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ORIGINAL RESEARCH ARTICLE

Birthweight of the subsequent singleton pregnancy following a first twin or singleton pregnancy

Prativa Basnet[1] | Rolv Skjærven[1,2] | Quaker E. Harmon[3] | Allen J. Wilcox[3] | Kari Klungsøyr[1,4] | Linn Marie Sørbye[5,6] | Nils-Halvdan Morken[7,8] | Liv G. Kvalvik[1]

[1]Department of Global Public Health and Primary Care, Faculty of Medicine, University of Bergen, Bergen, Norway

[2]Center for Fertility and Health, Norwegian Institute of Public Health, Oslo, Norway

[3]Epidemiology Branch, National Institute of Environmental Health Sciences, Durham, North Carolina, USA

[4]Division for Mental and Physical Health, Norwegian Institute of Public Health, Bergen, Norway

[5]Norwegian Research Center for Women's Health, Oslo University Hospital, Oslo, Norway

[6]Western Norway University of Applied Sciences, Faculty of Health and Social Sciences, Bergen, Norway

[7]Department of Clinical Science, University of Bergen, Bergen, Norway

[8]Department of Obstetrics and Gynecology, Haukeland University Hospital, Bergen, Norway

Correspondence

Prativa Basnet, Department of Global Public Health and Primary Care, Faculty of Medicine, University of Bergen, Alrek Helseklynge 17, Bergen 5020, Norway.
Email: prativa.basnet@uib.no

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Abstract

Introduction: Birthweight is an important pregnancy indicator strongly associated with infant, child, and later adult life health. Previous studies have found that second-born babies are, on average, heavier than first-born babies, indicating an independent effect of parity on birthweight. Existing data are mostly based on singleton pregnancies and do not consider higher order pregnancies. We aimed to compare birthweight in singleton pregnancies following a first twin pregnancy relative to a first singleton pregnancy.

Material and Methods: This was a prospective registry-based cohort study using maternally linked offspring with first and subsequent pregnancies registered in the Medical Birth Registry of Norway between 1967 and 2020. We studied offspring birthweights of 778 975 women, of which 4849 had twins and 774 126 had singletons in their first pregnancy. Associations between twin or singleton status of the first pregnancy and birthweight (grams) in subsequent singleton pregnancies were evaluated by linear regression adjusted for maternal age at first delivery, year of first pregnancy, maternal education, and country of birth. We used plots to visualize the distribution of birthweight in the first and subsequent pregnancies.

Results: Mean combined birthweight of first-born twins was more than 1000 g larger than mean birthweight of first-born singletons. When comparing mean birthweight of a subsequent singleton baby following first-born twins with those following first-born singletons, the adjusted difference was just 21 g (95% confidence interval 5–37 g).

Conclusions: Birthweights of the subsequent singleton baby were similar for women with a first twin or a first singleton pregnancy. Although first twin pregnancies contribute a greater combined total offspring birthweight including more extensive uterine expansion, this does not explain the general parity effect seen in birthweight. The physiological reasons for increased birthweight with parity remain to be established.

KEYWORDS

birthweight, parity effect, pregnancy, singleton pregnancy, twin pregnancy

Abbreviation: MBRN, Medical Birth Registry of Norway

1 | INTRODUCTION

Birthweight is an important pregnancy outcome strongly associated with infant, child, and later adult life health.[1,2] Previous research using both cross-sectional and longitudinal data indicates an independent effect of parity on birthweight, with subsequent singleton babies being 80–140 g larger than the first singleton.[3-6]

The reasons why birthweights of subsequent offspring are in general larger than the first are not fully understood. Possible mechanisms include functional and physiological adaptations during pregnancy, which likely impact the uterine function in subsequent pregnancy. For example, hemodynamic adaptations leading to increased uterine placental blood flow have been found in parous uteri, possibly allowing for more efficient oxygen and nutrient delivery to the fetus.[7,8] Structural changes in spiral arteries following a first pregnancy may improve vascular remodeling during the next pregnancy.[9] Also, pregnancy-related changes in the cardiovascular system, such as increased ventricular volume and cardiac output and decreased systemic vascular resistance, may be incompletely reversed postpartum, which may result in a more favorable uterine environment in a subsequent pregnancy.[10] Finally, uterine structural changes following the first pregnancy, including changes in connective tissue proteins, may provide a better uterine capacity in later pregnancies.[11,12] The current literature is, however, mostly based on successive singleton pregnancies and this association has not been studied for births following twins. Specifically, to our knowledge, no previous study has examined the patterns in birthweight of singletons following a twin pregnancy.

Women with twin pregnancies have larger placentas,[13] higher cardiac output,[14] evidence of systolic and diastolic dysfunction,[15] altered circulating angiogenic factors,[16] more pregnancy complications,[17,18] including shorter gestational age,[19] and greater fetal nutrition demand[20] than singleton pregnancies. In addition, twin pregnancies contribute a greater combined total offspring birthweight than singleton pregnancies. The resulting uterine capacity with twin pregnancy may be larger (combined birthweight, amniotic fluid, placental mass) and the uterine structural and functional changes may be greater than with singleton pregnancies. It remains unknown if these cardiovascular and uterine differences result in changes that impact birthweight in the subsequent pregnancy. Exploring birthweights of singletons following twin pregnancies may provide insight into the importance of factors resulting from pregnancy-related adaptation. In addition to physiological factors, other factors such as interpregnancy interval and pregnancy complications may differ based on the type of first pregnancy (twin or singleton). Women with singleton pregnancies with very short or long pregnancy interval are reported to be at increased risk of low birthweight[21] but, to our knowledge, no earlier studies have described the association among women with a first twin pregnancy.

We aimed to compare birthweight in singleton pregnancies following a first twin pregnancy relative to a first singleton pregnancy to get a better understanding of the general parity effect on birthweight. We also describe differences in interpregnancy interval and subsequent offspring's birthweight in women with first twin or singleton pregnancies. We hypothesized that the increased burden on a woman's physical capacity during a first twin pregnancy would be associated with a larger increase in a subsequent singleton's birthweights compared with a first singleton pregnancy. Our findings are relevant for clinicians who wonder whether a previous twin pregnancy could increase the risk of large subsequent singleton infant, suggesting a need for closer follow up towards term.

Key message

Although twin pregnancies contributed a greater combined offspring birthweight in the first pregnancy than a singleton pregnancy, birthweights of the subsequent singleton pregnancy were similar for offspring born after a twin pregnancy or after a singleton pregnancy.

2 | MATERIAL AND METHODS

2.1 | Study population

Data were obtained from the Medical Birth Registry of Norway (MBRN), a national population-based birth registry, established in 1967. Since then, the register has recorded all pregnancies lasting 16 or more gestational weeks (12th week since 2002) by mandatory notification. The unique national identification number provided to all residents in Norway allows women to be linked to all their pregnancies with women as the unit of observation. Our study population was restricted to women with a first pregnancy registered in the MBRN during 1967–2013 and followed for subsequent pregnancies until 2020. The main analyses consisted of a total of 4849 women who had a first twin pregnancy and a subsequent singleton pregnancy compared with 774 126 women with first and subsequent singleton pregnancies during the study period 1967–2020 (Figure 1). In our study, we excluded women who gave birth before gestational week 22 or after 44 weeks or had implausible *z*-score for birthweight by gestational age outside|5|. We further excluded triplet and quadruplet pregnancies because these pregnancies are both fewer in number than twin pregnancies and more complicated and might have different associations with birthweight and fetal growth in the subsequent pregnancy. Women who became pregnant through assisted reproductive technologies were more likely to have twins, and could have underlying conditions causing fertility problems that also affect birthweight. We therefore excluded the 0.4% of mothers who used assisted reproductive technologies in either their first or second pregnancies.

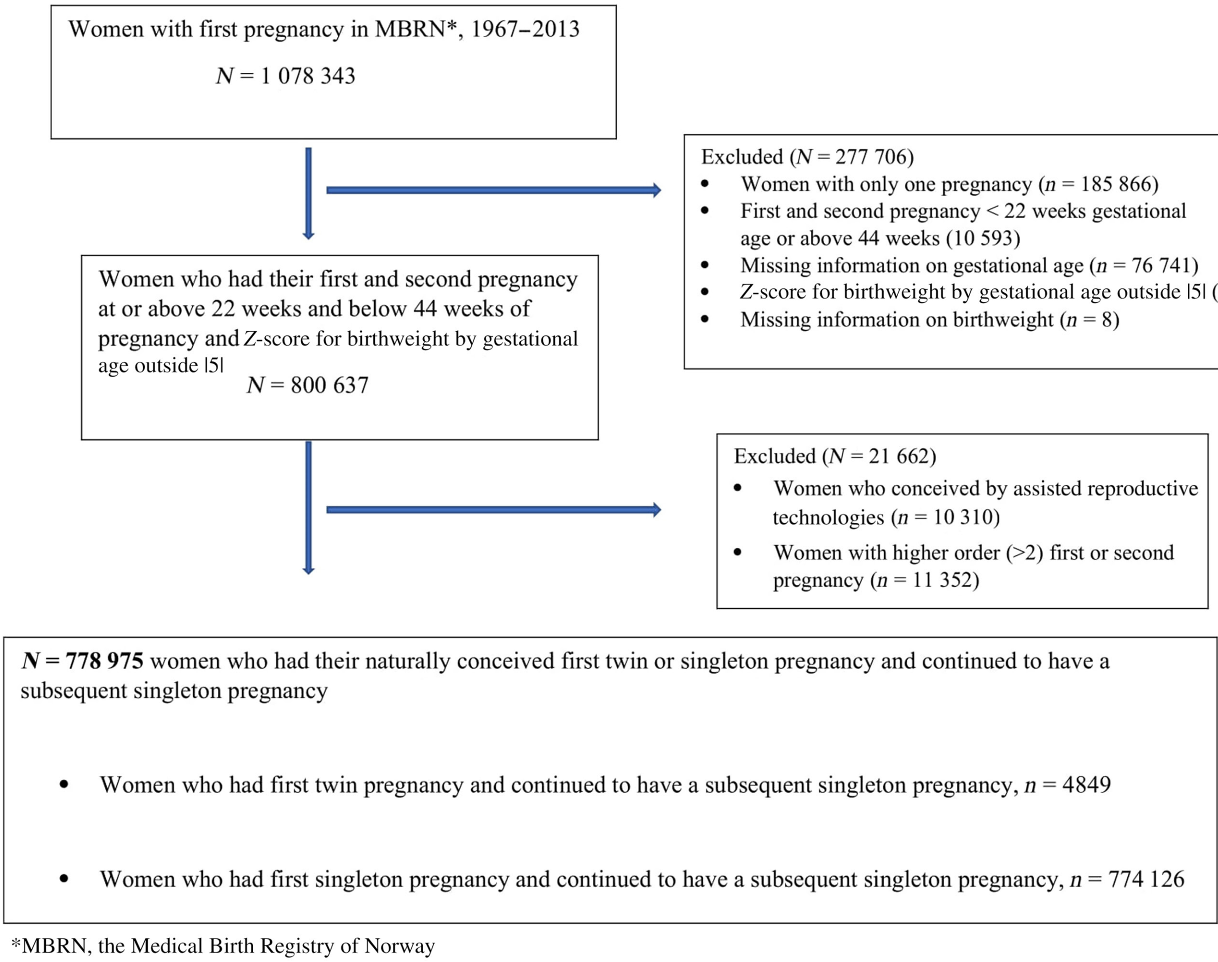

FIGURE 1 Flowchart of the study population.

2.2 | Exposure, outcome, and covariates

The exposure variable was twin or singleton status of the first pregnancy. Offspring birthweight was measured at delivery and recorded in grams (g) in the MBRN. Distribution of birthweights in first and subsequent singleton pregnancies was plotted using categories of absolute grams (ranging from 500 to 7000g). In first-born twins we used both sum of birthweights in twin pairs and individual infant weights to describe birthweight distributions. Gestational age estimates were based on reported last menstrual period. Ultrasound-based estimates have been recorded in the MBRN from 1999, and were used, when available, for women with missing information on last menstrual period or with a difference between ultrasound-based estimate and last menstrual period estimates of more than 10 days. *Z*-scores for birthweight by gestational age were derived based on national birthweight and gestational age distributions.[22] Our main outcome was birthweight in the subsequent singleton pregnancy.

We adjusted for possible confounding variables available in our data that could affect plurality in the first pregnancy and birthweight in the subsequent: secular trends year of first delivery (1967–1976, 1977–1986, 1987–1996, 1997–2006, and 2007–2020) and mother's age at first delivery (in years: ≤19, 20–25, 26–30, 31–35, and >35). Other potential confounders could be mother's body mass index (BMI), which we did not have data on. However, BMI is related to maternal education, we therefore also adjusted for highest level of maternal education (<11 years, 11–13 years, and ≥14 years). There are also studies describing different rates of twinning[23,24] and general differences in birthweight across countries,[25] so mother's country of birth was also included as a potential confounder (Nordic: women born in Norway, Finland, Sweden, Denmark, and Iceland; non-Nordic: women born outside the Nordic countries). Information on highest attained level of maternal education was obtained from the National Education Database at Statistics Norway, 2020.

The frequency of pregnancy complications in the first and second pregnancy as well as the interpregnancy interval were calculated by twin or singleton status of the first pregnancy. Interpregnancy interval was calculated as the date of the subsequent delivery minus the date of the first delivery minus the pregnancy length of the subsequent pregnancy. Pregnancy complications were obtained from the MBRN. The definition of preeclampsia in the MBRN has changed somewhat over time in accordance with the clinical criteria applied by the Norwegian

Society of Gynecology and Obstetrics.[26] The core criteria have been an increased blood pressure to at least 140mmHg systolic or 90mmHg diastolic combined with proteinuria (protein excretion of ≥0.3g/24h or ≥1+ on dip-stick) after 20weeks of gestation. Preterm delivery was defined as births before 37 completed weeks of gestation. Perinatal loss included pregnancy loss, stillbirths, and neonatal deaths during the first week after birth (one or both infants in the case of twins).

2.3 | Statistical analyses

All data were analyzed using STATA version 18 (StataCorp LLC, College Station, Texas). Descriptive statistics were presented as means with standard deviations (SD) for continuous variables (maternal age [years], gestational age [weeks], birthweight [grams] and interpregnancy interval [years]), and as numbers and percentage for categorical variables (maternal education, country of birth, initiation of delivery, pregnancy complications in the first and subsequent pregnancy). Association between twin and singleton status of the first pregnancy and birthweight for subsequent singleton pregnancies as a continuous factor was evaluated by linear regression adjusting for the confounders listed above. We also used plots to visualize the distribution of birthweight in the subsequent singleton pregnancy after a first twin or singleton pregnancy. Differences in length of interpregnancy intervals and birthweight at different interpregnancy intervals were explored visually using plots. Interpregnancy interval was expressed in 1-year increments initially but for graphical presentation of birthweight by interpregnancy interval, the longer interpregnancy intervals (>3.9years) were combined as 4–5.9, 6–7.9, 8–9.9, and 10–11.9years due to smaller numbers.

2.4 | Ethics statement

Norway by the Regional Committee for Medical Ethics Western Norway REC WEST 13818 on July 1, 2020.

3 | RESULTS

A flow chart of the study sample is presented in Figure 1. Missing values for the covariates (maternal education and country of birth) were rare (0.5% and <0.1%). These analyses are based on the 778975 women with complete data.

3.1 | Maternal and pregnancy characteristics of study population

Baseline characteristics of the 778975 women with a first twin (n=4849) or singleton (n=774126) birth and a subsequent singleton pregnancy are presented in Table 1. Mean maternal age at first delivery was similar in women with twin pregnancies (25.0years) and women with singleton pregnancies (24.6years). For women whose first two births were singletons, mean birthweight increased by an average of 151g from first to second birth.

Mean gestational age was shorter for first twin pregnancies (252days) than first singleton pregnancies (281days). Combined

TABLE 1 Baseline characteristics of 778975 women with a first twin (n=4849) or singleton (n=774126) pregnancy. Medical Birth Registry of Norway, 1967–2020.

	First twin pregnancy N=4849 Mean±SD or n (%)	First singleton pregnancy N=774126 Mean±SD or n (%)
Maternal age (years)	25.0±4.3	24.6±4.4
Gestational age (days)	252.1±28.7	280.9±14.9
Birthweight (g)[a]	4627.7±1390.2	3443.6±568.5
Maternal education		
Primary school	840 (17.3)	140630 (18.2)
High school	1778 (36.7)	300396 (38.8)
University	2208 (45.6)	329047 (42.5)
Missing education	23 (0.5)	4053 (0.5)
Women's country of birth		
Nordic	4521 (93.2)	718684 (92.84)
Non-Nordic	328 (6.8)	55432 (7.2)
Missing	0	10
Preterm delivery	2388 (49.3)	44166 (5.7)
Preeclampsia	634 (13.1)	32039 (4.1)
Perinatal loss	428 (8.8)	8698 (1.1)
Initiation of delivery		
Spontaneous	3088 (63.6)	636147 (82.2)
Induction	1171 (24.2)	119305 (15.4)
Cesarean section	590 (12.2)	18674 (2.4)
Interpregnancy interval (years)	4.2±3.1	2.9±2.4
<1	602 (12.4)	104737 (13.5)
1–1.9	704 (14.5)	226027 (29.2)
2–2.9	747 (15.4)	179713 (23.2)
3–3.9	686 (14.1)	100524 (13.0)
4–5.9	1047 (21.6)	89707 (11.6)
6–7.9	548 (11.3)	37418 (4.8)
8–9.9	272 (5.6)	17942 (2.3)
10–11.9	132 (2.7)	9065 (1.9)
>12	58 (1.2)	4691 (0.6)
Missing	53 (1.1)	4302 (0.6)
Preterm in subsequent pregnancy	218 (4.5)	32417 (4.2)
Preeclampsia in subsequent pregnancy	99 (2.0)	15182 (2.0)

Abbreviation: SD, standard deviation.

[a]Combined mean birthweight of two fetuses for a twin pair.

mean birthweight was 4628g for a twin pair and 3444g for a singleton in the first pregnancy. More than 90% of the women were born in Nordic countries. As expected, first twin pregnancies had a much higher occurrence of preterm delivery (49%), preeclampsia (13%), and perinatal loss (9%) than first singleton pregnancies (6%, 4%, and 1%, respectively), and the initiation of delivery was more frequently by prelabor cesarean section (12%) and induction of labor (24%) than in first-born singletons (2% and 15%, respectively). The occurrence of preterm delivery and preeclampsia in the subsequent singleton pregnancies was similar for women with a first twin pregnancy or a first singleton pregnancy (4.5% vs. 4.2% and 2.0% vs. 2.0%, respectively).

3.2 | Birthweight and gestational age in the subsequent singleton pregnancy by first twin or singleton pregnancy

Mean birthweight was 3621g in singleton pregnancies following a first twin pregnancy and 3595g in singletons after a first singleton pregnancy (Table 2), resulting in a crude mean difference of 26g. The mean gestational ages in the subsequent singleton pregnancy after a first twin or first singleton pregnancy were 39.6 and 39.7 weeks respectively. The *z*-scores for birthweight by gestational age in the subsequent singleton pregnancy were 0.15 and 0.08 after a first twin and first singleton pregnancy, respectively. The adjusted difference in mean birthweight in subsequent singletons among women with a first twin pregnancy compared with offspring of women with a first singleton was 21g (95% confidence interval 5–37) after adjusting for maternal age at first delivery, year of first delivery, maternal education, and country of birth.

The distributions of birthweight in the first (Figure 2A) and subsequent (Figure 2B) pregnancies show that although the birthweights of twin and singleton infants are markedly different in the first birth (Figure 2A), the birthweight distributions are almost identical in the subsequent singleton birth (Figure 2B).

3.3 | Birthweight in the subsequent singleton pregnancy by interpregnancy interval

Women with a first twin pregnancy had a mean±SD interpregnancy interval of 4.2±3.1 years, whereas women with a first singleton pregnancy had a mean±SD interpregnancy interval of 2.9±2.4 years. The

TABLE 2 Mean birthweight, gestational age, and *z*-score of 778975 infants born following a previous twin (*n*=4849) or singleton (*n*=774126) pregnancy, Medical Birth Registry of Norway, 1967–2020.

Subsequent singleton pregnancy	*n*	Birthweight (g), mean±SD	Gestational age (wk), mean±SD	*z*-score,[a] mean±SD	Difference in birthweight (g) unadjusted[b] (95% CI)	Difference in birthweight (g): adjusted[c] (95% CI)
First twin pregnancy	4849	3621 (575)	39.6 (1.9)	0.15 (1.05)	26.07 (10.29–41.85)	20.92 (5.19–36.67)
First singleton pregnancy	774126	3595 (559)	39.7 (1.9)	0.08 (1.01)	Reference	Reference

Abbreviations: CI, confidence interval; SD, standard deviation.

[a]*Z*-score for birthweight by gestational age.

[b]Linear regression.

[c]Adjusted for maternal age at first delivery, year of first delivery, maternal education, and country of birth.

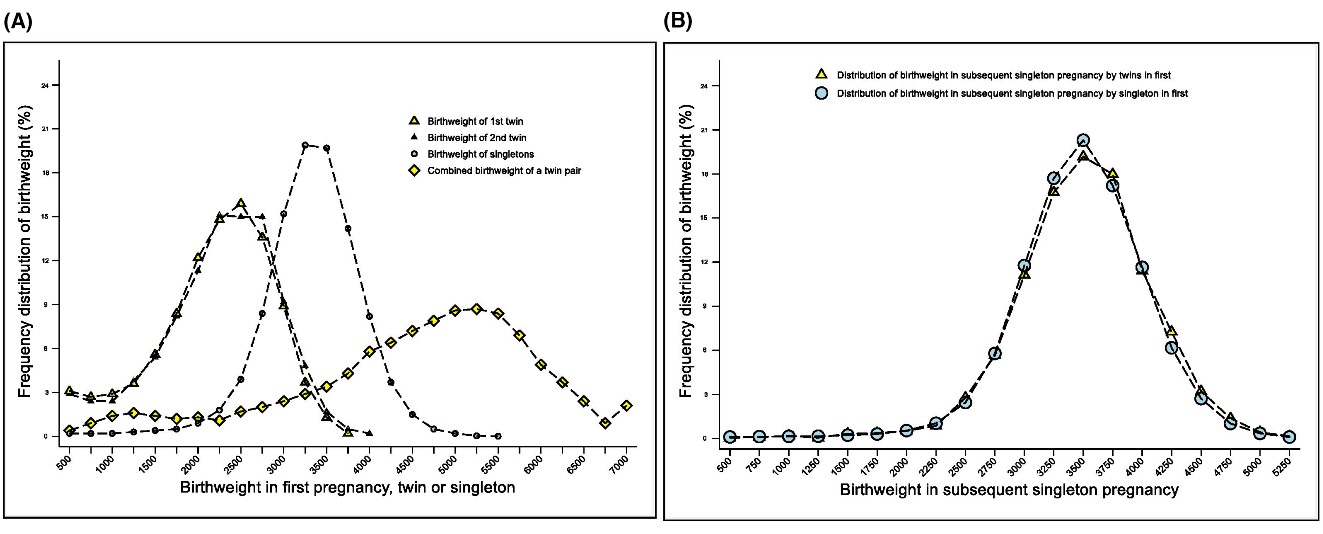

FIGURE 2 (A) Frequency distributions of mean birthweight in the first pregnancy, either twin or singleton. (B) Frequency distributions of mean birthweight in the subsequent singleton pregnancy by first twin or singleton pregnancy.

frequency distribution plots of interpregnancy interval showed that women who had singletons in the first pregnancy had a peak in frequency of a subsequent pregnancy at about 2 years (Figure 3A) and the majority (66%) of women with a first singleton pregnancy had interpregnancy interval of less than 3 years. In contrast the interpregnancy intervals in women with a first twin pregnancy were longer with a wider distribution and a less pronounced peak (Figure 3A). Following a first twin pregnancy only 42% of women had a subsequent pregnancy within 3 years. Although the birthweights of infants born within 3 years of a previous twin or singleton birth were similar (Figure 3B), there were differences in the birthweight patterns for longer interpregnancy intervals. Women with a first singleton pregnancy had an evident declining birthweight in the subsequent pregnancy with increasing interpregnancy intervals beyond 3 years, but a similar declining pattern was not observed among women with a first twin pregnancy.

4 | DISCUSSION

In this population-based cohort study using maternally linked sibship data in Norway, we found that although the combined birthweights of twins were on average more than a kilogram heavier than singleton pregnancies, the mean birthweight of singleton infants in the subsequent pregnancy were similar regardless of whether the earlier birth was twin or singleton. After a twin pregnancy, the adjusted mean weight of a singleton birth was only 21 g heavier than a singleton birth after a previous singleton pregnancy.

Earlier studies have suggested that birthweight is affected by differences in maternal physiological factors that change between the first and subsequent pregnancy.[3] These maternal physiological changes might impact the growth and size of the fetus. At the same time, growth of the fetus is also related to stable maternal factors, as women tend to have successive singleton babies of similar size.[27,28]

In our study, as expected, the mean total sum of birthweights in the first twin pregnancies was higher than the mean birthweight of first singletons. When amniotic fluid and placentas are also considered, it is likely that many women with twin pregnancies have a greater uterine distension than women with singleton pregnancies. This overdistension of the uterus in twin pregnancy has been hypothesized as a possible causal factor in the mechanisms leading to preterm delivery.[29,30] Increased birthweight in subsequent pregnancies might be the result of the improved uterine capacity and function

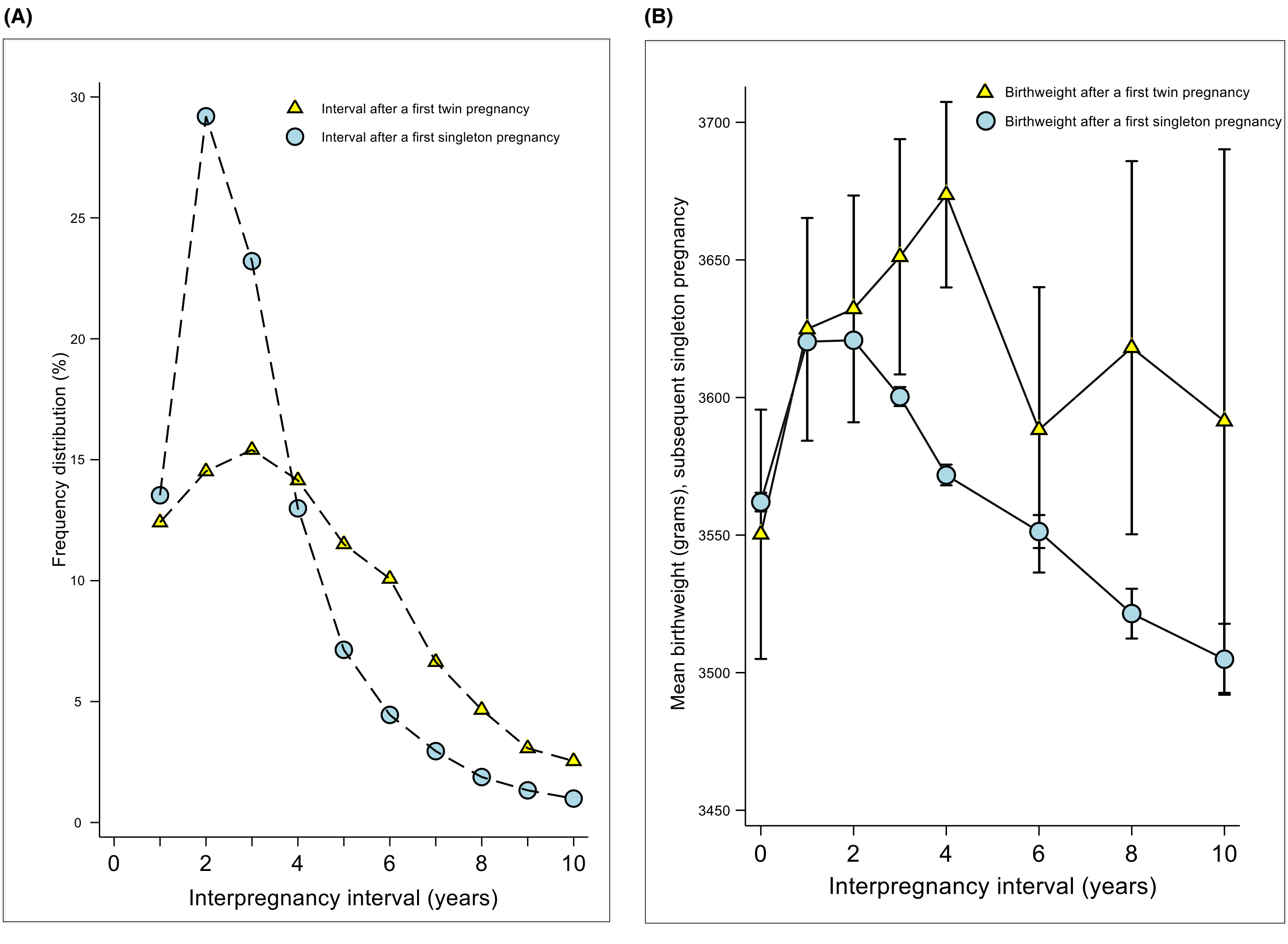

FIGURE 3 (A) Frequency distributions of interval between first and second pregnancy by plurality. (B) Mean birthweight (with 95% confidence interval) in the subsequent singleton pregnancy after a first twin or singleton pregnancy. In (B), interpregnancy interval in years is truncated as 0–0.9, 1–1.9, 2–2.9, 3–3.9, 4–5.9, 6–7.9, 8–9.9, and 10–11.9.

following a first pregnancy.[7,8,12] If this was the primary reason, we might expect that births following a first twin pregnancy would weigh substantially more than those following a first singleton pregnancy.

However, our data do not support this hypothesis. Although the combined birthweights of twin pregnancies were on average more than a kilogram heavier than singleton pregnancies, this additional weight and uterine expansion was associated with only a trivial increase in birthweight in the subsequent singleton pregnancy. The parity effect on birthweight (in the range of 80–140 g) therefore seems to be due to other mechanisms not yet understood.

The associations of birthweight with interpregnancy interval deserve special comment. We found that, after a singleton birth, the mean weight of the subsequent baby declined when the interpregnancy interval was longer than 3 years. This association probably reflects selection, in which the women who take longer to conceive after a singleton pregnancy are more likely to be subfertile and to have associated health problems that decrease birthweight. Such selection would not be as strong for mothers of twin babies, for whom having twins is itself a reason for a longer pregnancy interval (Figure 3A). After a twin birth, there are more healthy mothers with longer interpregnancy intervals, and less evidence of declining birthweights (Figure 3B). Further, adverse social factors like low education and change of partner may also be more frequent among singleton women with long interpregnancy interval compared with mothers of twins with long intervals. In this framework, pregnancy interval is not a confounder, and adjustment for pregnancy interval would not be justified. We can be further reassured that interpregnancy interval is not affecting our results by restricting to births within the first 2 years after delivery, during which time, selection should be less important. Within this time range, there is no evidence that a previous twin birth results in a heavier subsequent birth.

The main strength of our study is the maternally linked offspring design based on a population-based cohort with mandatory registration of mothers and offspring in Norway. This large cohort of births over 50 years provided sufficient sample size to study association in subsequent pregnancies. Another strength of the study is the valid measurement and reporting of birthweight, which has been consistent over time.[31]

We lacked information on some possible confounding factors such as smoking, gestational weight gain, and BMI resulting in possible residual confounding. Information on gestational diabetes was not available for the whole study period. Additionally, we did not have information on diet, weight change between pregnancies, and lifestyle factors that may have varied between first and subsequent pregnancy. Many of these factors are, however, related to maternal educational level, so by adjusting educational level we have likely reduced some of this residual confounding.

5 | CONCLUSION

Our study showed that women with a first twin pregnancy have singletons in the next pregnancy of similar birthweight to women with a first singleton pregnancy. Our findings indicate that the increased physiological and mechanical burden resulting from a twin pregnancy do not explain the general parity effect on the birthweight of first and second singleton births.

AUTHOR CONTRIBUTIONS

PB, RS, and LGK: Conceived and designed the study. PB: Performed statistical analysis and wrote the first draft of the manuscript. All authors contributed to analytical methods and discussion of results. RS: Is the guarantor of data quality. All authors took part in revision of the manuscript. All authors approved the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Norwegian Institute of Public Health. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from https://www.fhi.no/en/hn/health-registries/medical-birth-registry-of-norway/medical-birth-registry-of-norway/ with the permission of the Norwegian Institute of Public Health.

ORCID

Prativa Basnet https://orcid.org/0000-0001-9022-9957
Rolv Skjærven https://orcid.org/0000-0002-2983-1233
Quaker E. Harmon https://orcid.org/0000-0002-5866-848X
Allen J. Wilcox https://orcid.org/0000-0002-3376-1311
Kari Klungsøyr https://orcid.org/0000-0003-2482-1690
Linn Marie Sørbye https://orcid.org/0000-0002-3726-5198
Nils-Halvdan Morken https://orcid.org/0000-0002-8256-0778
Liv G. Kvalvik https://orcid.org/0000-0001-6520-9057

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