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Non-Western immigrant children have lower 25-hydroxyvitamin D than children from Western families

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Abstract

Objective: To determine if children aged 1–6 years from non-Western immigrant families have lower serum 25-hydroxyvitamin D (25(OH)D) levels than children from Western-born families and examine which factors influence this relationship.
Design: Cross-sectional study.
Setting: Toronto, Canada.
Subjects: Healthy children (*n* 1540) recruited through the TARGet Kids! practice-based research network. Serum 25(OH)D concentrations of non-Western immigrants were compared with those of children from Western-born families. Children from non-Western immigrant families were defined as those born, or their parents were born, outside a Western country. Univariate and multiple linear regression analyses were used to identify factors which might influence this relationship.
Results: Median age was 36 months, 51 % were male, 86 % had 'light' skin pigmentation, 55 % took vitamin D supplements, mean cow's milk intake was 1·8 cups/d and 27 % were non-Western immigrants. Median serum 25(OH)D concentration was 83 nmol/l, with 5 % having 25(OH)D < 50 nmol/l. Univariable analysis revealed that non-Western immigrant children had serum 25(OH)D lower by 4 (95 % CI 1·3, 8·0) nmol/l ($P = 0·006$) and increased odds of 25(OH)D < 50 nmol/l (OR = 1·9; 95 % CI 1·3, 2·9). After adjustment for known vitamin D determinants the observed difference attenuated to 0·04 (95 % CI −4·8, 4·8) nmol/l ($P = 0·99$), with higher cow's milk intake ($P < 0·0001$), vitamin D supplementation ($P < 0·0001$), summer season ($P = 0·008$) and increased age ($P = 0·04$) being statistically significant covariates. Vitamin D supplementation was the strongest explanatory factor of the observed difference.
Conclusions: There is an association between non-Western immigration and lower 25(OH)D in early childhood. This difference appears related to known vitamin D determinants, primarily vitamin D supplementation, representing opportunities for intervention.

Keywords
TARGet Kids!
Nutrition
Vitamin D
Non-Western immigrants
Early childhood

Vitamin D is an essential micronutrient and plays an important role in bone metabolism[1,2]. The Institute of Medicine and the American Academy of Pediatrics suggest that serum 25-hydroxyvitamin D (25(OH)D) concentration of 50 nmol/l will meet the needs of 97·5 % of the population for optimal bone-related health outcomes[3,4].

There is emerging evidence that low serum 25(OH)D levels may also be associated with a number of chronic health problems[5–8]. Observational epidemiological studies have suggested that low levels of vitamin D may play a role in fractures[9,10], asthma[11,12], respiratory infections[13] and

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obesity[14] in children. Identifying subgroups of children who are at risk of having low 25(OH)D is important, especially given the possibly long duration of exposure to low 25(OH)D beginning in childhood[1,2].

A number of determinants have been identified that affect 25(OH)D levels in children including skin pigmentation, breast-feeding without vitamin D supplementation, low intake of cow's milk (in Canada and the USA, cow's milk is fortified with approximately 2·5 μg (100 IU) of vitamin D per 250 ml), higher latitude and higher adiposity[15–29]. It has been suggested that immigration may also play a role in vitamin D status. Observational epidemiological data have suggested that non-Western adults immigrating to a Western country (Europe, North America, Australia or New Zealand) are at increased risk of having low 25(OH)D[30–34]. Further, children under 1 year of age from non-Western immigrant families living in a Western country appear to be at risk of developing vitamin D-deficiency rickets[35–37]. It is not known whether there is a relationship between non-Western immigration and 25(OH)D during early childhood (i.e. in children older than 1 year of age) and whether dietary, environmental or biological determinants of 25(OH)D might explain this effect.

The primary objective of the present study was to determine whether children older than 1 year of age from non-Western immigrant families have lower serum 25(OH)D levels than children from Western-born families. Our secondary objective was to evaluate whether known dietary, environmental or biological determinants of 25(OH)D influence this relationship.

Methods

The present study was a cross-sectional observational study of healthy children aged 1–6 years.

Participants

Children were recruited between December 2008 and July 2011 during a routine well-child doctor's visit at seven paediatric and family medicine group practices participating in TARGet Kids!, and represented a diverse sample of children in inner-city Toronto (latitude 43·4°N), the most culturally diverse city in Canada. Details of subject recruitment have been published elsewhere[38,39]. The TARGet Kids! practice-based research network was designed to collect data relevant to nutritional factors and dietary patterns in healthy infants and children. It was developed as a partnership between researchers at the Paediatric Outcomes Research Team at the Sick Kids Research Institute of The Hospital for Sick Children, the Applied Health Research Centre at the Li Ka Shing Knowledge Research Institute of St. Michael's Hospital, and primary-care providers in the Section on Community Paediatrics in the Department of Paediatrics and the Department of Family and Community Medicine at the University of Toronto. Exclusion criteria included any chronic illness (except for asthma), severe developmental delay, non-verbal English and medications known to affect vitamin D metabolism (i.e. anti-seizure medications).

Measurements

Survey data were collected through a parent-completed standardized data collection form adapted from the Canadian Community Health Survey[40]. Trained research assistants embedded in the practices obtained physical measurements and venous sampling occurred on site at the primary-care clinic by a trained phlebotomist. Blood samples were sent daily to the Mount Sinai Services Laboratory in Toronto (www.mountsinaservices.ca).

Serum 25(OH)D was measured using a competitive two-step chemiluminescence assay (Diasorin LIAISON®)[41]. This assay was regularly calibrated according to the internationally recognized Vitamin D External Quality Assessment Scheme[42]. Extensive testing and validation of this assay have been performed and demonstrated an intra-assay imprecision of 7·2 % at a concentration of 213 nmol/l and an inter-assay imprecision of 4·9 % at 32 nmol/l, 8·9 % at 77 nmol/l and 17·4 % at 213 nmol/l, values which are well within acceptable limits for biochemical measurements[43,44].

Our primary exposure variable was non-Western immigration determined by the parent(s) and child's country of birth. Non-Western immigration was defined as a child born outside Europe, North America, Australia or New Zealand or a child who has a parent (one or both) who emigrated from a non-Western country[45]. Thus first- and second-generation non-Western immigrant children were considered non-Western immigrants for the present analysis because dietary factors affecting young children likely reflect cultural patterns of their parents[46–51]. Immigration was measured by two open-ended questions: 'Where were your child's biological parents born?' and 'Where was your child born?'

Our primary outcome was serum total 25(OH)D (continuous outcome) and our secondary outcome was 25(OH)D < 50 nmol/l (binary outcome), based on the Institute of Medicine's reference cut-off point[3].

Clinically relevant covariates that we hypothesized might influence the relationship between non-Western immigration and 25(OH)D included ethnicity, sex, age, skin pigmentation, BMI, season, current vitamin D supplementation, cow's milk intake and outdoor play. Ethnicity was captured by the open-ended ethnicity question 'What were the ethnic or cultural origins of your child's ancestors (an ancestor is usually more distant than a grandparent)?' Two co-authors, J.A.O. and S.C., independently converted responses into the following five geographically based ethnicity categories: (i) East & South-east Asian; (ii) South-west Asian; (iii) African & Caribbean; (iv) mixed Western; and (v) mixed Western/non-Western[52]. Mixed Western included children born in families from Western countries (e.g. Western and Eastern

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Europe) and mixed Western/non-Western included children from mixed ethnic families from both non-Western countries (e.g. East Asian and Latin American) or families from Western and non-Western countries (e.g. South Asian and Western Europe). Differences in categorization between reviewers were identified less than 5 % of the time and subsequently resolved by consensus in each instance. The overall effect of ethnicity was tested using Western as the reference of the other four geographically based ethnic categories, identified above.

Each child's weight was measured using a precision digital scale (±0·025 %; Seca, Hamburg, Germany) and standing height was measured using a stadiometer (Seca). BMI was calculated as weight in kilograms divided by the square of height in metres[53,54]. BMI *Z*-scores were calculated using WHO growth standards[55]. Skin pigmentation was measured by trained research assistants using the Fitzpatrick scale, which is a skin pigmentation classification system widely used in dermatological research[56,57]. Cow's milk consumption was measured from parental report based on response to the following question: 'How many 250 ml cups of cow's milk does your child drink in a typical day?' All commercially available cow's milk in Canada is fortified with 2·5 μg (100 IU) of vitamin D per 250 ml cup[58,59]. Daily vitamin D supplementation was defined as currently taking a daily multivitamin and/or vitamin D supplement. In Canada, all over-the-counter multivitamins contain vitamin D and standard dosing of children's vitamin D-containing supplements is 10 μg (400 IU) per dose[60]. Outdoor play was defined as hours per week spent outside playing, which was used as a proxy for sun exposure.

Statistical analyses

Descriptive statistics were performed for the primary exposure, outcomes and covariates. For our primary analysis, univariate linear regression was used to determine the unadjusted association between our primary exposure (non-Western immigration) and our primary outcome (serum 25(OH)D as a continuous outcome) and univariate logistic regression was used to determine the unadjusted association between our primary exposure (non-Western immigration) and our secondary outcome (25(OH)D < 50 nmol/l as a binary outcome). For our secondary analysis, a multiple linear regression model was developed using our primary outcome, serum 25(OH)D, with adjustment for pre-specified, clinically relevant covariates (described above) to explore factors which might influence a relationship between non-Western immigration and 25(OH)D. All covariates were felt to be clinically important and were included in the final model regardless of *P* value.

To explore whether vitamin D supplementation and skin pigmentation may have different effects on 25(OH)D in non-Western immigrant children relative to Western-born children, two biologically plausible interactions were considered: (i) immigration and skin pigmentation; and (ii) immigration and vitamin D supplementation. To achieve a balance between over-fitting and interpretation and limit biases that can result from standard variable selection approaches, these interactions were tested together using a likelihood ratio test. If the *P* value for inclusion of the interactions was large (i.e. greater than 0·30), these interactions were considered to be unlikely and were not included in the final models.

Multicollinearity was assessed using the variance inflation factor, a measure of the degree that a regression coefficient is inflated when other independent variables contain similar information[61]. As the model did not contain large variance inflation factors (values not exceeding 5) multicollinearity was unlikely to be a problem, so each of the hypothesized covariates (including ethnicity and immigration) were considered independent variables[62].

Data were analysed using the statistical software package SAS 9·2 for Windows. The study was approved by the Research Ethics Board of St. Michael's Hospital and The Hospital for Sick Children, and parents of all participating children consented to participation in the study.

Results

Consent was obtained from parents of 3696 children; 1540 had complete survey, anthropometric and laboratory data and were included in the analysis (see Fig. 1). Children included and not included in the analysis appeared similar (see Table 1). The median age of included children was 36 months, 51 % were male, 86 % had 'light' skin pigmentation (Fitzpatrick scale I, II or III), 55 % took vitamin D supplements and mean cow's milk intake was 1·8 cups/d. Children from non-Western immigrant families made up 27 % of the population (see Table 2). Of non-Western immigrant families, 4 % of children and 96 % of parents were born outside Canada, in a non-Western country. Median serum 25(OH)D was 83 nmol/l. Eighty-one children (5 %) had 25(OH)D levels below 50 nmol/l (thirty-one (3 %) children from Western families and fifty (12 %) children from non-Western immigrant families).

For our primary analysis, univariable linear regression revealed that non-Western immigrant children had lower mean serum 25(OH)D concentrations than children from Western-born families (85 *v.* 89 nmol/l, respectively) with a difference of 4 (95 % CI 1·3, 8·0) nmol/l ($P = 0·006$). Univariable logistic regression revealed increased odds of 25(OH)D levels less than 50 nmol/l in non-Western immigrant children (OR = 1·9; 95 % CI 1·3, 2·9).

For our secondary analysis, multiple linear regression adjusted for clinically relevant covariates resulted in a reduction of the observed mean serum 25(OH)D difference between non-Western immigrant children and children from Western-born families to 0·04 (95 % CI −4·8, 4·8) nmol/l, which was no longer statistically significant ($P = 0·99$; see Table 3).

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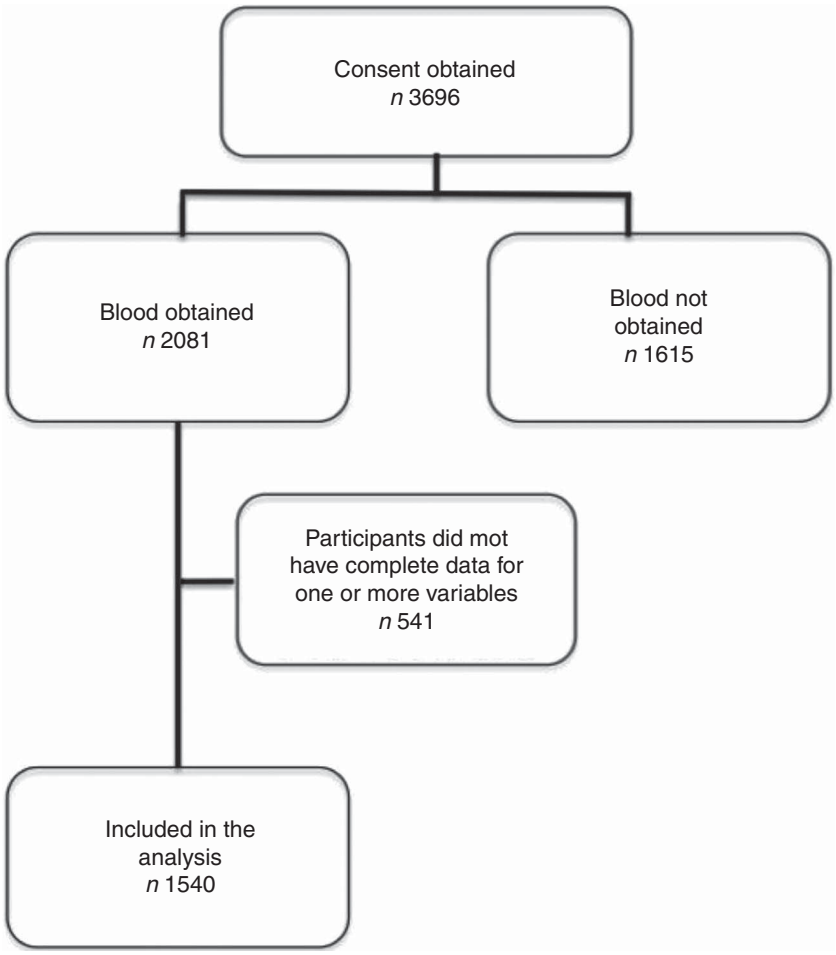

Fig. 1 Patient recruitment and enrolment flow chart

Covariates which appeared to attenuate the relationship between non-Western immigration and 25(OH)D included volume of cow's milk intake ($P<0{\cdot}0001$), vitamin D supplementation ($P=<0{\cdot}0001$), season ($P=0{\cdot}008$) and age ($P=0{\cdot}04$; see Table 3). Cow's milk intake, vitamin D supplementation, season and age were all associated with non-Western immigration and had an effect on 25(OH)D. However, only vitamin D supplementation changed the parameter estimate for non-Western immigration by more than 10 %, suggesting it was the strongest explanatory factor. We did not find that other variables, including ethnicity, skin pigmentation and outdoor play, were modifiers of the observed 25(OH)D difference (see Table 3).

Interactions between non-Western immigration and vitamin D supplementation and non-Western immigration and skin pigmentation were tested together which revealed $P=0{\cdot}9$, making these interactions unlikely. These interactions were not included in the final model.

Discussion

Immigration is a defining component of urban North America[63,64]. We have identified an association between non-Western immigration and lower 25(OH)D in early childhood. While the median 25(OH)D concentration was 83 nmol/l, well above the American Academy of Pediatrics' cut-off point of 50 nmol/l, non-Western immigrant children had nearly a twofold increased odds of 25(OH)D < 50 nmol/l when compared with children from Western-born families.

When biologically important covariates related to vitamin D intake and synthesis were included in our adjusted model, the observed 25(OH)D mean difference between immigration groups could largely be explained by known vitamin D determinants, with current vitamin D supplementation having the strongest effect. Cow's milk intake, season and age were significant covariates in the adjusted linear regression model but did not change the parameter estimate for non-Western immigration by more than 10 %, suggesting they were weaker explanatory factors.

To our knowledge, the present study is unique in documenting an association between 25(OH)D status and non-Western immigration in early childhood (children aged 1–6 years). Understanding non-Western immigration as an exposure is important due to the high frequency of

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Table 1 Population description for children included and not included in the analysis (children aged 1–6 years participating in TARGet Kids!, Toronto, Canada, December 2008 to July 2011)

	Children included in the analysis (*n* 1540)				Children not included in the analysis (*n* 1979)*			
Child characteristic	Frequency	%	Median	Range	Frequency	%	Median	Range
Age (months)	–	–	36	12–78	–	–	26	12–80
							Missing (*n* 0)	
Sex, male	785	51	–	–	1029	52	–	–
					Missing (*n* 1)			
Skin pigmentation, light	1320	86	–	–	1401	84	–	–
					Missing (*n* 316)			
BMI *Z*-score	–	–	0·2	−3·1 to 3·9			0.2	−3·4 to 3·9
							Missing (*n* 159)	
Ethnicity†								
Mixed Western	1004	65	–	–	1206	61	–	–
Mixed Western/non-Western	345	22	–	–	451	23	–	–
East Asian & South-east Asian	90	6	–	–	119	6	–	–
South-west Asian	70	5	–	–	92	5	–	–
African & Caribbean	31	2	–	–	51	3	–	–
					Missing (*n* 60)			
Season								
May-Sept (summer)	711	46	–	–	834	42	–	–
					Missing (*n* 0)			
Current cow's milk intake (ml)	–	–	500	0–1250	–	–	500	0–1250
							Missing (*n* 259)	
Vitamin D supplements								
Yes	850	55	–	–	1070	58	–	–
					Missing (*n* 136)			
Outdoor play								
1–4 h/week	629	41	–	–	729	40	–	–
5–7 h/week	911	59	–	–	1078	60	–	–
					Missing (*n* 172)			
Annual household income ($CAN)‡	–	–	56 000	15 000–335 000	–	–	56 800	15 000–269 000
							Missing (*n* 210)	
Serum 25(OH)D (nmol/l)	–	–	83	11–267	–	–	83	15–278
							Missing (*n* 1627)	

25(OH)D, 25-hydroxvitamin D.
*2176 children were not included in the analysis (blood not obtained for 1615 and 1540 did not have complete survey or anthropometric data). The table describes 1979 children; 197 were removed because they were outliers (fifteen children had BMI *Z*-score > 4, 181 had age <11·5 months or >84 months, and one had 25(OH)D of 352 nmol/l).
†Visible minorities in Toronto according to the 2006 census were 12·0 % South Asian, 2·6 % Arab or West Asian (totalling 14·6 % South-west Asian); 11·4 % Chinese, 4·1 % Filipino, 1·4 % Korean, 1·5 % South-east Asian, 0·5 % Japanese (totalling 18·9 % East Asian & South-east Asian); 8·4 % Black (totalling 8·4 % African & Caribbean); and multiple visible minority 1·3 %[72].
‡Median annual household income in Toronto in 2010 was $CAN 68 110[73].

non-Western immigration in much of urban North America[63]. Our finding that vitamin D supplementation appears to be the strongest explanatory factor of the observed difference in 25(OH)D suggests that vitamin D supplementation may be an excellent target for interventions to increase 25(OH)D among non-Western immigrant children.

Previous studies have identified a number of factors that affect 25(OH)D in children including factors related to cutaneous production of vitamin D such as skin pigmentation (melanin pigment decreases cutaneous synthesis)[15–17], ethnicity[65,66] and outdoor time[15–17,67,68]. We did not find that these factors were modifiers of the relationship between non-Western immigration and 25(OH)D. This could be a consequence of sun avoidance of young children or the relatively low frequency of 'dark' skin pigmentation in this population. If skin exposure to the sun were minimal, cutaneous production of 25(OH)D would also be expected to be minimal regardless of skin pigmentation, ethnicity or outdoor playtime.

Strengths of our study were the relatively large sample size with detailed clinical and laboratory data which allowed us to adjust for the many factors known to impact 25(OH)D concentrations in children. Further, our urban population included an ethnically diverse sample from one of the most multicultural cities in the world.

Limitations of the study include its cross-sectional design, from which causality cannot be inferred. Although the median 25(OH)D concentration was relatively high in our population and the majority of children had 25(OH)D levels above the American Academy of Pediatrics' cut-off point of 50 nmol/l, other Canadian-based studies including the national Canadian Health Measures Survey have found similar 25(OH)D levels in this age group[69–71]. There was a low representation of certain ethnic groups in the present study compared with visible minority groups in Toronto; however, this can be partially explained by the higher frequency of mixed ethnicities in our study[72]. Residual confounding from

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Table 2 Population description for children from Western-born families and from non-Western immigrant families (children aged 1–6 years participating in TARGet Kids!, Toronto, Canada, December 2008 to July 2011)

	Children from Western-born families (*n* 1119; 73 %)				Children from non-Western immigrant families (*n* 421; 27 %)			
Child characteristic	Frequency	%	Median	Range	Frequency	%	Median	Range
Age (months)	–	–	36	12–75	–	–	38	12–78
Sex, male	564	50	–	–	221	52	–	–
Skin pigmentation, light	1061	95	–	–	259	62	–	–
BMI *Z*-score			0·2	−3·0 to 3·8			0·12	−3·1 to 3·9
Ethnicity								
Mixed Western	958	86	–	–	46	11	–	–
Mixed Western/non-Western	143	13	–	–	202	48	–	–
East Asian & South-east Asian	8	1	–	–	82	19	–	–
South-west Asian	9	1	–	–	61	14	–	–
African & Caribbean	1	0·1	–	–	30	7	–	–
Season								
May-Sept (summer)	515	46	–	–	196	47	–	–
Current cow's milk intake (ml)	–	–	500	0–1250	–	–	500	0–1250
Vitamin D supplements								
Yes	633	57	–	–	217	52	–	–
Outdoor play								
1–4 h/week	399	36	–	–	230	55	–	–
5–7 h/week	720	64	–	–	191	45	–	–
Annual household income ($CAN)	–	–	58 000	15 000–335 000	–	–	50 000	15 000–269 000
Serum 25(OH)D (nmol/l)	–	–	84	12–267	–	–	80	11–210

25(OH)D, 25-hydroxvitamin D.

Table 3 Adjusted linear regression model for the association between immigration status and serum 25(OH)D (among children aged 1–6 years participating in TARGet Kids!, Toronto, Canada, December 2008 to July 2011)

Child characteristic	Difference in serum 25(OH)D (nmol/l)	*P* value
Immigration (non-Western *v.* Western)	–0·04	0·99
Age, months	−0·09	0·04*
Sex (male *v.* female)	–0·03	0·98
Skin type (dark *v.* light)	−2·40	0·37
BMI *Z*-score	–1·01	0·18
Ethnicity		
Mixed Western	Reference	0·09†
East Asian & South-east Asian	–5·15	
South-west Asian	−2·44	
African & Caribbean	−14·54	
Mixed Western/non-Western	–4·54	
Season (winter *v.* summer)	−4.15	0.008*
Daily cow's milk intake, 250 ml (1 cup)	5·00	<0·0001*
Vitamin D supplementation (yes *v.* no)	7·58	<0·0001*
Outdoor play (1–4 *v.* 5–7 h/week)	0·03	0·99

25(OH)D, 25-hydroxvitamin D.
*Indicates those variables that are independently associated with serum 25(OH)D ($P < 0·05$).
†The effect of ethnicity in the model was tested using mixed Western as the reference for the other four geographically based ethnic categories. The reported *P* value represents the statistical significance of a likelihood ratio test for all ethnicities tested in the model together relative to the reference.

unknown and unmeasured covariates is also a possibility, although such effects are likely to be small given that the adjusted 25(OH)D difference was small. Finally, a language barrier could have precluded some immigrant families from participating in the study. However, only 0·4 % of eligible children were actually excluded because of a language barrier yet almost a third of our population were non-Western immigrant families.

Conclusion

Children older than 1 year of age from non-Western immigrant families may be at increased risk of lower 25(OH)D. Vitamin D supplementation appeared to be the strongest explanatory factor of the observed difference in 25(OH)D, suggesting that targeted interventions to improve vitamin D supplementation among immigrant children beyond the first year of life may be successful at increasing the 25(OH)D status of non-Western immigrant children. Non-modifiable factors such as ethnicity and skin pigmentation did not appear to explain the observed difference.

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the research study. P.B.D., P.C.P. and C.S.B. helped to refine the study design. J.A.O., J.L.M. and K.E.T. analysed the data. M.K., S.C. and J.D. coordinated data collection. All authors contributed to the interpretation of results. J.A.O. and J.L.M. drafted the manuscript. All authors read and approved the final manuscript. *Acknowledgements:* The authors thank the practitioners, paediatric and family medicine practices and families who are currently involved in the TARGet Kids! research network.

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