

Exclusive Breastfeeding Duration Modified the Effects of Neonatal and Familiar Risk Factors on Childhood Asthma and Allergy: A Population-Based Study

Yabin Hu

Shanghai Childrens Medical Center Affiliated to Shanghai Jiaotong University School of Medicine <https://orcid.org/0000-0001-7622-5554>

Yiting Chen

Shanghai Jiao Tong University School of Medicine

Shijian Liu

Shanghai Childrens Medical Center Affiliated to Shanghai Jiaotong University School of Medicine

Fan Jiang

Shanghai Childrens Medical Center Affiliated to Shanghai Jiaotong University School of Medicine

Meiqin Wu

Shanghai Jiaotong University School of Medicine Xinhua Hospital

Chonghuai Yan

Shanghai Jiaotong University School of Medicine Xinhua Hospital

Jianguo Tan

Shanghai Meteorological Bureau

Guangjun Yu

Shanghai Children's Hospital: Children's Hospital of Shanghai

Yi Hu

Shanghai Children's Hospital: Children's Hospital of Shanghai

Yong Yin

Shanghai Childrens Medical Center Affiliated to Shanghai Jiaotong University School of Medicine

Jiajie Qu

Shanghai Municipal Education Commission

Shenghui Li

Shanghai Jiao Tong University School of Medicine

Shilu Tong (✉ tongshilu@scmc.com.cn)

Shanghai Childrens Medical Center Affiliated to Shanghai Jiaotong University School of Medicine <https://orcid.org/0000-0001-9579-6889>

Research

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Abstract

Background: Childhood asthma and allergic diseases are a significant global problem. There are inconsistent findings on the associations of delivery mode, the number of children in the household and breastfeeding with childhood asthma and allergic diseases. We assessed these associations and examined whether breastfeeding modified the effects of neonatal and familiar risk factors on childhood asthma and allergic diseases.

Methods: A population-based cross-sectional study was conducted in Shanghai, China. A total of 17 primary schools were randomly selected from 13 districts of Shanghai in this study. The International Study of Asthma and Allergies in Childhood questionnaire was adopted to assess the childhood asthma and allergic diseases. Multivariable logistic regression models were used to evaluate the associations between neonatal and familiar factors and childhood asthma and allergic diseases, and to examine the modification effects of breastfeeding on the associations assessed.

Results: Of 10,464 primary school children aged 6–11 years, the overall prevalence of childhood asthma, allergic rhinitis, urticarial, food allergy and drug allergy was 13.9%, 22.7%, 15.3%, 8.1% and 4.6%, respectively. Male sex, high socioeconomic status, cesarean section delivery, only one child in the household and having family history of allergy were among the major risk factors for childhood asthma and allergic diseases while longer exclusive breastfeeding duration (≥ 6 months) was a protective factor. Longer exclusive breastfeeding duration also attenuated the effects of neonatal and familiar risk factors on childhood asthma and allergic diseases.

Conclusions: Longer exclusive breastfeeding duration was a protective factor against childhood asthma and allergic diseases, and also reduced the adverse effects of neonatal and familiar risk factors on these diseases. Given the prevalence of childhood asthma and allergic diseases is rapidly rising across the globe, these findings may have important clinical and public health implications.

1. Introduction

The prevalence of childhood asthma and allergic diseases has elevated worldwide in the past 3 decades. For instance, the International Study of Asthma and Allergies in Childhood (ISAAC) phase 3 showed a significant increase in the prevalence of childhood asthma and allergic rhinitis (AR) in most of Asia-Pacific region from 2001 to 2010 [1]. With population and economic growth and urbanization, China has been experiencing a rapid increase in the prevalence of childhood asthma and allergic diseases [2–5]. These changes have brought heavy economic burdens to individuals, families and the society as a whole.

Mounting evidence suggests that prenatal and neonatal factors are associated with the development of childhood asthma and allergic diseases [6–8]. In China, a study conducted in Guangzhou, China found that male sex, high birth weight, cesarean section (CS) delivery, and only one child in the household were associated with the risks of allergic diseases in children aged 6–18 years [8]. Another study in Shanghai found that CS without medical indication was associated with increased risks of both childhood asthma and AR, and breastfeeding in early infancy attenuated these risks [6]. The Allergic Rhinitis Cohort Study for kids conducted in South Korea found that long-term breastfeeding (≥ 12 months) and a vaginal delivery were associated with a lower risk of developing childhood AR [7]. However, in two unselected populations using harmonised protocols in Australia, the association of CS with developing childhood allergy was weak, and no modification effects by breastfeeding duration were found [9].

Knowledge gaps exist in the associations between prenatal and neonatal factors and development of childhood asthma and allergic diseases. To assess these associations, and to examine whether breastfeeding duration modifies these associations, we conduct a population-based cross-sectional study among primary school children aged 6–11 years in Shanghai, the largest metropolitan city in China.

2. Materials And Methods

2.1 Study participants

Shanghai is located in the Yangtze River Delta region, east of China, E 120°52'–122°12', N 30°40'–31°53', which has over 27 million residents in 2020 [10]. A city-wide cross-sectional survey was conducted during April–June 2019 across Shanghai. To obtain a representative sample, a multi-stage and multi-strata sampling approach was used. Six urban districts (Huangpu, Hongkou, Changning, Xuhui, Putuo, and Yangpu) and seven suburban/rural districts (Pudong, Minhang, Jinshan, Songjiang, Qingpu, Baoshan, and Chongming) were randomly selected from 16 districts of Shanghai (7 urban districts and 9 suburban/rural districts). Then, a total of 17 primary schools were randomly selected. We firstly explained the purpose and content of the project to the principals and teachers in detail at a study launch meeting before the survey began. And then, teachers conveyed these messages to parents through parents' meetings at schools. Informed consent was then obtained from parents if they agreed to allow their children to take part. Each child's mother completed the questionnaire. Overall, 10700 participants completed the questionnaires. After the exclusion of some children with inappropriate ages (e.g. ≤ 6 years or ≥ 12 y), 10464 (97.8%) primary school children aged 6–11 years were finally included in this study.

The ethical application and the consent procedure of this study were approved by the Ethics Committees of Shanghai Jiao Tong University School of Medicine and Shanghai Children's Medical Center.

2.2 Questionnaire

The questionnaire included questions on childhood asthma and allergic diseases, general characteristics of children and parents, socioeconomic status (SES), allergy history of children and their family members, exposure during pregnancy, children's lifestyle habits, and home environmental exposures in early life. The Cronbach's alpha coefficient of the ISAAC allergic questionnaire in our sampled children was 0.91. The intra-class correlation coefficient of retest reliability at intervals of 2 weeks was 0.94. Validity presented by Kaiser-Meyer-Olkin test was 0.94. These results show the high validity of the questionnaire for the primary school children.

2.2.1 Assessment of asthma and allergic diseases

The core question of the ISAAC questionnaire was applied to assess asthma and allergic diseases status [11]. Asthma: Has your child ever been diagnosed with asthma by a doctor? A similar question was asked for AR, urticarial and drug allergy (DA). For food allergy (FA), the question was: Whether your child has a history of FA (red lips, rash, abdominal pain, etc. within 2 hours after eating)?

2.2.2 Assessment of independent variables

Mode of delivery included vaginal delivery (VD) and caesarean section (CS). Exclusive breastfeeding duration was divided into ≤ 6 and >6 months. The number of children in household was categorized as: only one child or not. A question about family history of allergy was: Does anyone at home have the following allergic diseases (Asthma, allergic dermatitis, FA, DA, AR, anaphylactic shock, etc.)? Socioeconomic status (SES) was measured as: Do you own the apartment or not?

2.3 Statistical analysis

Statistical descriptions were made utilizing the frequency and percentage for categorical variables. Pearson's chi-squared (χ^2) test was used to assess the differences among the prevalence of asthma and allergic diseases between different groups. Univariate logistic regression model was used to calculate the unadjusted odds ratios (OR) and 95% confidence interval (CI), and then multivariable logistic regression model was performed to calculate adjusted OR (AOR) and 95% CI, after adjustment for child's sex, age, and SES. All statistical analyses were conducted using R (version 3.6.3; R Core Team).

3. Results

In this study, the overall prevalence of childhood asthma, AR, urticarial, FA and DA was 13.9%, 22.7%, 15.3%, 8.1% and 4.6%, respectively. Table 1 depicts the summary statistics of characteristics among 10464 primary school children aged 6–11 years, and the prevalence rates of asthma and allergic diseases among different groups. This study included 5464 (52.2%) boys and 5000 (47.8%) girls, with higher prevalence of asthma and allergic diseases in boys than girls. Average age was 9.2 (standard deviation = 2.2) years. The prevalence of asthma, AR, urticarial and FA was significantly higher in CS group than VD group. The prevalence of asthma, AR, urticarial and DA was significantly lower in the group of breastfeeding duration >6 months, compared to that in the group of breastfeeding duration ≤ 6 months. The prevalence of childhood asthma and allergic diseases significantly increased ($P < 0.001$) in the group with higher SES (having the home ownership) or with family history of allergy or with only one child in the household.

Table 1 Summary statistics of characteristics and the prevalence of asthma and allergic diseases among different groups.

Variable	Total(%)	Asthma(%)	P-value	AR(%)	P-value	Urticarial(%)	p-value	FA(%)	P-value	DA(%)	p-value
Sex			0.001		0.001		0.010		0.091		0.031
Boys	5464(52.2)	883(16.2)		1429(26.2)		883(16.2)		468(8.6)		272(5.0)	
Girls	5000(47.8)	570(11.4)		943(18.9)		717(14.3)		383(7.7)		205(4.1)	
Age(year)			0.251		0.447		0.071		0.740		0.166
6-	713(6.8)	103(14.4)		145(20.3)		118(16.5)		63(8.8)		31(4.3)	
7-	2138(20.4)	290(13.6)		469(21.9)		360(16.8)		184(8.6)		86(4.0)	
8-	2092(20.0)	320(15.3)		498(23.8)		323(15.4)		174(8.3)		85(4.1)	
9-	2045(19.5)	289(14.1)		459(22.4)		277(13.5)		160(7.8)		90(4.4)	
10-	1988(19.0)	253(12.7)		459(23.1)		304(15.3)		148(7.4)		102(5.1)	
11-	1488(14.2)	198(13.3)		342(23.0)		218(14.7)		122(8.2)		83(5.6)	
Mode of delivery			0.001		0.001		0.001		0.010		0.094
Vaginal delivery	4224(40.4)	523(12.4)		878(20.8)		576(13.6)		308(7.3)		175(4.1)	
Caesarean section	6240(59.6)	930(14.9)		1494(23.9)		1024(16.4)		543(8.7)		3002(4.8)	
Exclusive breastfeeding			0.001		0.001		0.008		0.132		0.001
≤6m	5373(51.3)	825(15.4)		1388(25.8)		870(16.2)		458(8.5)		279(5.2)	
>6m	5091(48.7)	628(12.3)		984(19.3)		730(14.3)		393(7.7)		198(3.9)	
Birth weight			0.388		0.569		0.593		0.837		0.737
≤2500g	298(3.0)	50(16.8)		62(20.8)		52(17.4)		26(8.7)		11(3.7)	
2500-4000g	8896(88.5)	1251(14.1)		2054(23.1)		1379(15.5)		726(8.2)		414(4.7)	
≥4000g	855(8.5)	117(13.7)		190(22.2)		128(15.0)		74(8.7)		40(4.7)	
Gestational week			0.027		0.570		0.406		0.213		0.399
≤37w	946(9.1)	158(16.7)		222(23.5)		159(16.8)		91(9.6)		43(4.5)	
37-42w	8972(86.6)	1219(13.6)		2039(22.7)		1370(15.3)		722(8.0)		406(4.5)	
≥43w	440(4.2)	65(14.8)		92(20.9)		64(14.5)		33(7.5)		26(5.9)	
Only child			0.001		0.001		0.001		0.001		0.001
Yes	6524(62.3)	990(15.2)		1687(25.9)		1104(16.9)		590(9.0)		347(5.3)	
No	3940(37.3)	463(11.8)		685(17.4)		496(12.6)		261(6.6)		130(3.3)	
Family history of allergy			0.001		0.001		0.001		0.001		0.001
Yes	2450(23.4)	639(26.1)		1094(44.7)		636(26.0)		412(16.8)		205(8.4)	
No	8014(76.6)	814(10.2)		1278(15.9)		964(12.0)		439(5.5)		272(3.4)	
Home ownership			0.001		0.001		0.001		0.001		0.001
have	7743(74.0)	1179(15.2)		2015(26.0)		1345(17.4)		701(9.1)		391(5.0)	
Not have	2721(26.0)	274(10.1)		357(13.1)		255(9.4)		150(5.5)		86(3.2)	

Data were presented with frequency and percentage; P-value was calculated by Pearson's chi-squared (χ^2) test;

Figure 1–3 show the modification effects of exclusive breastfeeding duration on the associations of delivery mode, family history of allergy, only one child in the household with childhood asthma and allergic diseases after adjustment for child's sex, age, and SES. Figure 1 reveals that the AOR for childhood asthma, AR and DA in the group of CS and breastfeeding duration > 6 months (0.802, 95%CI: 0.691, 0.929, 0.753, 95%CI: 0.664, 0.855; and 0.758, 95%CI: 0.594, 0.967, respectively) was lower than that in the group of VD and breastfeeding duration ≤ 6 months (0.841, 95%CI: 0.712, 0.992; 0.969, 95%CI: 0.844, 1.112; and 0.891, 95%CI: 0.684, 1.162) compared to the reference group of VD and breastfeeding duration ≤ 6 months, which indicates that exclusive breastfeeding duration > 6 months might decrease the adverse effect of CS on childhood asthma, AR and DA. The AOR in the group of VD and breastfeeding duration > 6 months was lowest (0.780, 95%CI: 0.662, 0.918) for childhood asthma.

Figure 2 indicates that the AOR in the group of breastfeeding duration > 6 months and more than one child in the household was lowest for childhood asthma, AR and DA (0.720, 95%CI: 0.605, 0.858; 0.572, 95%CI: 0.492, 0.665; and 0.600, 95%CI: 0.448, 0.804, respectively).

Figure 3 depicts that the AOR in the group of breastfeeding duration > 6 months and without family history of allergy was lowest for childhood asthma, AR, urticarial, FA and DA (0.283, 95%CI: 0.240, 0.333; 0.191, 95%CI: 0.165, 0.220; 0.409, 95%CI: 0.349, 0.479; 0.300, 95%CI: 0.244, 0.368 and 0.331, 95%CI: 0.253, 0.431, respectively).

4. Discussion

In this population-based cross-sectional study, we found that the overall prevalence of childhood asthma, AR, urticarial, FA and DA among children aged 6–11 years was 13.9%, 22.7%, 15.3%, 8.1% and 4.6%, respectively, in Shanghai, China. Male sex, high SES, CS delivery, only one child in the household and having family history of allergy were among the major risk factors for childhood asthma and allergic diseases. The longer exclusive breastfeeding duration (≥6 months) was a protective factor for childhood asthma and allergic diseases, and could also attenuate the adverse effects of CS delivery, only one child in the household and having family history of allergy on childhood asthma and allergic diseases.

Our findings are consistent with most previous studies in which CS delivery, only one child in the household and formula feeding were associated with an increased risk of allergic diseases among children [6–8, 12–18]. Recently, a systematic review and meta-analysis reported that male sex, short duration of breastfeeding and having siblings were risk factors of early transient wheezing among children aged 3–18 years [19]. Our findings also show that male sex and short duration of breastfeeding were risk factors for childhood asthma and allergic diseases (Table 1), but in contrast, only one child (having no siblings) in the household was a risk factor for childhood asthma and allergic diseases. In addition, Chu et al [6] reported that breastfeeding attenuated the impacts of CS on childhood asthma and AR. However, Liao et al [9] suggest that the association of CS with developing childhood allergy was not modified by breastfeeding duration. Our results provide supportive evidence that breastfeeding duration modifies the association between CS and childhood allergy. The inconsistency between studies may be due to the differences in geographic locations, study designs and population characteristics.

Hygiene or old friends hypotheses involved gut microbiota exposure might partly explain the associations of CS, only one child in the household, and breastfeeding with childhood asthma and allergic diseases [20]. A meta-analysis reported an increase in the risk of childhood asthma after CS (OR = 1.20, 95% CI: 1.14, 12.6) [21]. Birth by CS causes development of the gut microbiota to be delayed and to take an unusual course [22]. Only one child, without siblings, also modulates the gut microbiota, leading to allergic disorders [23, 24]. However, breastfeeding could prevent allergy through regulating infant gut barrier function and microbiota [25], which may explain why longer breastfeeding duration attenuated the adverse effects of CS and only one child in the household on childhood asthma and allergic diseases. CS might boost inflammatory responses, affect bronchial epithelial barrier function, or associate with the metabolic syndrome, or both. In turn, breastfeeding could strengthen bronchial epithelial barrier function and boost innate immunity and regulatory immune responses [26].

Similar to previous studies [2, 17, 19, 27–29], we found that family history of allergy was strongly associated with the risk of childhood asthma and allergic diseases. Longer breastfeeding duration could reduce these risks. The World Health Organization issued a recommendation that mothers should breastfeed their children exclusively for 6 months at least [30]. Exclusive breastfeeding is the internationally preferred method of feeding babies during their first 6 months of life, and is recognized as one of the most natural and best forms of preventive medicine.

There are three major strengths in this study. First, a representative sample was obtained through a stringent multi-stage and multi-strata random sampling approach. Second, this population-based cross-sectional study achieved a high response rate (≈95%), so selection bias was probably minimal. Third, a wide range of childhood allergic diseases including asthma, AR, urticarial, FA and DA were considered in this study to explore their associations with CS, only one child in the household, family history of allergy and breastfeeding duration.

This study also has several limitations. First, recall bias was inevitable to some extent as all the information was obtained from questionnaires. We repeated the survey twice in a school to compare the accuracy and differences of the recalled information, and observed the high quality of collected data (Note: we provided some details in the Methods section). Second, the nature and severity of childhood asthma and allergic diseases was not measured in this study, and therefore, the determinants of mild and severe cases cannot be distinguished. Finally, a causal relationship cannot be established due to the cross-sectional study design. However, the independent variables included in the multivariable model (e.g., child's sex, CS, only one child in the household and family history of allergy) were significantly earlier than the diagnosis of childhood asthma and allergic diseases, so a certain temporal relationship exists.

Despite these limitations, the results from this study have demonstrated the contemporary prevalence of asthma and allergic diseases among children aged 6–11 years and their associations with CS, only one child in the household, family history of allergy and breastfeeding duration. Longer breastfeeding duration appeared to decrease the adverse effects of the neonatal and familiar risk factors on childhood asthma and allergic diseases. Our findings may be used to develop appropriate strategies to prevent and control childhood asthma and allergic diseases if they are confirmed by further research.

5. Conclusions

Among primary school children aged 6–11 years in Shanghai, born by CS delivery, only one child in the household, and having family history of allergy were among the major risk factors of childhood asthma and allergic diseases. Longer breastfeeding duration was associated with reduced risks of childhood asthma and allergic diseases, and could attenuate the adverse effects of neonatal and familiar risk factors on childhood allergic diseases. These findings may have important clinical and public health implications.

Abbreviations

AOR: adjusted odds ratios

AR: allergic rhinitis

CI: confidence interval

CS: cesarean section

DA: drug allergy

FA: food allergy

ISAAC: the International Study of Asthma and Allergies in Childhood

SES: socioeconomic status

Declarations

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Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

YH performed the statistical analysis and drafted the manuscript. YC was involved with study design and participants recruitment. SL and ST conceived the study, and developed its design, supervised the field work and revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The ethical application and the consent procedure of this study were approved by the Ethics Committees of Shanghai Jiao Tong University School of Medicine and Shanghai Children's Medical Center.

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Figures

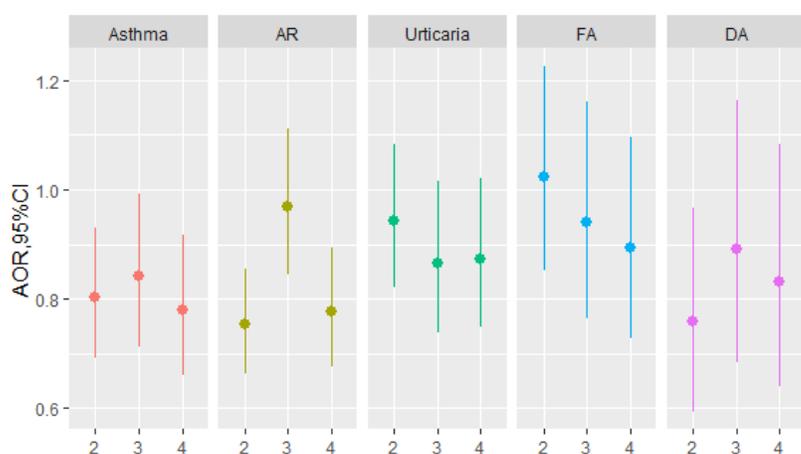


Figure 1

Combined effects of breastfeeding duration & mode of delivery on childhood asthma and allergic diseases. AR: allergic rhinitis; FA: food allergy; DA: drug allergy; Reference (1): CS & ≤6m; 2: CS & ≥6m; 3: VD & ≤6m; 4: VD & ≥6m.

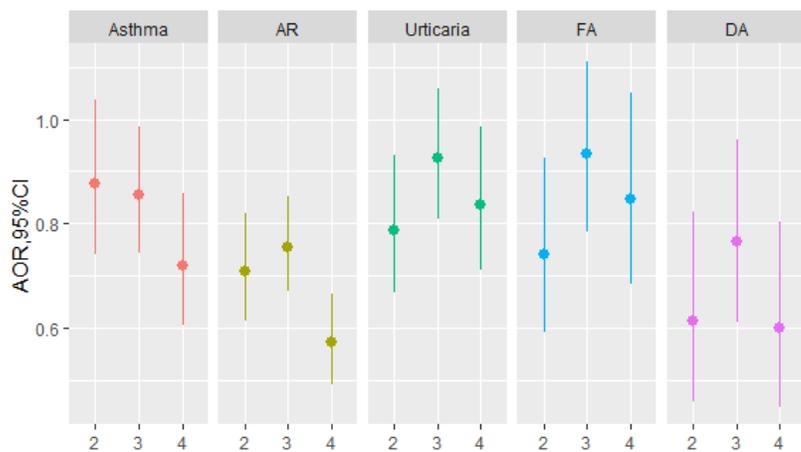


Figure 2

Combined effects of breastfeeding duration & only one child on childhood asthma and allergic diseases. AR: allergic rhinitis; FA: food allergy; DA: drug allergy; Reference (1): ≤6m & Yes; 2: ≤6m & No; 3: ≥6m & Yes; 4: ≥6m & No

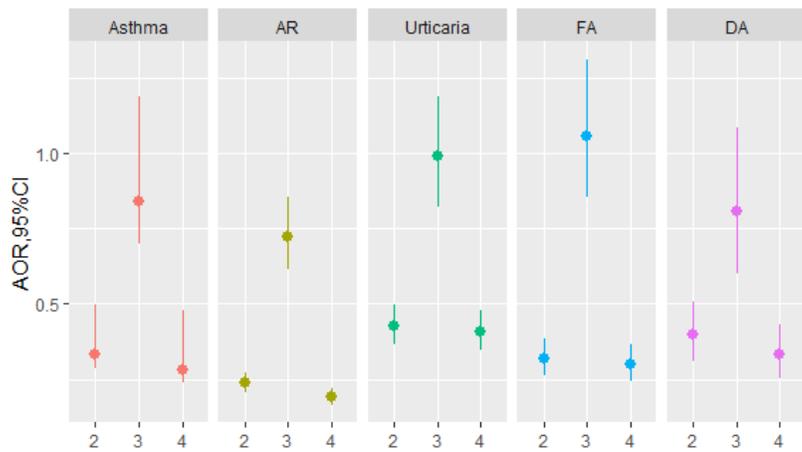


Figure 3
 Combined effects of breastfeeding duration & family history of allergy on childhood asthma and allergic diseases. AR: allergic rhinitis; FA: food allergy; DA: drug allergy; Reference (1): $\leq 6m$ & Yes; 2: $\leq 6m$ & No; 3: $> 6m$ & Yes; 4: $> 6m$ & No.