Estimated fetal weight percentiles and kindergarten-age child development: evaluating the predictive ability of the INTERGROWTH-21st and WHO fetal growth charts a cohort study

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Abstract

Objectives: To estimate the association between estimated fetal weight (EFW) percentiles on the INTERGROWTH-21st and WHO fetal growth charts and kindergarten-age childhood development, and identify the charts' percentile cut-offs that best predict kindergarten-age developmental challenges. Design: Retrospective cohort linkage study. Setting: Obstetrical ultrasound department of BC Women's Hospital, Vancouver, Canada. Population or Sample: Non-anomalous, singleton fetuses scanned [?] 28 weeks' gestation, 2000-2011 (n=3418). Methods: We classified EFWs into percentiles using the INTERGROWTH-21st and WHO charts. We used generalized additive modelling to link EFW percentile with routine province-wide kindergarten readiness test results. We calculated the AUC, as well as other measures of diagnostic accuracy with 95% confidence intervals (CI) at select percentile cut-points of the charts. Main Outcome Measures: Total Early Development Instrument (EDI) score (/50). Secondary outcomes: EDI sub-domain scores for language and cognitive development, and for communication skills and general knowledge; designation of 'developmentally vulnerable' or 'special needs'. Results: Fetuses with lower EFW percentiles had systematically lower EDI scores and increased risks of developmental vulnerability. However, the clinical significance of differences was modest in magnitude: e.g., total EDI score -2.8 [95% CI: -5.1, -0.5] in children with an EFW 3-9th percentile of INTERGROWTH chart (vs. reference of 31-90th). The charts' predictive abilities for adverse child development were limited (e.g., AUC<0.53 for both charts). Conclusions: Lower EFW percentiles on the INTERGROWTH-21st and WHO charts indicate increased risks of adverse kindergarten-age child development at the population level, but are not accurate individual-level predictors of adverse child development.

Introduction

The Society for Maternal-Fetal Medicine recommends that fetal growth restriction should be defined as an estimated fetal weight (EFW) or abdominal circumference below the 10th percentile of a population-based fetal growth reference. However, multiple population-based fetal growth references exist, and it is unclear which chart should be used. The fetal growth reference conventionally used in the United States, Hadlock's, was derived from a population of 392 predominantly middle-class white women who delivered over 30 years ago and has a number of methodological limitations. Although several new, high-quality population-based fetal growth charts that overcome the methodological limitations of existing charts have recently been published, such as the WHO fetal growth chart and the INTERGROWTH-21st fetal growth chart, research to date has yet to convincingly identify which chart- and which percentile cut-off on the chart- best predicts high-risk infants.

Most studies have focused on evaluating the new fetal growth charts in relation to neonatal health outcomes such as small-for-gestational age birth and adverse perinatal outcomes. However, fetal growth restriction also has longer-term consequences, and children with fetal growth restriction are also more likely to experience school-age developmental deficits than their normally-grown peers. While decisions about timing of delivery are likely to be made based on more immediate perinatal risks and outcomes, determination of which chart to use, and optimal thresholds on the charts, should also take these longer-term outcomes, which are important families, into account.

The goals of this study were to 1) estimate the association between estimated fetal weight percentiles on the INTERGROWTH-21st and WHO fetal growth charts and kindergarten-age childhood development, and 2) establish the percentile cut-offs on the INTERGROWTH-21st and WHO fetal growth charts that best identify fetuses at risk for developmental challenges at kindergarten age.

Methods :

Study population

We conducted a retrospective cohort study of non-anomalous, singleton fetuses receiving an outpatient obstetrical ultrasound between 28 weeks, 0 days and 41 weeks, 6 days gestational age at the British Columbia (BC) Women's Hospital, Vancouver, British Columbia, Canada between April 1 2000 to March 31 2011. BC Women's Hospital is a tertiary care teaching hospital of the University of British Columbia. It is the primary fetal and children's referral centre for the province of British Columbia, with an annual delivery volume of approximately 7000 births. Ultrasound records were linked with British Columbia population-level health and education databases, including the BC Perinatal Data Registry, which contains abstracted obstetrical and neonatal medical records for >99% of births in the province, and results from routine province-wide kindergarten readiness testing. We restricted our analytic cohort to fetuses with a valid estimate of fetal weight at or beyond 28 weeks' gestation, with no major anomalies (based on the US Center for Disease Control Definition of major anomalies). We obtained obstetrical and neonatal health outcomes for all births in British Columbia to help describe the source population from which our ultrasound cohort was drawn.

Estimated fetal weights

At the BC Women's Hospital, ultrasound assessment of fetal size is performed by sonographers certified in obstetrical ultrasound and verified by a Maternal Fetal Medicine or Radiology physician. Measurements are taken twice and the average of the two is used. The Hadlock3 formula, which combines head circumference, abdominal circumference, and femur length measurements was used to calculate estimated fetal weights. The most recent measurement before delivery was used. The accuracy of estimated fetal weights at our institution has previously been shown to be + 3.3% (SD 12.1), with 67% of fetuses having an estimated fetal weight within ±10% of their actual birthweight. Estimated fetal weights were converted into gestational age-specific percentiles using the previously published INTERGROWTH 21st and WHO standard. We used recommended methods to calculate exact percentiles for weights falling between published percentiles on the WHO chart.

Outcome

The Early Development Instrument (EDI) is a standardized assessment of early child development. The EDI is conducted in the latter half of the kindergarten year by a child's school teacher. It provides a holistic assessment of children's development through 104 questions across five domains: physical health and well-being, social competence, emotional maturity, language and cognitive development, and communication skills. The EDI has been shown to be psychometrically sound and a good predictor of adult health, education and social outcomes. In British Columbia, schools conduct the EDI in 3-year waves, so only approximately one third of children are tested in a given year.

Our primary outcome was the total EDI score (/50), and secondary outcomes included each of the two EDI sub-domain scores shown to be strongest predictors of later school performance - the language and cognitive development domain, and the communication skills and general knowledge domain – as well as the binary

indicators of 'developmental vulnerability' and a designation of 'special needs.' A child was considered to be developmental vulnerable if they had an EDI score that was equal to or lower than the score corresponding to the 10th percentile of all kindergarten children in one or more EDI sub-domain. 'Special needs' is a British Columbia Ministry of Education designation associated with allocation of additional funding to help cover the costs of additional staff, specialized learning materials, physical accommodations or equipment, and assessments to enable a student to meet their educational and social needs.

Statistical analysis

We summarized descriptive characteristics of the study cohort using means with standard deviations and frequencies with percentages. We calculated descriptive characteristics for all births in the province >28 weeks to help describe the source population from which our tertiary care cohort was drawn.

We estimated the relationship between fetal size percentiles and EDI score using generalized additive modelling, which allowed us to describe associations using smooth, non-linear patterns in risk. All models included age at testing (range 4 to 7 years, mean = 5.6 years) as a covariate. We then categorized estimated fetal weight into five categories (<3rd, 3-9th, 10-19th, 20-30th, 31st-90th), and compared EDI scores in each category with the reference category of 31-90th percentile using absolute mean differences with 95% confidence intervals. We repeated these calculations for the two EDI subdomains, and for our two binary outcomes (using generalized additive modelling and predicting risks and risk ratios for these). For comparative purposes, we calculated EDI scores for all other children in the province born at or beyond 28 weeks, overall and in gestation age categories of 28-33, 34-36, and 37-42 weeks.

To evaluate the charts' ability to predict developmental vulnerability at the individual level (i.e., discriminatory ability), we calculated the area under the receiver operating characteristic curve (AUC), as well as sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios with 95% confidence intervals at select percentile cut-points of the chart (3rd, 10th, 20th percentile). Because the 10th percentile of both charts classified considerably less than 10 percent of our population as small-for-gestational age, we additionally identified the percentile on each chart that corresponded to the 10th percentile weight in our cohort, and evaluated predictive ability at this cut-off. Optimal thresholds for low and high risk were established using Youden's Index.

Results

Study population

There were 10,366 births that underwent a prenatal ultrasound >28 weeks' gestation without major anomalies during our study period, of whom approximately one third (3,418) had available kindergarten-age Early Development Index scores (due to the three-year duration of testing waves across the province). Of these, 17 fetuses could not be assigned an estimated fetal weight using the WHO chart because their gestational age was beyond that covered by that chart.

As expected given the higher risk obstetrical population seen at our tertiary referal centre, our ultrasound population had a moderately higher risk profile than the overall British Columbia population. Women in our study population were slightly older at delivery (Mean 33 versus 30 years), more likely to be nulliparous, with slightly higher cesarean delivery rates and higher rates diabetes and hypertension (**Table 1**). Birthweights of babies our study cohort were also slightly lower. Median EDI scores were similar (41.7 in our study cohort; 41.5 in the BC population), as were rates of identified vulnerability on the EDI (29.8% study cohort; 29.7% general population). Our study cohort had slightly higher rates of special needs designation (3.9% versus 2.7%). As expected, developmental vulnerability and special needs designation was more common among infants born at younger gestational ages (**Table S1**).

Associations between EFW and kindergarten-age child development

For both the INTERGROWTH and WHO charts, estimated fetal weight percentile was positively associated with EDI scores, with lower median test scores and higher risks of developmental vulnerability among smaller

infants (**Figure 1**). However, the magnitude of the differences between smaller fetuses and those between the 31st to 90th percentile was generally modest (**Tables 2 and 3**). For example, children with an estimated fetal weight between the 31st to 90th centile of the INTERGROWTH chart had a mean EDI score of 40.6, while infants between the 3rd to 9th centile had a mean score of 37.8; a mean difference between the scores of only -2.8 [95% CI: -5.1, -0.5]. The most pronounced difference was observed among children who were <3rd percentile of the WHO chart, whose EDI scores were -4.7 [95% CI: -7.1,-2.3] lower than those with an EFW between the 31st and 90thpercentile.

The risks of developmental vulnerability were lowest among children with an EFW between the 31st and 90thpercentile (30.1% risk using the INTERGROWTH chart, 29.2% risk using the WHO chart). Risks were increased in lower EFW categories (e.g., 35-40% in categories <20th percentile of the INTERGROWTH chart, and 35-45% in categories<20th percentile of the WHO chart**, Tables 2 and 3**). Risk ratios for these differences were significantly different than the null for some, but not all of these lower percentile categories. Similar trends were observed for the two EDI subscales (**Figure S1**), and special needs designation (**Figure S2**), although small numbers for this latter outcome precluded firm conclusions.

Discriminatory ability

The ability of both charts to predict which fetuses would *vs*would not go on to develop developmentally vulnerability was poor (AUC of 53.0% for INTERGROWTH-21st; 52.8% for WHO; sensitivity of all cut-points < 67% [**Tables 4 and 5**]). For example, the 10th centile of the INTERGROWTH-21st had 3% sensitivity and 38% positive predictive value, while the 10th centile of the WHO chart had 6% sensitivity and 36% positive predictive value in identifying developmental vulnerability**.** It is noteworthy that the 10th percentile of both charts identified considerably less than 10 percent of our cohort as small-for-gestational age: 2.2% of our population was below the 10thpercentile of the INTERGROWTH-21st chart, and 4.9% was below the 10th percentile of the WHO chart. However, discriminatory ability at the percentile of the charts that classified 10 percent of our cohort as small-for-gestational age (the 33rd percentile of the INTERGROWTH chart, the 24th percentile of the WHO chart) was equally poor. The statistically-optimal threshold (i.e., that which maximizes both sensitivity and specificity, based on Youden's Index) was the 80th percentile of the INTERGROWTH-21st chart, and the 91stpercentile of the WHO chart.

Discussion

Principal findings

In this large, population-based linkage study of prenatal ultrasound findings with kindergarten child development testing, we found that estimated fetal weight percentiles were associated with child development test results, with lower scores and increased risks of developmental vulnerability among fetuses with lower EFW percentiles. However, the charts' value at predicting developmental vulnerability at the individual level (i.e., discriminatory ability) was limited, as evidenced by AUC of 53.0% for INTERGROWTH-21st; 52.8% for WHO and poor sensitivity across a range of cut-points.

Comparison with the literature

Results in the context of what is known

The literature on fetal growth and child cognitive development is highly heterogeneous in terms of how fetal growth restriction is defined (antenatal and/or postnatal) and how development is assessed (various measures of IQ and development are used); however, findings are consistent that infants with fetal growth restriction and/or small size are more likely to experience developmental challenges. Our finding that lower estimated fetal weight percentile is associated with greater developmental challenges is consistent with this literature. However, our study extends this work to move beyond population-level associations and evaluate the utility of estimated fetal weight charts as a clinical prediction tool, by examining measures such as sensitivity, specificity, positive predictive value, and negative predictive value. Our analyses highlight that, despite the population-level associations, EFW percentiles have limited ability as a tool to predict which specific children will go on to be developmentally vulnerable.

The magnitude of the association between EFW and developmental vulnerability observed in our study can be contextualized by comparing it to the effects of other determinants of developmental vulnerability. The link between low EFW percentile observed in our study (RR= 1.15 [95%CI: 0.65 to 1.86) and 1.49 [95%CI: 1.00 to 2.12] for fetuses <3rd percentile using the INTERGROWTH and WHO charts, respectively) are within the range of the magnitudes of increased risk associated with being born at late preterm gestation: Guthridge et al. found a two-fold increase of EDI developmental vulnerability in infants born between 34 and 36 weeks' gestation (OR= 2.08 [95%CI: 1.27 to 3.39]), while Bentley et al. likewise found that EDI developmental vulnerability increased as gestational age decreased: 26% higher risks [95% CI: 1.18 to 1.34] at 34-36 weeks' gestation compared with those born at 40 weeks.

Guthridge et al. found that a 5 minute Apgar <7 was associated with an 18% increased risk of developmental vulnerability on the EDI test [95% CI 0.46 to 3.01] whereas Razaz et al. reported that infants with 5-minute Apgar scores of 5,6,7, or 8 had increases in risk of EDI developmental vulnerability ranging from risk ratios of 1.1 to 1.5, compared with those with a 5-minute Apgar score of 10.

With regards to socio-economic factors, Guthridge et al found a two-fold increase of developmental vulnerability in infants of care-givers with 9 years or less of education [2.16 [95% CI: 1.40-3.33]). Likewise, Chittleborough et al. found that the most important early-life risks factors for developmental vulnerability at kindergarten age were socio-economic in nature (mother's age, mother's marital status, mother's occupation, father's occupation, number of previous pregnancies and smoking in the second half of pregnancy). Thus while risks of adverse child developmental outcomes are increased with lower EFW percentiles, they do not appear to be a dominant influence.

Not surprisingly, the association between low EFW percentile and developmental vulnerability is markedly lower than the association between low EFW and adverse neonatal outcomes. In previous work from this cohort of fetuses, we found that fetuses with an EFW less than the 10th centile were 3.1 fold more likely to have perinatal morbidity/mortality compared with fetuses between the 10th and 90th centile on the IG and WHO charts. However, this work, as well as that of others, also found that the charts have a poor ability to predict adverse outcomes at the individual level (i.e., poor sensitivity, specificity, and low AUC).

Strengths and Limitations

An important strength of our study was the linkage of our prenatal ultrasound cohort to population-based follow-up data. This enabled us to obtain longer-term child health outcome information without differential losses to follow-up, a common concern with prospectively-collected follow-up methods. This also enabled us to compare characteristics and outcomes in this higher-risk cohort (i.e., with an indication for third trimester prenatal ultrasound) to that of the general population. Our use of the Early Development Instrument, a validated indicator of kindergarten readiness and developmental vulnerability used in multiple jurisdictions worldwide, is also a strength as it enables our findings to be contextualized within a large body of literature on other risk factors for adverse child development.

Limitations of our study include the lack of EDI test results for a large fraction of the cohort. However, as these data are missing due to administrative reasons (the 3-year duration of testing waves across the province), this is unlikely to have introduced bias to our study. It did reduce our sample size, but our cohort of over 3400 children is still one of the largest studies of school-aged outcomes following prenatal ultrasound available. Our studied examined small fetal size (small for gestational age [SGA]), which is recognized to be a flawed indicator of the true pathological process of interest, fetal growth restriction. However, as fetal weight percentiles are widely used to screen for high-risk fetuses clinically, our evaluation of the predictive ability of SGA status provides pragmatic information on a commonly-used tool for clinical care.

Conclusions

This study found that although, on average, lower EFW percentiles on the INTERGROWTH-21st and WHO population fetal growth references are associated with increased risks of adverse child neurodevelopment at kindergarten age, they are not accurate individual-level predictors of adverse child development, across a

broad range of possible percentile cut-points. Our findings support recent calls to shift away from the reliance on fetal size percentiles for identifying growth restriction, and adopt a more comprehensive, multi-faceted approach to risk assessment.

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Disclosure of Interests

The authors declare that they have no competing interests. All inferences, opinions, and conclusions drawn in this study are those of the authors, and do not reflect the opinions or policies of the Data Steward(s).

Contribution to Authorship

AF contributed to the conception, planning, and carrying out of this work, and wrote the original draft of this manuscript. JL contributed to the conception, planning, and carrying out of this work, and wrote the original draft of this manuscript. CM contributed to the conception, planning, carrying out of this work, and reviewing the manuscript. AA contributed to the data analysis, carrying out of this work, and reviewing the manuscript. JAH contributed to the conception, planning, carrying out of this work, supervising data analysis, and reviewing the manuscript. All authors accept responsibility for the paper as published. The author(s) read and approved the final manuscript.

Details of Ethics Approval

This study was approved by the University of British Columbia/BC Children's & Women's Hospital Research Ethics Board, Certificate # H17–00798. This Research Ethics Board waived the requirement for consent from individual participants, under guidelines found here: https://ethics.research.ubc.ca/ore/ubc-clinical-research-ethics-general-guidance-notes. This study was conducted in accordance with the relevant guidelines and regulations of the Declaration of Helsinki.

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Figure 1. Association between estimated fetal weight percentiles as assigned by a) the INTERGROWTH-21st fetal growth chart, and b) the WHO fetal growth chart and kindergarten-age Early Development Index scores among 3,418 children with an ultrasound >28 weeks at the BC Women's Hospital, Vancouver, Canada, 2000-2011.

APPENDIX

Figure S1. Association between estimated fetal weight percentiles as assigned by a) the INTERGROWTH-21st fetal growth chart, and b) the WHO fetal growth chart and kindergarten-age Early Development Index Communication & General Knowledge and Language and Cognitive Development sub-scale scores among 3,418 children with an ultrasound >28 weeks at the BC Women's Hospital, Vancouver, Canada, 2000-2011.

Figure S2. Developmental vulnerability and Special Needs Designation by EFW centile by the a) the INTERGROWTH-21st fetal growth chart, and b) the WHO fetal growth chart among 3,418 children with an ultrasound >28 weeks at the BC Women's Hospital, Vancouver, Canada, 2000-2011.

Table S1. Early Development Index scores among 3,418 children with an ultrasound >28 weeks at the BC Women's Hospital, Vancouver, Canada, 2000-2011, by gestational age at birth.

References

Table 1. Descriptive characteristics of 3,418 children who underwent a prenatal ultrasound >28 weeks' gestation with available kindergarten-age Early Development Index scores, in British Columbia, April 1, 2000 to March 31, 2011

	Total Ultrasound Cohort Mean ± SD or n(%)	**Total British Col**
N	3,418	154,986
Maternal age (years)	32.7 ±5.4	30.1 ±5.6
Nulliparous	1,708 (50.0%)	70,247 (45.3%)
Type of labour induced	883 (25.8%)	33,287 (21.5%)
none	621 (18.2%)	19,648 (12.7%)
spontaneous	1,914 (56.0%)	102,050 (65.8%)
Mode of delivery elective CS	445 (13.0%)	16,594 (10.7%)
emergency CS	785 (23.0%)	27,456 (17.8%)
spontaneous vaginal	1,791 (52.4%)	94,446 (60.9%)
operative vaginal	397 (11.6%)	16,482 (10.6%)
GA at delivery (completed weeks)	38.1 ±2.3	38.9 ±1.7
Female	1,714 (50.1%)	75,590 (48.8%)
Birth weight (g)	3244.8 ±623.0	3455.7 ±520.3
APGAR at 5 minutes <7	27 (0.8%)	1,851 (1.2%)
EDI total score Median (IQR)	41.7 (35.5 - 46.3)	41.5 (35.5 - 46.1)
Bottom 10% of one or more EDI subscales	1,018 (29.8%)	46,104 (29.7%)
Designated Special Needs	135 (3.9%)	4,142 (2.7%)

Table 2. Kindergarten-age Early Development Index scores according to estimated fetal weight percentiles of the INTERGROWTH-21st fetal growth chart among 3,418 children with an ultrasound >28 weeks at the BC Women's Hospital, Vancouver, Canada, 2000-2011.

Outcome	**INTERGROWTH-21st EFW percentile**
	<3
N (%)	28 (0.8)
EDI Total Score, Mean (/50)	39.8
Mean Difference in EDI Total score [95% CI]	-0.9 [-3.8, 2.1]
Developmental vulnerability[a] n (%)	10 (35.7)
Risk ratio for developmental vulnerability [95% CI]	1.15 [0.65, 1.86]
Language & Cognitive Development score (/10)	8.1
Mean Difference in Language score [95% CI]	-1.1 [-4.1, 1.9]

Outcome	**INTERGROWTH-21st EFW percentile**
Communication & General Knowledge score (/10)	7.4
Mean Difference in Communication score [95% CI]	-0.2 [-1.4, 1.1]
Special Needs Designation n (%)	<5
Risk ratio for Special Needs Designation [95% CI]	2.2 [0.37, 6.82]
[a]<10th percentile on one or more subscale	[a]<10th percentile on one or more subscale
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Table 3. Kindergarten-age Early Development Index scores according to estimated fetal weight percentiles of the WHO fetal growth chart among 3,401 children with an ultrasound >28 weeks at the BC Women's Hospital, Vancouver, Canada, 2000-2011.

Outcome	**WHO chart EFW percentile [N=3,401)**	**WHO chart EFW percentile [N=3,401)**	**WHO chart EFW percentile [N=3,401)**	**WHO chart EFW percentile [N=3,401)**	**WHO chart EFW percentile [N=3,401)**
	<3	**3-9**	**10-19th**	**20-30th**	**31st -90th**
N (%)	43 (1.3)	125 (3.7)	120 (3.5)	167 (4.9)	1,673 (48.9)
EDI Total score (/50)	36.1	40.2	38.7	39.5	40.8
Mean Difference in EDI Total score [95% CI]	-4.7 [-7.1, -2.3]	-0.6 [-2.0, 0.8]	-2.1 [-3.5, -0.6]	-1.3 [-2.6, -0.1]	*reference*
Developmental vulnerability[a] n (%)	20 (46.5)	41 (32.8)	43 (35.8)	58 (34.7)	489 (29.2)
Risk ratio for developmental vulnerability [95% CI]	1.49 [1.00, 2.12]	1.13 [0.86, 1.47]	1.30 [0.99, 1.67]	1.21 [0.96, 1.51]	*reference*
Language & Cognitive Development score (/10)	7.5	9.1	9.0	8.3	9.0
Mean Difference in Language score [95% CI]	-1.5 [-3.7, 0.6]	0.08 [-1.2, 1.4]	-0.05 [-1.4, 1.3]	-0.7 [-1.8, 0.4]	*reference*
Communication & General Knowledge score (/10)	6.2	7.9	6.7	7.2	7.6
Mean Difference in Communication score [95% CI]	-1.4 [-2.4, -0.4]	0.3 [-0.3, 0.9]	-0.9 [-1.5, -0.3]	-0.4 [-1.0, 0.1]	*reference*
Special Needs Designation n (%)	5 (11.6)	7 (5.6)	9 (7.5)	7 (4.2)	50 (3.0)

Outcome	**WHO chart EFW percentile [N=3,401)**	**WHO chart EFW percentile [N=3,401)**	**WHO chart EFW percentile [N=3,401)**	**WHO chart EFW percentile [N=3,401)**	**WHO chart EFW percentile [N=3,401)**
Risk ratio for Special Needs Designation [95% CI]	4.44 [1.59, 9.97]	1.81 [0.77, 3.69]	2.31 [1.08, 4.42]	1.42 [0.60, 2.89]	*reference*
[a]<10th percentile on one or more subscale	[a]<10th percentile on one or more subscale	[a]<10th percentile on one or more subscale	[a]<10th percentile on one or more subscale	[a]<10th percentile on one or more subscale	[a]<10th percentile on one or more subscale

Table 4 . Discriminatory ability of select INTERGROWTH-21st fetal growth chart percentiles in identifying kindergarten age developmental vulnerability [bottom 10% of one or more Early Development Index subscales) among 3,418 children with an ultrasound >28 weeks at the BC Women's Hospital, Vancouver, Canada, 2000-2011.

Cut point (EFW percentile)	Study population defined as high risk by cut-point, n(%)	Sensitivity, % [95% CI)	Specificity [95% CI)	Positive predictive value [95% CI)	Negative predictive value [95% CI)	Positive likelihood ratio [95% CI)	Negative likelihood ratio [95% CI)
3	28 (0.8)	1 [0, 2]	99 [99, 100]	36 [19, 56]	70 [69, 72]	1.31 [0.61, 2.83]	1.00 [0.99, 1.00]
10	74 (2.2)	3 [2, 4]	98 [97, 99]	38 [27, 50]	70 [69, 72]	1.44 [0.90, 2.28]	0.99 [0.98, 1.00]
20	175 (5.1)	7 [5, 8]	96 [95, 96]	39 [32, 47]	71 [69, 72]	1.53 [1.14, 2.06]	0.98 [0.96, 0.99]
33[a]	331 (9.7)	11 [10, 14]	91 [90, 92]	35 [30, 41]	71 [69, 72]	1.29 [1.04, 1.60]	0.97 [0.95, 1.00]
80[b]	1,560 (45.6)	49 [46, 52]	56 [54, 58]	32 [30, 34]	72 [70, 74]	1.12 [1.03, 1.20]	0.91 [0.85, 0.97]

[a]percentile that identifies 10% of the cohort as high risk

[b]percentile that maximizes sensitivity and specificity using Youden's Index

Table 5 . Discriminatory ability of select WHO fetal growth chart percentiles in identifying kindergarten age developmental vulnerability [bottom 10% of one or more Early Development Index subscales) among 3,401 children with an ultrasound >28 weeks at the BC Women's Hospital, Vancouver, Canada, 2000-2011.Absolute risks of bottom 10% of one or more EDI subscales and test performance associated with WHO percentiles.

Cut point (EFW percentile)	Study population defined as high risk by cut-point, n(%)	Sensitivity, % [95% CI)	Specificity [95% CI)	Positive predictive value [95% CI)	Negative predictive value [95% CI)	Positive likelihood ratio [95% CI)	Negative likelihood ratio [95% CI)
3	43 (1.3)	2 [1, 3]	99 [99, 99]	47 [31, 62]	70 [69, 72]	2.04 [01.13, 3.71]	0.99 [0.98, 1.00]
10	168 (4.9)	6 [5, 8)	96 [95, 96]	36 [29, 44]	70 [69, 72]	1.34 [0.99, 1.82]	0.98 [0.97, 1.00]
20	288 (8.5)	10 [8, 12]	92 [91, 93]	36 [31, 42]	71 [69, 72]	1.33 [1.06, 1.67]	0.97 [0.95, 1.00]
24[a]	338 (9.9)	12 [10, 14]	91 [90, 92]	36 [30, 41]	71 [69, 72]	1.29 [1.05, 1.60]	0.97 [0.95, 1.00]
91[b]	2,204 (64.8)	67 [64, 70]	36 [34, 38]	31 [29, 33]	72 [69, 74]	1.04 [0.99, 1.10]	0.93 [0.84, 1.03]

[a]percentile that identifies 10% of the cohort as high risk

[b]percentile that maximizes sensitivity and specificity using Youden's Index

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