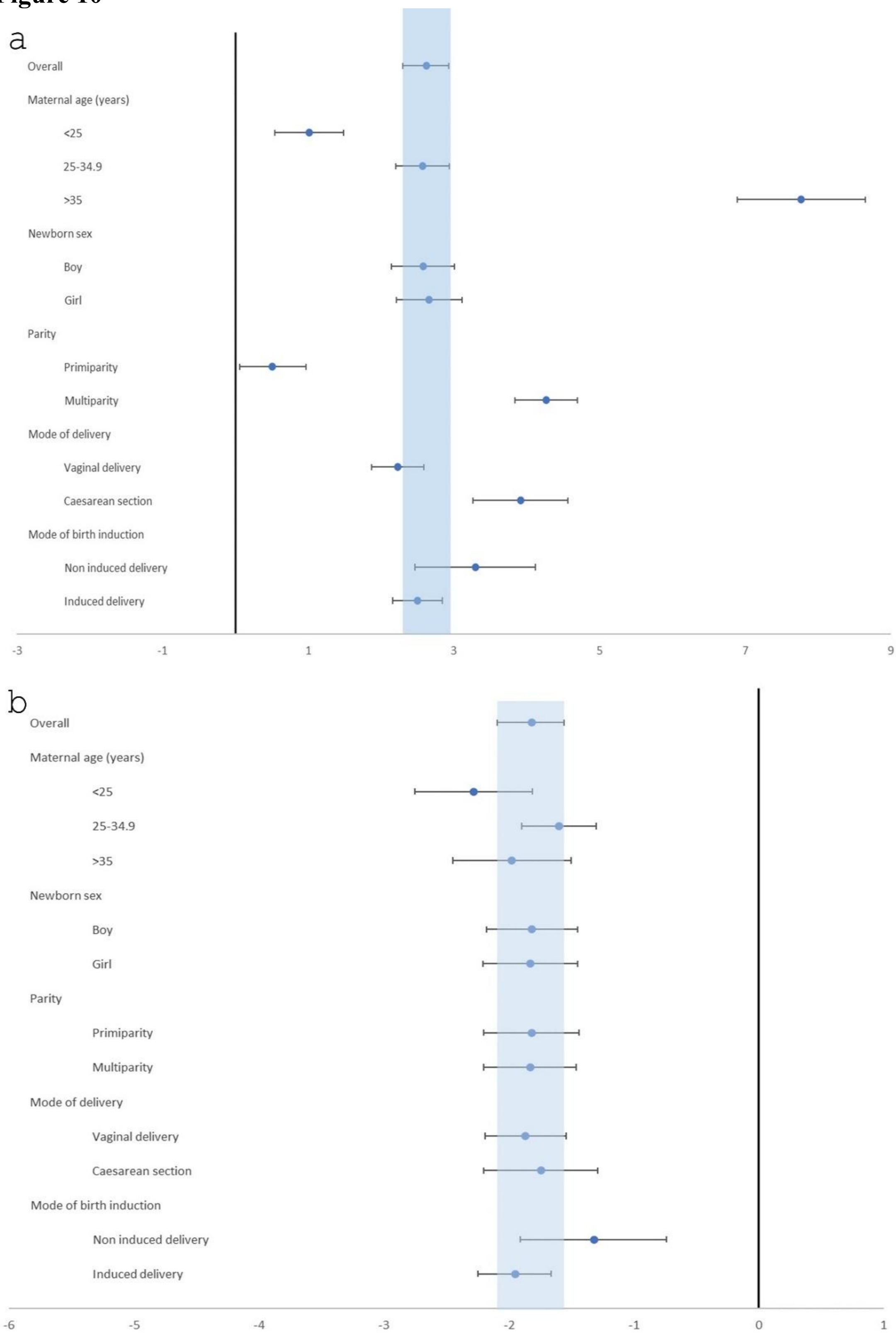
age at 39 weeks.
(week of delivery)^2 and (week of delivery)^3 refer to the quadratic and cubic terms of week of delivery. (maternal age)^2 refers to the quadratic term of maternal age in the linear model.

4.3.4 Interaction between selected maternal, fetal, and delivery related characteristics and calendar year

In the first period (1999-2008), we found a significant interaction between calendar time and maternal age ($p<0.0001$), showing the fastest increase in birth weight of mothers over 35 years of age (vs. a slower increase in both groups of younger mothers) leading to similar birth weights in all age groups by 2008. Similarly, there was a strong interaction with parity, with widening birth weight gap between multiparous and nulliparous women ($p<0.0001$) resulting from a slower increase in nulliparous and a faster increase in multiparous women. The mode of delivery was also related to the temporal increase in birth weights with a faster increase among those born by caesarean section ($p<0.0001$). No interaction between newborn sex ($p=0.801$) or the mode of induction ($p=0.080$) with calendar time on birth weights was found. (**Figure 10A, Figure 11**)

In the second period (2008-2018), we found a significant interaction with maternal age ($p=0.009$), however the direction of the interaction was the opposite compared to the previous period: newborns of the youngest mothers showed the fastest decline in birth weight over time. The interaction with parity ($p=0.773$) also changed, both primiparas and multiparas had a similar decrease in birth weights over time. Similarly to the first period, no interaction with sex of the newborn ($p=0.948$) was found. Furthermore, the rate of decrease in birth weight was similar in both types of deliveries ($p=0.672$) and was independent of presence or absence of induction ($p=0.059$). (**Figure 10B, Figure 12**)

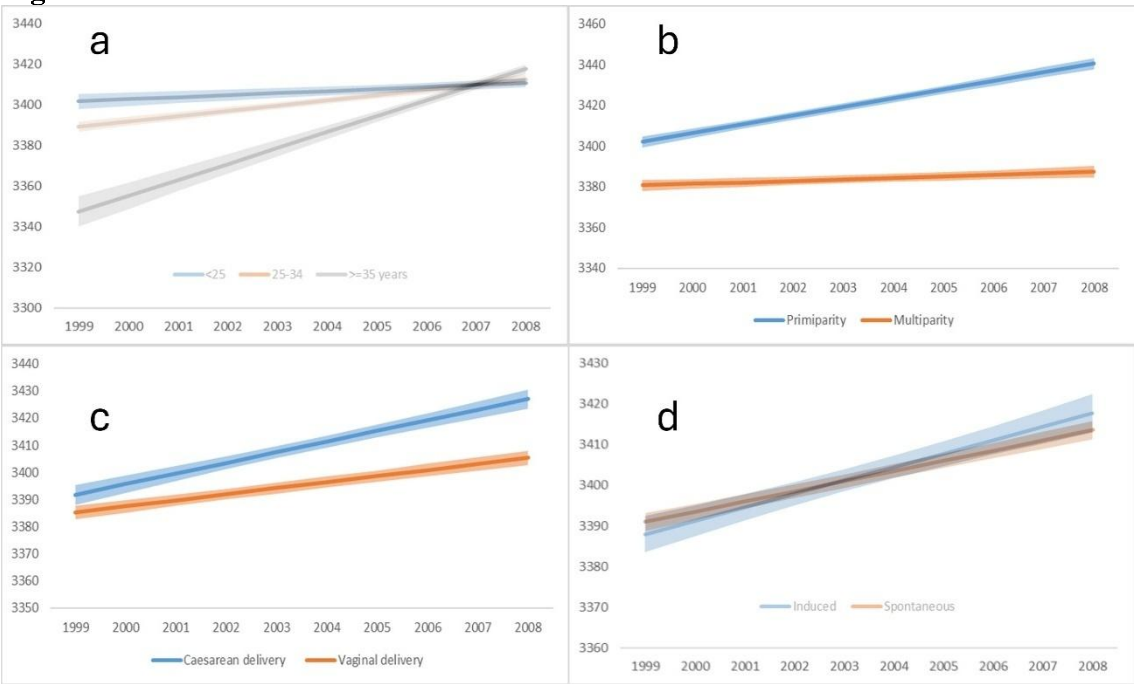
Figure 10



Yearly changes in birth weight of term newborns in 1999–2008 (a) and 2008-2018 (b).

Birth weights in grams.
All models are adjusted for gestational age at delivery (using linear, quadratic and cubic terms), maternal age (using linear and quadratic terms), parity, induced delivery, and caesarean section. Multiple linear regression. See further details in the Statistical analysis section.

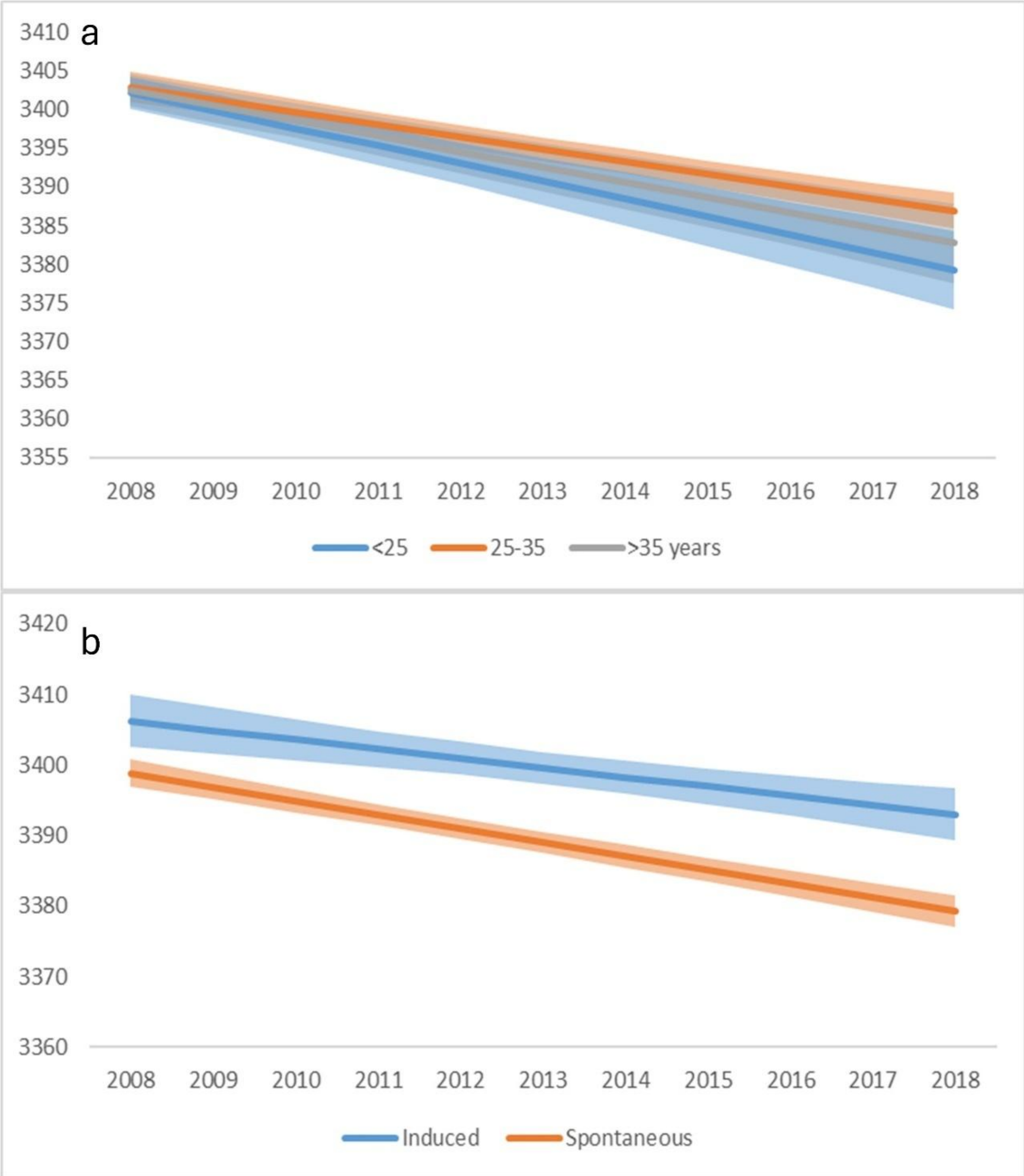
Figure 11



Birth weights by maternal age (a), parity (b), mode of delivery (c), and mode of birth induction (d) in 1999-2008.

Birth weights in grams, shaded areas represent 95% confidence bands.
Estimated marginal means for singleton term deliveries with the following characteristics: 48% female newborns, 47% primiparas, 76% vaginal deliveries, 85% non-induced deliveries, maternal age 28.0 years, gestational age at delivery 39.2 weeks.
See further details on the modelling approach in the Statistical analysis section.

Figure 12



Birth weights by maternal age (a), and mode of birth induction (b) in 2008-2018.

Birth weights in grams, shaded areas represent 95% confidence bands.
Estimated marginal means for singleton term deliveries with the following characteristics: 48% female newborns, 49% primiparas, 66% vaginal deliveries, 80% non-induced deliveries, maternal age 29.9 years, gestational age at delivery 39.1 weeks.
See further details on the modelling approach in the Statistical analysis section.

5 Discussion

5.1 Key results

5.1.1 Risk factors and consequences of term breech presentation

Using mandatory data collected on all pregnancies in Hungary over a period of 15 years (1996-2011), we found that the risk of term breech presentation increased in older, nulliparous women, in those with an abnormality in their obstetrical medical history (stillbirth, spontaneous abortions, non-spontaneous conception), and in women with hypertensive disorder or oligohydramnion during pregnancy. Fetal characteristics (including female sex, younger gestational age at delivery, SGA, lower fetal weight or a developmental abnormality) also increased the risk of breech presentation.

Even after controlling for the effect of the predictors of a breech pregnancy, we found that breech presentation in term pregnancies significantly increased the risk of pathological deliveries (Caesarean section and other interventions at parturition) and/or adverse fetal outcomes (low Apgar value, need for PIC treatment, intrauterine or perinatal death) by 12 times and 18%, respectively. These findings suggest breech presentation is a marker of a pathological pregnancy and not just a normal variant.

5.1.2 Updating the Hungarian birth weight percentiles

In the current analysis, we developed updated birth weight percentile data based on all pregnancies in Hungary that serves the needs of obstetricians. The average birth weight of boys is higher than girls. Furthermore, this difference between the sexes is widening as gestational age at delivery is increasing. For single pregnancies, birth weight percentiles follow an exponential curve over gestational age, while for twins, the curve is linear.

5.1.3 Birth weight trends and their explanatory factors

An analysis of almost all full-term births in Hungary in 1998-2018, clearly showed an increasing birth weight trend of 4.1 g/year until 2008, followed by a less steep decline of 2.5 g/year in 2008-2018. During the same period, important changes in maternal and delivery related characteristics were observed: gestational age at delivery decreased, maternal age increased, the proportion of first parities decreased, and the frequency of both caesarean sections and induced deliveries increased.

According to our multivariate models, most of the increase in birth weight in the first period was explained by the increasing maternal age, while a substantial part of the decrease in the second period was explained by decreasing duration of pregnancies (i.e., decreasing gestational age at delivery).

When we investigated interactions between pregnancy related factors and calendar time (i.e., subgroups with the least and most changes over time), we found that the most pronounced difference between the first and second period was in mothers over 35 years of age, who had the fastest increase in the first period followed by a similar to the younger age groups and the mean yearly change. Furthermore, the increase of birth weights in the first period was faster in newborns delivered by caesarean sections compared to vaginal deliveries, however no such interaction in the second period was found. Similarly, the increase in birth weights in the first period was more pronounced in multiparas compared to primiparas, while no interaction by parity in the second period was found.

5.2 Interpretation

5.2.1 Risk factors and consequences of term breech presentation

The 3.3% prevalence of breech presentation in term pregnancies observed in the present study is similar to those reported by other authors (23,84). Our findings also confirmed that mothers with breech presentation tend to be older than those with cephalic presentation (22,25,85,86).

We found a higher incidence of breech presentation if maternal obstetrical history was positive for prior stillbirths, postnatal deaths, and induced or spontaneous abortions. A similar higher (albeit non-significantly) risk of breech presentation after prior spontaneous abortions (6.0% vs. 4.5%, P = 0.07) has also been reported in Iranian data (87).

In the present study, the odds of breech presentation were found to be more than 50% higher if hormone treatment and 80% higher if assisted reproduction was utilised to facilitate conception. These findings correspond closely with a 50% increased risk in pregnancies conceived via assisted reproduction found in a Norwegian study (88).

Maternal pregestational and gestational diabetes, hypertension, severe oligohydramnion, and placenta praevia were all positively related in univariate analyses to breech presentation in our data. Rayl et al. reported higher frequencies of pregnancies with breech presentation in pregestational (0.7% vs. 0.3%, OR 2.8) but not in gestational diabetes (2.1% vs. 2.0%, OR 1.0) (22). Impaired glucose tolerance during pregnancy was associated with an over three-fold increased risk of breech presentation in a Chinese study (89). The association between breech presentation and oligohydramnion (26,90) and placenta praevia has also been reported previously (26).

Our finding of an increased risk of breech presentation in pregnancies with a female fetus confirms several prior observations (25,84,91–93). We found a slightly lower birth weight with breech presentation that also confirms previous observations (22,25,26,84,94).

Other factors that independently increased the risk of breech presentation in our data were primiparity, SGA, and developmental abnormality of the fetus. Fruscalzo et al. have also reported some of the factors observed by us: older maternal age, primiparity, premature birth, and female sex as independent factors predisposing to pregnancies with breech presentation (25). Other work has shown that premature babies (SGA) have an increased risk of breech presentation (95). Furthermore, the 2 to 5 fold increased risk of breech presentation associated with developmental abnormalities reported previously (22,25,26,92) corresponds closely to our OR of 1.65 (22,25,26,92).

Our results extend previous literature on risk factors of breech presentation and confirm that these risk factors are independently related to the development of breech presentation.

In the second part of our analysis, we focused on the consequences of breech presentation and attempted to establish whether breech presentation would increase the risk of these pathologies in the absence of confounding risk factors that are related to both breech presentation and to pathological pregnancies. As our preliminary analysis suggested a non-linear relationship between gestational age at delivery and breech presentation, with relative risks ranging from 1 to 9, we decided to exclude all premature births (<37 weeks of gestation). The association between prematurity and breech presentation is already well described in the literature (96).

The fact that deliveries with breech presentation have a younger gestational age at delivery may explain the finding that the odds of premature membrane rupture was higher in breech presentation in the unadjusted, but lower in the fully adjusted models. In prior work on 5,377 pregnancies and deliveries in Israel, a higher frequency of premature membrane rupture was observed in non-cephalic presentations (25.4% vs. 16.6%) (26). As in our findings the percentage of Caesarean section is higher in breech presentation (26), similarly intrapartum interventions (sterilisation, hysterectomy, manual control of the uterine cavity) (95).

Five-minute Apgar values were lower, and the rate of intrauterine death and perinatal mortality higher in fetuses from pregnancies with breech presentation compared with cephalic presentation. In addition, breech presentation fetuses required treatment in a PIC more frequently. A higher incidence of intrauterine death (OR 2.7 vs. our own OR 1.58) and perinatal mortality (OR 1.6 vs. our own OR 1.67) in pregnancies with breech presentation have also been observed in Swedish data (97).

Our finding of lower Apgar values in breech term babies replicates those from a previous study in Serbian data. The same study also found a several fold increased risk of perinatal mortality (OR 7.0) (96). The difference in odds ratios between studies may partly be related to adjustments for gestational age at delivery or the inclusion or exclusion of preterm deliveries from the analysis.

Our logistic models clearly showed that both delivery and fetal outcomes were negatively related to breech presentation independently from other pathological circumstances (including medical history and circumstances of the present pregnancy, such as congenital anomaly). These results again confirm the work of other authors (26,94,98,99).

Several factors are clearly involved in the development of breech presentation. We confirmed that, despite an increased rate of Caesarean sections in breech presentation, perinatal outcomes are poorer for these fetuses, and they are characterised by a higher perinatal morbidity and mortality in comparison to foetuses from a cephalic presentation. Our results suggest a bidirectional association between breech presentation and pathologies related to pregnancies: several factors complicating pregnancy (i.e. diabetes, hypertension, placenta praevia) increase the risk of breech presentation, and at the same time breech presentation in itself increases the risk of Caesarean section, prematurity, intrauterine death, and perinatal mortality.

5.2.2 Updating the Hungarian birth weight percentiles

5.2.2.1 Previous percentile charts for single pregnancies in Hungary

Joubert repeatedly reported birth weight percentile charts for the periods 1973-1978,(38) 1990-1996,(42) and 2000-2012(41).

The median (50th percentile) body weight of premature babies for both boys and girls (boy/girl at 24 weeks: 866/831g, 700/655g in 1990-1996, 673/638g in 2000-2012; and our own data 650/610g in 2011-2015; at 28 weeks: 1357/1321g in 1973-1978, 1155/1100g in 1990-1996, 1175/1116g in 2000-2012; and our own data 1195/1105g in 2011-2015) was substantially higher in 1973-1978 compared to the later periods. Birth weights at 24 weeks of gestation show a decreasing trend over the entire examination period, probably reflecting more accurate estimation of gestational age and better completeness of data and not decreasing birth weights over time. At 28 weeks of gestation, the only outlier (that significantly differs from the last period) is the first period (between 1973 and 1978), suggesting that data collection was less reliable in the first period. Not surprisingly, our birth weight data best corresponds to those collected between 2000 and 2012.

Birth weights of late premature babies are much more similar between the different observation periods (at 32 weeks of gestation [boy/girl]: 1954/1949g in 1973-1978, 1850/1800g in 1990-1996, 1904/1822g in 2000-2012, and our results 1870/1775g in 2011-2015; at 36 weeks of gestation: 2746/2657g, 2720/2620g, 2798/2868g, and our results 2750/2650g), as well as birth weights of mature newborns (at 40 weeks: 3373/3230g, 3500/3340g, 3555/3400g, and our results 3550/3400g, respectively). Median birth weights are higher at 32 weeks of gestation in the first period (1973-1978) than in the later periods, however birthweights are much more similar in the different examination periods after 36 weeks of gestation. Not surprisingly, our birth weight data best corresponds to those collected between 2000 and 2012. The shape of the birth weight percentile curves over gestational age are linear in 1973-1978, and exponential in 1990-1996, and in 2000-2012, similarly to our own percentile curves.

5.2.2.2 *Birth weights of single births in international comparison*

The observed birth weights in the multicentre, multinational INTERGROWTH-21st Project (n=20,486, data collection between 2009-2014) were lower (33 weeks: boy/girl 1950/1860g vs. 2100/ 1980g, 36th week: 2690/2600g vs. 2750/2650g, 40th week 3380/3260g vs. 3550/3400g) compared to our findings for each week of gestation suggesting that the INTERGROWTH charts are not directly adaptable to Hungarian newborns (100).

On the other hand, based on the data of >27,000 Polish newborns from the same period (2011-2016), similar median birthweights to ours for late preterm and mature newborns were published (33 weeks of gestation [boys/girls]: 2095/2001g vs our data 2100/1980g, 36 weeks of gestation: 2885 /2732g vs 2750/2650g, 40 weeks of gestation: 3676/3527g vs. 3550g/3400g) (101). In a larger study in Turkey between 2007-2013 (n=68,255 newborns), the trends in the birth weights of both premature and full-term newborns are similar to those measured by us, although the differences from our results are more pronounced compared to the Polish data (24 weeks of gestation [boys/girls]: 700/725g vs 650/610g, 28 weeks of gestation: 1110/1180g vs 1190/1105g, 32 weeks of gestation: 1980/1840 vs 1870/1775g, 36 weeks of gestation: 2850/2780 vs 2750/2650g: 40 weeks of gestation: 3370/3490g vs 3550/3400g) (102). From the European region, data are also available from Spain (; n=23,578 data collection: 2008-2011). Surprisingly, the birth weights of these Spanish newborns are nominally lower compared to our own data for each gestational week (28 weeks of gestation: boy/girl 1044/1012g vs 1190/1105g, 32 weeks of gestation: 1724/1697g vs 1870/1775g, 36 weeks of gestation: 2613/ 2534g vs 2750/2650g, 40 weeks of gestation: 3379/3243g vs 3550/3400g) (103). The shape of the birth weight percentile curves over gestational age in the studied European populations (similar to our results) is exponential rather than linear.

According to findings in United States conducted survey (n=3,252,011) in a slightly earlier period (between 1991-2011) are very similar to our own results (24 weeks of gestation: 706/652g vs. 650/610g, 28 weeks of gestation: 1177/1102g vs. 1190/1105g, 32 weeks of gestation: 1871/1784g vs 1870/1775g, 36 weeks of gestation: 2846/2734g vs 2750/2650 g, 40 weeks of gestation: 3572/3431g vs 3550/3400g) (104). The results of a Cuban survey including >16,000 newborns (data collection between 2008-2012) show similar percentiles charts to ours (32 weeks of gestation: 1945/1620g, 36 weeks of gestation: 2640/2560g, 40 weeks of gestation: 3450/3300g) (105).

Although the above surveys conducted in other high and middle income countries with mostly Caucasian populations show similar percentile charts to our Hungarian ones, their external validity in the Hungarian population is questionable given potentially different characteristics of the pregnant population (e.g., on BMI, age, socioeconomic status).

There are some birth weight centile data published for Asian populations. For example, median birth weights (except for term newborns) are higher in the Korean population (a high income country; data collection between 2010-2012, n=1,381,088) than the birth weights of Hungarian newborns (24 weeks of gestation: 720/669g vs 650/610g, 28 weeks of gestation: 1232/1147g vs 1190/1105g, 32 weeks of gestation: 1963/1861g vs 1870/1775g, 36 weeks of gestation: 2805/2698g vs 2750/2650g, 40 weeks of gestation: 3408/3292g vs 3550/3400g) (106). In contrast, in the southern part of India (a low-to-middle income country; data collection between 1996-2010, n=41,055), birth weights are lower than the birth weights we found (32 weeks of gestation [first-repeat pregnancy]: 1630g-1795/1426-1731g vs 1870/1175g, 36 weeks of gestation: 2472–2600/1393-2511g vs 2750/2650g, 40 weeks of gestation: 3065–3187/3058 2977g vs 3550/3400g) (107). It should be noted that the shape of the percentile curves over gestational age similar to ours is exponential.

5.2.2.3 Birth weight data of twin pregnancies in international comparison

Significantly less published data is available on birth weight centiles of twins. The previously presented Korean study (data collection between 2010-2012, n=42,314) also reports birth weight data of multiple pregnancies (106). Birth weights of twins are higher for both boys and girls compared to our results except for gestational weeks 36 to 39 (24 weeks of gestation: 713/664g vs 666/350g, 28 weeks of gestation: 1198/1124g v. 1140/1060g, 32 weeks of gestation: 1198/1124g vs 1140/1060g, 36 weeks of gestation: 1833/1739g vs 1830/1705g, 36 weeks of gestation: 2479/2382g vs 2480/2400g, 40 weeks of gestation: 2946/2880g vs 2928/2775g). The shape of the percentile curves similarly to ours is linear for twin newborns. In contrast, data from another high income country (Taiwan, data collection between 1998 and 2002) shows lower birth weights of twins compared to our results (108).

A report comparing birth weights of monochorionic and dichorionic twins from India (data collection between 1991-2005), found different shapes of the percentile lines: monochorionic twins showed exponential, while dichorionic twins linear curves (109). While we were unable to compare mono- and dichorionic twins, our overall charts showed linearly increasing birth weights over gestational age. Furthermore, the birth weights of twins were lower than that of singletons, that is similar to our results.

Birth weight of Chinese twins (data collection between 2006 and 2015, n=22,507) are similar to the Hungarian data, although the Hungarian twins are slightly heavier at term (28 weeks of gestation: 1200/1130g vs. 1140/1060g, 32 weeks of gestation: 1800/1700g vs. 1830/1705g, 36 weeks of gestation: 2500/2400g vs 2480/2400g, 40 weeks of gestation: 2770/2660g vs 2928/2775g) (110). It is noteworthy that the shape of the percentile curves of Chinese twin newborns are exponential rather than linear.

5.2.2.4 Temporal trends of mean birth weights between 1996 and 2015

In addition to the period between 2011 and 2015, we compared mean birth weights of 3 5-year periods (from 1996 to 2010) to the reference period of 2011-2015. We found significant heterogeneity of birthweights in these 4 periods for boys between 37 and 39 weeks of gestation and for girls between 36 and 38 weeks of gestation. In general, we found that birth weights of term deliveries increased until 2006-2010 followed by a decrease in 2011-2015. We could not confirm a similar tendency in twins (probably partly due to the lack of statistical power).

Similar to our results, decreasing birth weights of term deliveries were reported in the US in recent years. This may be due to a higher frequency of inductions and terminations due to a higher frequency of pathological pregnancies (probably related to better diagnostics) (111). Other studies found relatively stable birth weights in Australia between 1997 and 2007 (11), in Vietnam between 2007 and 2012 (112), and in South Korea (106). It is worth noting that while our results were similar to those observed in other high income countries with predominantly Caucasian populations, the observed temporal trends showed wide heterogeneity worldwide.

Data on twin births are equivocal: birth weights decreased in Australia (113) and in China (114) in recent years, while birth weight increased for term newborns in South Korea (106). Our data well corresponds to the latter trends: birth weights of mature twins increased overall in the last 20 years.

5.2.3 Birth weight trends and their explanatory factors

5.2.3.1 Birth weight trends in international comparison

The increasing birth weight trend observed in the first period (1999-2008) parallels with similar observations from other high income countries (50–58,61) including those from Croatia (59), Poland (115) and a regional database analysis from Hungary (77).

During the second period we found declining birth weight trends. This is in line with observations from the U.S., where the average birth weight of term pregnancies declined from 3,315g in 1990 to 3,247g in 2013, a decrease of 67g (66). The validity of this observation was confirmed by other reports from Japan (62,63), the U.S. (64–69), Norway (73,74), Portugal (72), China (70,71), Chile (116), and Germany (75). Overall, a similar decrease to the one observed in Hungary was also found in most developed countries, however the decrease started mostly a decade earlier than in Hungary. In contrast, birth weights did not change significantly in low and middle-income countries from Africa, Asia and Central America between 2013 and 2018 (117).

5.2.3.2 Decreasing gestational age at delivery

Gestational age at delivery declined by two days between 1999 and 2018. This trend is similar to other surveys, however the magnitude of the decline varies between less than 1 to almost 3 days between 1990 and 2013 in the different studies (64,66,67,75,117–119). Furthermore, there is evidence at least from the US that the decreasing gestational age at delivery is driven by labour inductions and early term caesarean deliveries (117).

5.2.3.3 Increasing maternal age over time

We found that median maternal age at delivery increased from 26.2 years in 1999 to 30.5 years in 2018, corresponding to an increase in the proportion of older mothers (≥30 years) from 24% to 53%. An increasing trend in maternal age is reported from most countries worldwide (58,120). For example, the mean age of primiparas increased from 24.9 years to 26.3 years in the U.S. between 2000 and 2014 (121).

5.2.3.4 Decreasing parity over time

During the 20-year observation period, the proportion of primiparas increased from 46.4% to 49.6%. Our results are somewhat different from those in other developed countries. For example, the proportion of primiparity remained constant (43.3%) in France between 1998-2003 (57), while it decreased (37.3% to 33.7%) in the US between 2000 and 2008 (65).

5.2.3.5 Increasing rates of caesarean sections and induced deliveries

The rate of caesarean sections and labour inductions more than doubled (from 17.6% to 39.7% and from 12.7% to 26.2%, respectively) in Hungary between 1999 and 2018. This is in line with observations from almost all countries. The rate of scheduled or induced deliveries almost tripled reaching over 30% in the US between 1990 and 2013 (65,66,117). Similar, but smaller increase (25.9% to 33.6%) was observed in Scotland in 1988-2012 (122). The rate of caesarean sections increased in the US (117) and similarly in India (from 28.2% to 42.0% in 2010-2017) (123) and Brazil (from 34.1% to 57% in 1997-2014) (124,125), while the increase was minimal in Norway (13.6% to 16.3% in 1999-2016) (126).

5.2.3.6 Potential explanation for the increasing birth weight trends in the first period

According to our hierarchical logistic regression models, maternal age explained a large proportion (5.4 g/year vs. 2.4 g/year – 55.5%) of the increasing birth weight trend over time. This is in agreement with findings from other studies from high-income countries (52,53,56–58,63,77).

While maternal age may be directly related to birth weight, it could be a marker of other determinants, such as anthropometric, lifestyle or social factors that are also reported to be related to the increasing birth weight trends (53,55–59,63,116). For example, maternal smoking might decrease with maternal age (53,56). Similarly, maternal weight increases with aging and maternal BMI is a known predictor of newborn weight (127). Indeed, there is an increasing trend in obesity among fertile aged women in Hungary in the last decades (128). Furthermore, older age is associated with better socioeconomic circumstances that is associated with larger birth weights (129). As advanced maternal age is also associated with higher risk of adverse obstetrical and perinatal outcomes (130), as well as elective deliveries (65) the changes observed during the first period could be associated with worsening pregnancy outcomes.

5.2.3.7 Potential explanation for the decreasing birth weight trends in the second period

We found that a large proportion of the decreasing birth weight trend was explained by gestational age at delivery (i.e. length of pregnancy) similarly to other authors (62–64,67,68,72). The decreasing length of gestation over time is strongly related to the fact that the proportion of induced deliveries and caesarean sections more than doubled over the examination period. Other authors that found similar decreasing birth weight trends explained this observation by the increasing rates of early term caesarean deliveries and induced labours (50,64,66–68). This is supported by the fact that births became much less likely to occur beyond gestational week 40 and much more likely to occur during weeks 37-39 (51). In addition to shorter pregnancies, some authors proposed that decreased fetal growth per se explain part of the decreasing birth weight trend (65,68).

It is plausible that the worsening short term pregnancy outcomes associated with advanced maternal age is compensated by early term pregnancies (67).

However, the question remains how the approach to early term deliveries will modify long-term consequences. It is known that caesarean sections are associated with an increased risk of severe acute maternal morbidity and mortality, and a higher risk of adverse outcomes in subsequent pregnancies (131). In terms of newborn outcomes, caesarean sections are associated with increased risks of fetal respiratory problems (132) and long-term consequences (i.e. asthma, overweight, obesity, allergy) (131).

5.2.3.8 Subgroups driving increasing and decreasing birth weight trends

We found the fastest increase in birth weight among the oldest mothers (≥35 years of age), among those with multiparity, and among newborns delivered by a caesarean section in the first part of the observation period. These findings may suggest that the approach to deliveries was reactive by obstetricians: wait in the high-risk groups (older mothers, multiparas) for delivery induction or caesarean delivery until the fetus becomes large. This notion is supported by the Spanish observation that term newborns from caesarean deliveries were larger than from vaginal deliveries and newborns of multiparas were larges than those of primiparas (133).

We found the fastest decline in birth weight among the youngest mothers (<25 years of age) in the second part of the observation period. Furthermore, newborns of multiparas and those of caesarean deliveries were no longer associated with faster increases in birth weights. These findings are compatible with the hypothesis of a proactive management of delivery, where pregnancy is terminated in high-risk women before fetal weight reaches abnormal levels.

5.3 Strengths and limitations

5.3.1 General strengths and limitations of the Tauffer database

Our analysis builds on a large population sample that represents most Hungarian pregnancies with an ascertainment rate of over 90%. The huge number of records allowed us to adjust for several risk factors and to provide robust risk estimates. The data entry software comes with detailed instructions that assure high quality of the collected outcome variables. Therefore, our results can be considered representative at the population level. Although births missing from the system can potentially lead to a distortion of the results, there is no data available on them, so the imputation of the missing data is not possible.

Although it is mandatory to fill in the data after giving birth, this unfortunately does not happen in all cases. The accuracy and completeness of the data is not monitored by regular quality assurance. If, in addition to the random error, bias occurs during the measurement of for example birth weight at obstetrical departments, this may result in a systematic error in the data that we published. In addition, certain maternal parameters (e.g. pre-pregnancy weight, height, weight gain, smoking habits, race ethnicity, social circumstances) that are important covariates in our analyses are missing from database.

5.3.2 Risk factors and consequences of term breech presentation

With over a million pregnancies and 40,000 pregnancies with breech presentations, our study is one of the largest on the risk factors and consequences of breech presentation to date. Another strength relates to the detailed information on previous pregnancies of the mother, providing several covariates for our investigation.

As with other administrative databases, several limitations have to be acknowledged: maternal post-partum complications are not collected systematically, excluding the possibility of including them in the analysis. Similarly, data on fetal treatments are limited to the first 2-3 days of life as most of the data are entered at time of parturition and updated at hospital discharge. Although the possibility of some misclassification of outcomes and covariates cannot be excluded, it should be noted that the Tauffer database is not used for reimbursement purposes and thus selective, intentional over- or under-diagnosis is unlikely to bias our estimates.

5.3.3 Updating the Hungarian birth weight percentiles

The clinical benefit of our results is obvious: obstetricians can classify newborns from singleton and twin pregnancies according to gestational age and sex as average (25-75th percentile), below and above average (10-25th and 75-90th), and SGA and LGA (<10 and >90 percentile) groups, that is an important determinant of the care required by the newborn as well as their long term outcomes.

Although birth weight data is prone to measurement error, it should be noted that weight is the least sensitive to distortion among the anthropometric data, and obstetric departments also have a fundamental interest in and legal obligation to ensuring optimal quality of anthropometric measurements. However, given the lack of more precise anthropometric data with standardized measurements and external quality assurance on a representative national sample, we believe that the percentile data based on the present analysis is the best estimate of the distribution of birth weights by gestational age and sex in Hungary.

There is no data in the database on the method of gestational age determination. However, the basis of gestational age is crown-rump length (CRL) measured the first trimester (between 10 and 14 weeks of gestation), as it is stated by Hungarian and international recommendations and professional guidelines (82,83,134). Although the Tauffer database does not indicate the method of the determination of gestational age, we assumed that most gynaecologists would follow the above professional guidelines and hypothesized that gestational age was determined accurately. Furthermore, the exact determination of the gestational age is a legal obligation, as it is recorded in official registries (Obstetrics and Neonatology Records, Central Statistical Office) and it also affects the further care and treatment of the newborn.

While it is possible to increase the number of cases by extending the reference period, and thus to reach smoother percentile curves, this analysis would be biased by the temporal trends we also described. In the present study, we tried to find the optimal way to handle these competing aspects. Given the low number of births during 22-23 and 42-43 weeks of gestation, we had to combine these periods to draw stable estimates. The percentile curves were not smoothed by statistical methods because in our opinion the raw data better reflects reality. The percentile curves from twin pregnancies are even less uniform compared to singleton pregnancies, but they are still clinically relewvant and accurate.

5.3.4 Birth weight trends and their explanatory factors

The huge number of records allowed adjustment for several risk factors and to provide narrow CIs. The data entry software comes with detailed instructions that assures high quality of the collected variables (79).

Our analyses are limited in several ways. First, there is no way to measure changes in the obstetric decision-making process in official administrative data. The role of unmeasured confounding cannot be downplayed. It is possible that the increases and decreases in birth weights were responding to unobserved factors. Individual measures of maternal behaviours, characteristics, and other risk factors for obstetric interventions were also quite limited. Potentially key details about maternal health risk factors related to obstetric decisions (such as obesity) may also be missing. This limitation is especially relevant for our secondary objective (drivers of increasing and decreasing birth weight trends over time), and thus our results on this objective should be considered as hypothesis generating only.

6 Conclusions

6.1 Risk factors and consequences of term breech presentation

Our results clearly show that breech presentation is not only a consequence of pathological pregnancies but also leads to pathological processes, thus increasing the risk of gestational complications even in term pregnancies. We propose that closer management of pregnancies with breech presentation is justifiable even in the absence of other pregnancy related pathologies.

6.2 Updating the Hungarian birth weight percentiles

The knowledge of the percentile values of birth weight for each gestational week and both sexes is very important not only for obstetricians, but also for neonatological, pediatric specialist and even for physicians caring for adults. Small for gestational age newborns and fetuses have a high likelihood of intrauterine growth retardation that also a risk factor for perinatal morbidity and mortality (135). These morbidities include hypoglycemia, respiratory distress, hypothermia, necrotizing enterocolitis, and retinopathy (136). In children and young adults, endocrinological disturbances (early adrenarche and polycystic ovary syndrome) and growth retardation could be a problem (137–140). In adulthood, an increased risk of hypertension, obesity, dyslipidemia, type 2 diabetes, and cardiovascular diseases were found (135,141). In contrast, large for gestational age newborns (LGA) that present with excessive fetal growth have an increased risk of fetal morbidity, complications during delivery (shoulder impingement, prolonged delivery, caesarean section), as well as late cardiometabolic diseases in childhood (142).

6.3 Birth weight trends and their explanatory factors

Given the strong association between large birth weight and an adverse metabolic profile in children and young adults (47,48), our findings of an increasing birth weight trend between 1999 and 2008 may forecast an increased risk of cardiometabolic diseases in offsprings born in this period. Our results also suggest that the changes in birth weights in this period are mostly related to the aging of the mothers.

In contrast, after 2008, birth weights were decreasing. While these changes may reflect some beneficial effects in term of reduced perinatal morbidity (49), the long term effect of this decreasing birth weight trajectory cannot be predicted, as the trend is explained by the shorter pregnancies (lower gestational age at delivery) and not changes in other drivers of macrosomia (such as maternal age or BMI). Furthermore, the increasing trend in the age of the mothers is continuing unabated.

6.4 Novel findings

1. The risk of term breech presentation increased in older, nulliparous women, in those with an abnormality in their obstetrical medical history (stillbirth, spontaneous abortions, non-spontaneous conception), and in women with hypertensive disorder or oligohydramnion during pregnancy.
2. Fetal characteristics (including female sex, younger gestational age at delivery, SGA, lower fetal weight or a developmental abnormality) also increased the risk of breech presentation.
3. The breech presentation in term pregnancies significantly increased the risk of pathological deliveries (Caesarean section and other interventions at parturition) by 12 times.
4. The adverse fetal outcomes (low Apgar value, need for PIC treatment, intrauterine or perinatal death) also significantly increased the risk in breech presentation by 18%.
5. Breech presentation is a marker of a pathological pregnancy and not just a normal variant.
6. The knowledge of the novel percentile values of birth weight in single or twin pregnancies both sexes for each gestational week is very important for obstetricians, neonatologists and other clinicians.
7. The birthweight in term deliveries by single pregnancies are increased from 2006 and after 2010 decreased. This trend was not proved in term deliveries by twin pregnancies.

8. During accurately examination the birthweight trend by single pregnancies in term deliveries increased continuously from 2008 to 2008. In 2008 was the plateau and from 2008 to 2018 decreased the birthweight.
9. The increased birth weight trend (between 1999-2008) was explained the increasing aging of the mothers.
10. After 2008 although the maternal age is increased further but the cause of decreased birth weight is the declined gestational age. The increased caesarean section rate and decreased gestational age verify that the decreasing birth weight trends explained this observation by the increasing rates of early term caesarean deliveries and induced labours the clinicians.
11. We found the fastest increase in birth weight among the oldest mothers (≥35 years of age), among those with multiparity, and among newborns delivered by a caesarean section in the first part of the observation period. These findings may suggest that the approach to deliveries was reactive by obstetricians: wait in the high-risk groups (older mothers, multiparas) for delivery induction or caesarean delivery until the fetus becomes large.
12. We found the fastest decline in birth weight among the youngest mothers (<25 years of age) in the second part of the observation period. Furthermore, newborns of multiparas and those of caesarean deliveries were no longer associated with faster increases in birth weights. These findings are compatible with the hypothesis of a proactive management of delivery, where pregnancy is terminated in high-risk women before fetal weight reaches abnormal levels.

7 Summary

Introduction – Well phenotyped registries are rich data sources. The present thesis aims to (1) describe predictors and outcomes of breech presentation, (2) update birth weight percentile charts for Hungary, and (3) describe birthweight trends and their drivers with the use of the Tauffer Obstetric database. **Material and Methods –** For all 3 analyses, we used a data from the Tauffer Statistics (a compulsory data collection of obstetrical data) in 1996-2018. For aim (1), we analysed all term (≥37 weeks), singleton pregnancies with cephalic and breech presentation (n=41,796) using multivariable logistic regression to investigate predictors of, as well as delivery and fetal outcomes related to breech presentation. For aim (2) we developed birth weight centile charts for each gestational week by sex for singleton and twin pregnancies. For aim (3) we modelled birth weight trends in 1999-2008 and 2008-2018 using hierarchical linear regression models adjusted for calendar year and other determinants. **Results –** Breech presentation was independently associated with maternal age, medical history (e.g., stillbirth), maternal morbidities (e.g., hypertension), and fetal factors (e.g., sex, gestational age at delivery). An adverse delivery outcome was 11.7 (95%CI 11.3-12.0) and an adverse fetal outcome was 1.39 (95%CI 1.33-1.45) times more frequent in breech vs cephalic pregnancies. We present birth weight centiles for live births in both tabular and graphical form using data in 2011-2015. Median birth weights increased from 3250/3400g (girl/boy) to 3300/3440g from 1999 to 2008 and decreased to 3260/3400g in 2018. When we adjusted for gestational age the increase in the first period became more pronounced (5.4 g/year). During the second period, similar adjustment decreased the rate of decline (2.5 to 1.4g/year). Further adjustment for maternal age halved the rate of increase to 2.4g/year in the first period. **Conclusions –** Breech presentation is not only a marker of pathological pregnancies, but an independent risk factor of complications. Given the substantial change in birth weights during the past 20 years, renewal of the commonly used percentile tables is necessary. Our findings of an increasing birth weight trend (mostly related to the aging of mothers) in 1999-2008 may forecast increased risk of cardiometabolic diseases in offsprings born in this period. In

contrast, the decreasing trends after 2008 may reflect some beneficial effects on perinatal morbidity. However, its the long-term effects cannot be predicted, as the trend is mostly explained by the shorter pregnancies.

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9 Bibliography of the candidate's publications

9.1 Publications directly related to the PhD Thesis

9.1.1 Peer reviewed articles

1. **Zsirai László**, Csákány M. György, Vargha Péter, Szepesi János, Egyed Jenő, Török Miklós, Tamás Gyula: Medencevégű terhességek gyakorisága, jellemzőik és a farfekvésre hajlamosító lehetséges okok elemzése. Az Országos Szülészeti és Nőgyógyászati Intézet 1997-2006 közötti adatbázisának elemzése. *Magyar Nőorvosok Lapja,* 2011; 74 (5): 19-26.
2. **László Zsirai**, György M Csákány, Péter Vargha, Vilmos Fülöp, Ádám G Tabák: Breech presentation: its predictors and consequences. An analysis of the Hungarian Tauffer Obstetric Database (1996-2011). *Acta Obstet Gynecol Scand* 2016; 95(3): 347-354.
3. **László Zsirai**, M György Csákány, György Végh, Gy Ádám Tabák: A születési súlyok megoszlása 2011 és 2015 között és a percentilisértékek változása 1996 és 2015 között. *A Tauffer-adatbázis feldolgozása* (Distribution of birth weights between 2011 and 2015 and changes in percentile figures between 1996 and 2015. *Analyis of the Tauffer database). Orvosi Hetilap* 2019; 160(36): 1426-1436.
4. **László Zsirai**, Attila Kun, Gergely Á Visolyi, Márk M Svébis, Beatrix A Domján, Ádám G Tabák: Birth weight trends and their explanatory factors in Hungary between 1999 and 2018: an analysis of the Hungarian Tauffer registry. *Reprod Health* 2024;21(1):52.

9.2 Publications not directly related to the PhD thesis:

9.2.1 Peer reviewed articles

1. Murányi Zoltán, Illyés Miklós, Vajda Miklós, **Zsirai László**, Végh György, Drávucz Sándor: 24 órás ambuláns vérnyomás monitorozással szerzett tapasztalataink patológiás terhességekben. *Magyar Nőorvosok Lapja* 2000; 63 (6), 439-443.
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5. Madarász Eszter, Tabák Gy. Ádám, **Zsirai László**, Wudi Krisztina, Kerényi Zsuzsanna, Tamás Gyula: Napjában többször alkalmazott inzulin és inzulinpumpa-kezelés 1-es típusú diabeteses terhességben: változik-e az inzulinigény (Multiple daily injection and pump insulin therapy in type 1 diabetes complicated by pregnancy: changing insulin doses)? *Magyar Belorvosi Archivum* 2011;64:344-348.
6. **Zsirai László**, Csákány M. György, Vargha Péter, Szepesi János, Egyed Jenő, Török Miklós, Tamás Gyula: A terhességek befejezésének trendje tíz év alatt, medencevégű fekvés esetén. Vajon jobb-e a császármetszés? Merre tovább a szülés módját illetően? *Magyar Nőorvosok Lapja*, 2013; 76 (4): 11-19.
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9.2.2 Published conference abstracts

1. Madarász E., Kerényi Zs., **Zsirai L.**, Wudi K., Tabák Gy.Á., Tamás Gy.: Inzulinpumpa alkalmazás és hagyományos inzulinkezelés összehasonlítása 1-es típusú diabéteszes terhességben (Comparison of continuous subcutaneous infusion and human regular insulin treatment during pregnancy complicated by type 1 diabetes). Diabetologia Hungarica 16 (Suppl. 1):76, 2008
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3. Szabó E., **Zsirai L.**, Csákány M. Gy., Svébis M., Tabák Gy.Á.: 1-es típusú cukorbeteg (T1DM) és a kontroll magyar lakosság újszülötteinek születési súlya 1996-2011 között a Tauffer adatbázis alapján (Birth weight of type 1 diabetic (T1DM) and control women in the Tauffer Obstetric Database between 1996 and 2011). Diabetologia Hungarica 25 (Suppl 2.):86-87, 2017
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