

INFLUENCE OF MATERNAL HEIGHT ON BIRTHWEIGHT CLASSIFICATION AND SEVERE ADVERSE PERINATAL OUTCOMES IN SINGLETON AT TERM BIRTHS IN THE NETHERLANDS

Name: S. (Suzanne) Mentink
Student number: 6912761
Status: Master Thesis
Date: 25-06-2021
Studies: Utrecht University
Master Clinical Health Sciences
Master's program Health Sciences for Healthcare Professionals
UMC Utrecht
Supervisor: dr. Jens Henrichs
Teacher: dr. Rob Zwitterlood
Research institute: Amsterdam UMC (Location VUmc), Amsterdam
Department of Midwifery Science
Protocol: STROBE Statement
Intended Journal: British Journal of Obstetrics and Gynaecology
Wordcount: 3737/3800
Wordcount abstract: 294/300
Wordcount abstract (NL): 283/300

ABSTRACT

Background: An accurate birthweight classification is important to prevent severe adverse perinatal outcomes (SAPO). Neonates who are small for gestational age (SGA, $p \leq 10$) or large for gestational age (LGA, $p \geq 90$) have a higher risk for SAPO.

Aim: To assess the association between maternal height and birthweight in low-risk pregnancies and to investigate the effect of maternal height on the classification of birthweight as SGA and LGA. Secondly, to investigate whether maternal height has a predictive value for the risk of SAPO.

Method: An observational study using prospectively precollected data from the IRIS study was conducted ($n=6970$). The influence of maternal height on birthweight and SAPO was analysed. The number of neonates classified as SGA and LGA was calculated. Subsequently, the changes in classification from SGA and LGA to appropriate for gestational age (AGA) were calculated.

Results: A significant association was found between maternal height and birthweight ($p < .001$) and maternal height and SAPO ($p = .023$). Shorter and taller women had a higher risk for SAPO. A logistic regression with maternal height squared showed that this curvilinear effect was not significant ($p = .062$). The incidence of SGA was 7.2% (decreasing from 17.9% to 2.9% in the shortest to tallest height categories) and LGA was 9.5% (increasing from 2.7% to 15.5%). A shift in classification was found for 18.1% of the SGA and 17.5% of the LGA neonates when controlling for maternal height.

Conclusion: Maternal height is significantly associated with birthweight and SAPO. Customised birthweight charts based on maternal height changes the classification of around one in five SGA or LGA neonates at term.

Recommendations: Validation studies to assess the predictive value of a customised birthweight chart based on maternal height on SAPO.

Keywords: Maternal height, Birthweight, Small for gestational age, Large for gestational age, Adverse perinatal outcomes.

SAMENVATTING

Achtergrond: Een betrouwbare geboortegewichtsclassificatie is belangrijk om ernstige perinatale uitkomsten (EPU) te voorkomen. Neonaten die dysmatuur ($\leq p10$) of macrosoom ($\geq p90$) zijn hebben een hoger risico op EPU.

Doel: Het onderzoeken van de associatie tussen maternale lengte en geboortegewicht bij laag risico zwangeren en het onderzoeken van het effect van maternale lengte op geboortegewichtsclassificatie als dysmatuur of macrosoom. Daarnaast, het onderzoeken of er een samenhang is tussen maternale lengte en EPU.

Methode: Een observationele studie met bestaande prospectieve data van de IRIS studie werd uitgevoerd (n=6970). De invloed van maternale lengte op geboortegewicht en EPU werd geanalyseerd. Het aantal neonaten geclassificeerd als dysmatuur of macrosoom werd berekend. Vervolgens werd het verschil in classificaties als dysmatuur en macrosoom ten opzichte van een normaal geboortegewicht berekend.

Resultaten: Er werd een significante associatie gevonden tussen maternale lengte en geboortegewicht ($p < .001$) en voor maternale lengte en EPU ($p = .023$). Kortere en langere vrouwen hadden een hoger risico voor EPU. Een logistische regressie met maternale lengte in het kwadraat toonde aan dat dit paraboolvormige verband niet significant was ($p = .062$). De incidentie van dysmaturiteit was 7.2% (afnemend van 17.9% tot 2.9% van de kortste tot langste vrouwen) en macrosomie was 9.5% (toenemend van 2.7% tot 15.5%). Een verschuiving in de classificatie werd gevonden voor 18.1% van de dysmatuur neonaten en bij 17.5% van de macrosome neonaten bij het controleren voor maternale lengte.

Conclusie: Maternale lengte is significant geassocieerd met geboortegewicht. Geboortegewichtscurven aangepast op maternale lengte zorgen voor een verschillende classificatie als dysmatuur of macrosoom bij ongeveer één op de vijf a terme neonaten.

Aanbevelingen: Validiteitsonderzoek naar de voorspellende waarde van een geboortegewichtscurve op basis van maternale lengte op EPU is noodzakelijk.

Kernwoorden: Maternale lengte, Geboortegewicht, Dysmaturiteit, Macrosomie, Ernstige perinatale uitkomsten

INTRODUCTION

The birthweight of neonates is the end-result of the intrauterine growth. Neonatal birthweight is classified by using birthweight charts specified for gestational age. Birthweight can be classified as appropriate for gestational age (AGA), small for gestational age (i.e., birthweight less than or equal to the 10th percentile) or large for gestational age (i.e., birthweight greater than or equal to the 90th percentile)¹⁻⁹.

An abnormal birthweight, small for gestational age (SGA) or large for gestational age (LGA), is associated with short- and long-term morbidity and perinatal mortality such as stillbirth, sepsis or traumatic delivery¹⁻⁹. Birthweight classification is used in clinical practice by healthcare professionals to identify neonates at risk for complications resulting in adverse perinatal outcomes¹⁻⁹.

The neonatal birthweight potential depends on various different determinants such as genetic factors, maternal ethnicity, maternal height and gender^{10,11}. In addition, there are many other determinants that influence the neonatal birthweight potential. These determinants include an abnormal (<18.5 or >25.0 kg/m²) maternal body mass index (BMI), smoking, gestational weight gain, gestational diabetes, parity, foetal and infectious diseases^{12,13}.

The Dutch Birthweight chart by Hoftiezer (further referred to as the Dutch Birthweight chart) is used in the Netherlands to classify neonatal birthweight. This chart was developed with data from the Netherlands Perinatal Registry (Perined)¹⁴. Cases with risk factors for SGA or LGA were excluded when this chart was developed. Information on maternal BMI is not registered in Perined and information on smoking is limited in this database. Neonatal gender is a constitutional factor in the Dutch Birthweight chart^{14,15}.

The Dutch Birthweight chart is not customised for maternal factors like maternal height, weight or ethnicity^{14,15}. While maternal height and ethnicity are correlated to neonatal birthweight. Tall mothers give birth to constitutionally larger neonates and smaller mothers to smaller neonates^{11,16-18}. Ethnicity also has an influence on birthweight¹⁹. However, maternal height and ethnicity are correlated since maternal height varies not only between but also within ethnic groups. A German survey has shown that mothers from different ethnic groups with similar height have similar mean birthweights and similar SGA and LGA rates²⁰. This suggests that maternal height is a stronger predictor for birthweight than ethnicity.

In the Netherlands, maternal height is currently not considered as a factor that may influence the classification of neonatal birthweight. Research from Zeegers et al. (2020) based on a Dutch low-risk cohort shows that maternal height is significantly associated with neonatal birthweight. Customised birthweight charts for maternal height changed the classification in one out of six SGA or LGA neonates at term²¹.

A total of 17,3% of SGA neonates and 21,1% of LGA neonates were classified differently with the maternal height birthweight chart. Neonates previously considered SGA would be classified normal in shorter women (<167cm) while the same amount of AGA neonates were classified as SGA in taller women. The opposite happened for LGA neonates. An increased number of LGA neonates would be found in shorter women while this number would decrease for taller women²¹.

However, it is still unknown if this shift in classification results in an altered detection rate of adverse perinatal outcomes. Research by Marshall et al. (2019) did show a strong association between maternal height and perinatal risk in addition to risks that are associated with variations in maternal weight. The study concluded that among women with a normal BMI an individualized screening could optimize outcomes for mothers and neonates²².

Maternal height seems to be an important predictor for neonatal birthweight and might therefore improve the prediction of short- and long-term morbidity and perinatal mortality that is associated with LGA and SGA. Using precollected prospective data from the IRIS study, a nationwide prospective clinical trial in the Netherlands, this study aims to explore if a customised birthweight chart based on maternal height alters the classification of SGA and LGA neonates in comparison to the current Dutch Birthweight chart^{23,24}. Secondly, this study explores the association between maternal height and SAPO.

AIM

This study aims to assess the association between maternal height and birthweight in low-risk pregnancies and to investigate the effect of maternal height on the classification of birthweight as small for gestational age (SGA) and large for gestational age (LGA). Furthermore, this study aims to investigate the association between maternal height and severe adverse perinatal outcomes (SAPO).

METHODS

This observational study used prospectively precollected data from the IRIS study. The IRIS study was a nationwide, pragmatic, multicentre, stepped wedge cluster randomised trial that took place in the Netherlands evaluating the (cost-)effectiveness of universal third trimester ultrasonography in reducing severe adverse perinatal outcomes compared to usual care. Women with a low-risk pregnancy in primary care at enrolment (around 22 weeks of gestation) from different midwifery practices in the Netherlands were studied in the IRIS study. Participants were enrolled through 60 midwifery practices between February 1st 2015 and February 29th 2016^{23,24}.

Study procedures

This study is a secondary analysis of prospectively collected data from the IRIS study and was carried out between February 2021 and June 2021. For this trial, data from the 13,520 women who participated in the IRIS study was used^{23,24}. For 13,046 of the cases any data from Perined or hospital records was available on perinatal or peripartum outcomes. The exact study procedure from the IRIS study can be found in the original trial²³.

The precollected data consists of information from Perined, demographic information collected at baseline by the participating midwifery practices and hospital records of mothers and neonates at risk for severe adverse perinatal outcomes or pathology^{14,23,24}. Women were asked for permission to use the data from their records and were asked to sign a written informed consent form.

Inclusion criteria for women in the IRIS study were: receiving antenatal care in a participating midwifery practice in mid-pregnancy, a singleton pregnancy, age sixteen years or older, no major obstetric or medical risk factors and a reliable expected date of delivery (based on a term dating scan or a reliable first day of the last menstrual period).

For the current study, records with missing data on foetal gender, birthweight, maternal height, weight before pregnancy, parity, gestational age, SGA (classified by the Dutch Birthweight chart), LGA (classified by the Dutch Birthweight chart), SAPO and smoking were excluded from the IRIS study sample. Furthermore, records with preterm (<37 weeks of gestation) and post term (>41 weeks of gestation) birth were excluded from the IRIS study sample since only at term births were studied.

BMI was calculated as weight before pregnancy (kg) divided by squared maternal height (m²). Weight was based on self-reported weight before pregnancy and maternal height was reported by the participants' midwife during the first appointment. BMI was classified according to the classification from the WHO²⁵.

Maternal height was categorised in different groups (≤152, 153-157, 158-162, 163-167, 168-172, 172-177, 178-182, 183-187 and ≥188 cm). Smoking and parity were

dichotomised, smoking or not smoking during pregnancy and nulliparous or multiparous. Gestational age was classified in different categories (week 37, week 38, week 39, week 40 and week 41).

To create a healthy subsample only participants without risk factors that influence intrauterine growth were included for further analysis. Women who smoked during pregnancy and women with an BMI outside the normal range (18.5-25.0 kg/m²) were excluded. Furthermore, women with extremes in maternal height (≤ 152 and ≥ 188 cm) were excluded after analysing baseline characteristics since numbers were too small.

Parameters

This study focused on the classification of SGA (a birthweight below or equal to the 10th percentile) and LGA (a birthweight above or equal to the 90th percentile) based on the maternal height birthweight classification in comparison to the Dutch Birthweight chart.

The main study parameter for this study was Severe Adverse Perinatal Outcomes (SAPO). SAPO is a dichotomous composite measure previously used in the IRIS study^{23,24}. It contains twelve adverse perinatal outcomes occurring up to seven days after birth: perinatal death between 28 weeks of gestation and seven days after birth, an Apgar score <4 at five minutes, impaired consciousness (coma, stupor, or decreased response to pain), asphyxia (with arterial base excess of cord blood less than -12 mmol/L), seizures on at least two occasions within 72 hours of birth, assisted ventilation by endotracheal tube for more than 24 hours started within 72 hours of birth, septicaemia confirmed by blood culture, meningitis confirmed by culture of cerebrospinal fluid, bronchopulmonary dysplasia requiring oxygen after 36 weeks of gestation and confirmed by radiography, intraventricular haemorrhage grade 3 or 4 confirmed by ultrasonography or autopsy, cystic periventricular leucomalacia confirmed by ultrasonography or necrotising enterocolitis confirmed by radiography, surgery, or autopsy^{23,24}.

Data analysis

Analysis of the precollected data from the IRIS study was carried out using IBM SPSS Statistics 26.0²⁶. Descriptive statistics were performed on the demographic data, computing the data into means and percentages.

To analyse the primary study parameters p10 and p90 of birthweights based on the maternal height chart from the precollected data were compared with the Dutch Birthweight chart for girls and boys separately^{14,15}. Moreover, a multiple linear regression analysis was performed to assess the association between maternal height (per cm) and birthweight (in grams) with adjustment for gender, gestational age and parity. BMI was not included as an independent variable in the model since all included participants had a normal BMI (18.5-

25.0 kg/m²), The 'enter' regression method was used, regarding $p < 0.05$ as statistically significant. Effect size, R^2 , was calculated and classified by the benchmarks of Cohen. R^2 was classified as followed: < 0.09 a small effect size; $0.10-0.24$ a moderate effect size and ≥ 0.25 a large effect size²⁷.

In this study neonates with a birthweight below or equal to the 10th percentile on the Dutch Birthweight chart were classified as SGA. Neonates with a birthweight above or equal to the 90th percentile on the Dutch Birthweight chart were classified as LGA. Incidences of SGA, LGA and SAPO were calculated for the total group and within seven different maternal height categories (153-157cm, 158-162 cm, etc.) to observe the association between maternal height and SGA, LGA and SAPO.

Furthermore, the study examined absolute numbers and percentages of SGA, LGA and SAPO for all height categories to understand the influence of different maternal heights on birthweight classification. The absolute number of cases classified as SGA or LGA by the current Dutch Birthweight chart and the cases that would be classified differently with a birthweight chart customised for maternal height were calculated. The overall incidence of SGA, LGA cases was not changed, assuming a constant incidence of these factors in all height categories.

Results from all analyses are shown graphically to further explore the association between maternal height and birthweight classification and to explore the influence of maternal height on severe adverse perinatal outcomes. A multiple logistic regression analysis was performed to investigate the association between maternal height and SAPO. After entering the linear term of maternal height into the first model, a squared term of maternal height was entered in a second model. These analyses were adjusted for gender, gestational age and parity. The 'enter' regression method was used, regarding $p < 0.05$ as statistically significant. Odds ratios and 95% CI were calculated.

Finally, a sensitivity analysis was performed to explore if the patterns found in the healthy subsample were present in the complete sample, including women who smoked during pregnancy and with all BMI categories.

Ethical issues

This study was conducted following the principles of the Declaration of Helsinki (2013). This study was not subject to the Medical Research Involving Human Subjects Act (WMO) since it is a secondary analysis of precollected data from the IRIS study. The IRIS study was approved by the Dutch Institutional Review Board of the VU Medical University Centre Amsterdam (reference No 2013.409)^{23,24}.

RESULTS

The original sample from the IRIS study contained data from 13,046 women with singleton pregnancies in primary care. Cases with missing data on foetal gender, birthweight, maternal height, weight before pregnancy, parity, gestational age, SGA (classified by the Dutch Birthweight chart), LGA (classified by the Dutch Birthweight chart), SAPO, smoking, neonates born pre- or postterm were excluded. After exclusion the total sample contained 12,017 complete cases. From this sample a healthy subsample with non-smokers and women with a normal BMI was subtracted, a total of 7039 subjects were left for further analyses (**Figure 1**).

The healthy subsample and the total sample showed a similar mean maternal age, length, ethnicity and similar distribution of neonates over maternal height categories. Highest level of education differed between groups. A higher percentage of participants completed HBO/University in the healthy subsample in comparison to the total sample, 66.0% versus 54.5%. Furthermore, mean birthweights were nearly the same in both samples. A mean birthweight of 3523g (SD 458) in the total sample compared to a mean birthweight of 3525g (SD 446) in the healthy subsample (**Table1**).

Further analyses were performed with the healthy subsample (n=6970), excluding extreme short and tall records (≤ 152 and ≥ 188 cm) (**Figure 1**). For girls the p10 curve of the healthy subsample was mostly above the p10 curve of the Dutch Birthweight chart, on average 12g. The p90 curve for girls of the healthy subsample was slightly below the de p90 curve of the Dutch Birthweight chart, on average 5g less (**Figure 2**). The birthweight curves for boys showed a different pattern. Although minimal, both the p10 and p90 curve in the healthy subsample were mostly below the p10 and p90 curve of the Dutch Birthweight chart. Respectively, 3g and 17g (**Figure 2**).

A multiple linear regression showed a significant association between maternal height and birthweight with a 15.1g higher birthweight per extra cm maternal height (95% CI 13.8-16.5; $p < .001$; $R^2 = 0.29$). R^2 was 0.29 which is a strong effect size. Corrected for confounders, maternal height explained 29.0% of the variance in neonatal birthweight.

The incidence of neonates labelled as SGA using the Dutch Birthweight chart in the healthy subsample with maternal height between 153-187cm was 7.2% (n=504). While examining the incidences of SGA in different maternal height categories a substantial difference was found between groups. The incidence declined from 17.9% SGA in the shortest women to 2.9% in the group with tallest women (**Figure 3**). The incidence of LGA in the healthy subsample was 9.5% (n=663). Between different maternal height groups, the incidence increased profoundly from 2.7% in the shortest height category to 15.5% in the tallest category (**Figure 3**).

The incidence of SAPO was 1.1% (n=77) in the healthy subsample. The incidence

was higher than average for women <167cm (1.4-2.7%) and \geq 183cm (1.5%). The incidence for women with a height between 168-182cm was slightly lower than average, 0.6-1.1% (**Figure 3**). While correcting for confounders, a multiple logistic regression to investigate the association between maternal height and SAPO showed a significant negative association ($p=.023$; OR 0.961, 95% CI 0.928-0.995). With increasing height, the risk of SAPO decreases. The curvilinear association between maternal height and SAPO was not significant (**Figure 3**). A multiple logistic regression exploring the association between maternal height squared and SAPO showed no significant association ($p=.062$; OR 1.003; 95% CI 1.000-1.007).

The implications of using a birthweight chart based on maternal height were explored while working with the assumption that the same number ($n=504$ or 7.2%) of neonates was classified as SGA when controlling for maternal height. Spreading the 7.2% smallest birthweights over the different maternal height categories. A shift in classification was calculated for a substantial 91 out of 504 neonates (18.1%). A total of 91 neonates previously considered SGA would be classified as AGA in women <167cm when controlling for maternal height, 91 neonates previously considered AGA would be classified as SGA in taller women. This implies that a customised birthweight chart for maternal height might reduce the number of neonates labelled as SGA among shorter women and increase this number among taller women (**Figure 4(a)**). Exploring the same effect for the classification of LGA showed a shift in classification of 116 out of 663 cases (17.5%). The number of neonates labelled as LGA in taller women decreases while among shorter women the number of LGA labelled neonates increases (**Figure 4(b)**).

To explore if the same patterns were found in the total sample a sensitivity analysis was conducted. All women, including smokers and women with all BMI were included. Women \leq 152cm and \geq 188cm were excluded since numbers were too small ($n=11,889$). The same trend of SGA and LGA over the different maternal height categories was found. The incidence of SGA declined from 17.6% to 3.1% from the shortest tot tallest maternal height categories. The incidence of LGA increased from the smallest tot the tallest women, from 3.8% to 18.7%. When controlling for maternal height 17.1% of the SGA and 15.8% of the LGA neonates would be reclassified as AGA.

DISCUSSION

This study shows a significant positive association between maternal height and neonatal birthweight in low-risk pregnancies. The incidence of SGA decreased from the shortest height category to tallest height category, 17.9% to 2.9%. For LGA the opposite effect was found, the incidence increased while maternal height increased. For the shortest women the incidence of LGA was 2.7%, while for the tallest women this was 15.5%. With a customised birthweight chart based on maternal height 18.1% of SGA neonates would be reclassified as AGA, while for LGA neonates this was 17.5%. The incidence of SAPO was higher than average in relatively short women (<168cm) and tall women (≥ 183 cm). A significant negative association between maternal height and SAPO was found. However, no significant curvilinear association between maternal height and SAPO was found.

A regression coefficient of 15.1g extra birthweight per centimetre was found, this is in line with prior studies^{20,21,28}. For example, women with a height of 160cm compared to women with a height of 180cm give birth to neonates with a mean birthweight that is 300g lower. This 300g makes a substantial difference in classification of birthweight considering the relatively small range in neonatal birthweight. Previous studies in the Netherlands have found similar associations between maternal height and birthweight. Taller women have the lowest risk for SGA and the highest for LGA and vice versa for shorter women^{10,21}.

This study found a narrower range of p10 and p90 curves for both genders in the healthy subsample in comparison to the Dutch Birthweight chart¹⁴. This narrower range reflects the low risk and homogenous profile of the healthy subsample. Furthermore, the incidence of SGA (7.2%) and LGA (9.5%) shows the low risk and homogenous profile of the healthy subsample. The incidences of SGA and LGA are lower than the cut-off 10.0% (below 10th percentile and above 90th percentile) from the Dutch Birthweight chart¹⁴.

Prior studies confirm that customised birthweight charts, taking maternal height into account, lead to a different classification of at term neonates as SGA with a stronger association with adverse perinatal outcomes²⁹⁻³³. Various customised birthweight charts use ethnicity as a predictor for intrauterine growth²⁹⁻³³. However, ethnicity is becoming increasingly harder to determine. The number of inter-ethnic women increases in many countries like the Netherlands. Customising for ethnicity can become more problematic. Therefore, maternal height is more feasible than ethnicity in the development of customised birthweight charts^{20,21}.

Research by Voigt et al. (2020) showed a clinically significant difference in birthweight percentiles when stratified by maternal height. Maternal anthropometry, length and weight, could provide a higher specificity and more individual prediction of perinatal risk³⁴. Furthermore, research by Marshall et al. (2019) found a strong association between maternal height and perinatal risks. For women with a normal BMI individualized screening based on

maternal height could optimize perinatal outcomes for mothers and neonates²². This is in line with the significant association between maternal height and SAPO that was found in this study. Customising birthweight charts for height, and possibly BMI, could help prevent adverse perinatal outcomes.

Strengths and limitations

A strength of this study was that it was based on a healthy subsample of pregnant women who were non-smokers and had a normal BMI. In a healthy sample the impact of pathological factors on intrauterine growth is limited, providing the opportunity to study the impact of maternal height on neonatal birthweight. The healthy subsample had the same distribution of maternal height and age, gestational age and foetal gender as the total sample. Furthermore, the healthy subsample shows very similar distribution of these variables as prior studies in the Netherlands²¹.

Besides this strength, a second strength of this study is that the data from the IRIS-study was prospectively collected^{23,24}. The data also included a composite measure for severe adverse perinatal outcomes and contained combined information from Perined and hospital records. These hospital records were collected and examined by trained researchers^{23,24}.

A limitation of this study is that paternal height is missing from the data. Both paternal and maternal height effect the intrauterine growth. However, maternal height has a far greater influence on birthweight^{35,36}. A second limitation is that not all factors that influence birthweight were excluded. The sample consisted of a low-risk population: non-smoking women with a normal BMI and with a normal 20-week scan without anomalies. Other placental, foetal and other genetic factors that could possibly affect the intrauterine growth were not excluded^{37,38}.

Implications for clinical practice and future research

The findings from this study and a prior study from Zeegers et al. (2020) show promising results for a birthweight chart customised for maternal height. Suggesting that it could be useful to develop new prescriptive birthweight charts. These new prescriptive birthweight charts should be based on data from a similar low-risk cohort but have to take into account unhealthy life-style factors like a low or high BMI and smoking.

Maternal height should be used as a predictor of intrauterine growth and neonatal birthweight, rather than ethnicity. New cut-off points for SGA and LGA should be determined. Finally, a validation study should be performed to determine if a customised birthweight chart with new cut-off points for SGA and LGA leads to a better identification of neonates at risk for adverse perinatal outcomes.

Conclusion

This study contributes new information to the association between maternal height and neonatal birthweight by investigating this hypothesis in a healthy sample low-risk, non-smoking women with a normal BMI. A significant positive association of maternal height and birthweight was found while a significant negative association between maternal height and SAPO was found. Using the Dutch Birthweight chart leads to a misclassification of around one out of five neonates classified as SGA or LGA. Validation studies are needed evaluating whether birthweight charts customised for maternal height have the potential to improve the classification of SGA and LGA as a predictor for adverse perinatal outcomes.

REFERENCES

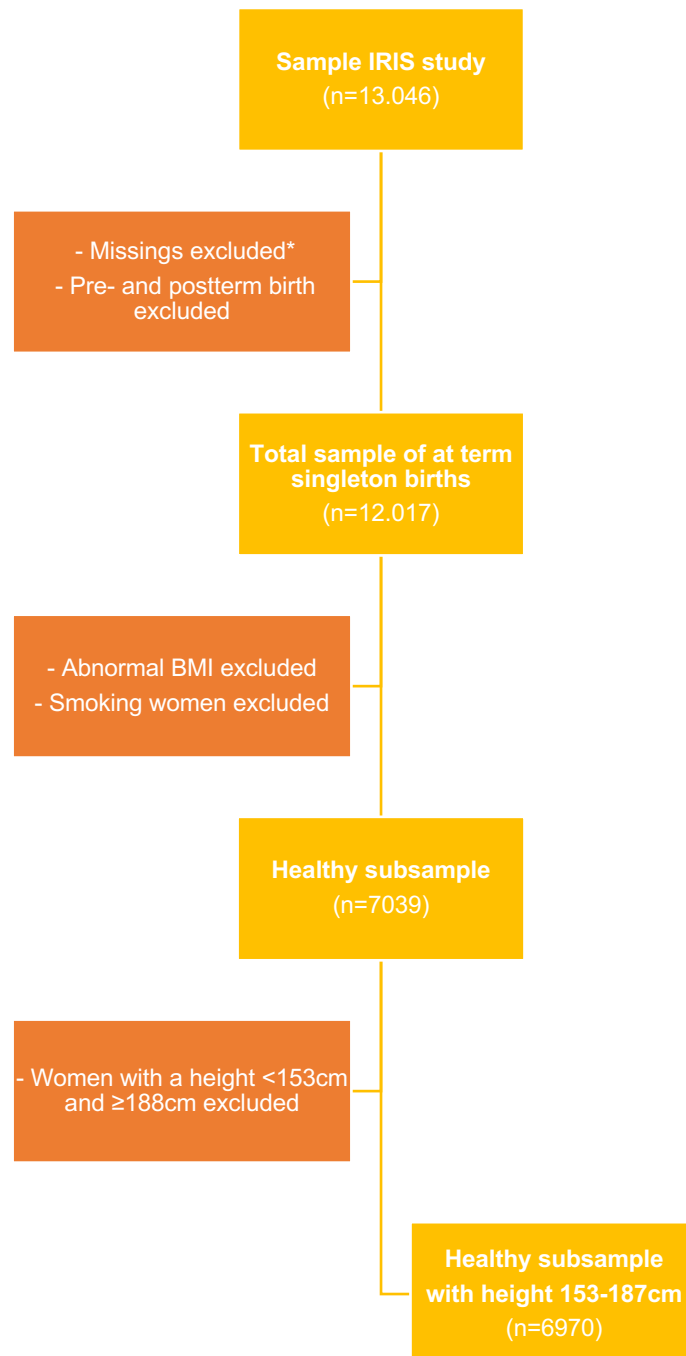
1. Chauhan SP, Rice MM, Grobman WA, et al. Neonatal morbidity of small- and large-for-gestational-age neonates born at term in uncomplicated pregnancies. *Obstet Gynecol*. 2017;130(3):511–519.
2. Dowdall D, Flatley C, Kumar S. Birth weight centiles, risk of intrapartum compromise, and adverse perinatal outcomes in term infants. *J Matern Fetal Neonat Med*. 2017;30(17):2126–2132.
3. Henriksen T. The macrosomic fetus: a challenge in current obstetrics. *Acta Obstet Gynecol Scand*. 2008;87(2):134–145.
4. Pilliod RA, Cheng YW, Snowden JM, et al. The risk of intrauterine fetal death in the small-for-gestational-age fetus. *Am J Obstet Gynecol*. 2012;207(4):318.e1–318.e6.
5. McIntire DD, Bloom SL, Casey BM, et al. Birth weight in relation to morbidity and mortality among newborn infants. *N Engl J Med*. 1999;340(16):1234–1238.
6. Murray E, Fernandes M, Fazel M, et al. Differential effect of intrauterine growth restriction on childhood neurodevelopment: a systematic review. *BJOG*. 2015;122(8):1062–1072.
7. Malin GL, Morris RK, Riley RD, et al. When is birthweight at term (≥ 37 weeks' gestation) abnormally low? A systematic review and meta-analysis of the prognostic and predictive ability of current birthweight standards for childhood and adult outcomes. *BJOG*. 2015;122(5):634–642.
8. Longo S, Bollani L, Decembrino L, et al. Short-term and long-term sequelae in intrauterine growth retardation (IUGR). *J Matern Fetal Neonat Med*. 2013;26(3):222.
9. Gluckman PD, Hanson MA, Cooper C, et al. Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med*. 2008;359(1):61–73.
10. Ay L, Kruithof CJ, Bakker R, et al. Maternal anthropometrics are associated with fetal size in different periods of pregnancy and at birth. The Generation R Study. *BJOG*. 2009;116(7):953–963.
11. Trojner Bregar A, Blickstein I, Steblovnik L, et al. Do tall women beget larger babies? *J Matern Fetal Neonat Med*. 2016;29(8):1311–1313.
12. McCowan L, Horgan RP. Risk factors for small for gestational age infants. *Best Pract Res Clin Obstet Gynaecol*. 2009;23(6):779–793.
13. Jolly MC, Sebire NJ, Harris JP, et al. Risk factors for macrosomia and its clinical consequences: a study of 350,311 pregnancies. *Eur J Obstet Gynecol Reprod Biol*. 2003;111(1):9–14.
14. Perined Perinatale Zorg in Nederland 2016. Perined: Utrecht, 2018.
15. Hoftiezer L, Hof MHP, Dijs-Elsinga J, et al. From population reference to national standard: new and improved birthweight charts. *Am J Obstet Gynecol*. 2018;220(4):383.e1–383.e17.

16. Voigt M, Rochow N, Jahrig K, et al. Dependence of neonatal small and large for gestational age rates on maternal height and weight – an analysis of the German Perinatal Survey. *J Perinat Med.* 2010;38(4):425–430.
17. Olbertz DM, Knie A, Straube S, et al. Somatic development at birth as influenced by maternal characteristics – an analysis of the German Perinatal Survey. *J Perinat Med.* 2018;46(8):889–892.
18. Polzlberger E, Hartmann B, Hafner E, et al. Maternal height and pre-pregnancy weight status are associated with fetal growth patterns and newborn size. *J Biosoc Sci.* 2017;49(3):392–407.
19. Mikolajczyk RT, Zhang J, Betran AP, et al. A global reference for fetal-weight and birthweight percentiles. *Lancet.* 2011;377(9780):1855–1861.
20. Rochow N, AlSamnan M, So HY, et al. Maternal body height is a stronger predictor of birth weight than ethnicity: analysis of birth weight percentile charts. *J Perinat Med.* 2018;47(1):22–29.
21. Zeegers B, Offerhaus P, Peters L, et al. Impact of maternal height on birthweight classification in singleton births at term: a cohort study in The Netherlands, *The Journal of Maternal-Fetal & Neonatal Medicine*, 2020. DOI: 10.1080/14767058.2020.1814246
22. Marshall NE, Biel FM, Boone-Heinonen J, Dukhovny D, Caughey AB, Snowden JM. The Association between Maternal Height, Body Mass Index, and Perinatal Outcomes. *Am J Perinatol* 2019;36(6):632-640.
23. Henrichs J, Verfaillie V, Jellema P, Viester L, Pajkrt E, Wilschut J, et al. Effectiveness of routine third trimester ultrasonography to reduce adverse perinatal outcomes in low risk pregnancy (the IRIS study): nationwide, pragmatic, multicentre, stepped wedge cluster randomised trial. *BMJ* 2019;367:l5517.
24. Henrichs J, Verfaillie V, Viester L, et al, IRIS Study Group. Effectiveness and cost effectiveness of routine third trimester ultrasound screening for intrauterine growth restriction: study protocol of a nationwide stepped wedge cluster-randomized trial in The Netherlands (The IRIS Study). *BMC Pregnancy Childbirth* 2016;16:310. doi:10.1186/s12884-016-1104-8.
25. Weir CB, Jan A. BMI Classification Percentile And Cut Off Points. StatPearls Treasure Island (FL): StatPearls Publishing LLC; 2021.
26. IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.
27. Cohen J. (1988). *Statistical Power Analysis for the Behavioral Sciences*, 2nd Ed. Hillsdale, NJ: Laurence Erlbaum Associates
28. Voigt M, Rochow N, Guthmann F, et al. Birth weight percentile values for girls and boys under consideration of maternal height. *Z Geburtshilfe Neonatol.* 2012;216(5):212–219.

29. Agarwal P, Rajadurai VS, Yap F, et al. Comparison of customized and cohort-based birthweight standards in identification of growth-restricted infants in GUSTO cohort study. *J Matern Fetal Neonat Med*. 2015;29(15): 1–22.
30. Anderson NH, Sadler LC, Stewart AW, et al. Maternal and pathological pregnancy characteristics in customised birthweight centiles and identification of at-risk small-for-gestational-age infants: a retrospective cohort study. *BJOG*. 2012;119(7):848–856.
31. Clausson B, Gardosi J, Francis A, et al. Perinatal outcome in SGA births defined by customised versus population-based birthweight standards. *BJOG*. 2001; 108(8):830–834.
32. Gardosi J, Francis A, Turner S, et al. Customized growth charts: rationale, validation and clinical benefits. *Am J Obstet Gynecol*. 2018;218(2S):S609–S618.
33. Sovio U, Smith GCS. The effect of customization and use of a fetal growth standard on the association between birthweight percentile and adverse perinatal outcome. *Am J Obstet Gynecol*. 2018;218(2): S738–S744.
34. Voigt M, Rochow N, Landau-Crangle E, Meyer-Kahrweg LM, Olbertz DM, Kunze M, Nikischin W, Wittwer-Backofen U, Rochow M, Däbritz J, Hentschel R. Individualized sex-specific birth weight percentiles for gestational age based on maternal height and weight. *J Perinat Med*. 2020 Aug 31;49(1):94-103. doi: 10.1515/jpm-2020-0119. PMID: 32866126.
35. Griffiths LJ, Dezateux C, Cole TJ. Differential parental weight and height contributions to offspring birth-weight and weight gain in infancy. *Int J Epidemiol*. 2007;36(1):104–107.
36. Pomeroy E, Wells JC, Cole TJ, et al. Relationships of maternal and paternal anthropometry with neonatal body size, proportions and adiposity in an Australian cohort. *Am J Phys Anthropol*. 2015;156(4):625–636.
37. Sharma D, Sharma P, Shastri S. Genetic, metabolic and endocrine aspect of intrauterine growth restriction: an update. *J Matern Fetal Neonatal Med*. 2017 Oct;30(19):2263-2275. doi: 10.1080/14767058.2016.1245285. Epub 2016 Oct 26. PMID: 27718783.
38. Sharma D, Shastri S, Sharma P. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. *Clin Med Insights Pediatr*. 2016 Jul 14;10:67-83. doi: 10.4137/CMPed.S40070. PMID: 27441006; PMCID: PMC4946587.

TABLES AND FIGURES

Figure 1. Flow-chart of selected cases.



* Records with missing data on: foetal gender, birthweight, maternal height, weight before pregnancy, parity, gestational age, SGA (classified by the Dutch Birthweight chart), LGA (classified by the Dutch Birthweight chart), SAPO and smoking.

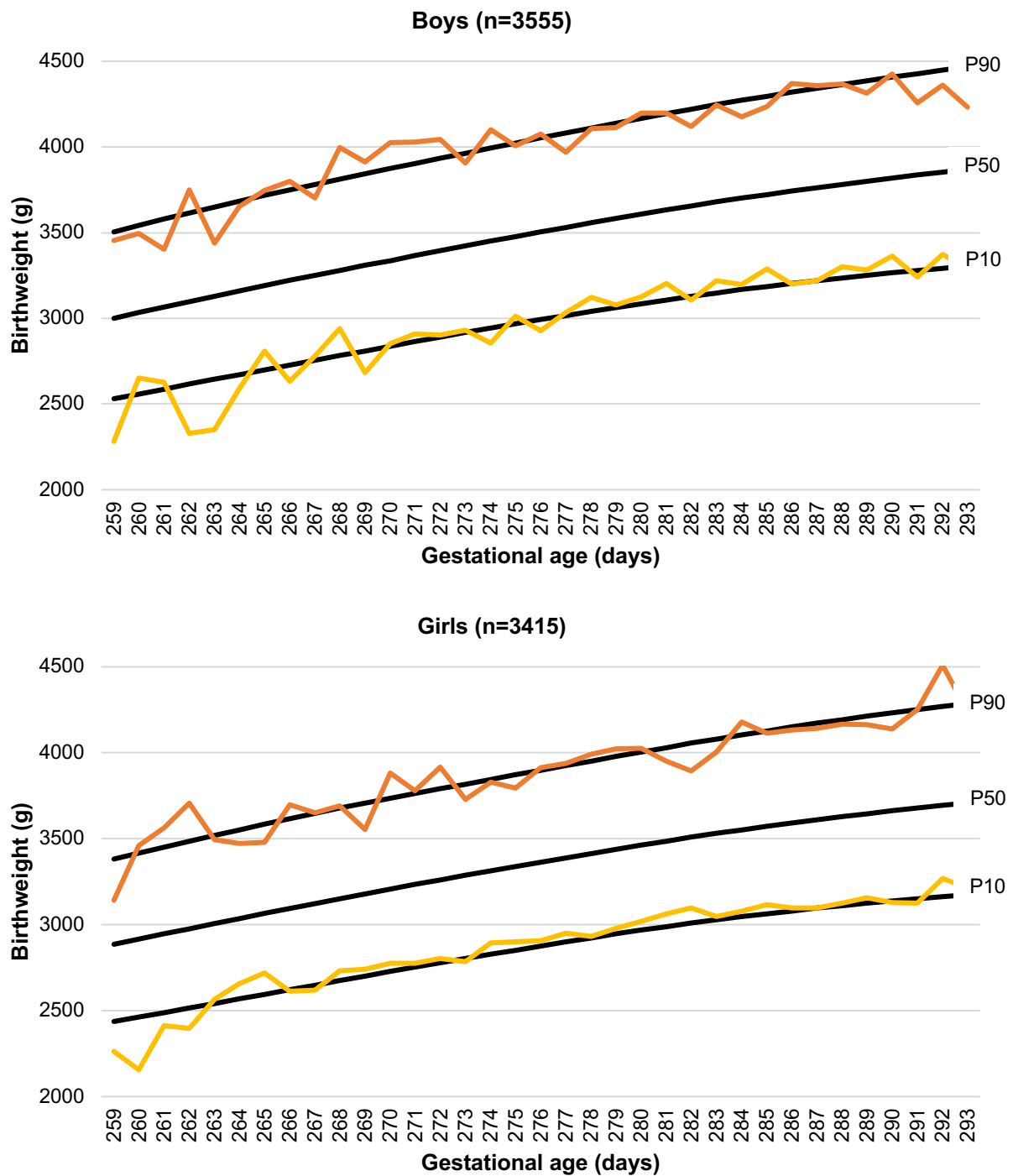
Table 1. Baseline characteristics of the study population.

	At term singleton births	
	Total sample (n=12,017)	Healthy subsample of pregnant women with normal BMI and non-smoking (n=7039)
Maternal characteristics		
Age, years (mean)	30.8 (SD 4.4)	31.2 (SD 4.1)
Height, cm (mean)	169.6 (SD 6.8)	170.1 (SD 6.8)
Height category, cm		
≤ 152	90 (0.7%)	44 (0.6%)
153-157	353 (2.9%)	184 (2.6%)
158-162	1255 (10.4%)	645 (9.2%)
163-167	2498 (20.8%)	1387 (19.2%)
168-172	3752 (31.2%)	2244 (31.9%)
173-177	2452 (20.4%)	1499 (21.3%)
178-182	1264 (10.5%)	805 (11.4%)
183-187	315 (2.6%)	206 (2.9%)
≥ 188	38 (0.3%)	25 (0.4%)
Weight, kg (mean)	68.8 (SD 13.1)	63.4 (SD 6.8)
BMI, kg/m ² (mean)	23.9 (SD 4.2)	21.9 (SD 1.7)
BMI category, kg/m ²		
<18.5	392 (3.3%)	-
18.5-24.9	8027 (66.8%)	7039 (100.0%)
25.0-29.9	2517 (20.9%)	-
30.0-34.9	806 (6.7%)	-
35.0-39.9	245 (2.0%)	-
≥40.0	30 (0.2%)	-
Smoking		
Yes	1676 (13.9%)	-
No	10,341 (86.1%)	7039 (100.0%)
Ethnicity		
Dutch	9029 (75.2%)	5361 (76.2%)
Turkish	265 (2.2%)	125 (1.8%)
Moroccan	223 (1.9%)	122 (1.6%)
Surinam	61 (0.5%)	20 (0.3%)
Antillean/Aruban	17 (0.1%)	7 (0.1%)
African	164 (1.4%)	67 (1.0%)
North-African	169 (1.4%)	78 (1.1%)
Asian	392 (3.3%)	255 (3.6%)
Middle Eastern	53 (0.4%)	30 (0.4%)
Other Non-Western	144 (1.2%)	77 (1.1%)
Other Western	1240 (10.3%)	788 (11.2%)
Other	109 (0.9%)	48 (0.7%)
Creole	76 (0.6%)	26 (0.4%)
Hindustan	68 (0.6%)	40 (0.6%)
Missing	7	5
Education		
None	72 (0.6%)	17 (0.2%)
Elementary school	153 (1.3%)	59 (0.8%)
LBO	169 (1.4%)	59 (0.8%)
MAVO	776 (6.5%)	273 (3.9%)
MBO	3728 (31.3%)	1702 (24.4%)
HAVO/VWO	502 (4.2%)	260 (3.7%)
HBO	3823 (32.1%)	2540 (36.4%)
University	2670 (22.4%)	2069 (29.6%)
Missing	124	60
Gestational characteristics		
Parity		
Nulliparous women	5705 (47.5%)	3391 (48.2%)
Multiparous women	6312 (52.5%)	3648 (51.8%)
Gestational age		
Week 37	689 (5.7%)	351 (5.0%)
Week 38	1840 (15.3%)	975 (13.9%)
Week 39	3309 (27.5%)	1963 (27.9%)
Week 40	3872 (32.2%)	2350 (33.4%)
Week 41	2307 (19.2%)	1400 (19.9%)
Neonatal characteristics		
Gender		
Male	6100 (50.8%)	3590 (51.0%)
Female	5917 (49.2%)	3449 (49.0%)
Birthweight, g (mean)	3523 (SD 458)	3525 (SD 446)
Birthweight, g (mean)		
Week 37	3056 (SD 426)	3032 (SD 399)
Week 38	3322 (SD 433)	3310 (SD 419)
Week 39	3458 (SD 417)	3452 (SD 405)
Week 40	3624 (SD 416)	3622 (SD 409)
Week 41	3747 (SD 425)	3740 (SD 405)
SGA <p10	7.8%*	7.4%*/7.2%**
LGA >p90	10.8%*	9.5%*
SAPO	1.3%	1.1%

* Classified using the Dutch Birthweight chart (15)

** Percentage in the healthy subsample of pregnant women with normal BMI and non-smoking

Figure 2. Description of birthweight percentiles by gender*.



* Black lines; Dutch Birthweight chart (p10, p50 and p90), orange lines; birthweight p90 in subsample of non-smoking women with a normal BMI, yellow lines; birthweight p10 in subsample of non-smoking women with a normal BMI.

Figure 3. Incidences of SGA (<p10), LGA (p>90) and SAPO in different maternal height categories.

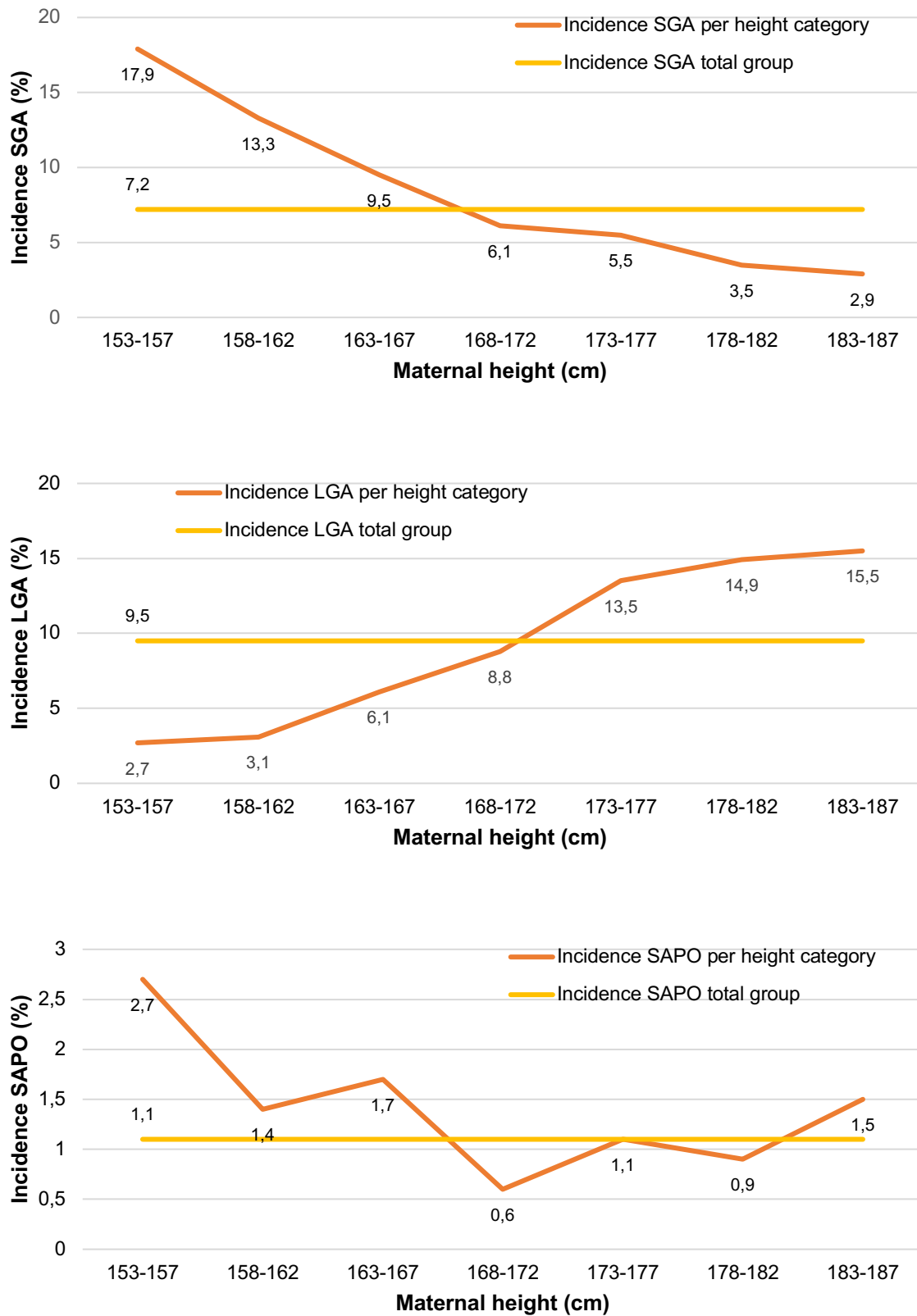
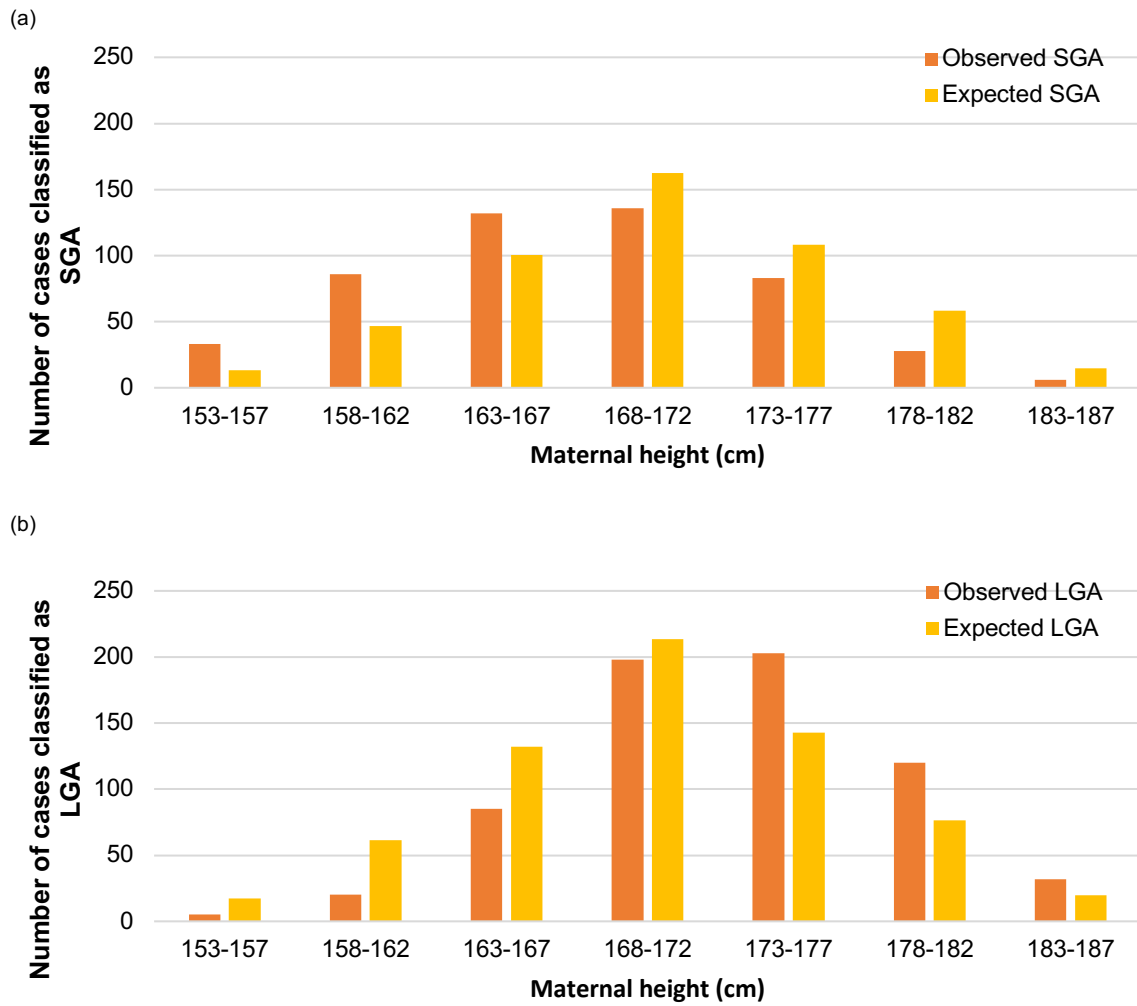


Figure 4. Differences in classification of neonates as SGA, LGA and cases with SAPO (n=6970).



(a) Observed number of cases classified as SGA ($<p10$) using the Dutch Birthweight chart (incidence 7.2%). Calculated number in case reference stratified by maternal height category (7.2% of cases classified as SGA per stratum).

(b) Observed number of cases classified as LGA ($<p10$) using the Dutch Birthweight chart (incidence 9.5%). Calculated number in case reference stratified by maternal height category (9.5% of cases classified as LGA per stratum).