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The associations of economic growth and anaemia for school-aged children in China

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Abstract

Economic growth has brought improvements in many areas of child health, but its effects on anaemia among school-aged children remain unknown. However, this is important because iron deficiency anaemia is common and is the main cause of disability-adjusted life years for school-aged children. In this study, we included 429,222 Chinese children aged 7–17 years from five consecutive national cross-sectional surveys during 1995–2014. Using altitude-adjusted haemoglobin concentration measured from capillary blood samples, we defined anaemia status according to World Health Organization's recommendation. We used logistic regressions weighted by provincial population to examine the association between provincial gross domestic product (GDP) per capita and anaemia, adjusting for sex, age, urban–rural location, regional socio-economic status (SES), fixed effect of province, and clustering of schools. We used generalised additive mixed models to evaluate a potentially non-linear relationship. For each 100% growth in GDP per capita, there was a 40% (odds ratio [OR] = 0.60; 95% confidence interval [CI; 0.56, 0.65]) reduction in anaemia. However, the association was weaker for girls and in cities with a lower SES. The association was weaker across 2005–2014 (OR = 0.75, 95% CI [0.62, 0.90]) compared with 1995–2005 (OR = 0.52; 95% CI [0.44, 0.61]), reflecting a weaker association when GDP per capita reaches around $2,000. The results were similar for moderate-to-severe anaemia. We concluded that economic growth has been associated with reductions in anaemia among school-aged children in China but with fewer benefits for girls and those in poorer settings. Further economic development in China is unlikely to bring similar reductions in anaemia, suggesting that additional population level and targeted interventions will be needed.

KEYWORDS
adolescent, anaemia, child, China, economic development, gross domestic product, haemoglobin

Dongmei Luo and Rongbin Xu contributed equally to this paper.

1 | INTRODUCTION

Anaemia is an important global health problem with children and pregnant women most at risk (Balarajan, Ramakrishnan, Ozaltin, Shankar, & Subramanian, 2011). Iron deficiency is one of the key causes of anaemia and is the leading cause of disability-adjusted life years among children aged 7–14 years in 2017 (GBD 2017 DALYs and HALE Collaborators, 2018). Anaemia can impair motor and cognitive development, with lower academic performance and unfulfilled potential (Balarajan et al., 2011; Granthammcgregor & Ani, 2001; Mccann & Ames, 2007). Inadequate nutrient intake and infectious diseases, two leading causes of anaemia (Balarajan et al., 2011; Tolentino & Friedman, 2007), are both associated with economic growth (Smith & Haddad, 2002). Higher household income improves food availability and dietary diversity, and improved socio-economic status (SES) is generally accompanied by reductions in infectious diseases (i.e., soil-transmitted helminths and schistosomiasis; Smith & Haddad, 2002).

However, only a few studies have examined the association between economic growth and childhood anaemia, and they showed conflicting findings (Alderman & Linnemayr, 2009; Chen, Wu, Wang, Deng, & Jia, 2011; Wu, Yang, Yin, Zhu, & Gao, 2015). Alderman and Linnemayr (2009), using data from 40 demographic and health surveys in 32 countries from 1995 to 2006, found that, on average, anaemia prevalence among children under 5 declined roughly a quarter as fast as gross national income per capita increases. Chen et al. (2011) examined the impact of the 2008 global economic crisis in China and found that the anaemia prevalence of children under 5 was relatively stable during and after the crisis, suggesting that in this case, economic fluctuations had minimal effects on childhood anaemia. Wu et al. (2015) used aggregated time series data from nationally representative surveys in China from 1992 to 2010 and reported no significant correlation between gross domestic product (GDP) per capita and anaemia prevalence among children under 5.

Apart from the contradictory findings, these three studies have several limitations (Alderman & Linnemayr, 2009; Chen et al., 2011; Wu et al., 2015). First, they all relied on aggregated measures of anaemia rather than individual-level data, raising a possibility of an ecological fallacy (Piantadosi, Byar, & Green, 1988). Second, using aggregated data reduced statistical power and raised a possibility of false negative results. Furthermore, all studies were conducted among preschool-aged children, and no study has examined the links between anaemia and economic growth in school-aged children and adolescents are largely overlaped. Older children are also vulnerable to anaemia, with a global prevalence of 25.4% (95% confidence interval [CI; 19.9, 30.9]), corresponding to 305 million (95% CI [238, 371]) children (World Health Organization [WHO], 2008). Even though it carries implications for both future health and that of the next generation (Patton et al., 2018), anaemia in school-aged children has been poorly monitored compared with preschool children, pregnant women, and women of reproductive age (WHO, 2008).

Key messages

- Chinese economic growth was associated with anaemia reductions in school-aged children but with fewer gains in girls and those in poorer settings.
- The association between economic growth and anaemia was weaker across 2005–2014 compared with 1995–2005, reflecting a weaker association when gross domestic product per capita reaches around $2,000.
- The results suggest that additional population level and targeted interventions will be needed to tackle persisting high levels of childhood anaemia in China, and this may well be true for other countries.

China has undergone rapid transitions in health, demography, nutrition, and economic growth in recent decades, providing an opportunity to investigate the effects of economic development on childhood anaemia. In this study, we use school-based, cross-sectional surveys from 26 mainland provinces and 4 municipalities from 1995 to 2014 to investigate the extent to which economic growth has been accompanied by reductions in anaemia among school-aged children.

2 | METHODS

2.1 | Literature review

We searched PubMed and Google Scholar for articles whose title and abstract included children (search terms "child," "children," and "adolescent"), economic growth (search terms "economic" and "growth"), and anaemia (search terms "anemia," "anaemia," "hemoglobin," "haemoglobin," "Hb," and "Hgb") published in English from January 1, 1990 to November 6, 2019. We identified only three studies of the association between economic growth and childhood anaemia. These three studies were described in the Section 1.

2.2 | Design and participants

The Chinese National Survey on Students' Constitution and Health (CNSSCH): This project comprises a series of school-based, cross-sectional surveys that monitored the health status in Chinese children aged 7–18 years (CNSSCH Association, 1987, 1997, 2002, 2007, 2012, 2016). The CNSSCH was first conducted in 1985 and used the same multistage stratified random cluster sampling procedure in 1995, 2000, 2005, 2010, and 2014 (Figure 1). The SES within a province of a city (upper, intermediate, and lower) was assessed at the study onset (in 1985) and remained unchanged. The design yields a representative sample for each province.

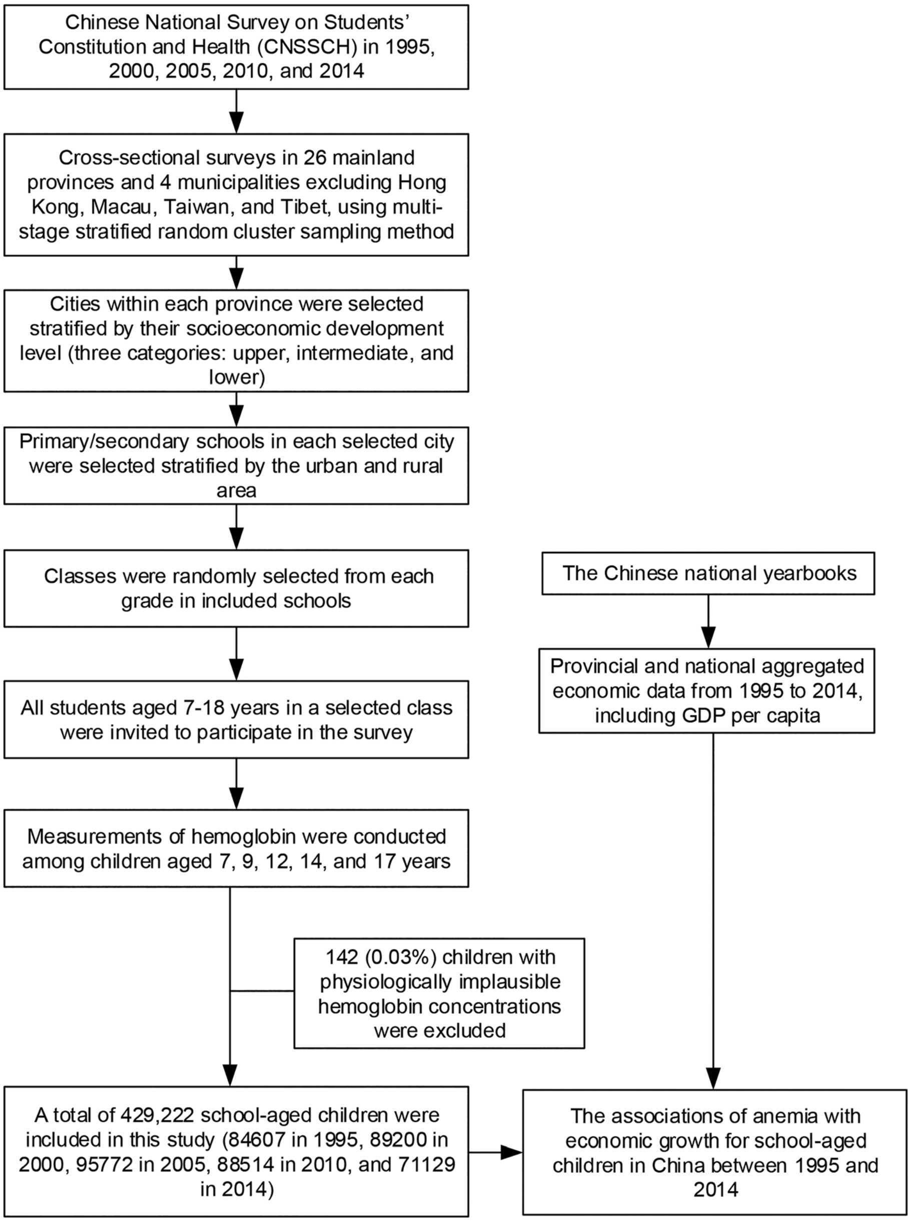

FIGURE 1 Participant flow chart for the Chinese National Survey on Students' Constitution and Health. The three categories (upper, intermediate, and lower) of socio-economic development level were determined based on five different characteristics: regional gross domestic product (GDP), total yearly income per capita, average food consumption per capita, natural growth rate of population, and the regional social welfare index. The measurements of haemoglobin are missing for children in 1995 in Qinghai and Chongqing (when it was not regarded as a municipality) and for children aged 17 years in 2014

Measurements of haemoglobin were conducted in the surveys from 1995 to 2014 in 30 regions, among children aged 7, 9, 12, 14, and 17 years. However, the measurements of haemoglobin are missing for children in 1995 in Qinghai and Chongqing (when it was not regarded as a municipality) and for children aged 17 years in 2014.

Informed consent was obtained verbally from both students and parents. To protect participants' privacy, we used anonymous data for all our analyses.

2.3 | Measurement of anaemia

Capillary blood samples were collected at school from each selected child aged 7, 9, 12, 14, and 17 years after discarding the first drop. In 1995–2010, haemoglobin concentration measurement was performed by laboratory technicians using spectrophotometric determination of cyanide-haemoglobin whereas in 2014 using Hemo-Cue201+ (Origin: Sweden; Model: HemoCue201+; Manufacturer: HemoCue AB).

According to the recommendation of WHO (2011), we adjusted the measured haemoglobin concentration based on the altitude of the corresponding cities and then used altitude-adjusted haemoglobin concentrations to define anaemia and its severity: (a) for children aged 7 and 9 years, non-, mild, moderate, and severe anaemia are respectively defined as altitude-adjusted haemoglobin concentration ≥ 115, 110–114, 80–109, and <80 g/L; (b) for children 12 and 14 years of age and girls 17 years of age, non-, mild, moderate, and severe anaemia are respectively defined as altitude-adjusted haemoglobin concentration ≥ 120, 110–119, 80–109, and <80 g/L; (c) for boys 17 years of age, non-, mild, moderate, and severe anaemia are respectively defined as altitude-adjusted haemoglobin concentration ≥ 130, 110–129, 80–109, and <80 g/L. We used both anaemia (yes/no) and moderate-to-severe anaemia (MS anaemia; yes/no) as primary outcomes; the prevalence of severe anaemia was negligible.

Outliers were defined as observations with sex- and age-specific altitude-adjusted haemoglobin concentration outside the range of mean ± 5SD. They were excluded from the analyses due to their physiologically implausible haemoglobin concentration.

2.4 | Other data

The Chinese national yearbooks (National Bureau of Statistics of the People's Republic of China, 2015): These data sets were used to obtain the provincial and national aggregated economic data from 1995 to 2014, including the nominal GDP per capita and the population size. We adjusted the nominal GDP for consumer price index to get the real GDP in a constant price referenced to 2014. To make our analyses internationally comparable, we transformed the currency unit into U.S. dollars according to an average exchange rate of 2014 (RMB ¥1 = $0.16).

2.5 | Statistical analysis

At the provincial level, we used scatter plots and Pearson correlation coefficient to assess the association between log GDP per capita and anaemia or MS anaemia prevalence. In the scatter plots, GDP per capita was presented on a natural logarithmic scale.

At the individual level, we used logistic regression models to examine the association between economic growth and anaemia. GDP per capita for specific provinces and survey years was assigned to all corresponding individuals. The GDP per capita in natural logarithmic unit (log GDP per capita) was added to the regression model as the independent variable. The associations were quantified as odds ratios (ORs) of anaemia or MS anaemia associated with 100% growth in GDP per capita (Vollmer et al., 2014). All models were adjusted for sex, age, urban or rural area of residence, baseline regional SES within province when appropriate, fixed effects of province, and clustering of schools. All models were weighted by population of corresponding province and year. We did not incorporate fixed effects for years as they were consistently insignificant in all models.

Stratified analyses were conducted by sex, age, urban–rural location, different time periods (1995–2005 vs. 2005–2014), and regional SES within province (upper, intermediate, and lower); *p* values for difference tested the subgroup difference in the effect estimates, and they were estimated by adding interaction term to the model. For the time period, as adding interaction term is not possible, we used meta-regression to estimate the *p* value for difference.

We used generalised additive mixed models (GAMM; Anderson-Cook, 2007) to fit the non-linear relationship between GDP per capita and anaemia or MS anaemia, weighted by provincial population and adjusting for the same covariates and random effects of schools as logistic models mentioned above. A spline function was used for GDP per capita in the GAMM. Akaike information criterion was used to choose the smoothing parameter, and finally, a smoothing parameter of one was attributed to all models. In those plots, we stratified GDP per capita into four strata according to World Bank's international classification of country affluence in 2014 (The World Bank, n.d.): low income (≤$1,045), lower middle income ($1,046–4,125), upper middle income ($4,126–12,735), and high income (>$12,735).

We viewed a *p* value less than.05 as statistically significant. The GAMM and meta-regression were performed on R (version 3.3.3) by “gamm4” package (version 0.2-5) and "mvmeta" package (version 0.4.11), respectively. All the other analyses were done with Stata (version 14.0).

2.6 | ETHICAL STATEMENT

The Chinese National Survey on Students' Constitution and Health (CNSSCH) was approved by the Medical Research Ethics Committee of Peking University Health Science Center (IRB00001052-18002). Informed consent was obtained from each participant. To protect participants' privacy, we used anonymous data for all our analyses.

3 | RESULTS

A total of 429,222 school-aged children were included in this study, after excluding 142 (0.03%) children with physiologically implausible haemoglobin concentrations (Figure 1). The sample sizes for the five surveys ranged from 71,129 to 95,772. The ratio of girl/boy or rural/urban approximately equalled 1 in each survey. The proportions of students at different ages were approximately equivalent in each survey (except that children aged 17 years were not included in 2014; Table 1).

3.1 | The economic growth and anaemia prevalence during 1995–2014

From 1995 to 2014, China had experienced a sustained economic boom. The national GDP per capita has increased by more than 500% from $1,263.3 to $7,594.3. Meanwhile, the anaemia and MS anaemia prevalence dropped from 19.9% and 7.2% in 1995 to 8.9% and 3.1% in 2014, respectively. However, the reduction in anaemia or MS anaemia prevalence occurred predominantly during 1995–2005 rather than 2005–2014, despite consistent economic growth across the 19-year period (Table 1; Figure S1).

The trends of anaemia and MS anaemia prevalence varied substantially across the 30 regions in our study. The largest six declines (more than 20%) in anaemia prevalence from 1995 to 2014 happened in Sichuan, Jiangxi, Yunnan, Tianjin, Hunan, and Anhui. In contrast, Hainan, Heilongjiang, and Ningxia had an increased prevalence of anaemia over this time with Hainan increasing by 10.4 percentage points. In 2014, there was a very large inter-province

TABLE 1 The characteristics of samples included in the analyses, by survey year

	Survey year				
	1995	2000	2005	2010	2014
Sample size	84,607	89,200	95,772	88,514	71,129
Boys, *n* (%)	42,544 (50.3)	44,694 (50.1)	48,035 (50.2)	44,213 (50.0)	35550 (50.0)
Urban, *n* (%)	42,823 (50.6)	44,730 (50.1)	48,189 (50.3)	44,404 (50.2)	35611 (50.1)
Age, *M* ± *SD*	11.9 ± 3.5	11. 8 ± 3.5	11.8 ± 3.5	11.8 ± 3.5	10.5 ± 2.7
7 years, *n* (%)	16,361 (19.3)	17,934 (20.1)	19,220 (20.1)	17,838 (20.2)	17,852 (25.1)
9 years, *n* (%)	16,368 (19.3)	17,858 (20.0)	19,265 (20.1)	17,798 (20.1)	17,798 (25.0)
12 years, *n* (%)	17,316 (20.5)	17,963 (20.1)	19,096 (20.0)	17,769 (20.1)	17,749 (25.0)
14 years, *n* (%)	17,316 (20.5)	17,869 (20.0)	18,989 (19.8)	17,643 (19.9)	17,730 (24.9)
17 years, *n* (%)	17,246 (20.4)	17,576 (19.7)	19,202 (20.0)	17,466 (19.7)	0 (0.0)
Anaemia, *n* (%)	16,811 (19.9)	14,212 (15.9)	10,098 (10.5)	10,174 (11.5)	6,316 (8.9)
Moderate-to-severe anaemia, *n* (%)	6,131 (7.2)	4,359 (4.9)	3222 (3.4)	3,634 (4.1)	2,181 (3.1)
Provincial GDP per capita ($), ±*SD*[a]	1,100.1 ± 728.2	1,987.4 ± 1,500.8	3,501.3 ± 2,354.3	6,247.4 ± 3,165.2	8,381.0 ± 3,597.5
National GDP per capita ($)[a]	1,263.3	1,799.5	3,036.9	5,634.0	7,594.3

Abbreviation: GDP, gross domestic product.
[a]GDP per capita were all in 2014 price.

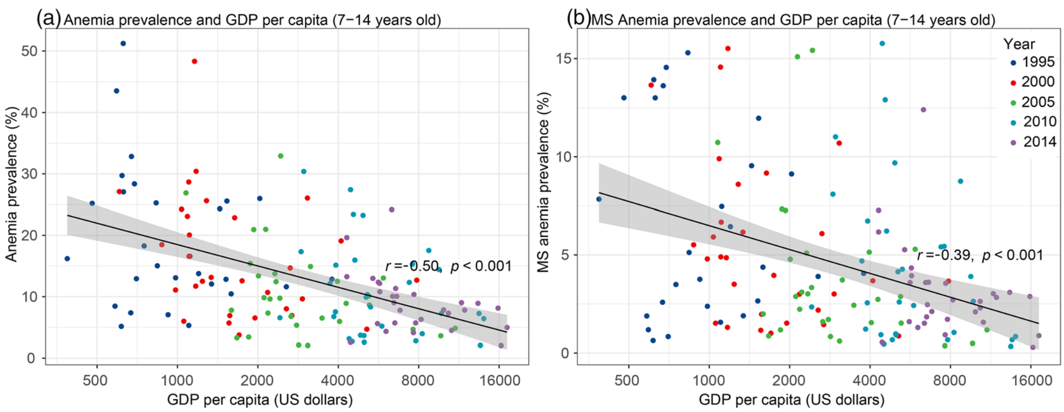

FIGURE 2 Correlation between (a) anaemia or (b) moderate-to-severe anaemia (MS anaemia) and gross domestic product (GDP) per capita for children 7–14 years of age. GDP per capita was presented on a natural logarithmic scale. *r* represents Pearson correlation coefficient between anaemia or MS anaemia prevalence and log GDP per capita. Data are missing for Qinghai and Chongqing in 1995. Sichuan province had an extremely high prevalence of MS anaemia in 1995 (33.3%) and was excluded from plot (b). The shadows represent 95% confidence intervals

variation in anaemia prevalence in school-aged children, ranging from 2.0% in Beijing to 24.2% in Hainan (Figure S2; Table S1).

3.2 | The association between economic growth and anaemia or MS anaemia

At provincial level, anaemia prevalence was inversely and moderately correlated with log GDP per capita (Pearson correlation $r = -0.50$, $p < .001$; Figure 2a). MS anaemia prevalence was less substantially correlated with log GDP per capita compared with anaemia ($r = -0.39$, $p < .001$; Figure 2b).

At an individual level, every 100% growth in GDP per capita was associated with a 40% (OR = 0.60, 95% CI [0.56, 0.65]) reduction in anaemia. The associations did not show significant difference between different ages and between urban and rural (*p* value for difference > .05). However, the associations were weaker for girls compared with boys (*p* value for difference < .05) and were weaker for children in cities with lower regional SES compared with upper regional SES (*p* value for difference < .05). This association was significantly lower across 2005–2014 (OR = 0.75, 95% CI [0.62, 0.90]) compared with 1995–2005 (OR = 0.52, 95% CI [0.44, 0.61]; Figure 3a).

The results were similar for MS anaemia. Every 100% growth in GDP per capita was associated with a 44% (OR = 0.56, 95% CI [0.50, 0.64]) reduction in MS anaemia. During 2005–2014, the association between GDP per capita and MS anaemia attenuated to null (OR = 0.78, 95% CI [0.60, 1.01]) compared with 1995–2005 (Figure 3b).

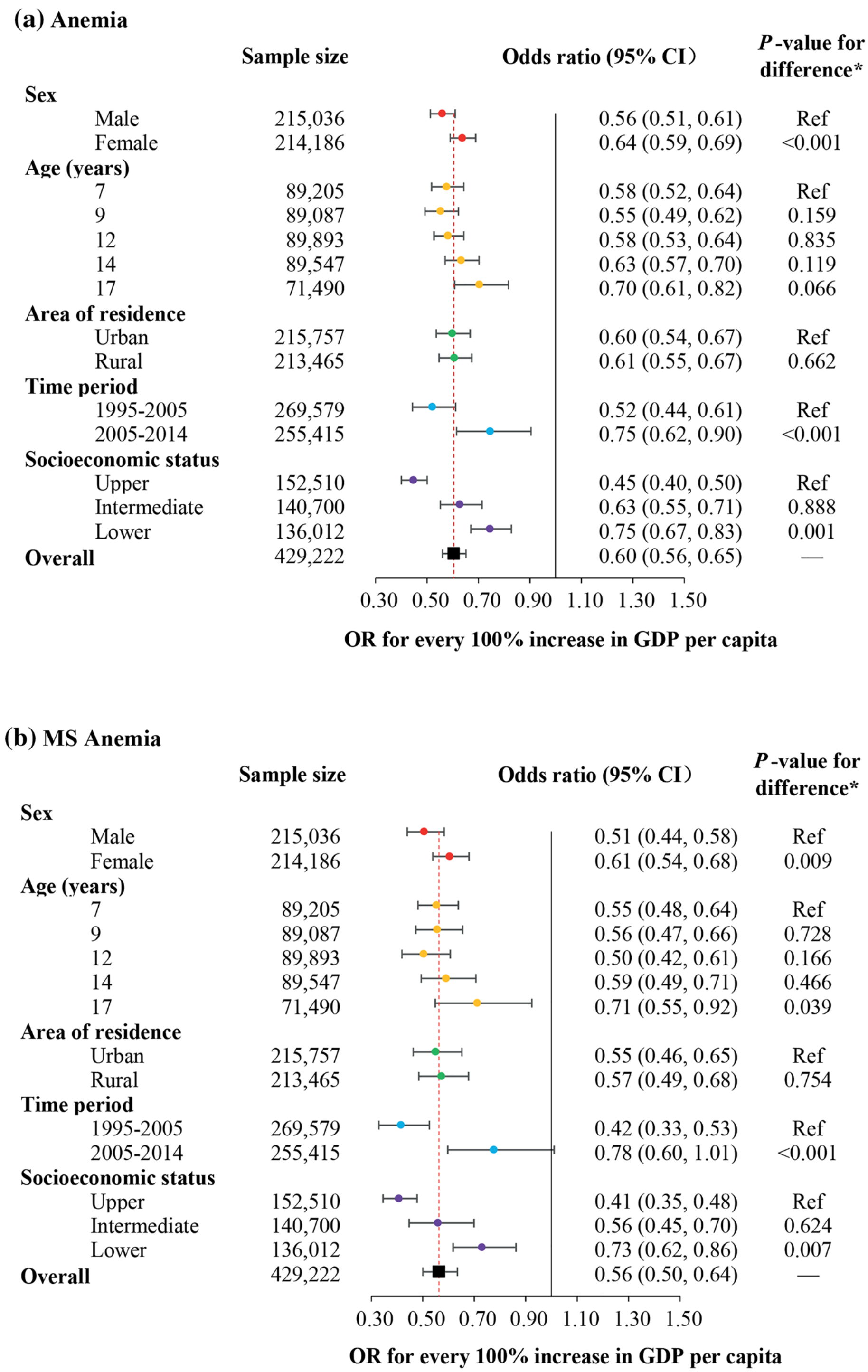

FIGURE 3 The association between (a) anaemia or (b) moderate-to-severe anaemia (MS anaemia) and every 100% increase in gross domestic product (GDP) per capita; *p* values for difference tested the subgroup difference in the effect estimates, and they were estimated by adding interaction term to the model. For the time period, adding interaction term is not possible; we used meta-regression to estimate the *p* value for difference. Abbreviations: CI, confidence interval; OR, odds ratio

The lower associations between economic growth and anaemia or MS anaemia since 2005 were likely to be a result of a non-linear relationship with a decrease of OR of anaemia less once GDP per capita reached around $2,000 (Figure 4).

4 | DISCUSSION

This is the first study that has evaluated the association between economic growth and anaemia reduction among school-aged children. Based on surveys of 429,222 school-aged children from five national surveys between 1995 and 2014, we found that every 100% increase in GDP per capita was accompanied by a 40% reduction in anaemia and 44% reduction in MS anaemia. However, the benefits from economic growth were less in girls and for children growing up in poorer areas. The association between economic growth and anaemia has been lower since 2005, suggesting that income is a major driver of anaemia below a $2,000 per capita.

Economic growth is likely to contribute to anaemia reduction by improving food availability and dietary diversity and by bringing

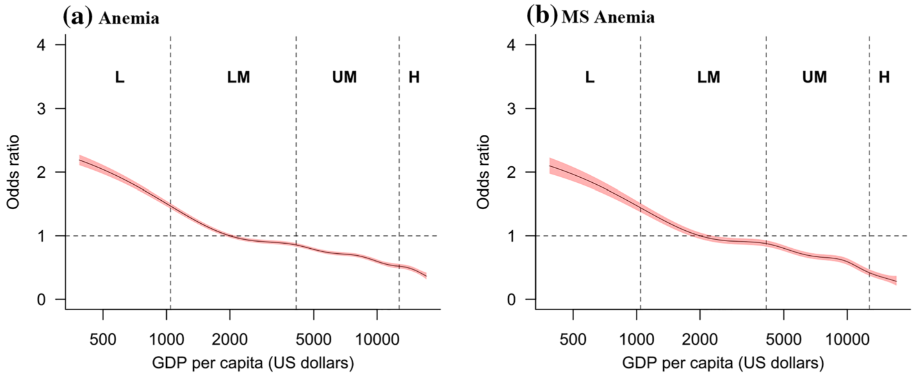

FIGURE 4 Non-linear relationship between gross domestic product (GDP) per capita and (a) anaemia or (b) moderate-to-severe anaemia (MS anaemia). GDP per capita was presented on a natural logarithmic scale. The shadows represent 95% confidence intervals. Abbreviations: H, high income; L, low income; LM, lower middle income; UM, upper middle income

reductions in intestinal infectious diseases (i.e., soil-transmitted helminths and schistosomiasis; Smith & Haddad, 2002). The underlying reasons for the sex and socio-economic inequality in the benefit of economic growth are unclear. One explanation is that Chinese girls prefer to be slim leading to dietary restriction (23.6% in girls vs. 9.1% in boys according to a national survey in 2005) and thus benefit less from food availability or diversity (Song, Wang, Ma, & Wang, 2013). Alternatively, school-aged girls enter puberty about 2 years earlier (Song et al., 2014; Song et al., 2016), and menstruation may increase girls' vulnerability to anaemia (Friedman et al., 2012) and lesser reduction with economic growth.

As we measured SES within province, socio-economic inequality is due to the intraprovincial income inequality. In each province, the economic and political resources were generally centralised to the upper SES cities (usually the capital cities), with those cities having faster economic growth compared with lower SES cities in the same province. This could be supported by the increased intraprovincial income inequality during 1998–2007 (Gravier-Rymaszewska, Tyrowicz, & Kochanowicz, 2010). Moreover, a fiscal decentralisation policy since 1995 has further exaggerated intraprovincial inequality, because the local governments had to rely more on themselves rather than the provincial government's support (Liu, Martinez-Vazquez, & Wu, 2014). Thus, lower SES cities often lack money to invest in school health, such as improving sanitation, preventing intestinal infectious diseases, and improving students' diet.

One possible reason for the diminished association with economic growth since 2005 might be that increases in regional income have not been equally shared by disadvantaged populations, who are more vulnerable to anaemia (Balarajan et al., 2011). A second possibility is that the pattern of risk factors for anaemia changes with economic development (Balarajan et al., 2011). From 1995 to 2005, economic growth is likely to have brought greater dietary diversity and improved sanitation; between 1992 and 2002, the average consumption of livestock and poultry meat in China increased from 58.9 to 78.6 g (Zhao et al., 2016); from 1988–1992 to 2001–2004, the estimated number of soil-transmitted nematodes-infected people also declined from 536 million to 129 million (Xu et al., 2005). For this reason, other risks including a limited awareness of anaemia symptoms and lack of understanding about anaemia prevention may have come to play a bigger role since 2005. Such risk factors may be less affected by economic growth alone. This “bottleneck” stage of anaemia reduction has also been reported in other countries (Gupta, Perrine, Mei, & Scanlon, 2016; Stevens et al., 2013).

Although China continues to have rapid economic growth rate, we expect that any further gains in childhood anaemia will be modest due to the diminished association with growth since 2005. Further reductions in anaemia seem likely to require more targeted interventions with a particular focus on high-risk subgroups. For the government, there is a strong rationale in that prevention, and treatment of anaemia is likely to improve work capacity and cognitive development and ultimately promote economic growth (Balarajan et al., 2011; Horton & Ross, 2003).

Targeted interventions, tailored to the local context, are now needed to further reduce anaemia in school-aged children in China. Local governments should assess the context-specific determinants of anaemia, especially in provinces where anaemia prevalence remains relatively high or has rebounded. For example, the high prevalence of anaemia in 2014 of Hainan may be partly due to its prevalent soil-transmitted helminths infection, especially hookworm and pinworm, although it is uncertain whether the infection is associated with the rebound in anaemia prevalence (Zang, Zhang, & Chen, 2013). In this case, iron supplementation and deworming would be sensible interventions (Pasricha, Drakesmith, Black, Hipgrave, & Biggs, 2013). In provinces with relatively low and stable anaemia prevalence (e.g., Beijing and Shanghai), efforts should be more focused on nutritional education and diet modification (Pasricha et al., 2013). Other potential risk factors beyond dietary iron deficiency and infectious diseases, like vitamin B12 and folic acid deficiency due to the dietary shifts, prevalent vitamin D deficiency partly due to insufficient outdoor time, tea culture, and increased coffee consumption (Balarajan et al., 2011), should be considered. Governments also need to pay special attention to the anaemia status of high-risk subgroups, such as children from low SES and girls, and to monitor and evaluate existing nutrition improvement programmes to ensure their effectiveness.

As the first multilevel examination of the association between economic growth and anaemia in school-aged children, our study has several strengths. First, our school-based sample is representative of the childhood population, especially children under 15 years of age. In 2014, the gross enrollment rates of primary and junior and senior secondary education in China were estimated to be 99.8%, 87.9%, and 69.7%, respectively (Yuan, He, & Li, 2017). Second, our sample is large enough and geographically diverse. In addition, including individual-level data of anaemia allowed us to tackle the challenge of the ecological fallacy that confounds earlier studies (Alderman & Linnemayr, 2009; Chen et al., 2011; Wu et al., 2015). Nevertheless, there are some limitations. For data collection, haemoglobin data for children aged 17 years in 2014 were not available. However, the analyses stratified by age were largely consistent with the main results. A second limitation relates to the haemoglobin measurements. In the survey in 2014, using the HemoCue method rather than the direct cyanmethemoglobin method to measure haemoglobin concentration brought a potential for measurement error. However, the prevalence of anaemia appears similar when assessed using these two methods for both venous blood and capillary blood (Sari et al., 2001). Besides, the haemoglobin concentration measured with these two methods are highly correlated with a Pearson's correlation coefficient of.917 ($p < .05$), and the haemoglobin concentration measured by HemoCue method is on average 1.8 (95% CI [0.8, 2.8]) g/L higher than that measured by the direct cyanmethemoglobin method (venous blood), which indicates that the association of economic growth and anaemia reduction was even smaller across 2005–2014 (Sari et al., 2001). Another limitation is that there is a possibility that we did not account for provincial factors that may have confounded associations between economic growth and anaemia (Smith & Haddad, 2002). We addressed this issue by incorporating province fixed effects into our models. It is less likely to be a problem as in studies comparing countries because provinces in the same country have greater similarities around political and institutional environments, education systems, and social norms. In this context, there is also the possibility that the effect of economic growth may have been attenuated by the capacity of central government to reallocate national income across provinces.

In summary, economic growth was associated with reductions in anaemia among school-aged children but with fewer gains in girls and those in poorer settings. Further economic growth alone is unlikely to bring continued falls in childhood anaemia, and there is now a need to develop and evaluate interventions targeted to the local context and high-risk subgroups.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

RX, DL, and YS conceived and designed the study. JM, YS, PH, DL, and RX supported the data collection. DL, RX, and XY performed the statistical analysis. DL and RX wrote the first draft of manuscript. GP, HR, YS, JM, and CJ contributed to significant edit and critical review. All authors reviewed and revised the manuscript. All authors read and approved the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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