Effects on developmental outcomes after cesarean birth versus vaginal birth in Chinese children aged 1-59 months: A cross-sectional community-based survey

Hong Zhou 1,2, Yuan Ding 1, Yuning Yang 3, Siyu Zou 1, Xueqi Qu 1, Anqi Wang 1,4, Xi Wang 5, Yue Huang 1, Li Xintong 6, Xiaona Huang 3, Yan Wang 1,2

1 Department of Maternal and Child Health, School of Public Health, Peking University, Beijing, China
2 Environmental and Spatial Epidemiology Research Center, National Human Genetic Resources Center, Beijing, China
3 UNICEF China, Beijing, China
4 Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA, Los Angeles, United States of America
5 Children’s Hospital of Philadelphia, Philadelphia, United States of America
6 Beijing Camford Royal School, Beijing, China

Corresponding Author: Xiaona Huang
Email address: xhuang@unicef.org

OBJECTIVE: It is controversial whether the mode of delivery is associated with developmental outcome, and little was known about growth and development of cesarean children in poor rural areas in China. We aim to measure the development of both cesarean and vaginal-delivered children by Ages and Stages Questionnaires (ASQ) and explore the association between mode of delivery and developmental outcome in poor rural areas in China.

METHODS: Data were collected from a cross-sectional community-based survey, which recruited 1755 vaginal delivered and cesarean children ages 1 to 59 months in eight counties of China. Caregivers of those children completed the Chinese version of ASQ-3 (ASQ-C) while physical examination and questionnaires on socio-demographic and neonatal characteristics were conducted. Multivariate logistic regressions were used to measure the association between developmental delay and mode of delivery as well as each socio-demographic factor, respectively, after adjusting other socio-demographic characteristics.

RESULTS: The prevalence of suspected overall developmental delay was 23.4% in the cesarean group, compared with 21.3% in the vaginal delivered group, yet without statistical difference (p>0.05). Developmental delay was also not significantly different between cesarean and vaginal delivered group in five ASQ domains of communication (7.7% vs. 7.8%, p=0.949), fine motor (7.0% vs. 6.1%, p=0.538), gross motor (8.5% vs. 6.4%, p=0.154), problem solving (7.2% vs. 6.7%, p=0.722) and personal social (8.0% vs. 7.9%, p=0.960).

CONCLUSIONS: Our findings suggest that cesarean delivery does not increase or decrease the risk of suspected developmental in children delay as compared with vaginal delivery.
Effects on developmental outcomes after cesarean birth versus vaginal birth in Chinese children aged 1-59 months: A cross-sectional community-based survey

Hong Zhou 1,2, Yuan Ding 1, Yuning Yang 3, Siyu Zou 1, Xueqi Qu 1, Anqi Wang 1,4, Xi Wang 5, Yue Huang 1, Xintong Li 6, Xiaona Huang 3*, Yan Wang 1,2

1Department of Maternal and Child Health, School of Public Health, Peking University, Beijing, China
2Environmental and Spatial Epidemiology Research Center, National Human Genetic Resources Center, Beijing, China
3UNICEF China, Beijing, China
4Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA
5Children’s Hospital of Philadelphia, Philadelphia, United States of America
6Beijing Camford Royal School, Beijing, China

Corresponding Author:
Xiaona Huang, 12 Sanlitun Lu, Chaoyang District, Beijing, 100600, P.R. China, Email address: xhuang@unicef.org

ABSTRACT

OBJECTIVE: It is controversial whether the mode of delivery is associated with developmental outcome, and little was known about growth and development of cesarean children in poor rural areas in China. We aim to measure the development of both cesarean and vaginal-delivered children by Ages and Stages Questionnaires (ASQ) and explore the association between mode of delivery and developmental outcome in poor rural areas in China.

METHODS: Data were collected from a cross-sectional community-based survey, which recruited 1755 vaginal delivered and cesarean children ages 1 to 59 months in eight counties of China. Caregivers of those children completed the Chinese version of ASQ-3 (ASQ-C) while physical examination and questionnaires on socio-demographic and neonatal characteristics were conducted. Multivariate logistic regressions were used to measure the association between developmental delay and mode of delivery as well as each socio-demographic factor, respectively, after adjusting other socio-demographic characteristics.
**RESULTS:** The prevalence of suspected overall developmental delay was 23.4% in the cesarean group, compared with 21.3% in the vaginal delivered group, yet without statistical difference (p>0.05). Developmental delay was also not significantly different between cesarean and vaginal delivered group in five ASQ domains of communication (7.7% vs. 7.8%, p=0.949), fine motor (7.0% vs. 6.1%, p=0.538), gross motor (8.5% vs. 6.4%, p=0.154), problem solving (7.2% vs. 6.7%, p=0.722) and personal social (8.0% vs. 7.9%, p=0.960).

**CONCLUSIONS:** Our findings suggest that cesarean delivery does not increase or decrease the risk of suspected developmental in children delay as compared with vaginal delivery.

**Introduction**

According to published data from 150 countries in 1990-2014 (Betran et al. 2016), the global cesarean section rate rose to 18.6%, which was higher than the 15% recommended cesarean section rate proposed by WHO in 1985 (1985). With the change of time, cesarean section rate has risen rapidly in both developed and developing countries, and the worldwide increasing trend caused many concern (Betran et al. 2016; Vogel et al. 2015).

With the development of perinatal care, the safety of cesarean section has been greatly improved, and cesarean section plays an important role in reducing maternal and neonatal mortality. When cesarean section rate rose from less than 5% to 10%, the cesarean section rate was significantly associated with the decreased maternal and neonatal mortality, especially in low-income countries where cesarean section was not available (Althabe et al. 2006). However, WHO pointed out that caesarean section can effectively reduce the maternal and neonatal death only when it is medically justified, and there is no evidence that caesarean delivery can provide benefit to the mother and child who do not require the procedure in 2015 (Betran et al. 2016; Hannah et al. 2000). At population level, once cesarean section rate reached 10%, its further increased rate is not associated with a reduction of maternal, neonatal, and infant mortality rates (Ye et al. 2014).

There were some mechanisms explaining how the process of cesarean section may affect children’s neurodevelopment. First, cesarean children lack the normal extrusion process of birth canal. The birth canal extrusion during vaginal delivery can effectively help with fetal lung
expansion. In the delivery, the baby's head and chest are constantly squeezed, stimulating the respiratory center and removing excess fluid from the lung, which help the baby to breathe smoothly after birth (Hooper, Harding 1995; Milner, Saunders, Hopkin 1978; Vyas, Milner, Hopkins 1981). The sympa-tho-adrenal activity in the fetal body also increased significantly to face against the pressure (Falconer, Poyser 1986), which not only help the baby face the whole delivery process, but also make them better adapted to the outer environment and promote their neurobehavioral development. Second, instrumental and surgical delivery was associated with compromised early mother-infant interaction and a higher risk of breastfeeding failure (Rowe-Murray, Fisher 2001). The postnatal recovery for vaginal delivery is faster, only taking 1-3 days. Women can eat immediately after childbirth and get out of bed the day or the following day after the delivery of a baby. In contrast, it usually takes 5-7 days for women to get recovered after cesarean section (Donowitz, Wenzel 1980; Rortveit et al. 2003). Therefore, women after vaginal delivery have more time and energy to take care of the newborn and establish a good maternal-child interaction, which may benefit neonatal neurological development (Robson et al. 2015; Rowe-Murray, Fisher 2001). In addition, women after vaginal delivery have fewer complications (Arikan et al. 2012) and can begin breastfeeding sooner than cesarean born infants. The early interaction and sucking behavior are of great importance in establishing successful breastfeeding (Sakalidis et al. 2013). Women who had cesarean section had a higher proportion of breastfeeding difficulties and a less breastfeeding rate (Hobbs et al. 2016; Prior et al. 2012). Breastfeeding can strengthen the maternal-child interaction and attachment, which plays an important role in young children’s emotional development.

However, the existing research evidence is not consistent relating to the effects of cesarean section on child health outcomes. For example, some studies have shown that the cesarean section was not associated with a reduction in risk of death or neurodevelopmental delay in children (Asztalos et al. 2016; Bahl et al. 2007; Dekeunink et al. 2016; Haque et al. 2008; Joseph et al. 2015; Kimura et al. 2017; Robson et al. 2015; Spinillo et al. 1992; Whyte et al. 2004; Zhu et al. 2014), while others argued that cesarean section significantly reduced the risk of children neurodevelopmental delay in a specific case (Molkenboer et al. 2006). Some other studies showed that cesarean section may have a negative impact on the baby's respiratory system and immune system (Lee et al. 2014; Shearer 1993). According to WHO's statement, the impact of cesarean section on maternal and
child health still remains unclear, and more research is needed to understand the short- and long-term effects of cesarean section on children’s health outcomes.

As China's cesarean section rate was up to 46% according to WHO survey in 2008, and up to date, it has remained at the highest level in the world (Lumbiganon et al. 2010), this has provided a good opportunity for the study of effects of cesarean section on child health outcomes. According to the latest research covering 2865 counties in mainland China’s 31 provinces, China's overall cesarean section rate is 34.9%, with the rate declining in some of the largest cities and still rising up in poor rural areas (Lee et al. 2014). Moreover, China's rural areas have a large birth population, it is imperative to understand the impact of high cesarean section level on children's physical, psychological and intellectual development.

**Objective**

We aim to measure the development of both cesarean and vaginal-delivered children by Ages and Stages Questionnaires (ASQ) and explore the association between mode of delivery and developmental outcome in poor rural areas in China.

**Design**

Our study was a cross-sectional community-based survey on early child development as part of maternal and child health program funded by UNICEF in 2016. The study covered 8 rural counties of four provinces in China (Xinjiang, Qinghai, Jiangxi and Ningxia), with the total population of 3,639,000 in the year of 2016. The annual income per capita of the project counties was 8997 RMB, lower than the national average of 12,363 RMB in rural areas in 2016.

Setting and subjects

Multistage sampling method was used to select the townships and villages from each county. First, 15 administrative villages per county and then 2 nature villages per administrative village were selected at random with population proportional to size (PPS). Second, within each selected nature village, 10 households with a child under 3 years of age were selected by simple random sampling approach according to the children registration list provided by local village doctors. All the sampling processes were completed by the staff members of the program and random numbers for
selection criteria were generated by a random number table. The study was approved by Ethical Committee of Peking University Health Science Centre (IRB00001052-16041). The study procedures were explained to all the caregivers involved in the study and their written informed consent to the study was obtained prior to their participation in the study.

In our study, the statistical significance (α) was set at 0.05 level and the power of the test (1-β) was 80%. As the study was designed to collect relevant baseline data for an intervention project, we assumed the baseline prevalence of suspected development delay (p0) would be 40% and expected a relative 20% decrement of prevalence (p1− p0) / p0. Finally, in consideration of an 80% response rate, the needed total sample size of children would be 1354 (677:677). The following formula was used to calculate the sample size:

\[ n = \frac{2p_0q(Z_{\alpha} + Z_{\beta})^2}{(p_1 - p_0)^2}, \quad \beta = (p_1 + p_0) / 2, \quad \alpha = 1 - \beta \]

**Main Outcome Measures**

Chinese version of the Ages & Stages Questionnaires, Third Edition (ASQ-C) was used to evaluate children’s neurodevelopment in our study (Bian et al. 2012; Wei et al. 2015). The ASQ-C is a series of 21 parent/caregiver-completed questionnaires designed as an alternative screening assessment of developmental performance among children aged 1-66 months, and the difficulty of the questions increases with the increasing age of the children. The ASQ-C contains 5 major developmental domains (communication, gross motor, fine motor, problem solving and personal-social skills), and each domain consists 6 questions. A caregiver was asked about her/his child’s behaviour, such as “Does your baby pick up a crumb or Cheerio with the tips of his thumb and a finger”. The response to each question is one of the following: “yes”, “sometimes” or “not yet” and scores are 10, 5, 0 points respectively. The score on each of the 6 questions was summed to obtain an ASQ-C domain score. We considered a certain domain score as abnormal if it was less than two standard deviations from the mean of the Chinese reference group. In our study, the ASQ result is considered to be abnormal if the score for any 1 of the 5 domains is abnormal (Squires, Potter, Bricker 1995). The abnormal ASQ result indicated a suspected developmental delay of the child. The assessment process took approximately 10–15 minutes.

Information on child’s age, gender (boys and girls), birth order (1, 2, 3, or more), birthweight, gestational age at birth and delivery method (cesarean section or vaginal delivery) was included in our study, and information on caregiver’s education (illiterate, primary school, secondary school, college, and above) and income (poorest, poor, middle, richer, and richest) was also collected. All
data collection was accomplished by tablet computers with the Good Data entry system. Our
questionnaire was adjusted based on a pilot survey conducted in the Yulong County in Yunnan
Province. Before the formal fieldwork was conducted, all the interviewers involved were trained
by the study guideline, including the procedure to use the digital survey equipment, to conduct a
household survey, and to understand the standards and requirements of ASQ assessments.

**Statistical Analysis**

All children involved in our study were full-term delivered single children, with 37–42 weeks of
gestation. They were divided into two groups according to the different ways of delivery: cesarean
and vaginal-delivered

The prevalence of suspected developmental delay in cesarean and vaginal-delivered children were
calculated and compared using chi-square tests. Then the multivariate logistic regression analyses
were used to examine the relationship between all the socio-demographic factors (especially the
method of delivery) and the suspected developmental delay, leading to crude, adjusted odds ratios,
and 95% confidence interval for the suspected developmental delay. The socio-demographic
factors included the child’s age, gender, birth order, birthweight, delivery method and the
caregiver’s education and income. All analyses were conducted using SPSS version 25.0.

**Results**

As shown in Table 1, a total of 1755 children aged 1-59 months were included in our study.
Among 1755 children, 401(22.8%) of them were delivered by cesarean section. There were
significant differences in gestational age weeks (p<0.001) and the caregiver’s education(p<0.001) between cesarean and vaginal delivered children (Table 1).

The prevalence of suspected developmental delay in cesarean and vaginal delivered groups was
similar (23.4 % vs 21.3%; p=0.37) (Figure 1). There was no significant difference in the five
separate ASQ domains between the two groups (Figure 1).

Table 2 showed the bivariate and multivariate regression output of risk factors associated with
suspected developmental delay among children in 8 counties in China. The variations of abnormal
ASQ scores significantly differed by household income. Children from the poorest quintile
families tended to have the poorest performance on ASQ, with abnormal rate of 27.0% and
adjusted OR of 1.48 (95%CI: 1.04-2.11, p<0.05). Boys had a higher proportion of abnormal ASQ
scores in comparison to girls (24.5% vs. 18.7%, adjusted OR=1.31, 95%CI: 1.03-1.67). The
cesarean group had a higher proportion of abnormal ASQ scores as compared to vaginal delivery group (23.4% vs. 21.3%, adjusted OR=1.24, 95%CI: 0.94-1.64), but the difference is not significant.

Discussion

Our study shows that there is no significant difference in neurodevelopmental behaviors between cesarean and vaginal-delivered children. The abnormal ASQ rate was a reflection of developmental delay in children, but we did not find any significant difference in general result or each ASQ domain between the two groups of children.

Our results are consistent with other studies regarding full-term, preterm, breech presentation children or twins, and these studies also found no significant difference in developmental and behavioral outcomes between cesarean and vaginal-delivered groups (Asztalos et al. 2016; Bahl et al. 2007; Dekeunink et al. 2016; Haque et al. 2008; Joseph et al. 2015; Kimura et al. 2017; Robson et al. 2015; Spinillo et al. 1992; Zhu et al. 2014). However, previous studies have found some negative outcomes due to cesarean delivery. For example, Cesarean delivery was related to an increased risk of attention-deficit/hyperactivity disorder or autism spectrum disorder (Curran et al. 2015a; Curran et al. 2015b; Talge, Allswede, Holzman 2016). Studies in the UK, and Iceland found that birth by caesarean section was associated with an increased risk of attention-deficit/hyperactivity disorder (ADHD) or autism spectrum disorder (ASD) compared with spontaneous vaginal delivery, especially birth by emergency cesarean section, or by cesarean section plus induction of labor (Curran et al. 2015a; Curran et al. 2016; Valdimarsdottir et al. 2006). Cesarean children also reported more hearing screening failure than vaginal delivered children (Smolkin et al. 2013; Xiao et al. 2015).

Notably, the rate of cesarean section in our study area was 22.8%, lower than the national average rate (Li et al. 2017), but still above the 10-15% recommended by WHO. The same trend was also shown in other economic developed and developing counties in China. Reasons for the increased rate of cesarean delivery were complicated, and many women chose cesarean delivery without medical indications because of their fear of pain and the belief that cesarean delivery was more beneficial for both mother and baby than vaginal delivery (Huang et al. 2012). Another reason is the affordability of the cost of cesarean section in China. As China's new cooperative medical scheme (NCMS) was launched in 2003 to provide families health insurance in rural areas that more
and more families in rural areas could afford cesarean section (Huang et al. 2012). This result is consistent with the studies in USA, Italy and Brazil that the rate of caesarean section in private hospitals was significantly higher than in public hospitals, possibly because women who had private insurance would like to choose cesarean sections, many of which had no medical indications (Giani et al. 2011; Hopkins, de Lima Amaral, Mourao 2014; Lipkind et al. 2009). Cesarean sections not only brought financial burden to patients and their families especially in poor areas (Bogg et al. 2010; Deboutte et al. 2015), but also placed an economic burden on already highly stressed medical systems worldwide (Druzin, El-Sayed 2006).

WHO recommends that cesarean section should be performed according to medical indications to minimize unnecessary cesarean section. It is still unclear whether all the caesarean sections conducted in the surveyed area were necessary. Further studies were needed to discover the appropriate rate of cesarean section for Chinese rural areas. Robson classification system, as a global standard for assessing and monitoring caesarean section (Betran et al. 2016), is not widely adopted in most poor rural areas of China. We need to establish a reliable and internationally recognized classification system especially in Chinese rural areas, which can be further compared with the international results.

We also noticed other sociodemographic factors were associated with developmental outcomes. In our study, boys are at higher risk of developmental delay, and similar results were also found in Dutch, Norway, UK and Egypt among children aged 4-60 months, showing a significantly higher average ASQ score of girls especially in communication, personal social and fine motor domains (Abo El Elella et al. 2017; Kerstjens et al. 2009; Morley et al. 2015; Richter, Janson 2007). Low income is another high risk factor affecting the development of young children, which was also reflected in previous studies (Handal et al. 2007; Noble et al. 2015; Seguin et al. 2005).

There are a number of limitations in the present study. First, only ASQ-C screening scale, was used to evaluate the developmental status of children. Children who have developmental delay cannot be firmly diagnosed. Second, a cross-sectional study was used that whether cesarean section had an impact on children's long-term behavior or psychological development was not determined. Future study using longitudinal study design is needed to investigate the effects of cesarean section on child health outcomes. Third, insufficient information was collected to assess if the cesarean...
deliveries were in line with medical indications, so we were not able to distinguish the impact of necessary and unnecessary cesarean section on the child developmental outcomes.

In conclusion, our study showed the prevalence of suspected developmental delay in cesarean and vaginal delivered were similar in poor rural areas in China. Therefore, our findings suggest that cesarean delivery does not increase or decrease the risk of suspected developmental in children delay as compared with vaginal delivery.

Acknowledgments
This work was funded by a grant from UNICEF China (YH702). We would like to thank research teams from Lanzhou University and Capital Medical University for their hard work in orchestrating the field work and identifying study population. We also want to thank all of family members who participated in this study from the 8 counties in rural China.

ADDITIONAL INFORMATION AND DECLARATIONS

Conflict of interests
None.

Authorship
Hong Zhou formulated the research question and the first draft of the article. Yan Wang, Hong Zhou, Xiaona Huang and Yuning Yang designed study and carried it out. Yuan Ding, Xueqi Qu, Anqi Wang, Xi Wang and Xintong Li did literature review and polished the language of this article. Yue Huang, Siyu Zou and Yuan Ding analyzed the data. Yan Wang, Xiaona Huang and Hong Zhou provided overall guidance to the study. All authors contributed to the writing and revision of the article.

“What is already known on this topic”
Cesarean section plays an important role in reducing maternal and neonatal mortality
Cesarean section may affect children’s neurodevelopment
China's cesarean section rate was up to 46%, remained at the highest level in the world
“What this study adds” What This Study Adds

The rate of cesarean section in our study area was 22.8%, still above the 10-15% recommended by WHO.

Our study did not find significant difference in developmental and behavioral outcomes between cesarean and vaginal-delivered groups.

In cesarean delivered children group, low birthweight was significantly associated with the abnormal ASQ performance in children.
References

1985. Appropriate technology for birth. *Lancet* 2:436-437.

Abo El Elella SS, Tawfik MAM, Abo El Fotoh WMM, Barseem NF. 2017. Screening for developmental delay in preschool-aged children using parent-completed Ages and Stages Questionnaires: additional insights into child development. *Postgrad Med J* 93:597-602. 10.1136/postgradmedj-2016-134694

Althabe F, Sosa C, Belizan JM, Gibbons L, Jacquerioz F, Bergel E. 2006. Cesarean section rates and maternal and neonatal mortality in low-, medium-, and high-income countries: an ecological study. *Birth* 33:270-277. 10.1111/j.1523-536X.2006.00118.x

Abo El Elella SS, Tawfik MAM, Abo El Fotoh WMM, Barseem NF. 2017. Screening for developmental delay in preschool-aged children using parent-completed Ages and Stages Questionnaires: additional insights into child development. *Postgrad Med J* 93:597-602. 10.1136/postgradmedj-2016-134694

Arikan I, Barut A, Harma M, Harma IM, Gezer S, Ulubasoglu H. 2012. Cesarean section with relative indications versus spontaneous vaginal delivery: short-term outcomes of maternofetal health. *Clin Exp Obstet Gynecol* 39:288-292.

Asztalos EV, Hannah ME, Hutton EK, Allen AC, Armson BA, Gafni A, Joseph KS, Ohlsson A, Ross S, Sanchez JJ, Manguoff K, Barrett JF. 2016. Twin Birth Study: 2-year neurodevelopmental follow-up of the randomized trial of planned cesarean or planned vaginal delivery for twin pregnancy. *Am J Obstet Gynecol* 214:371.e371-371.e319. 10.1016/j.ajog.2015.12.051

Bahl R, Patel RR, Swingler R, Ellis M, Murphy DJ. 2007. Neurodevelopmental outcome at 5 years after operative delivery in the second stage of labor: a cohort study. *Am J Obstet Gynecol* 197:147.e141-146. 10.1016/j.ajog.2007.03.034

Betran AP, Torloni MR, Zhang JJ, Gulmezoglu AM. 2016. WHO Statement on Caesarean Section Rates. *Bjog* 123:667-670. 10.1111/1471-0528.13526

Bian X, Yao G, Squires J, Hoselton R, Chen C-I, Murphy K, Wei M, Fang B. 2012. Translation and Use of Parent-Completed Developmental Screening Test in Shanghai. *Journal of Early Childhood Research* 10:162-175.

Boggs L, Huang K, Long Q, Shen Y, Hemminki E. 2010. Dramatic increase of Cesarean deliveries in the midst of health reforms in rural China. *Soc Sci Med* 70:1544-1549. 10.1016/j.socscimed.2010.01.026

Boggs L, Huang K, Long Q, Shen Y, Hemminki E. 2010. Dramatic increase of Cesarean deliveries in the midst of health reforms in rural China. *Soc Sci Med* 70:1544-1549. 10.1016/j.socscimed.2010.01.026

Curran EA, Dalman C, Kearney PM, Kenny LC, Cryan JF, Dinan TG, Khashan AS. 2015a. Association Between Obstetric Mode of Delivery and Autism Spectrum Disorder: A Population-Based Sibling Design Study. *JAMA Psychiatry* 72:935-942. 10.1001/jamapsychiatry.2015.0846

Curran EA, Khashan AS, Dalman C, Kenny LC, Cryan JF, Dinan TG, Kerney PM. 2016. Obstetric mode of delivery and attention-deficit/hyperactivity disorder: a sibling-matched study. *Int J Epidemiol* 45:532-542. 10.1093/ije/dyw001

Curran EA, O'Neill SM, Cryan JF, Kenny LC, Dinan TG, Khashan AS, Kearney PM. 2015b. Research review: Birth by caesarean section and development of autism spectrum disorder and attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. *J Child Psychol Psychiatry* 56:500-508. 10.1111/jcpp.12351

Deboutte D, O'Dempsey T, Mann G, Faragher B. 2015. User cost of Caesarean section: case study of Bunia, Democratic Republic of Congo. *Int J Health Plann Manage* 30:88-97. 10.1002/hpm.2208

Dekunink GM, Goossens SM, Matthijs v, Senden RH, Beckers CM, Roumen FJ. 2016. Neurodevelopmental outcome of twins at two years of age according to the planned mode of delivery. *J Matern Fetal Neonatal Med* 29:303-308. 10.3109/14767058.2014.999232

Donowitz LG, Wenzel RP. 1980. Endometritis following cesarean section. A controlled study of the increased duration of hospital stay and direct cost of hospitalization. *Am J Obstet Gynecol* 137:467-469.
Druzin ML, El-Sayed YY. 2006. Cesarean delivery on maternal request: wise use of finite resources? A view from the trenches. *Semin Perinatol* 30:305-308. 10.1053/j.semperi.2006.07.012

Falconer AD, Poyser LM. 1986. Fetal sympa-tho-adrenal mediated metabolic responses to par turition. *Br J Obstet Gynaecol* 93:747-753.

Giani U, Bruzzese D, Pugliese A, Saporito M, Triassi M. 2011. [Risk factors analysis for elective caesarean section in Campania region (Italy)]. *Epidemiol Prev* 35:101-110.

Handal AJ, Lozoff B, Breilh J, Harlow SD. 2007. Sociodemographic and nutritional correlates of neurobehavioral development: a study of young children in a rural region of Ecuador. *Rev Panam Salud Publico* 21:292-300.

Hannah ME, Hannah WJ, Hewson SA, Hodnett ED, Saigal S, Willan AR. 2000. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial.

Haque KN, Hayes AM, Ahmed Z, Wilde R, Fong CY. 2008. Caesarean or vaginal delivery for preterm very-low-birth weight (< or =1,250 g) infant: experience from a district general hospital in UK. *Arch Gynecol Obstet* 277:207-212. 10.1007/s00404-007-0438-x

Hobbs AJ, Mannion CA, McDonald SW, Brockway M, Tough SC. 2016. The impact of caesarean section on breastfeeding initiation, duration and difficulties in the first four months postpartum. *BMJ Pregnancy Childbirth* 16:90. 10.1186/s12884-016-0876-1

Hooper SB, Harding R. 1995. Fetal lung liquid: a major determinant of the growth and functional development of the fetal lung. *Clin Exp Pharmacol Physiol* 22:235-247.

Hopkins K, de Lima Amaral EF, Mourao AN. 2014. The impact of payment source and hospital type on rising cesarean section rates in Brazil, 1998 to 2008. *Birth* 41:169-177. 10.1111/birt.12106

Huang K, Tao F, Bogg L, Tang S. 2012. Impact of alternative reimbursement strategies in the new cooperative medical scheme on caesarean delivery rates: a mixed-method study in rural China. *BMJ Health Serv Res* 12:217. 10.1186/1472-6963-12-217

Joseph KS, Pressey T, Lyons J, Bartholomew S, Liu S, Muraca G, Liston RM. 2015. Once more unto the breech: planned vaginal delivery compared with planned cesarean delivery. *Obstet Gynecol* 125:1162-1167. 10.1097/aog.0000000000000824

Kerstjens JM, Bos AF, ten Vergert EM, de Meer G, Butcher PR, Reijnveld SA. 2009. Support for the global feasibility of the Ages and Stages Questionnaire as developmental screener. *Early Hum Dev* 85:443-447. 10.1016/j.earlhumdev.2009.03.001

Kimura T, Takeuchi M, Imai T, Tanaka S, Kawakami K. 2017. Neurodevelopment at 3 Years in Neonates Born by Vaginal Delivery versus Cesarean Section at <26 Weeks of Gestation: Retrospective Analysis of a Nationwide Registry in Japan. *Neonatology* 112:258-266. 10.1159/000477293

Lee SY, Yu J, Ahn KM, Kim KW, Shin YH, Lee KS, Hong SA, Jung YH, Lee E, Yang SI, Seo JH, Kwon JW, Kim BJ, Kim HB, Kim WK, Song DJ, Jang GC, Shim YJ, Lee SY, Kwon JY, Choi SJ, Lee KJ, Park HJ, Won HS, Yoo HS, Kang MJ, Kim HY, Hong SJ. 2014. Additive effect between IL-13 polymorphism and cesarean section delivery/prenatal antibiotics use on atopic dermatitis: a birth cohort study (COCOA). *PLoS One* 9:e96603. 10.1371/journal.pone.0096603

Li HT, Luo S, Trasande L, Hellerstein S, Kang C, Li JX, Zhang Y, Liu JM, Blustein J. 2017. Geographic Variations and Temporal Trends in Cesarean Delivery Rates in China, 2008-2014. *Jama* 317:69-76. 10.1001/jama.2016.18663

Lipkind HS, Duzyj C, Rosenberg TJ, Funai EF, Chavkin W, Chiasson MA. 2009. Disparities in cesarean delivery rates and associated adverse neonatal outcomes in New York City hospitals. *Obstet Gynecol* 113:1239-1247. 10.1097/AOG.0b013e3181a4c3e5

Lumbiganon P, Laopaiboon M, Gulmezoglu AM, Souza JP, Taneepanichskul S, Ruyan P, Attygalle DE, Shrestha N, Mori R, Nguyen DH, Hoang TB, Rathavy T, Chuyun K, Cheang K, Festin M, Udomprasertgul V, Gernar MJ, Yanqui G, Roy M, Carroli G, Ba-Thike K, Filipatova E, Villar J. 2010.
Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007-08. *Lancet* 375:490-499. 10.1016/s0140-6736(09)61870-5

Milner AD, Saunders RA, Hopkin IE. 1978. Effects of delivery by caesarean section on lung mechanics and lung volume in the human neonate. *Arch Dis Child* 53:545-548.

Molkenboer JF, Roumen FJ, Smits LJ, Nijhuis JG. 2006. Birth weight and neurodevelopmental outcome of children at 2 years of age after planned vaginal delivery for breech presentation at term. *Am J Obstet Gynecol* 194:624-629. 10.1016/j.ajog.2005.09.009

Morley D, Till K, Ogilvie P, Turner G. 2015. Influences of gender and socioeconomic status on the motor proficiency of children in the UK. *Hum Mov Sci* 44:150-156. 10.1016/j.humov.2015.08.022

Noble KG, Houston SM, Brito NH, Bartsch H, Kan E, Kuperman JM, Akshoomoff N, Amaral DG, Bloss CS, Libiger O, Schork NJ, Murray SS, Casey BJ, Chang L, Ernst TM, Frazier JA, Gruen JR, Kennedy DN, Van Zijl P, Mostofsky S, Kaufmann WE, Kenet T, Dale AM, Jernigan TL, Sowell ER. 2015. Family income, parental education and brain structure in children and adolescents. *Nat Neurosci* 18:773-778. 10.1038/nn.3983

Prior E, Santhakumaran S, Gale C, Philippes LH, Modi N, Hyde MJ. 2012. Breastfeeding after cesarean delivery: a systematic review and meta-analysis of world literature. *Am J Clin Nutr* 95:1113-1135. 10.3945/ajcn.111.030254

Richter J, Janson H. 2007. A validation study of the Norwegian version of the Ages and Stages Questionnaires. *Acta Paediatr* 96:748-752. 10.1111/j.1651-2227.2007.00246.x

Robson SJ, Vally H, Abdel-Latif ME, Yu M, Westrupp E. 2015. Childhood Health and Developmental Outcomes After Cesarean Birth in an Australian Cohort. *Pediatrics* 136:e1285-1293. 10.1542/peds.2015-1400

Rortveit G, Daltveit AK, Hannestad YS, Hunskaar S. 2003. Urinary incontinence after vaginal delivery or cesarean section. *N Engl J Med* 348:900-907. 10.1056/NEJMoa021788

Rowe-Murray HJ, Fisher JR. 2001. Operative intervention in delivery is associated with compromised early mother-infant interaction. *Bjog* 108:1068-1075.

Sakalidis VS, Williams TM, Hepworth AR, Garbin CP, Hartmann PE, Paech MJ, Al-Tamimi Y, Geddes DT. 2013. A comparison of early sucking dynamics during breastfeeding after cesarean section and vaginal birth. *Breastfeed Med* 8:79-85. 10.1089/bfm.2012.0018

Seguin L, Xu Q, Gauvin L, Zunzunegui MV, Potvin L, Frohlich KL. 2005. Understanding the dimensions of socioeconomic status that influence toddlers' health: unique impact of lack of money for basic needs in Quebec's birth cohort. *J Epidemiol Community Health* 59:42-48. 10.1136/jech.2004.020438

Shearer EL. 1993. Cesarean section: medical benefits and costs. *Soc Sci Med* 37:1223-1231.

Smolkin T, Awawdeh S, Blazer S, Mick O, Makhoul IR. 2013. Delayed first otoacoustic emissions test decreases failure on neonatal hearing screening after caesarean delivery. *Acta Paediatr* 102:e194-199. 10.1111/apa.12175

Spinillo A, Stronati M, Ometto A, Fazzi E, de Seta F, Iasci A. 1992. The influence of presentation and method of delivery on neonatal mortality and infant neurodevelopmental outcome in nondiscordant low-birthweight ( < 2500 g) twin gestations. *Eur J Obstet Gynecol Reprod Biol* 47:189-194.

Squires J, Potter LW, Bricker D. 1995. The ASQ user's guide for the Ages & Stages Questionnaires: A parent-completed, child-monitoring system.

Talge NM, Allswede DM, Holzman C. 2016. Gestational Age at Term, Delivery Circumstance, and Their Association with Childhood Attention Deficit Hyperactivity Disorder Symptoms. *Paediatr Perinat Epidemiol* 30:171-180. 10.1111/ppe.12274

Valdimarsdottir M, Hrafnsdottir AH, Magnusson P, Gudmundsson OO. 2006. [The frequency of some factors in pregnancy and delivery for Icelandic children with ADHD]. *Laeknabladid* 92:609-614.
Vogel JP, Betran AP, Vindevoghel N, Souza JP, Torloni MR, Zhang J, Tuncalp O, Mori R, Morisaki N, Ortiz-Panozo E, Hernandez B, Perez-Cuevas R, Qureshi Z, Gulmezoglu AM, Temmerman M. 2015. Use of the Robson classification to assess caesarean section trends in 21 countries: a secondary analysis of two WHO multicountry surveys. *Lancet Glob Health* 3:e260-270. 10.1016/s2214-109x(15)70094-x

Vyas H, Milner AD, Hopkins IE. 1981. Intrathoracic pressure and volume changes during the spontaneous onset of respiration in babies born by cesarean section and by vaginal delivery. *J Pediatr* 99:787-791.

Wei M, Bian X, Squires J, Yao G, Wang X, Xie H, Song W, Lu J, Zhu C, Yue H, Zhu G, Wang Q, Xu R, Wan C, Sun S, Chen J. 2015. [Studies of the norm and psychometrical properties of the ages and stages questionnaires, third edition, with a Chinese national sample]. *Zhonghua Er Ke Za Zhi* 53:913-918.

Whyte H, Hannah ME, Saigal S, Hannah WJ, Hewson S, Amankwah K, Cheng M, Gafni A, Guselle P, Helewa M, Hodnett ED, Hutton E, Kung R, McKay D, Ross S, Willan A. 2004. Outcomes of children at 2 years after planned cesarean birth versus planned vaginal birth for breech presentation at term: the International Randomized Term Breech Trial. *Am J Obstet Gynecol* 191:864-871. 10.1016/j.ajog.2004.06.056

Xiao T, Li Y, Xiao L, Jiang L, Hu Q. 2015. Association between mode of delivery and failure of neonatal acoustic emission test: a retrospective analysis. *Int J Pediatr Otorhinolaryngol* 79:516-519. 10.1016/j.ijporl.2015.01.019

Ye J, Betran AP, Guerrero Vela M, Souza JP, Zhang J. 2014. Searching for the optimal rate of medically necessary cesarean delivery. *Birth* 41:237-244. 10.1111/birt.12104

Zhu JJ, Bao YY, Zhang GL, Ma LX, Wu MY. 2014. No relationship between mode of delivery and neonatal mortality and neurodevelopment in very low birth weight infants aged two years. *World J Pediatr* 10:227-231. 10.1007/s12519-014-0497-6
Figure 1

*Figure 1: Comparison of prevalence of suspected developmental delay in cesarean section and vaginal delivery groups in 8 counties of China, 2016.*

There was difference in the prevalence of overall suspected developmental delay between cesarean group (23.4%) and vaginal delivered group (21.3%), but this difference was not statistical significant (p=0.37). Meanwhile, the rate of suspected developmental delay in cesarean group for communication, fine motor, gross motor, problem solving and personal social was 7.7%, 7.0%, 8.5%, 7.2% and 8.0%, respectively, and there was no significant difference in these five separate ASQ domains between two groups.
Manuscript to be reviewed

- Communication: Vaginal delivery: 7.8, Cesarean section: 7.7, p=0.949
- Fine motor: Vaginal delivery: 6.1, Cesarean section: 7.0, p=0.583
- Gross motor: Vaginal delivery: 6.4, Cesarean section: 8.5, p=0.154
- Problem solving: Vaginal delivery: 7.9, Cesarean section: 7.2, p=0.722
- Personal social: Vaginal delivery: 6.7, Cesarean section: 8.0, p=0.960

Total: Vaginal delivery: 21.3, Cesarean section: 23.4, p=0.370
Table 1 (on next page)

Table 1: Characteristics of children aged 1-59 months with cesarean section and vaginal delivery groups in 8 counties in China (2016).
| Characteristics                          | Cesarean section | Vaginal delivery | P     |
|-----------------------------------------|------------------|------------------|-------|
| Total, n(%)                             | 401(22.8)        | 1354(77.2)       |       |
| Gestational age weeks, mean (range)     | 39+0(37+0-41+6)  | 39+2(37+0-41+6)  | <0.001|
| Birthweight g, mean (range)             | 3198(1500-4600)  | 3187(1700-5000)  | 0.757 |
| Age of child, months, n(%)              |                  |                  | 0.601 |
| 1-11                                    | 83(20.7)         | 255(18.8)        |       |
| 12-23                                   | 99(24.7)         | 361(26.7)        |       |
| 24-59                                   | 219(54.6)        | 738(54.5)        |       |
| Gender of Child, n(%)                   |                  |                  | 0.467 |
| Boys                                    | 210(52.4)        | 737(54.4)        |       |
| Girls                                   | 191(47.6)        | 617(45.6)        |       |
| Birth order of child, n(%)              |                  |                  | 0.051 |
| 1                                       | 175(43.6)        | 519(38.3)        |       |
| 2                                       | 169(42.1)        | 580(42.8)        |       |
| >=3                                      | 57(14.2)         | 255(18.8)        |       |
| Caregiver’s education, n(%)             |                  |                  | <0.001|
| Illiteracy                              | 46(11.5)         | 181(13.4)        |       |
| Primary                                 | 80(20.0)         | 334(24.7)        |       |
| Secondary                               | 224(55.9)        | 757(55.9)        |       |
| College and above                       | 51(12.7)         | 82(6.1)          |       |
| Low birthweight, n(%)                   |                  |                  | 0.219 |
| Yes                                     | 24(6.1)          | 60(4.6)          |       |
| No                                      | 368(93.9)        | 1248(95.4)       |       |
| Income, n(%)                            |                  |                  | 0.080 |
| Poorest                                 | 93(24.1)         | 289(22.0)        |       |
|      |      |      |
|------|------|------|
| Poor | 50(13.0) | 246(18.7) |
| Middle | 85(22.0) | 283(21.6) |
| Richer | 58(15.0) | 159(12.1) |
| Richest | 100(25.9) | 336(25.6) |
Table 2

Table 2: Socio-demographic factors for abnormal ASQ scores among children in 8 counties in China (2016).
| Characteristics                  | N   | n   | % (95% CI) | Crude OR (95% CI) | Adjusted OR (95% CI)* |
|---------------------------------|-----|-----|------------|-------------------|-----------------------|
| **Total**                       | 1755| 383 | 21.8 (19.9-23.8) |                   |                       |
| **Age of child, months**        |     |     |            |                   |                       |
| 1-11                            | 338 | 64  | 18.9 (14.8-23.1) | 1                 | 1                     |
| 12-23                           | 460 | 113 | 24.6 (20.6-28.5) | 1.39 (0.98-1.96)  | 1.39 (0.97-2.00)      |
| 24-59                           | 957 | 206 | 21.5 (18.9-24.1) | 1.17 (0.85-1.60)  | 1.17 (0.85-1.63)      |
| **Gender of Child**             |     |     |            |                   |                       |
| Boys                            | 947 | 232 | 24.5 (21.8-27.2) | 1.41 (1.12-1.77)* | 1.31 (1.03-1.67)*     |
| Girls                           | 808 | 151 | 18.7 (16.0-21.4) | 1                 | 1                     |
| **Birth order of child**        |     |     |            |                   |                       |
| 1                               | 694 | 132 | 19.0 (16.1-21.9) | 1                 | 1                     |
| 2                               | 749 | 170 | 22.7 (19.7-25.7) | 1.25 (0.96-1.61)  | 1.14 (0.87-1.51)      |
| >=3                             | 312 | 81  | 26.0 (21.1-30.8) | 1.49 (1.08-2.04)* | 1.31 (0.93-1.83)      |
| **Caregiver’s education**       |     |     |            |                   |                       |
| Illiteracy                      | 227 | 45  | 19.9 (14.6-25.0) | 1.68 (0.92-3.08)  | 1.45 (0.73-2.90)      |
| Primary                         | 414 | 109 | 27.5 (22.1-30.6) | 2.43 (1.40-4.24)* | 2.28 (1.20-4.32)*     |
| Secondary                       | 981 | 212 | 19.6 (19.0-24.2) | 1.88 (1.10-3.19)* | 1.88 (1.02-3.46)*     |
| College and above               | 133 | 17  | 15.9 (7.1-18.5)  | 1                 | 1                     |
| **Income**                      |     |     |            |                   |                       |
| Poorest                         | 382 | 103 | 27.0 (22.5-31.4) | 1.66 (1.19-2.32)* | 1.48 (1.04-2.11)*     |
| Poor                            | 296 | 63  | 21.3 (16.6-25.9) | 1.22 (0.84-1.76)  | 1.13 (0.77-1.67)      |
| Middle                          | 368 | 81  | 22.0 (17.8-26.2) | 1.27 (0.90-1.80)  | 1.21 (0.84-1.75)      |
| Richer                          | 217 | 50  | 23.0 (17.4-28.6) | 1.35 (0.90-2.01)  | 1.46 (0.96-2.21)      |
| Richest                         | 436 | 79  | 18.1 (14.5-21.7) | 1                 | 1                     |
| **Low birthweight, n(%)**       |     |     |            |                   |                       |
| Yes                             | 84  | 22  | 26.2 (16.8-35.6) | 1.31 (0.79-2.16)  | 1.37 (0.82-2.29)      |
| No                              | 1616| 344 | 21.3 (19.3-23.3) | 1                 | 1                     |
| **Mode of delivery, n(%)**      |     |     |            |                   |                       |
|                | Cesarean section | Vaginal delivery |
|----------------|------------------|------------------|
|                | Count | n | Median (IQR) | Odds ratio (95% CI) | Odds ratio (95% CI) |
| Cesarean section | 401   | 94 | 23.4(19.3-27.6) | 1.12(0.86-1.47) | 1.24(0.94-1.64) |
| Vaginal delivery | 1354  | 289| 21.3(19.2-23.5) | 1                | 1                |

2 Adjusted for all the variables in Table 2.

3 * p < 0.05