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## New birthweight percentiles by sex and gestational age in Southern China and its comparison with the INTERGROWTH-21st Standard

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We first showed the sex- and gestational age (week)-specific birthweight distributions from primiparous and multiparous mothers. Birthweight percentiles were created by using the Lambda Mu Sigma (LMS) method. We established the birthweight percentiles in Southern China and provide clinicians and researchers with up-to-date population norms of birthweight percentiles. Then we use the data from Birth Certificate System between Jan 1st, 2017 and Oct 31st, 2017, which included 1,245,364 live births to calculate SGA and LGA ratio by these three birthweight references- the new INTERGROWTH-21st standard, China's 2015 research standard and our birthweight percentiles. The overall prevalence of SGA estimated by our standards, the China's 2015 research standards and INTERGROWTH-21st standards, were 10.21%, 12.93% and 7.98%, respectively, whereas the overall prevalence of LGA was 9.88%, 4.48% and 8.37%, respectively.

Neonatal birthweight has been an important indicator of common concern in obstetrics and neonatology. This factor is critical for the study of adverse pregnancy outcomes and the prediction of neonatal mortality and morbidity. Extreme (large or small) neonatal birthweight increase the risks of diseases in adulthood<sup>1,2</sup>. The birthweight percentile is used to monitor the clinical measurement within the population value of the individual within the range. Infants who are SGA or LGA, are commonly defined as below the 10th or above the 90th centiles according to the birthweight percentile reference standard<sup>3,4</sup>. Brazil, India, Korea, Canada, United States, Japan, and Australia have published studies for assessing birthweight for gestational age (week)<sup>5-11</sup>. Nowadays, INTERGROWTH-21st reported a new global newborn birthweight standard, and attempted to define an international birthweight standard in the context of optimal maternal health and fetal growth<sup>12</sup>.

In our analysis, we first showed the sex- and gestational age (week)-specific birthweight distributions for primiparous and multiparous mothers separately. Using the birth certificate data in 2017, the SGA ratio and the LGA ratio obtained through the standards' 10th and 90th percentile values. Standards included the new INTERGROWTH-21st standard and China's 2015 research standard then we compare the ratios. In China, the Chinese newborn collaboration network also produced a newborn birthweight standard in 2015<sup>13</sup>. Since birthweight may differ by race and ethnicity, and there have been increasing number of older and multiparous mothers after the general implementation of two-child policy in China since 2016, the birthweight standard may change and the outdated classification of infants as SGA or LGA may not be accurately defined. This paper is to establish our birthweight standard in Guangdong province in Southern China and study up-to-date birthweight changes and abnormal birthweight risk factors.

### Materials and Methods

All birth data were obtained from the Guangdong Provincial Birth Certificate System, about 1900 medical institutions, which collected all information about infants who were admitted to medical institutions accredited to midwifery in Guangdong Province. After the birth, maternity medical workers would bare the baby on the electronic scales, read the stable weight data, weighing accuracy is 1 g; on the other hand, health care attendants

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| GA<br>(weeks) | Male babies smoothed percentiles |      |      |      |      |      |      |      |       |      |     | Female babies smoothed percentiles |      |      |      |      |      |      |      |       |      |     |
|---------------|----------------------------------|------|------|------|------|------|------|------|-------|------|-----|------------------------------------|------|------|------|------|------|------|------|-------|------|-----|
|               | N                                | C3   | C10  | C25  | C50  | C75  | C90  | C97  | L     | M    | S   | N                                  | C3   | C10  | C25  | C50  | C75  | C90  | C97  | L     | M    | S   |
| 25            | 64                               | 555  | 632  | 700  | 772  | 848  | 926  | 1022 | -0.26 | 772  | 326 | 23                                 | 635  | 705  | 768  | 834  | 903  | 972  | 1054 | -0.23 | 834  | 153 |
| 26            | 228                              | 634  | 715  | 787  | 862  | 940  | 1022 | 1124 | -0.28 | 862  | 459 | 107                                | 694  | 776  | 850  | 929  | 1011 | 1095 | 1197 | -0.26 | 929  | 654 |
| 27            | 572                              | 722  | 810  | 887  | 967  | 1052 | 1140 | 1251 | -0.33 | 967  | 137 | 310                                | 757  | 855  | 942  | 1035 | 1133 | 1236 | 1367 | -0.35 | 1035 | 544 |
| 28            | 1273                             | 810  | 911  | 1000 | 1092 | 1189 | 1291 | 1422 | -0.37 | 1092 | 365 | 790                                | 826  | 943  | 1047 | 1157 | 1275 | 1402 | 1571 | 0.14  | 1157 | 358 |
| 29            | 1698                             | 889  | 1011 | 1117 | 1228 | 1344 | 1468 | 1630 | -0.29 | 1228 | 289 | 1118                               | 900  | 1040 | 1163 | 1293 | 1433 | 1589 | 1805 | 0.15  | 1293 | 408 |
| 30            | 2626                             | 966  | 1110 | 1234 | 1363 | 1499 | 1646 | 1839 | -0.28 | 1363 | 309 | 1670                               | 981  | 1147 | 1289 | 1437 | 1599 | 1781 | 2037 | 0.09  | 1437 | 321 |
| 31            | 3795                             | 1058 | 1223 | 1365 | 1512 | 1668 | 1835 | 2056 | 0.17  | 1512 | 305 | 2328                               | 1087 | 1273 | 1433 | 1599 | 1777 | 1976 | 2253 | 0.16  | 1599 | 346 |
| 32            | 5605                             | 1181 | 1366 | 1525 | 1689 | 1862 | 2047 | 2289 | -0.13 | 1689 | 306 | 3750                               | 1223 | 1427 | 1602 | 1784 | 1977 | 2186 | 2465 | -0.15 | 1784 | 338 |
| 33            | 8513                             | 1326 | 1528 | 1702 | 1882 | 2070 | 2270 | 2526 | -0.08 | 1882 | 346 | 5726                               | 1385 | 1601 | 1790 | 1986 | 2191 | 2408 | 2685 | -0.10 | 1986 | 338 |
| 34            | 15824                            | 1477 | 1695 | 1883 | 2078 | 2280 | 2492 | 2760 | 0.06  | 2078 | 336 | 11030                              | 1569 | 1796 | 1995 | 2204 | 2420 | 2644 | 2920 | 0.08  | 2204 | 359 |
| 35            | 28548                            | 1659 | 1888 | 2087 | 2294 | 2507 | 2728 | 3000 | 0.12  | 2294 | 360 | 20166                              | 1768 | 2001 | 2208 | 2426 | 2651 | 2881 | 3158 | 0.11  | 2426 | 363 |
| 36            | 66292                            | 1849 | 2085 | 2295 | 2513 | 2737 | 2966 | 3240 | 0.18  | 2513 | 367 | 46054                              | 1980 | 2209 | 2418 | 2641 | 2872 | 3107 | 3387 | 0.13  | 2641 | 372 |
| 37            | 239695                           | 2068 | 2303 | 2517 | 2744 | 2978 | 3213 | 3490 | 0.16  | 2744 | 366 | 165833                             | 2214 | 2431 | 2635 | 2859 | 3094 | 3331 | 3609 | 0.16  | 2859 | 369 |
| 38            | 621082                           | 2319 | 2540 | 2750 | 2979 | 3217 | 3455 | 3730 | 0.15  | 2979 | 367 | 474002                             | 2399 | 2602 | 2800 | 3022 | 3257 | 3492 | 3762 | 0.14  | 3022 | 361 |
| 39            | 849913                           | 2504 | 2713 | 2918 | 3147 | 3388 | 3627 | 3897 | 0.15  | 3147 | 372 | 751125                             | 2510 | 2708 | 2907 | 3132 | 3372 | 3610 | 3878 | 0.33  | 3132 | 362 |
| 40            | 709857                           | 2610 | 2818 | 3025 | 3260 | 3507 | 3750 | 4018 | 0.14  | 3260 | 383 | 688392                             | 2564 | 2769 | 2976 | 3210 | 3458 | 3702 | 3974 | 0.30  | 3210 | 374 |
| 41            | 187571                           | 2654 | 2870 | 3087 | 3332 | 3590 | 3841 | 4115 | 0.13  | 3332 | 392 | 197254                             | 2634 | 2849 | 3064 | 3308 | 3565 | 3816 | 4093 | 0.28  | 3308 | 385 |
| 42            | 21317                            | 2731 | 2954 | 3178 | 3431 | 3696 | 3953 | 4232 | -0.28 | 3431 | 410 | 22022                              | 2623 | 2846 | 3070 | 3324 | 3594 | 3858 | 4151 | -0.23 | 3324 | 406 |

**Table 1.** Smoothed percentiles for birthweight (grams) of male and female.

or midwives would fill in the newborns' delivery information in the regional maternal and child information system. The system setting logic was corrected to ensure the correct range. At last, regional maternal and child information would upload to Guangdong Provincial Birth Certificate System. The Chief of Midwives and the Chief of Physicians in hospitals confirmed the information after data entry. Before the birth certificate is issued, the Department of Medical Administration and parents also confirmed the birth information. All the information was verified by the medical professional. The birth registry database maintains the date of birth, gestational age (week) at birth, birthweight, infant sex, parents' ages, registered residence and parity. We included the babies in the study which were born except for stillbirth, death within seven days, and birth defects. Our analyses were based on 5,516,173 births after exclusions. The study was reviewed and approved by Ethics Committee of Guangdong Women and Children Hospital.

The raw data of all newborns (1,771,534 in 2014, 1,627,254 in 2015, and 1,757,385 in 2016) were analyzed. The gestational age (week) was measured combining with mother-reported last menstrual period, early pregnancy ultrasound, and postnatal gestational age (week) assessment. It was expressed in completed weeks. The birthweight was measured immediately after the delivery with measurement accurate to 1 gram. Birthweight percentiles were created by using the Lambda Mu Sigma (LMS) method, which can be fitted within the GAMLSS package by assuming that the birthweight has a Box-Cox Cole and Green (BCCG) distribution<sup>14,15</sup>. The smoothed data were represented by the BW percentile curves. The curves appeared at intervals of one week by gestation and separated into all single births. We also constructed separate curves and tables for male and female newborns for the 3rd, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97th percentiles from 25 to 42 completed weeks based on smoothed estimated curves. The charts and tables were stratified by gender and parity for the 3rd, 5th, 10th, 50th, 90th, 95th and 97th percentiles, and SD were obtained after smoothing. SGA was defined as weight below the 10th percentile of a sex- and gestational age (week)-specific birthweight curve.

Then we use the data from Birth Certificate System between Jan 1<sup>st</sup>, 2017 and Oct 31<sup>st</sup>, 2017, which included 1,245,364 live births to calculate SGA and LGA ratio by three birthweight references. The 10th percentile values of the above three birthweight references were compared against each other, and the difference in cutoff weight at each gestational age (week) was calculated. The same comparison was performed for the 90th percentile values. The GAMLSS package (version 5.0.6) for R statistical software (version 3.4.2) was used for the analysis.

## Results

A retrospective survey for data pertaining to birthweight, maternal parity and infant gender was conducted on 5,516,173 singleton live births at gestational age (week)s 25–42 weeks from January 1<sup>st</sup>, 2014 to December 31<sup>st</sup>, 2016. We included the babies in the study which were born except for stillbirth, death within seven days, and birth defects. After exclusion of birthweight outliers, we included 5,516,173 single neonates in the analysis, comprising 710,480 firstborn boys, 649,882 firstborn girls, 2,053,993 later-born boys, and 1,741,818 later-born girls. Males comprised 53.61% of the births, and 25.70% of infants were firstborn. Late premature infants born at 34–36 weeks' gestation and premature infants born at <34 weeks' gestation accounted for 3.64% and 0.78% of the total infant population, respectively. 20 to 34 years-old mothers accounted for 84.10% of all pregnant women, among which 8.90% were above 35 years-old, and was 18.20% of fathers were older than 35 years-old. Vaginal delivery and cesarean section delivery accounted for 72.10% and 27.70% respectively, while the remaining delivery modes were unclear.

| GA (weeks) | First born male babies smoothed percentiles |      |      |      |      |      |      |      |       |      |     | First born female babies smoothed percentiles |      |      |      |      |      |      |      |       |      |      |
|------------|---|------|------|------|------|------|------|------|-------|------|-----|---|------|------|------|------|------|------|------|-------|------|------|
|            | N   | C3   | C10  | C25  | C50  | C75  | C90  | C97  | L     | M    | S   | N   | C3   | C10  | C25  | C50  | C75  | C90  | C97  | L     | M    | S    |
| 25         | 12  | 657  | 725  | 788  | 856  | 926  | 993  | 1067 | -0.26 | 856  | 326 | 6   | 600  | 673  | 738  | 805  | 872  | 936  | 1007 | -0.27 | 805  | 798  |
| 26         | 58  | 721  | 803  | 878  | 958  | 1040 | 1120 | 1210 | -0.28 | 958  | 459 | 28  | 667  | 753  | 830  | 910  | 990  | 1069 | 1157 | -0.27 | 910  | 1252 |
| 27         | 138   | 792  | 892  | 982  | 1077 | 1174 | 1271 | 1383 | -0.33 | 1077 | 137 | 80  | 732  | 833  | 923  | 1016 | 1112 | 1207 | 1318 | -0.30 | 1016 | 1102 |
| 28         | 307   | 869  | 993  | 1101 | 1213 | 1327 | 1443 | 1584 | -0.37 | 1213 | 365 | 198   | 803  | 920  | 1025 | 1135 | 1249 | 1366 | 1506 | -0.39 | 1135 | 1161 |
| 29         | 440   | 953  | 1101 | 1227 | 1355 | 1487 | 1624 | 1796 | -0.29 | 1355 | 289 | 297   | 883  | 1021 | 1144 | 1273 | 1408 | 1550 | 1725 | -0.39 | 1273 | 1352 |
| 30         | 670   | 1047 | 1216 | 1358 | 1502 | 1650 | 1807 | 2008 | -0.28 | 1502 | 309 | 448   | 968  | 1128 | 1270 | 1419 | 1577 | 1743 | 1955 | -0.26 | 1419 | 1443 |
| 31         | 979   | 1162 | 1352 | 1511 | 1671 | 1838 | 2014 | 2243 | 0.17  | 1671 | 305 | 606   | 1065 | 1250 | 1413 | 1582 | 1760 | 1948 | 2189 | 0.27  | 1582 | 1602 |
| 32         | 1450  | 1300 | 1508 | 1684 | 1862 | 2046 | 2241 | 2490 | -0.13 | 1862 | 306 | 1018  | 1190 | 1400 | 1581 | 1768 | 1962 | 2165 | 2420 | 0.06  | 1768 | 1764 |
| 33         | 2129  | 1461 | 1680 | 1869 | 2063 | 2262 | 2468 | 2726 | -0.08 | 2063 | 346 | 1573  | 1351 | 1574 | 1766 | 1964 | 2167 | 2376 | 2633 | -0.12 | 1964 | 1975 |
| 34         | 4195  | 1640 | 1867 | 2067 | 2273 | 2483 | 2697 | 2954 | 0.06  | 2273 | 336 | 3054  | 1547 | 1776 | 1976 | 2181 | 2391 | 2604 | 2859 | -0.23 | 2181 | 2193 |
| 35         | 7699  | 1824 | 2058 | 2266 | 2482 | 2701 | 2919 | 3173 | 0.12  | 2482 | 360 | 5813  | 1752 | 1984 | 2189 | 2403 | 2620 | 2837 | 3092 | -0.10 | 2403 | 2418 |
| 36         | 17663                                       | 2040 | 2272 | 2483 | 2704 | 2930 | 3152 | 3406 | 0.18  | 2704 | 367 | 12894   | 1956 | 2182 | 2387 | 2604 | 2826 | 3046 | 3302 | 0.19  | 2604 | 2614 |
| 37         | 59435                                       | 2274 | 2495 | 2702 | 2927 | 3159 | 3388 | 3648 | 0.16  | 2927 | 366 | 43413   | 2182 | 2394 | 2595 | 2813 | 3040 | 3266 | 3525 | 0.11  | 2813 | 2828 |
| 38         | 151706                                      | 2461 | 2668 | 2872 | 3099 | 3337 | 3572 | 3835 | 0.15  | 3099 | 367 | 122852  | 2368 | 2566 | 2761 | 2979 | 3209 | 3438 | 3697 | 0.25  | 2979 | 2996 |
| 39         | 222147                                      | 2579 | 2784 | 2990 | 3223 | 3469 | 3710 | 3975 | 0.15  | 3223 | 372 | 206784  | 2485 | 2680 | 2876 | 3098 | 3334 | 3567 | 3827 | 0.15  | 3098 | 3116 |
| 40         | 709857                                      | 2610 | 2818 | 3025 | 3260 | 3507 | 3750 | 4018 | 0.14  | 3260 | 383 | 187135  | 2547 | 2748 | 2951 | 3183 | 3428 | 3667 | 3930 | 0.14  | 3183 | 3199 |
| 41         | 187571                                      | 2654 | 2870 | 3087 | 3332 | 3590 | 3841 | 4115 | 0.13  | 3332 | 392 | 58249   | 2622 | 2829 | 3040 | 3281 | 3535 | 3780 | 4046 | 0.14  | 3281 | 3297 |
| 42         | 21317                                       | 2731 | 2954 | 3178 | 3431 | 3696 | 3953 | 4232 | -0.28 | 3431 | 410 | 5434  | 2603 | 2817 | 3035 | 3286 | 3549 | 3803 | 4075 | -0.20 | 3286 | 3297 |

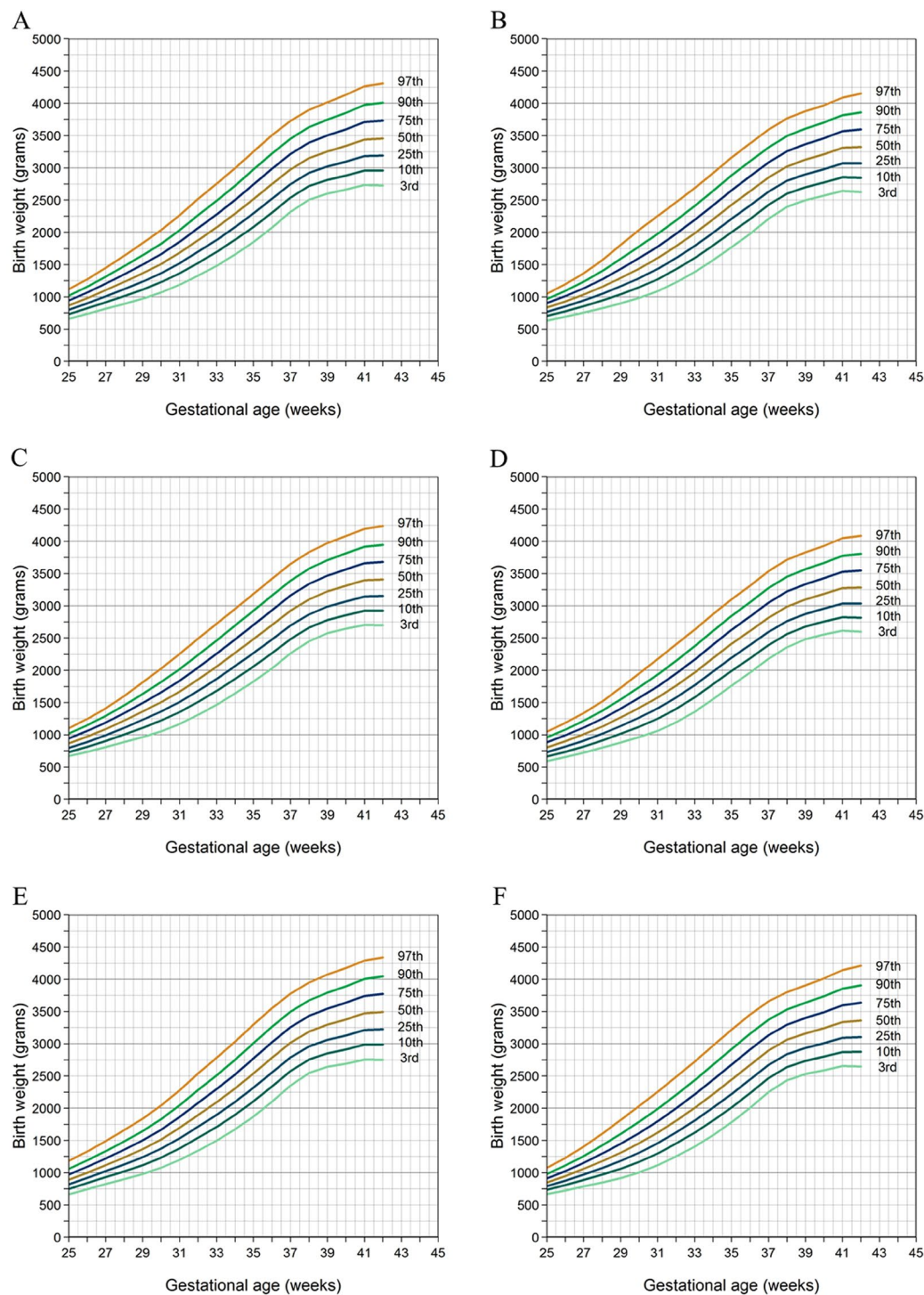
**Table 2.** Smoothed percentiles for birthweight (grams) of first born male and female.

| GA (weeks) | Later born male babies smoothed percentiles |      |      |      |      |      |      |      |       |      |     | Later born female babies smoothed percentiles |      |      |      |      |      |      |      |       |      |     |
|------------|---|------|------|------|------|------|------|------|-------|------|-----|---|------|------|------|------|------|------|------|-------|------|-----|
|            | N   | C3   | C10  | C25  | C50  | C75  | C90  | C97  | L     | M    | S   | N   | C3   | C10  | C25  | C50  | C75  | C90  | C97  | L     | M    | S   |
| 25         | 52  | 625  | 712  | 787  | 865  | 947  | 1035 | 1153 | -0.36 | 865  | 211 | 17  | 619  | 685  | 747  | 814  | 885  | 959  | 1050 | -0.20 | 814  | 146 |
| 26         | 170   | 722  | 814  | 892  | 974  | 1060 | 1153 | 1276 | -0.38 | 974  | 316 | 79  | 688  | 769  | 843  | 923  | 1008 | 1098 | 1211 | -0.33 | 923  | 499 |
| 27         | 434   | 817  | 919  | 1008 | 1100 | 1197 | 1303 | 1442 | -0.33 | 1100 | 252 | 230   | 760  | 858  | 947  | 1042 | 1143 | 1252 | 1393 | -0.23 | 1042 | 630 |
| 28         | 966   | 898  | 1019 | 1124 | 1233 | 1349 | 1475 | 1642 | -0.35 | 1233 | 339 | 592   | 835  | 953  | 1058 | 1168 | 1288 | 1419 | 1594 | -0.25 | 1168 | 394 |
| 29         | 1258  | 971  | 1113 | 1236 | 1365 | 1502 | 1650 | 1849 | -0.30 | 1365 | 258 | 821   | 916  | 1054 | 1176 | 1304 | 1443 | 1598 | 1814 | -0.23 | 1304 | 416 |
| 30         | 1956  | 1062 | 1226 | 1368 | 1517 | 1675 | 1847 | 2074 | -0.25 | 1517 | 287 | 1222  | 1003 | 1165 | 1305 | 1452 | 1613 | 1795 | 2054 | -0.23 | 1452 | 336 |
| 31         | 2816  | 1187 | 1370 | 1529 | 1696 | 1871 | 2059 | 2305 | 0.27  | 1696 | 288 | 1722  | 1105 | 1290 | 1450 | 1618 | 1800 | 2006 | 2297 | 0.21  | 1618 | 347 |
| 32         | 4155  | 1335 | 1535 | 1708 | 1888 | 2077 | 2278 | 2535 | -0.23 | 1888 | 330 | 2732  | 1234 | 1438 | 1615 | 1802 | 2001 | 2221 | 2518 | -0.12 | 1802 | 354 |
| 33         | 6384  | 1483 | 1701 | 1889 | 2084 | 2287 | 2500 | 2769 | -0.18 | 2084 | 343 | 4153  | 1391 | 1607 | 1796 | 1995 | 2205 | 2428 | 2716 | -0.33 | 1995 | 336 |
| 34         | 11629                                       | 1664 | 1894 | 2094 | 2302 | 2516 | 2739 | 3016 | 0.08  | 2302 | 353 | 7976  | 1575 | 1800 | 1999 | 2208 | 2426 | 2652 | 2931 | 0.11  | 2208 | 369 |
| 35         | 20849                                       | 1859 | 2096 | 2306 | 2524 | 2750 | 2981 | 3262 | 0.22  | 2524 | 380 | 14353   | 1774 | 2007 | 2214 | 2432 | 2659 | 2890 | 3169 | 0.16  | 2432 | 373 |
| 36         | 48629                                       | 2081 | 2317 | 2531 | 2759 | 2995 | 3234 | 3517 | 0.28  | 2759 | 383 | 33160   | 1991 | 2221 | 2430 | 2653 | 2885 | 3121 | 3404 | 0.36  | 2653 | 385 |
| 37         | 180260                                      | 2336 | 2557 | 2767 | 2996 | 3236 | 3476 | 3753 | 0.36  | 2996 | 376 | 122420  | 2231 | 2447 | 2651 | 2875 | 3110 | 3348 | 3627 | 0.27  | 2875 | 373 |
| 38         | 469376                                      | 2521 | 2730 | 2934 | 3163 | 3404 | 3643 | 3914 | 0.35  | 3163 | 371 | 351150  | 2412 | 2614 | 2812 | 3033 | 3269 | 3504 | 3772 | 0.25  | 3033 | 362 |
| 39         | 627766                                      | 2622 | 2831 | 3039 | 3273 | 3520 | 3763 | 4033 | 0.25  | 3273 | 376 | 544341  | 2519 | 2716 | 2914 | 3139 | 3379 | 3616 | 3883 | 0.24  | 3139 | 364 |
| 40         | 526358                                      | 2661 | 2878 | 3095 | 3341 | 3600 | 3852 | 4128 | 0.15  | 3341 | 392 | 501257  | 2568 | 2772 | 2978 | 3213 | 3461 | 3706 | 3978 | 0.09  | 3213 | 376 |
| 41         | 134437                                      | 2738 | 2962 | 3188 | 3443 | 3709 | 3968 | 4249 | 0.34  | 3443 | 403 | 139005  | 2633 | 2847 | 3063 | 3308 | 3566 | 3818 | 4094 | 0.24  | 3308 | 389 |
| 42         | 16498                                       | 2714 | 2949 | 3187 | 3457 | 3742 | 4018 | 4319 | -0.25 | 3457 | 424 | 16588   | 2617 | 2843 | 3070 | 3327 | 3599 | 3865 | 4160 | -0.17 | 3327 | 415 |

**Table 3.** Smoothed percentiles for birthweight (grams) of later born male and female.

The percentile charts (3rd, 5th, 10th, 50th, 90th, 95th and 97th centiles) were stratified by sex and mother's parity. First of all, we showed smoothed percentiles for birthweight by gestational age (week) for male and female babies in Table 1. Then all infants from the primiparous mothers were grouped based on gestational age (week), and the data at the 3rd, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97th percentiles were presented in Table 2. Infants from the multiparous mothers were plotted in the same way. The Table 3 showed smoothed percentiles for birthweight (in grams) of later-born male and female. As the gestational age (week) increases, the growth curves for various percentiles are smooth and increasing steadily. In the 10th, 50th, and 90th percentile graphs of singleton births, boys showed higher BWs than those of girls in the total infant graphs at each GA; moreover, Single births showed weight gained the most at 36–37 weeks, and growth slowed after 37 weeks (Fig. 1).

We use the Birth certificate data between Jan 1<sup>st</sup>, 2017 and Oct 31<sup>st</sup>, 2017 as our test dataset which were categorized into the 10<sup>th</sup> and 90<sup>th</sup> percentiles of birthweight for gestational age (week) (i.e., SGA, LGA) using cut points derived from our research standards, China's 2015 research standards<sup>13</sup> and INTERGROWTH-21st standards. The Table 4 provides the sex-specific proportions of these births at 25–42 gestational age (week) ranges.



**Figure 1.** Smoothed percentiles for weight (gms) by gestational age (week) (weeks) for (A) male and (B) female babies. Smoothed percentiles for weight (gms) by gestational age (week) (weeks) for (C) male and (D) female babies from primiparous mothers. Smoothed percentiles for weight (gms) by gestational age (week) (weeks) for (E) male and (F) female babies from multiparous mothers. (A) We first showed the male and gestational age (week)-specific birthweight distributions from mothers who may have ever delivered or did not give birth ever. Curve fitting of the third percentile birthweight of each gestational age (week) (25–42 gestational age (week)) was presented. Above the third percentile, it is the 10th percentile, the 25th percentile, the 50th percentile, the 75th percentile, the 90th percentile, and the 97th percentile of each gestational age (week). (B) Showed the female and gestational age (week)-specific birthweight distributions from mothers who may give birth once or not. (C) Representative the male and gestational age (week)-specific birthweight distributions from primiparous mothers. (D) Representative the female and gestational age (week)-specific birthweight distributions from primiparous mothers. (E) Representative the male and gestational age (week)-specific birthweight distributions from multiparous mothers. (F) Representative the female and gestational age (week)-specific birthweight distributions from multiparous mothers.

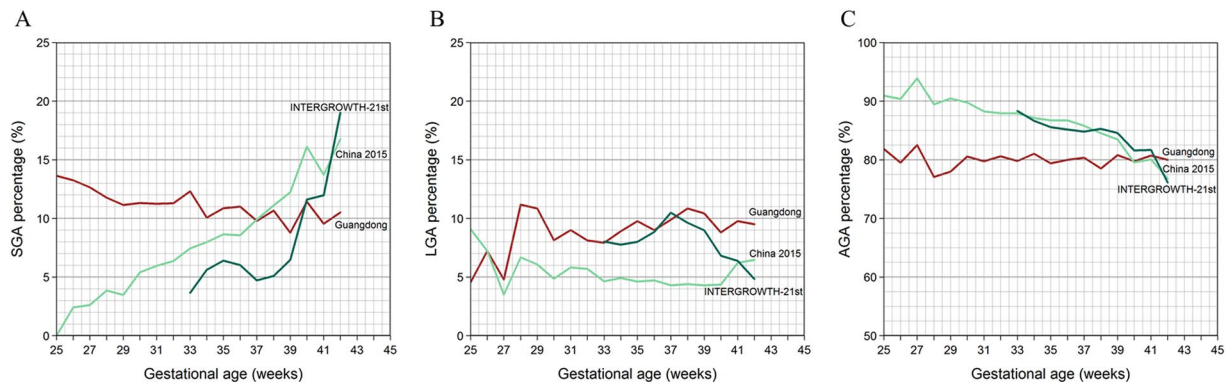
| GA (weeks) | N       | Guangdong Standard |        |        | China's 2015 Standard |        |        | INTERGROWTH-21st Standard |        |        |
|------------|---------|--------------------|--------|--------|-----------------------|--------|--------|---------------------------|--------|--------|
|            |         | SGA(%)             | AGA(%) | LGA(%) | SGA(%)                | AGA(%) | LGA(%) | SGA(%)                    | AGA(%) | LGA(%) |
| 25         | 22      | 13.64              | 81.82  | 4.55   | 0                     | 90.91  | 9.09   |                           |        |        |
| 26         | 83      | 13.25              | 79.52  | 7.23   | 2.41                  | 90.36  | 7.23   |                           |        |        |
| 27         | 229     | 12.66              | 82.53  | 4.80   | 2.62                  | 93.89  | 3.49   |                           |        |        |
| 28         | 493     | 11.76              | 77.08  | 11.16  | 3.85                  | 89.45  | 6.69   |                           |        |        |
| 29         | 691     | 11.14              | 78.00  | 10.85  | 3.47                  | 90.45  | 6.08   |                           |        |        |
| 30         | 946     | 11.31              | 80.55  | 8.14   | 5.39                  | 89.75  | 4.86   |                           |        |        |
| 31         | 1343    | 11.24              | 79.75  | 9.01   | 5.96                  | 88.24  | 5.81   |                           |        |        |
| 32         | 2090    | 11.29              | 80.57  | 8.13   | 6.36                  | 87.94  | 5.69   |                           |        |        |
| 33         | 3448    | 12.30              | 79.79  | 7.92   | 7.45                  | 87.91  | 4.64   | 3.65                      | 88.31  | 8.03   |
| 34         | 6562    | 10.06              | 81.04  | 8.90   | 7.99                  | 87.11  | 4.91   | 5.61                      | 86.64  | 7.76   |
| 35         | 11507   | 10.87              | 79.37  | 9.76   | 8.65                  | 86.73  | 4.62   | 6.41                      | 85.57  | 8.01   |
| 36         | 26147   | 11.01              | 79.97  | 9.01   | 8.57                  | 86.71  | 4.72   | 6.02                      | 85.15  | 8.84   |
| 37         | 93877   | 9.78               | 80.33  | 9.89   | 9.90                  | 85.81  | 4.29   | 4.71                      | 84.81  | 10.48  |
| 38         | 262138  | 10.67              | 78.49  | 10.84  | 11.10                 | 84.50  | 4.40   | 5.10                      | 85.27  | 9.62   |
| 39         | 376992  | 8.79               | 80.78  | 10.43  | 12.23                 | 83.47  | 4.30   | 6.46                      | 84.56  | 8.99   |
| 40         | 377739  | 11.43              | 79.76  | 8.80   | 16.12                 | 79.53  | 4.35   | 11.61                     | 81.58  | 6.82   |
| 41         | 75187   | 9.55               | 80.69  | 9.76   | 13.72                 | 80.07  | 6.21   | 11.96                     | 81.66  | 6.38   |
| 42         | 5870    | 10.51              | 79.98  | 9.51   | 16.75                 | 76.78  | 6.47   | 19.01                     | 76.15  | 4.84   |
| total      | 1245364 | 10.21              | 79.91  | 9.88   | 12.93                 | 82.59  | 4.48   | 7.98                      | 83.65  | 8.37   |

**Table 4.** Comparison with the China's 2015 Standard and INTERGROWTH-21st Standard.

The curves show the incidence of SGA at each gestational age (week), and the three criteria are compared (Fig. 2). In the same way, the incidence of LGA and the incidence of AGA in each gestational age (week) was observed by these three criteria. As the INTERGROWTH-21st national standards only cover 33–42 weeks of gestational age (week), we only calculate the 10th and 90th percentiles of birthweight for gestational age (week) (i.e., SGA, LGA) at 33–42 weeks using this reference. As expected, the thresholds derived from INTERGROWTH-21st standards below the 10th and above the 90th percentile across all gestational age (week) categories were from 3.65% to 19.01%. On the other hand, the thresholds derived from China's 2015 research standards captured a greater proportion of SGA births (16.75% in 42 gestational age (week), while included only 9.09% (25 gestational age (week)) of LGA births within the gestation ranges in their research dataset. In our research, the 10th and 90th-percentile proportions of birthweight for gestational age (week) were relatively stable. The maximum value was found in SGA of 25 gestational age (week) (13.64%), while the minimum value is found in LGA of 25 gestational age (week) (4.55%). The overall prevalence of SGA estimated by our standards, the China's 2015 research standards and INTERGROWTH-21st standards, were 10.21%, 12.93% and 7.98%, respectively, whereas the overall prevalence of LGA was 9.88%, 4.48% and 8.37%, respectively.

## Discussion

The birthweight references included newborns with adverse pregnancy outcomes. These references served the purpose of comparing newborns with the general population, but they were not the prescribed criteria on how newborns should grow under the optimal pregnancy conditions. Infant birthweight is influenced by both environmental and genetic factors; therefore, it is important to identify the percentile distribution of birthweight during pregnancy using recent data to evaluate infants<sup>16</sup>. The birthweight standard for Chinese infants was published in 1988, which was nearly three-decade old and cannot reflect the current newborns' situation<sup>17</sup>. The male birthweight is bigger than that of female; thus, the birthweight curve should be sex-specific. For example, a cross-sectional population-based study in Australia between 1998 and 2007, by comparing term babies of the same gestational age (week), the median birthweight is 0–25 g heavier for male infants, and 5–45 g higher for female infants than 10 years ago<sup>11</sup>. In our analyses, from 25 gestational age (week) to 42 gestational age (week), the average birthweight of males is from 903 g to 3470 g. The average birthweight of females is from 844 g to 3341 g. The 3rd, 5th, 10th, 50th, 90th, 95th and 97th centiles birthweight of males is heavier than that of girls. In 1988, Zhang *et al.*<sup>18</sup> reported the physical development of different gestational age (week) neonates in 15 cities in China. Their study showed that from 28 gestational age (week) to 42 gestational age (week), the birthweight of the male neonate from 50th were from 1234 g to 3405 g. The 50th birthweight of female newborns were from 1103 g to 3292 g. In 2015, a nationwide neonatology network in China made a survey in 63 hospitals. And the mean birthweight of male was (3271 ± 576) g, the mean birthweight of female was (3188 ± 528) g<sup>13</sup>. Compared with references using previously published percentiles in Australia, increases in age-specific 10th and 90th percentiles observed from current data will therefore increase the rate of SGA and decrease the rate of LGA for term births<sup>11</sup>. In the United States, the 50th percentile birthweight of male and female at 40 gestational age (week) were respectively 3572 g and 3431 g in 2011<sup>9</sup>, which were higher than those published in China's 2015 research birthweight standard (3482 g for male and 3349 g for female). In Guangdong population, the birthweight at 50 percentiles was 3339 g and 3213 g for male and female respectively. In general, birthweight in China is smaller compared to that in the developed countries, while the BWs in Guangdong province is even smaller than China's average.



**Figure 2.** Comparison with the China 2015 Standard and INTERGROWTH-21st Standard. **(A)** In each gestational age (week), the SGA rate is calculated by dividing the number of infants who are judged as SGA by the total number of infants born during this gestational age (week). The number of AGA infants were determined by three criteria. **(B)** The LGA rate is calculated by dividing the number of infants who are judged as LGA by the total number of infants born during this gestational age (week). The number of LGA infants were determined by three criteria. **(C)** The AGA rate is calculated by dividing the number of infants who are judged as AGA by the total number of infants born during this gestational age (week). The number of AGA infants were determined by three criteria.

The average birthweight of primipara male infants at 40 gestational age (week) was 120 g higher than that of female. The largest mean birthweights gap between the male and the female infants was 135 g at 41 gestational age (week). These gender differences are bigger than the ones in India where the term firstborn males were found to be 45 g heavier than females on average (the mean birthweight were 2934 g and 2889.5 g for males and females respectively). When considering later born preterm babies, the males outweighed the female babies by 111 grams. The mean birthweight were 2089 g and 1978 g respectively<sup>19</sup>.

In Australia, a mean increase in birthweight of 23 g from 1990 to 2005 for male babies in New South Wales could be translated into an 18% increase in those identified as SGA, or 21% increase in those identified as LGA for females. The test data from 2017 shows between 25 and 27-week gestational age (week), we observed the highest prevalence (12.66–13.64%) of SGA by applying the new Guangdong Province birthweight standard. In contrast, by applying the same standard, the incidence of SGA was the lowest (8.79%) in 39 gestational age (week). Relative to the other two standards, the prevalence of LGA was the highest estimated by our research standards in general. The use of the other two percentiles may lead to the unnecessary intervention and anxiety to the parents of babies whose weight fall in the range of lower and upper centiles according to our centiles. With the China's 2015 research standards, the total incidence of SGA is the largest (12.93%), while the total incidence of SGA by our research and International standards is 10.21% and 7.98% respectively. On the contrary, the total incidence of LGA by the 2015 China standard is lowest (4.48%) compared to the other two standards.

A study has shown that infants defined by Guangdong new birthweight reference (a new reference) as SGA, 15.3–47.7% (depending upon gestational age (week)) were considered appropriate for gestational age (week) (AGA) by the currently used reference of China. Of the infants defined as SGA by the new reference, 92% with gestational age (week) between 34 and 36 weeks and 14.3% between 37 and 41 weeks were considered AGA by the global reference<sup>20</sup>.

Our method to assess gestational age (week) may be constrained by methodology. Ideally, gestational age (week) should be combined with the assessment of mother's last menstrual period, prenatal ultrasound measurement, and postnatal assessment; such practice could be found from the National Perinatal Data Collection (NPDC) of the Australian Institute of Health and Welfare (AIHW) National Perinatal Statistics Unit<sup>11,21</sup> and Scottish neonatal birthweight percentiles by Bonellie *et al.*<sup>22</sup>. However, in actual clinical practice in Guangdong, the gestational age (week) assessment was mainly assessed by mother's last menstrual period. If the conditions of midwifery technical services of medical institutions allow, the early pregnancy ultrasound correction of gestational age (week) may have been carried out. Although the ultrasound examination to assess the gestational age (week) has been commonly used, and the regular pregnancy test performed in the early gestational age (week) also becomes popular, it is difficult to collect obstetric information; and therefore, most of the newborn's gestational age (week)s are still solely based on mother's last menstrual time.

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### Author Contributions

Prof Zhao and Fei Yao conceptualized and designed the study and the data collection instruments, and coordinated and supervised data collection, critically reviewed the manuscript, and approved the final manuscript as submitted. Huazhang Miao carried out the main data processing and analysis, drafted the initial manuscript, and approved the final manuscript as submitted. Bing Li and Yuntao Wu participated in the data collection and carried out the initial analyses. Prof Zhao and Fei Yao assisted the data processing and model construction, critically reviewed the manuscript. All authors have reviewed and revised the manuscript, and approved the final manuscript as submitted.

### Additional Information

**Competing Interests:** The authors declare no competing interests.

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