Original Article

Vitamin A status and recurrent respiratory infection among Chinese children: A nationally representative survey

Yixin Zhang MSc[1], Zifang Du MSc[1], Wenbo Ma MSc[1], Keliang Chang MSc[1], Chunmei Zheng MSc[2]

[1]*Department of Statistics, Renmin University of China, Beijing, China*
[2]*Beijing Harmony Health Medical Engineering Technology Research Institute, Beijing, China*

Background and Objectives: Vitamin A is involved in immune function, vision, reproduction, and cell differentiation and is essential for child growth. Vitamin A deficiency (VAD) contributes significantly to mortality and morbidity in developing countries. This study assessed the current vitamin A status in Chinese children. **Methods and Study Design:** A cross-sectional survey was conducted in 26 provinces in China between 2015 and 2018, and 277,064 children aged 0–14 years were enrolled. Data on sociodemographic factors and dietary supplements were obtained through interviews with their parents. Serum vitamin A concentrations were measured using HPLC. To reduce the sampling error, a weighted distribution was produced to estimate the distribution of serum vitamin A concentration in Chinese children. A new method was used calculate the CI. **Results:** The results revealed that 10.4% (23.9 million) (95% CI: 10.1%–10.8%) of Chinese children aged 0–14 years were at risk of suffering from subclinical VAD (SVAD) (<0.2 mg/L). Sick children, especially those with recurrent respiratory infections (21.3%, 95% CI: 20.5%–22.2%), were vulnerable to SVAD. A high prevalence of SVAD was observed in western and northeastern areas in China. Serum vitamin A concentrations in ethnic minority groups were significantly lower than those in Han Chinese children (*p*<0.01). **Conclusions:** VAD is still a moderate public health problem in Chinese children, especially in those with respiratory symptoms. Regular consumption of vitamin A–rich foods should be promoted through nutrition education for parents.

Key Words: vitamin A, distribution, deficiency, children, China

INTRODUCTION

Vitamin A is an essential fat-soluble micronutrient[1] that promotes growth and maintains physiological functions.[2] Although the living standards have risen worldwide, vitamin A deficiency (VAD) remains a major public health threat in low- and middle-income countries.[3] An estimated 190 million (33.3%) of preschool-age children globally are at risk of VAD.[4] VAD impairs immune functions, making children less able to fight common infections, such as measles and respiratory infections, and leads to night blindness.[5,6] Many studies have identified a significant correlation between VAD and child mortality.[7,8]

Even though VAD no longer leads to death in some areas, the prevalence of VAD and child mortality in South Asia, Southeast Asia, and Sub-Saharan Africa remains high.[4] Numerous small-scale surveys have indicated that VAD continues to be a serious public health problem for preschool-age children in China.[9-12] However, the extent of VAD in school age and young adolescent children remains unclear. Furthermore, most of the surveys were local and conducted by doctors on their patients, and therefore the samples might not reflect the entire Chinese population. A comprehensive and up-to-date assessment of vitamin A status in Chinese children is thus necessary.

This study therefore assessed the latest vitamin A status in Chinese children aged 0–14 years using a histogram to represent the distribution of serum vitamin A concentration. A new method was developed to estimate the CIs for the probability within each bin.

METHODS

Study population and data collection

The sample came from two departments. One part of the sample were children aged 0–14 years who visited health care centers from August 9, 2016, to June 18, 2018. A total of 65,965 healthy children (Group A) from 17 provinces were randomly selected. The data were stored in the Laboratory Information System (LIS) at Beijing Harmony Health Medical Engineering Technology Research Institute, Beijing, China.

The other part of the sample were children aged 0–14 years who visited pulmonary clinics from March 1, 2015, to April 30, 2018. A face-to-face survey was conducted by pediatric pulmonologists with the children's parents or principal caregivers using a structured questionnaire comprising sociodemographic factors, respiratory health status, and dietary intake in the past month. Respiratory infection is the most common childhood illness in China, accounting for 75% of pediatric hospitalizations.[13] Self-reported respiratory symptoms in the past 12 months were necessary to assess the children's health status. A total of 211,099 children from 25 provinces were randomly selected; of them, 159,650 children reported their respiratory health status. According to the diagnostic criteria of recurrent respiratory infections (RRI) (Table 1), these children were divided into four groups (B1, B2, C1, and C2) (Table 2).[14] This research project was directed by the Capital Institute of Pediatrics. This project was approved by the National Health Commission of the People's Republic of China. All children's parents were requested to sign a consent form.

Measurements of vitamin A
Serum vitamin A concentration was measured by Beijing Harmony Health Medical Engineering Technology Research Institute using HPLC. HPLC has been demonstrated to be a fast, straightforward, and reliable method.[15] Serum samples were treated with an equal volume of ethanol and then extracted three times with an equal volume of hexane. The hexane extracts were pooled and dried under nitrogen. Serum vitamin A concentrations were quantified by measuring the absorbance at 295 nm. External control samples were used to ensure accuracy. In this study, serum vitamin A concentrations were divided into five levels (<0.1, 0.1–0.2, 0.2–0.3, 0.3–0.7, and >0.7 mg/L). Serum vitamin A concentration <0.2 mg/L was defined as subclinical VAD (SVAD) and 0.2-0.3 mg/L as suspected subclinical VAD (SSVAD).[14]

Statistical analysis
R Studio version 3.5.0 was used for all analyses. Duplicate data were removed. If a child was enrolled two or more times, only the first information was used. Histograms were used to display the distributions of serum vitamin A concentration. Continuous variables are presented as mean ± standard deviation (SD), and categorical variables as percentages. An independent-samples student's t test and non-parametric methods such as the Kruskal–Wallis test were used to compare continuous variable data. Results were considered significant at $p<0.05$.

Estimating methodology
Previous studies have tended to investigate serum vitamin A concentrations in healthy children. However, a certain percentage of children are always sick at any given moment. RRI is one of the most common pediatric diseases with an overall morbidity of 20% in China.[16-21] A significant difference in vitamin A status has been noted between children with RRI and healthy children.[22-25] In statistical surveys, when subpopulations within an overall population vary, it can be advantageous to sample each subpopulation independently. Therefore, when estimating the distribution of serum vitamin A concentrations in Chinese children, it was necessary to combine the two distributions of serum vitamin A concentrations in healthy children and children with RRI.

The sample was considered for post-event stratification. All children were divided into two independent strata according to their respiratory health status: with or without RRI. Individuals in Group B were randomly selected from children with RRI, and individuals in Group A were randomly selected from healthy children. A weighted population distribution was calculated according to the two subpopulation distributions (Figure 1). The population weight of stratum RRI was 20%, which is the overall morbidity of RRI.[16-21]

The distribution of serum vitamin A was estimated with 95% CI based on normal distribution. Histograms were used to present the distributions of serum vitamin A concentration. A new method was proposed to estimate CI for histograms. For simplicity, a histogram was assumed to partition the set into several bins. The bins were sorted in descending order, and the probabilities were assumed to

Table 1. Diagnostic criteria of RRI

Age	Upper respiratory tract infection	Tracheitis/ bronchitis/ pneumonia
6months - 2years	≥7 times	≥3 times (Pneumonia ≥2 times)
2-5years	≥6 times	≥2 times
5-14years	≥5 times	≥2 times

RRI: recurrent respiratory infections.

Table 2. Data structure

Data source	Group	
Part 1 LIS	Healthy Children (Group A)	Healthy (Group A)
Part 2 HIS	RRI (Group B)	RI symptoms (Group B1)
		No RI symptoms (Group B2)
	Non RRI (Group C)	RI symptoms (Group C1)
		No RI symptoms (Group C2)

LIS: laboratory information system; HIS: hospital information system; RRI: recurrent respiratory infections; RI: respiratory infections.
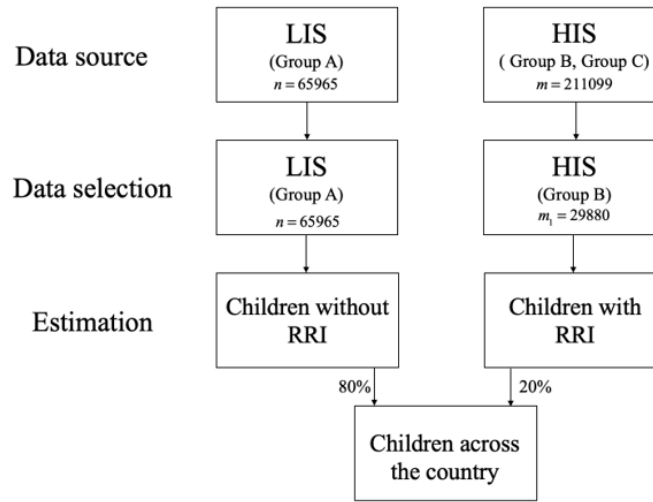
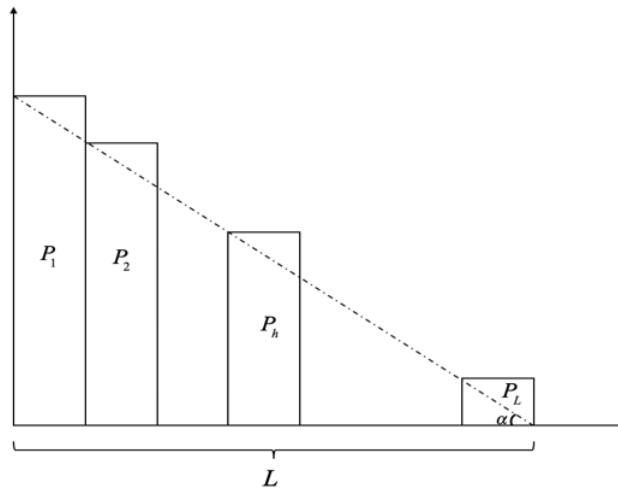**Figure 1.** Estimation of population distribution.

Figure 2. Histogram bins in a descending order.

demonstrate a linear decay (Figure 2). At L number of bins, the following partition was obtained:

$B_1 = [0,1]$, $B_2 = [1,2]$, ….., $B_L = [L-1, L]$,
$P_1 \geq P_2 \geq …… \geq P_L$

In this case,

P_h = [(*number of observations within B_h*)/ *n*]*[1/ length of bin]

$$= \sum_{i=1}^{n} I\ (X_i \in B_h)/\ n \qquad (1)$$

It was assumed that
$\Sigma\ |P_h - P_h| = \Sigma\ d_h = d = L\bar{d}$,
$\Sigma\ |P_h - P_h\ | = \Sigma\ r_h\ P_h = \bar{r}$

where d_h is the absolute error and $\bar{r}$ is the average relative error.

According to the central limit theorem,

$\frac{\hat{P}_L - P_L}{\frac{\sqrt{P_L(1-P_L)}}{\sqrt{n}}} \sim N(0,1)$, where $n \to \infty$

$P\ (\frac{|\hat{P}_L - P_L|}{\frac{\sqrt{P_L(1-P_L)}}{\sqrt{n}}} < \frac{d_L}{\frac{\sqrt{P_L(1-P_L)}}{\sqrt{n}}}) = 1- \alpha$

$$\sqrt{n} = \frac{Z_{\alpha/2}\sqrt{P_L(1-P_L)}}{d_L} \qquad (2)$$

According to the correlation between P_L and P_1, $P_L = P_1 / L$, P_1 was used to estimate the population distribution because P_1 was the largest proportion and was the most stable and accessible.

$$1/n = 1/\ [(Z_{\alpha/2}\ /\ \bar{r})^2(L/\ P_1 - 1)] + (1/N) \qquad (3)$$

According to equation (3), when sample size (n), population size (N), and confidence level were given, the average $\bar{r}$ was calculated. The general form of CI was $[P_h - P_h\bar{r}, P_h + P_h\bar{r}]$.

RESULTS
Study population
In total, 277,064 children (0–14 years) from 26 provinces representing the eastern, western, and central areas of China were enrolled (Figure 3). Table 3 presents the study population characteristics. The study population was divided into three groups according to their health status: Group A (healthy children), Group B (children with RRI), and Group C (children with other diseases).

Vitamin A status in the study population
Descriptive statistics of serum vitamin A concentration are presented in Table 4. Mean and SD were used to measure
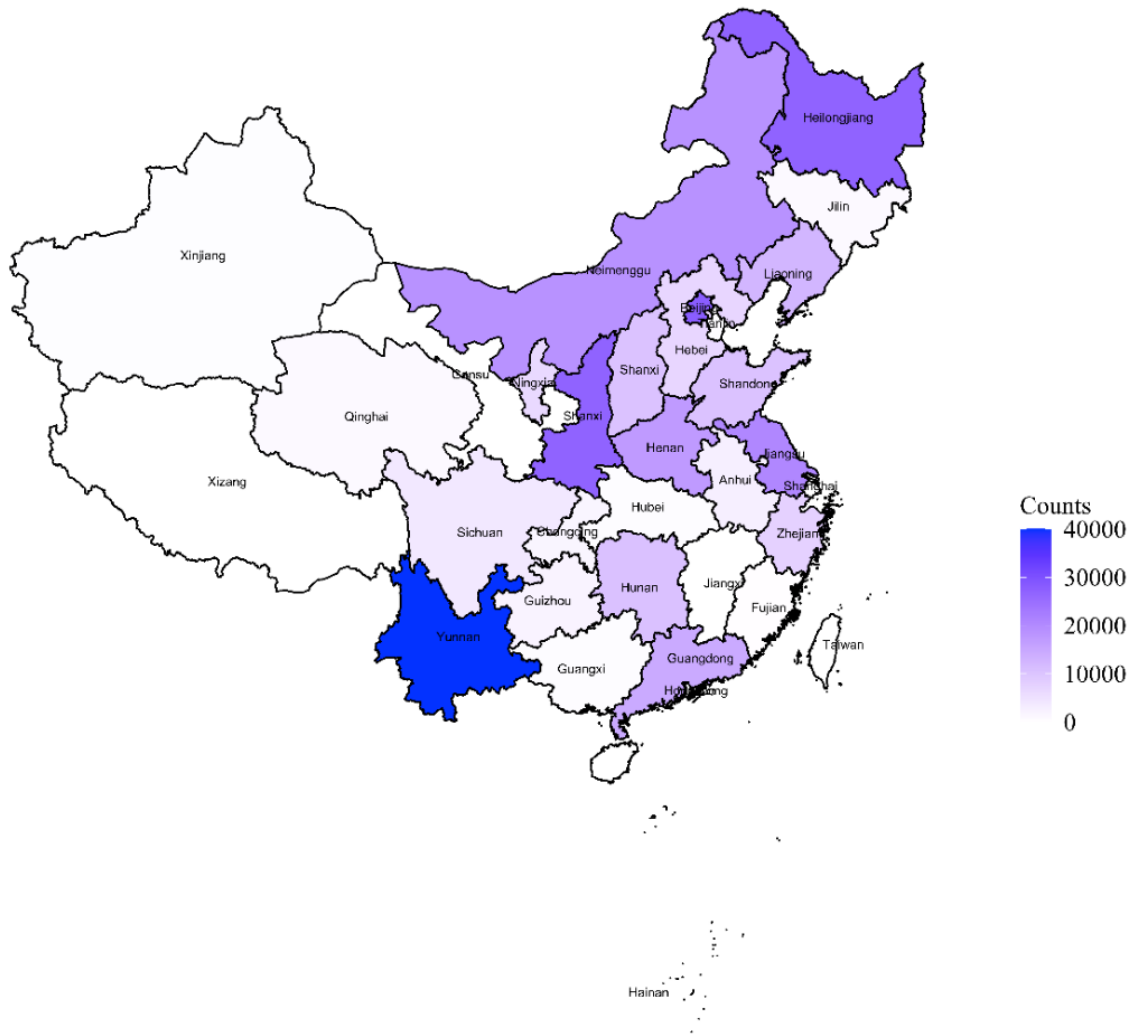
Figure 3. Geographic distribution of the participants

the average values and dispersion of serum vitamin A concentration. The extent of the prevalence of SVAD and SSVAD among the children in different groups was calculated.

Generally, the distributions of serum vitamin A concentration were significantly different between the three groups ($p<0.01$) (Figure 4). The mean serum vitamin A concentration in Group A (0.309 ± 0.082 mg/L) was significantly higher than those in Group B (0.276 ± 0.114 mg/L) ($p<0.01$) and Group C (0.298 ± 0.181 mg/L) ($p<0.01$). However, the prevalence of SVAD was still high even in Group A (7.7%). The highest prevalence of SVAD (21.3%) was observed in Group B. A significant association between RRI and serum vitamin A concentration was noted ($p<0.01$). The vitamin A status was not significantly different between boys and girls in Groups A ($p=0.127$) and B ($p=0.169$). Serum vitamin A concentrations increased significantly ($p<0.01$) with age. Serum vitamin A concentrations in Group A from west and northeast areas were significantly lower than those in east and central areas ($p<0.01$). Serum vitamin A concentrations in children with minority ethnicity were lower than those in Han Chinese children. A small but significant difference was noted in serum vitamin A concentrations between children in urban and rural areas in Group C ($p<0.01$), but the difference was nonsignificant in Group B ($p=0.835$).

Children who mainly ate staple foods, such as rice and wheat, were likely to have lower serum vitamin A concentrations among Group B (0.273 ± 0.106 mg/L) and Group C (0.288 ± 0.128 mg/L). In group C, children who ate more meat (0.425 ± 0.42 mg/L) tended to have a higher serum vitamin A concentration compared with those who ate more vegetables (0.34 ± 0.257 mg/L) ($p<0.01$). Furthermore, 23.3% of children who drank <100 mL milk daily were at risk of SVAD. Approximately 60% of children in Group C had eaten foods containing liver in the past month. The prevalence of SVAD among non–liver eaters (21.2%) was significantly higher than that among liver eaters ($p<0.05$). A lower prevalence of SVAD (12.7%) was observed in children who ate lamb liver in the past month compared with those who didn't.

The distributions of serum vitamin A concentration were significantly different between Groups A and B ($p<0.05$), indicating different vitamin A statuses among the subpopulations. Thus, the two distributions were weighted when the overall population distribution was estimated. Because 20% of Chinese children have RRI,[16-21] first, the distributions of serum vitamin A were estimated separately among healthy children and children with RRI using 95% CI based on normal distribution. According to equation (3), the sample size of Group A was large enough to yield a relative error of estimation <3% under 95% CI, whereas

Table 3. Characteristics of the subjects

Characteristic	Group A 65965 (100)	Group B 29880 (100)	Group C 129770 (100)
Sex			
Boy	35758 (55)	18598 (62)	78412 (60)
Girl	29641 (45)	11282 (38)	20090 (40)
Age (years)			
0-1	21663 (33)	1429 (5)	30657 (15)
1-2	15804 (24)	3422 (11)	16214 (24)
2-3	7119 (11)	4710 (16)	35580 (13)
3-6	14663 (22)	13520 (45)	24344 (27)
6-12	6112 (9)	6331 (21)	2885 (19)
12-14	583 (1)	468 (2)	1025 (2)
Areas			
East	39083 (59)	8247 (28)	33048 (25)
West	7726 (12)	10602 (35)	56557 (44)
Central	6896 (10)	5965 (20)	21185 (16)
Northeast	12260 (19)	5066 (17)	18980 (15)
Ethnicity			
Han	-	28930 (97)	125917 (97)
Man	-	164 (1)	674 (1)
Hui	-	192 (1)	749 (1)
Other	-	594 (1)	2430 (1)
Residence			
Urban	-	22966 (77)	110453 (85)
Rural	-	6300 (21)	16457 (13)
Mixed	-	614 (2)	1846 (1)
Major food sources of micronutrients			
Staple foods	-	26,372 (88)	109,288 (84)
Meat	-	846 (3)	3209 (2)
Eggs	-	1024 (3)	6040 (5)
Vegetables	-	485 (2)	1597 (1)
Fruits	-	776 (3)	2508 (2)
Meat (fists[†])			
0–0.5	-	16,289 (55)	59,521 (46)
0.5–1	-	5872 (20)	20,037 (15)
1–1.5	-	6285 (21)	34,761 (27)
1.5–2	-	229 (1)	1465 (1)
2–2.5	-	882 (3)	5803 (4)
>2.5	-	298 (1)	5776 (4)
Daily milk consumption (mL)			
0–100	-	14,627 (49)	76,633 (59)
100–200	-	3493 (12)	8530 (7)
200–300	-	5829 (20)	20,462 (16)
300–500	-	3429 (11)	13017 (10)
500–1000	-	2260 (8)	10137 (8)
>1000	-	261 (1)	744 (1)
Liver			
Pork	-	9946 (33)	58,551 (45)
Lamb	-	509 (2)	4137 (3)
Chicken	-	1860 (6)	11327 (9)
Duck	-	345 (1)	3642 (3)
None	-	14,883 (50)	52,156 (40)

[†]Children's fist was used to measure the portion size.

for Group B, this was <4%. The estimated distributions of serum vitamin A concentration with 95% CI among Groups A and B are presented in Figures 5 and 6. The prevalence of SVAD was 7.7% (95% CI: 7.5%–7.9%) in Group A and 21.3% (95% CI: 20.5%–22.2%) in Group B. Children with RRI were thus more vulnerable to SVAD.

A weighted population distribution was calculated according to the two subpopulation distributions. The population weight of the RRI stratum was 20%, which was the overall morbidity of RRI.[16–21] The overall prevalence of SVAD was 10.4% (95% CI: 10.1%–10.8%) (Figure 7) and the prevalence of SSVAD was 37.5% (95% CI: 36.3%–38.7%). The average relative error of the estimate was 4%.

DISCUSSION
This study used the latest data to systematically estimate vitamin A status among various population groups. By pooling the data of many organizations, the study sample

Table 4. Descriptive characteristics of serum vitamin A among the three groups

Characteristics	Group A			Group B			Group C		
	Mean (SD) (mg/L)	Prevalence of SVAD (%)	Prevalence of SSVAD (%)	Mean (SD) (mg/L)	Prevalence of SVAD (%)	Prevalence of SSVAD (%)	Mean (SD) (mg/L)	Prevalence of SVAD (%)	Prevalence of SSVAD (%)
All	0.309 (0.082)	7.73	36.5	0.276 (0.114)	21.3	41.7	0.298 (0.181)	20.4	36.1
Sex									
Boy	0.310 (0.082)	7.61	36.9	0.277 (0.116)	21.1	41.7	0.296 (0.174)	20.5	36.5
Girl	0.310 (0.083)	7.97	36.0	0.275 (0.111)	21.8	41.5	0.301 (0.190)	20.1	35.6
Age (years)									
0-1	0.268 (0.075)	16.4	50.4	0.263 (0.108)	27.1	40.1	0.276 (0.189)	27.1	40.6
1-2	0.318 (0.081)	5.79	33.8	0.278 (0.102)	21.0	39.9	0.298 (0.196)	21.1	38.0
2-3	0.338 (0.075)	2.08	26.5	0.272 (0.108)	22.5	42.3	0.304 (0.178)	18.8	35.0
3-6	0.334 (0.072)	2.13	27.0	0.273 (0.118)	22.4	42.3	0.292 (0.176)	21.6	36.2
6-12	0.332 (0.080)	2.75	30.6	0.285 (0.118)	18.3	41.8	0.313 (0.160)	14.8	32.4
12-14	0.375 (0.084)	1.03	14.1	0.327 (0.103)	8.76	29.0	0.362 (0.161)	6.62	22.38
Areas									
East	0.318 (0.081)	5.71	34.4	0.268 (0.104)	22.6	42.4	0.278 (0.111)	21.4	36.4
West	0.293 (0.095)	16.8	34.4	0.267 (0.109)	24.7	41.6	0.293 (0.112)	18.5	34.3
Central	0.316 (0.079)	5.64	34.4	0.286 (0.095)	16.9	39.7	0.341 (0.360)	28.1	38.1
Northeast	0.288 (0.073)	9.67	45.8	0.299 (0.151)	17.6	42.9	0.299 (0.130)	15.7	38.9
Ethnicity									
Han	-	-	-	0.277 (0.115)	21.1	41.7	0.299 (0.182)	20.3	36.1
Man	-	-	-	0.272 (0.091)	19.5	44.5	0.281 (0.097)	17.7	40.8
Hui	-	-	-	0.254 (0.095)	29.2	41.1	0.257 (0.092)	27.2	41.2
Other	-	-	-	0.251 (0.092)	30.1	41.3	0.275 (0.113)	23.1	37.5
Residence									
Urban	-	-	-	0.276 (0.116)	21.7	41.6	0.296 (0.158)	19.4	35.6
Rural	-	-	-	0.276 (0.109)	20.8	41.8	0.309 (0.285)	26.4	39.8
Mixed	-	-	-	0.288 (0.088)	13.1	42.3	0.293 (0.145)	19.7	36.0

SD: standard deviation; SVAD: subclinical vitamin A deficiency; SSVAD: suspected subclinical vitamin A deficiency.
[†]Children's fist was used to measure the portion size.

Table 4. Descriptive characteristics of serum vitamin A among the three groups (cont.)

Characteristics	Group A			Group B			Group C		
	Mean (SD) (mg/L)	Prevalence of SVAD (%)	Prevalence of SSVAD (%)	Mean (SD) (mg/L)	Prevalence of SVAD (%)	Prevalence of SSVAD (%)	Mean (SD) (mg/L)	Prevalence of SVAD (%)	Prevalence of SSVAD (%)
Major food sources of micronutrients									
Staple foods	-	-	-	0.273 (0.106)	21.5	42.0	0.288 (0.128)	19.7	36.3
Meat	-	-	-	0.328 (0.196)	15.8	35.9	0.425 (0.42)	15.8	29.3
Eggs	-	-	-	0.281 (0.139)	22.8	41.5	0.445 (0.478)	22.4	33.5
Vegetables	-	-	-	0.292 (0.144)	20.4	39.4	0.34 (0.257)	16.4	36.8
Fruits	-	-	-	0.311 (0.163)	16.5	37.4	0.302 (0.153)	17.1	39.4
Meat (fists[†])									
0-0.5	-	-	-	0.274 (0.106)	20.6	42.2	0.281 (0.149)	22.8	39.0
0.5-1	-	-	-	0.274 (0.112)	22.6	41.7	0.288 (0.14)	20.5	37.8
1-1.5	-	-	-	0.284 (0.132)	20.9	40.6	0.291 (0.127)	19.4	35.2
1.5-2	-	-	-	0.279 (0.122)	22.7	44.1	0.302 (0.117)	15.8	35.9
2-2.5	-	-	-	0.276 (0.127)	27.0	35.2	0.308 (0.117)	14.4	32.8
>2.5	-	-	-	0.269 (0.116)	24.5	48.7	0.349 (0.115)	6.70	14.5
Daily milk consumption (mL)									
0-100	-	-	-	0.274 (0.104)	21.1	42.1	0.286 (0.177)	23.3	38.1
100-200	-	-	-	0.278 (0.113)	19.2	44.2	0.314 (0.228)	18.0	37.2
200-300	-	-	-	0.277 (0.131)	22.5	41.0	0.324 (0.19)	14.8	30.7
300-500	-	-	-	0.281 (0.134)	22.9	40.2	0.316 (0.183)	16.0	33.8
500-1000	-	-	-	0.278 (0.098)	20.9	38.9	0.302 (0.13)	16.7	34.1
>1000	-	-	-	0.297 (0.116)	17.6	38.7	0.283 (0.142)	21.2	36.9
Liver									
Pork	-	-	-	0.287 (0.115)	17.7	38.4	0.298 (0.174)	19.6	34.8
Lamb	-	-	-	0.282 (0.103)	20.4	39.3	0.502 (0.538)	12.7	31.0
Chicken	-	-	-	0.278 (0.134)	20.1	42.6	0.388 (0.384)	16.4	33.3
Duck	-	-	-	0.297 (0.106)	14.8	38.5	0.55 (0.586)	18.6	26.7
None	-	-	-	0.271 (0.104)	21.7	44.0	0.287 (0.145)	21.2	37.5

SD: standard deviation; SVAD: subclinical vitamin A deficiency; SSVAD: suspected subclinical vitamin A deficiency.
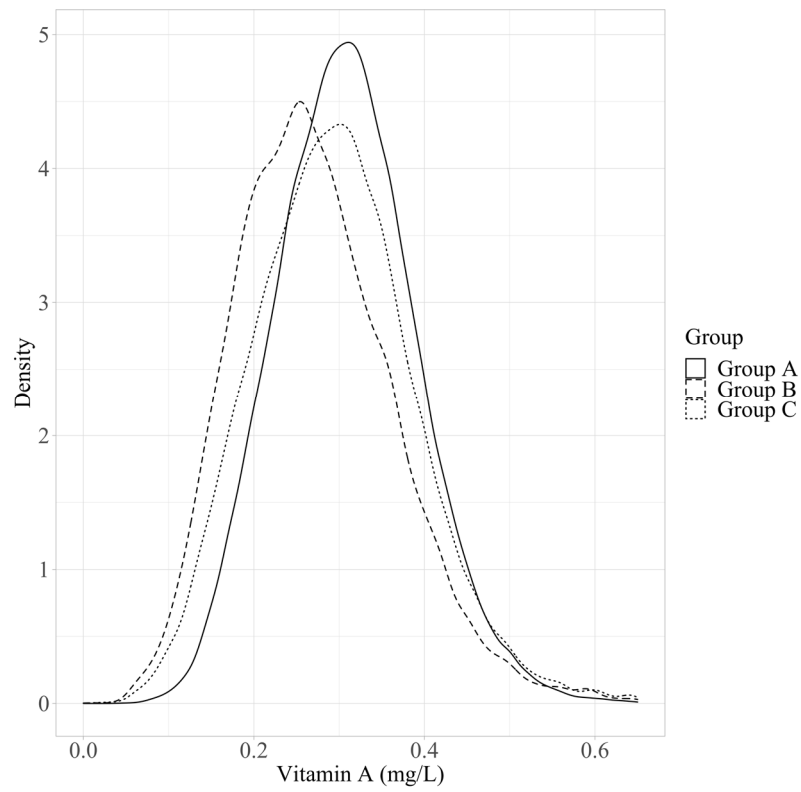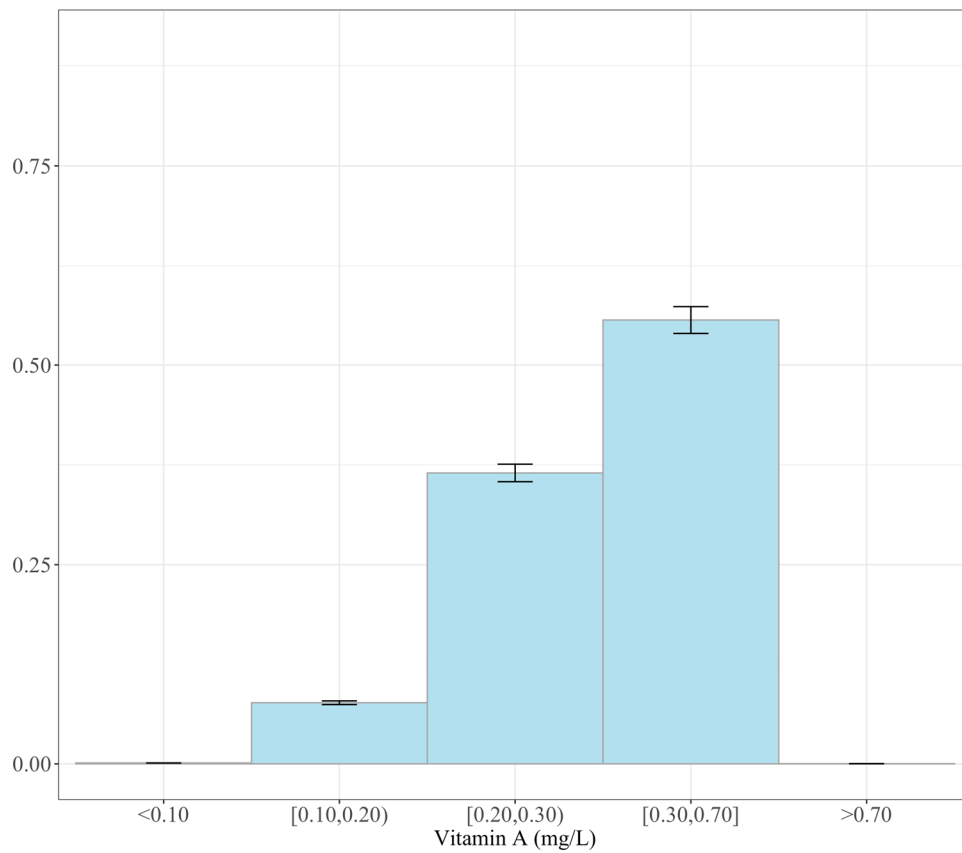[†]Children's fist was used to measure the portion size.

Figure 4. Vitamin A status in the three groups

	<0.10	[0.10,0.20)	[0.20,0.30)	[0.30,0.70]	>0.70
Lower	0.1%	7.4%	35.4%	54.1%	0%
Percentage	0.1%	7.6%	36.5%	55.8%	0%
Upper	0.1%	7.8%	37.6%	57.4%	0%

Figure 5. Estimated distribution of serum vitamin A concentration with 95% CI among healthy children

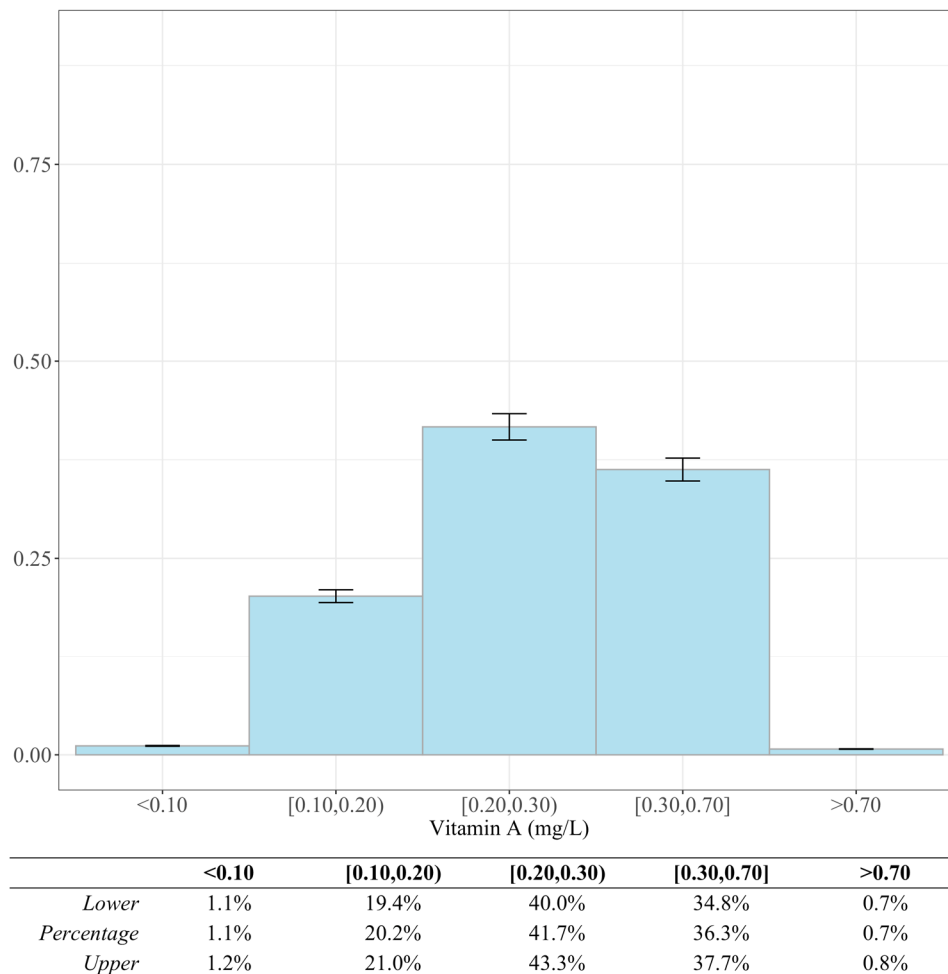|	<0.10	[0.10,0.20)	[0.20,0.30)	[0.30,0.70]	>0.70
Lower	1.1%	19.4%	40.0%	34.8%	0.7%
Percentage	1.1%	20.2%	41.7%	36.3%	0.7%
Upper	1.2%	21.0%	43.3%	37.7%	0.8%

Figure 6. Estimated distribution of serum vitamin A concentration with 95% CI among children with RRI

included more comprehensive information than that obtained from any other individual investigation. The study sites covered most of the provinces in China, and the results are therefore likely to reflect the true status of vitamin A in the whole of China.

Estimates confirmed 10.4% (95% CI: 10.1%–10.8%) of Chinese children aged 0–14 years were at risk of SVAD. The average relative error of the estimate was 4%. According to National Bureau of Statistics, there are approximately 230 million children aged 0–14 in China. Thus, approximately 23.9 million (95% CI: 23.2–24.8) of them are at risk of SVAD. The prevalence of SVAD was highly variable in the different groups. The correlation between RRI and VAD was significant ($p<0.01$), but correlation does not imply causation. The cross-sectional design of the present study does not allow for causality to be inferred insofar as the relationship of RRI and VAD is concerned. But sick children were more likely to have a low serum vitamin A.

The prevalence of SVAD was inversely related to children's age. Serum vitamin A concentration appears to be the lowest in infants. Generally, infants are born with low serum vitamin A concentration and are dependent on external sources, particularly breast milk, for vitamin A. Infants may not receive adequate amounts of vitamin A from the breast milk if the maternal nutritional status is poor. Higher dietary vitamin A intake is thus necessary for breastfeeding mothers. Moreover, using the same cutoff

points for all age groups might not be a proper choice.[26] Age-specific cutoff points for defining low serum vitamin A concentration are necessary and should be considered in future studies.

No significant difference in vitamin A status was observed between boys and girls, which was consistent with other studies.[27] A high prevalence of SVAD was observed in western and northeastern areas in China. Serum vitamin A concentration of Han Chinese children, which is the majority ethnicity in China, was higher than that in the ethnic minority groups. Most minority groups live in western and northeastern areas, which are lower income regions compared with the eastern areas. Moreover, the ethnic minority groups and the Han Chinese have different dietary patterns. Vitamin A is derived from animal sources (retinoids) and plant sources (provitamin A carotenoids).[28] Liver has a higher retinoid content than any other food. Liver as a source of vitamin A is essential because among liver eaters, 39%–48% of total vitamin A intake is derived from liver-containing foods.[29] However, foods high in vitamin A, such as animal liver, meat, and eggs, are expensive in China. Vegetarians may add a dash of oil into salad to help improve the absorption of provitamin A from plant sources. The body cannot produce vitamin A by itself, and thus the vitamin must be provided from diets. Some food groups are better sources of certain micronutrients than others, so that a diverse diet can ensure adequate vitamin A among other micronutrient intakes. Nutrition education, particu-
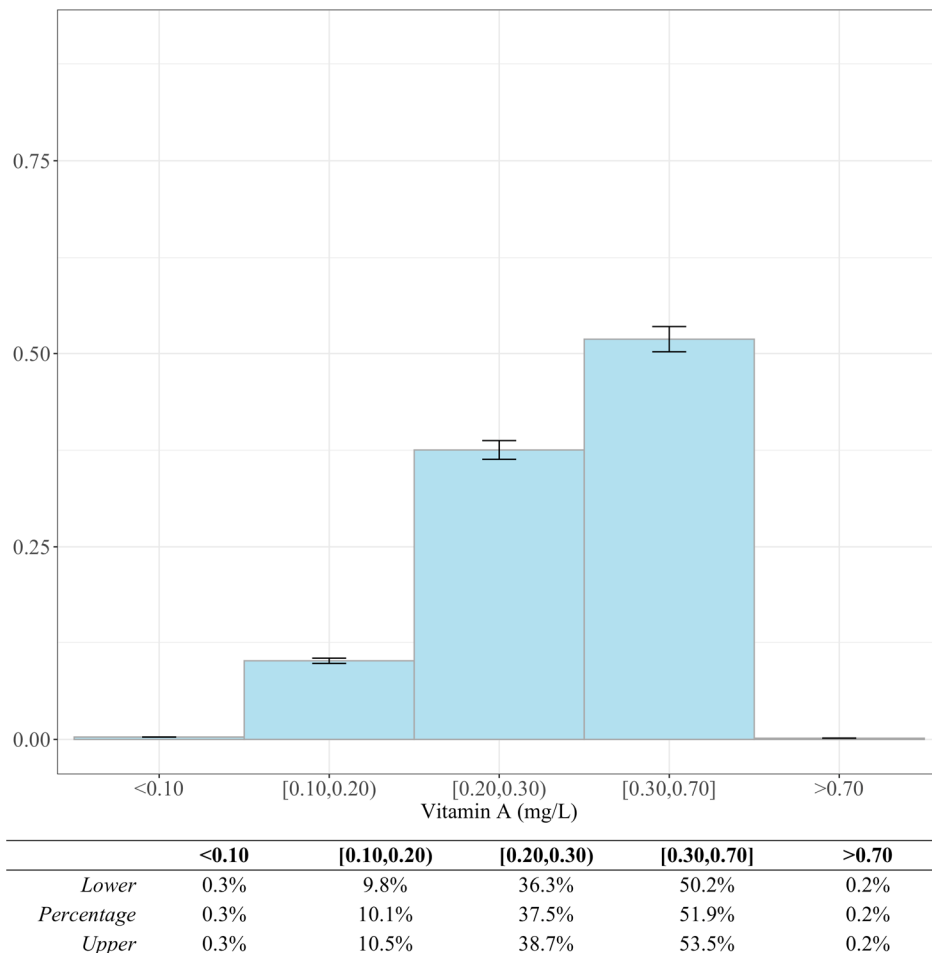
	<0.10	[0.10,0.20)	[0.20,0.30)	[0.30,0.70]	>0.70
Lower	0.3%	9.8%	36.3%	50.2%	0.2%
Percentage	0.3%	10.1%	37.5%	51.9%	0.2%
Upper	0.3%	10.5%	38.7%	53.5%	0.2%

Figure 7. Estimated distribution of serum vitamin A concentration with 95% CI among all Chinese children

larly in the benefits of consuming micronutrient-rich foods, might greatly curtail the overall risk and prevalence of VAD, especially among minority groups.

The difference of vitamin A status between children in rural and urban areas was small but significant due to the very large sample size. The reason might be the development of the social economy: Increased family income enables parents in rural areas to provide various micronutrient-rich foods for their children.[30]

This study had several limitations. A certain percentage of children developed diseases other than RRI. The morbidity of some of the diseases was not available and might vary in different regions. Therefore, the results of this study may underestimate the magnitude of VAD among Chinese children.

In summary, this study elucidated the gravity of VAD as a moderate public health problem in China. Children who were sick, of ethnic minority, and of a younger age were prone to VAD. Vitamin A supplementation should be offered to these groups during clinical treatment. Regular consumption of vitamin A–rich foods should be promoted using nutrition education for breastfeeding mothers and in families of a minority ethnicity.

REFERENCES
1. Demissie T, Ali A, Mekonen Y, Haider J, Umeta M. Magnitude and distribution of vitamin A deficiency in Ethiopia. Food Nutr Bull. 2010;31:234-41. doi: 10.1177/156482651003100206.
2. Biesalski HK, Nohr D. New aspects in vitamin A metabolism: The role of retinyl esters as systemic and local sources for retinol in mucous epithelia. J Nutr. 2004;134(12 Suppl): 3453S-7S. doi: 10.1093/jn/134.12.3453S.
3. Stevens GA, Bennett JE, Hennocq Q, Lu Y, De-Regil LM, Rogers L et al. Trends and mortality effects of vitamin A deficiency in children in 138 low-income and middle-income countries between 1991 and 2013: A pooled analysis of population-based surveys. Lancet Glob Heal. 2015;3(9): e528-36. doi: 10.1016/S2214-109X(15)00039-X.
4. World Health Organization. Global prevalence of vitamin A deficiency in populations at risk 1995-2005 : WHO global database on vitamin A deficiency. 2009 [cited 2019/12/18]; Available from: http://apps.who.int//iris/handle/10665/44110.
5. Tienboon P, Wangpakapattanawong P. Nutritional status, body composition and health conditions of the Karen hill tribe children aged 1-6 years in Northern Thailand. Asia Pacific J Clin Nutr. 2007;16:158-62.
6. Akhtar S, Ahmed A, Randhawa MA, Atukorala S, Arlappa N, Ismail T, Ali Z. Prevalence of vitamin A deficiency in South Asia: causes, outcomes, and possible remedies. J Heal Popul Nutr. 2013;31:413-23. doi: 10.3329/jhpn.v31i4.19975.

7. Schultink W. Use of under-five mortality rate as an indicator for vitamin A deficiency in a population. J Nutr. 2002;132(9 Suppl):2881S-3S. doi: 10.1093/jn/132.9.2881S.

8. Fawzi WW, Herrera MG, Spiegelman DL, El Amin A, Nestel P, Mohamed KA. A prospective study of malnutrition in relation to child mortality in the Sudan. Am J Clin Nutr. 1997;65:1062-9. doi: 10.1093/ajcn/65.4.1062.

9. Jin C, Wang X, Zhang L, Zhang Y, Li N, Wang J et al. Analysis of fat-soluble vitamins A, D, E levels in the serum of healthy children. Chinese J Clin Nutr. 2016;24:349-53. doi: 10.3760/cma.j.issn.1674-635X.2016.06.005.

10. Ye ZC. An analysis of children's vitamin deficiency in Shanghai. Chinese J Heal Birth Child Care. 2014;20:15-7. doi: 10.3969/j.issn.1007-3434.2014.01.005.

11. Jiang JX, Lin LM, Lian GL, Greiner T. Vitamin A deficiency and child feeding in Beijing and Guizhou, China. World J Pediatr. 2008;4:20-5. doi: 10.1007/s12519-008-0004-z.

12. Tan ZW, Ma GF, Lin LM, Liu CY, Liu YL, Wang L et al. Survey on serum vitamin A levels among 0-6 years children of China. Chinese Journal of Child Health Care. 2002;5:303-6. doi: 10.3969/j.issn.1008-6579.2002.05.006. (In Chinese)

13. Li YQ, Yang SY. Correlation between vitamin A and respiratory infections in children. Jilin Med. 2018;39:3-5. doi: 10.3969/j.issn.1004-0412.2018.01.001.

14. Hu YM, Jiang ZF, Shen KL. Zhu Futang practice pediatrics 8th edition. Beijing: People's Medical Publishing House; 2014. (In Chinese)

15. Corradini D, Eksteen E, Eksteen R, Schoenmakers P, Miller N. Handbook of HPLC. 2011 [cited 2020/03/20]; Available from: https://books.google.com/books?id=4mj_DArD5n0C.

16. Chen YN, Wang Y, Li G. Analysis of recurrent respiratory tract infection in preschool children in friendship area of baoshan district, Shanghai. Contemp Med. 2019;25:6-10. doi: 10.3969/j/issn.1009-4393.2019.19.002.

17. Liu PH, Cheng Q, Zhang JR, Chi CT, Meng W, Qu ZQ. Prevalence and influencing factors of recurrent respiratory tract infection among preschool children in Mudanjiang city. Chinese Journal of Public Health. 2017;33:1004-7. doi: 10. 11847/zgggws2017-33-06-37. (In Chinese)

18. Ye QC. Repeated respiratory tract infections. Journal of Applied Clinical Pediatrics. 1999;14:361-2. doi: 10.3969/j. issn.1003-515X.1999. 06.037.

19. Gui Y, Li XL. Correlation between cough variant asthma in children and repeated mycoplasma pnenumonia infection. J Clin Lung. 2017;12:276-9. doi: 10.3969/j.issn.1009-

6663.2017.02.002.

20. Zhao YZ. Advances in the treatment of recurrent respiratory tract infections in children. Proceeding of Clinical Medicine. 2011;20: 609-10. doi: 10.3969/j.issn.1671-8631.2011.08.024.

21. Ji HX. Study on the relationship between recurrent respiratory tract infection and mycoplasma pneumoniae in children. Contemp Med. 2018;24:69-71. doi: 10.3969/j.issn.1009-4393.2018.05.013.

22. Zhang J, Sun RR, Yan ZX, Yi WX, Yue B. Correlation of serum vtamin A, D, and E with recurrent respiratory infection in children. Eur Rev Med Pharmacol Sci. 2019;23: 8133-8. doi: 10.26355/eurrev_201909_19033.

23. Arora P, Kumar V, Batra S. Vitamin A status in children with asthma. Pediatr Allergy Immunol. 2002;13:223-6. doi: 10. 1034/j.1399-3038.2002.00010.x.

24. Pinnock CB, Douglas RM, Badcock NR. Vitamin A status in children who are prone to respiratory tract infections. Aust Paediatr J. 1986;22:95-9. doi: 10.1111/j.1440-1754.1986. tb00197.x.

25. Sivakumar B, Reddy V. Absorption of labelled vitamin A in children during infection. Br J Nutr. 1972;27:299-304. doi: 10.1079/BJN19720094.

26. Tanumihardjo SA, Russell RM, Stephensen CB, Gannon BM, Craft NE, Haskell MJ, Lietz G, Schulze K, Raiten DJ. Biomarkers of nutrition for development (BOND)-vitamin A review. J Nutr. 2016;146:1816S-48S. doi: 10.3945/jn.115. 229708.

27. World Health Organization. Vitamin and mineral requirements in human nutrition. 2005 [cited 2020/02/14]. Available from: https://apps.who.int/iris/bitstream/handle/ 10665/42716/9241546123.pdf.

28. Pizzorno JE, Murray MT, Joiner-Bey H. The clinician's handbook of natural medicine. Edinburgh: Churchill Livingstone; 2016.

29. Finnish Food Safety Authority Evira. Intake of vitamin A from liver foods among Finnish 1, 3- and 6 year old children. 2008 [cited 2020/02/18]. Available from: https://www.ruokavirasto.fi/globalassets/henkiloasiakkaat/ti etoa-elintarvikkeista/intake-of-vitamin-a-from-liver-foods-among-finnish-1--3--and-6-year-old-children---quantative-risk-assessment.pdf.

30. Wei SG, Ju LR, Li M, Wang W. Child health and nutrition: Getting better and facing new challenges in China. Australas Med J. 2011;4:123-32. doi: 10.4066/AMJ.2011.584.