

Hypovitaminosis D in Migrant Children in Switzerland: a Retrospective Study

Olivia Fahmi (✉ olivia.fahmi@gmail.com)

Universite de Geneve Faculte de Medecine <https://orcid.org/0000-0002-6578-1034>

Alexandra Wilhelm-Bals

Geneva University Hospitals: Hopitaux Universitaires Geneve

Klara M. Posfay-Barbe

Geneva University Hospitals: Hopitaux Universitaires Geneve

Noémie Wagner

Geneva University Hospitals: Hopitaux Universitaires Geneve

Research Article

Keywords: Vitamin D, Hypovitaminosis D, Supplementation, Children, Migrant, Refugee

Posted Date: March 10th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-281204/v1>

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Abstract

Cholecalciferol (vitamin D₃) is essentially known for its part in the phospho-calcic metabolism and associated pathologies, such as rickets. In Switzerland, 40 to 50% of children are vitamin D deficient. Due to skin colour, poor nutrition, living condition and cultural practices, migrant population is particularly at risk. Our aim is to attest the vitamin D status of the children arriving in Switzerland and compare the cost-effectiveness of two supplementation strategies.

We retrospectively assessed 528 children's vitamin D status and parathyroid hormone, phosphates and calcium levels between 2015 and 2018 by electrochemiluminescence and spectrophotometry. Cholecalciferol was considered insufficient under 50 nmol/L and severely deficient below 25 nmol/L. Supplementation strategies' costs were based on local prices.

Seventy-three percent of children showed hypovitaminosis D and 28% had a severe deficit. Highest prevalence of deficit was found in children from Eastern Mediterranean (80%) and African regions (75%). Severe deficit was highest in the South East Asian (39%) and Eastern Mediterranean regions (33%) and higher in females than males. Deficit was predominant and more severe in winter. Hypovitaminosis increased with age. 0.4% of children presented with biological rickets. The most cost-effective supplementation strategy was to systematically supplement all children at arrival and in winter, reducing costs by 25% compared to vitamin D level-based supplementation.

Conclusion: A majority of migrant children presented with hypovitaminosis D. They must be supplemented to prevent complications. A cost-effective strategy could be to supplement all children at arrival and during wintertime without systematic vitamin D level check.

Summary

What is known

- Hypovitaminosis D is frequent in children and can lead to bone-related complications.
- Migrant children are particularly at risk of deficit.

What is new

- Three-quarters of migrant children evaluated at our migrant clinic in Geneva's children hospital are deficient in vitamin D, one third severely.
- A cost-effective strategy to correct the deficit is to supplement all migrant children at arrival and in winter.

Introduction

Vitamin D₃ (cholecalciferol) is classically known for its role in the calcium and phosphate metabolism. It is absorbed by ingestion (20%) or synthesized by the skin during sun exposure (80%) [1, 2]. In the setting of hypovitaminosis D, calcium and phosphate absorption will drop. Parathyroid hormone (PTH) will increase to normalize the calcium levels, resulting in normal to low serum calcium, high PTH and low phosphate [3, 1]. Severe deficit can induce rickets or osteomalacia due to abnormal bone mineralization [1, 4, 2, 3]. Vitamin D also seems involved in cancer prevention, autoimmune and cardiovascular diseases [5–8] and, in children, hypovitaminosis D has additionally been associated to respiratory infections, eczema and asthma [9, 8, 10].

Symptoms of hypovitaminosis D are variable (Table 1). The more severe the deficit, the more symptomatic children will be. Teenagers are more prone to subtle symptoms (irritability, tiredness, ...) than younger children [9, 11].

Table 1
Main symptoms of vitamin D deficit [9, 11]

Skeletal	Neurologic
Bone deformities: distal bowing of the legs, rickety rosary, cupping of the metaphyseal growth plate, Harrison's sulci, craniotabes, ... Poor growth	Hypotonia Motor developmental delay Tetany Seizures Muscular pain and weakness Tiredness Irritability

In Switzerland, 40 to 50% of native children are deficient in vitamin D [12]. Most of the vitamin D needed for health (80–90%) is produced by the skin as a result of ultraviolet radiation from the sun. In late autumn, winter and early spring, cloudy cover and weaker sun in this region does not allow the skin to produce enough vitamin D. In summer, because of the increased use of solar cream recommended by the society of dermatology to prevent skin cancer, skin exposure might also be insufficient. Moreover, fortified food is rare in Switzerland [11, 9, 10].

Due to nutritional deprivations, cultural practices (clothing, time spent indoors, ...) and darker skin phenotype (decreased cutaneous synthesis), migrant children are even more at risk [13–16, 3, 9].

Swiss guidelines (Federal Office of Public Health and Swiss Federal Commission for Nutrition) recommend a yearly prophylaxis for the first three years of life [11, 17]. The latter also suggests a yearly

supplementation for all children and teenagers, as well as screening for groups at risks (including dark-skinned people) [11]. Long-term compliance with daily supplementation seems however difficult to obtain [11, 18]. Paediatricians have the responsibility to assess if their patients can reach the recommended daily intake without supplementation and look for deficit symptoms, in particular in case of risk factors.

It is widely admitted that children older than one year old and teenagers should have a daily vitamin D intake of 600 IU (400 IU in infants younger than one) through sun, diet and, if necessary, supplementation [19, 10, 20]. In case of severe or symptomatic deficit, higher doses may be needed [11, 9].

Specific supplementation recommendations vary between countries, notably due to differences in milk and food fortification in vitamin D. The American Academy of Pediatrics only recommends that fully or partially breastfed infants and children (or children ingesting low quantities of fortified milk/food) should be supplemented, as their milk and food is fortified [21]. The French Society of Paediatrics recommend yearly supplementation for children up to 18 months and winter supplementation up to 5 years old and in teenagers [22]. The Scientific Advisory Committee on Nutrition in the United Kingdom recommends daily supplementation for all partially and fully breastfed infants up to 1 year old and systematic daily prophylaxis from 1 to 4 years old [23]. In our institution, all migrant children are routinely screened at arrival since 2015 and supplemented when necessary.

This study's primary aim is to determine the prevalence of vitamin D deficit in migrant children at arrival in Geneva and according to origin, age, sex and season. The secondary outcome is to analyse two supplementation strategies and propose cost-effective guidelines.

Materials And Methods

Study population

Migrant children arriving in our region are evaluated at a migrant clinic in Geneva's children hospital. Since 2015, they benefit from a global work-up at first consultation, amongst which vitamin D, calcium, phosphate and PTH are measured. We retrospectively analysed the medical records of 1246 children between 2015 and 2018 to assess serum 25-hydroxyvitamin D (25(OH)D), calcium, phosphate and PTH.

Inclusion criteria were: children aged 0–16 years old; first consultation between January 2015 and December 2018.

Exclusion criteria were: born in Switzerland; prior stay in Switzerland; no 25(OH)D results; 25(OH)D measured later than 6 months after first consultation.

We also collected information about demographics, country of origin and season of blood draw. Four age categories (age at first consultation) were defined: <3 years old, 3 to < 5 years old, 5 to < 10 years old and \geq 10 years old.

Geographic zones followed World Health Organization zones, except for Somalia, which was included in the African Region [24].

Laboratory tests

Cholecalciferol and PTH were measured by electrochemiluminescence and calcium and phosphate by spectrophotometry, using Roche Diagnostics kits (Switzerland) in our routine clinical laboratory. Various cutoffs to stratify vitamin D levels exist. Following the WHO, European Academy of Paediatrics and Swiss Federal Commission for Nutrition, we defined deficit as a 25(OH)D concentration of ≤ 50 nmol/L (20 ng/ml) and severe deficit as < 25 nmol/L (10 ng/ml) [19, 11, 25]. These thresholds are based on bone outcomes with increased PTH below 50 nmol/L and risk of rickets/osteomalacia below 25 nmol/L [11, 9]. Serum calcium was considered normal between 2.2 nmol/L and 2.52 nmol/L and PTH between 1.1 pmol/L and 6.8 pmol/L. Phosphate values were adapted to age according to the CALIPER program [26, 27].

Supplementation strategies

Two strategies were analysed to compare costs (Table 2) by simulating each method with our patient's data. They were only used for children older than 3 years old, as all children in Switzerland are supplemented up to 3 years old. Strategy 1 was a vitamin D level-based arrival supplementation. Strategy 2 was a systematic arrival supplementation without vitamin D assessment. For both, arrival supplementation was followed by winter supplementation for 10 years as winter deficit is expected and thus supplementation necessary in the long run. Migrant children are usually followed for about 10 years in our consultation.

Table 2
Supplementation strategies

Strategy	Arrival supplementation	Winter supplementation
Strategy 1	25(OH)D level assessment. If deficit, daily supplementation of 600 IU/day for 3 months ^a	Two oral doses of 100'000 IU in November and February for 10 years ^b
Strategy 2	No 25(OH)D level assessment. Systematic daily supplementation of 600 IU/day for 3 months	Two oral doses of 100'000 IU in November and February for 10 years ^b
^a If severe deficit, 25(OH)D level control after supplementation.		
^b If arrival in winter, no winter supplementation for the first year (arrival supplementation only)		

Arrival supplementation consisted in daily doses of 600 IU for three months and costed 8,50 CHF (~ 9,50\$ in february 2021). Winter supplementation consisted in two oral doses of 100'000 IU in November and

February and costed 18.50 CHF per year (~ 21\$). While less physiologic, the latter approach was chosen for winter supplementation to increase compliance [9, 28]. The price of the vitamin D check was 53 CHF (~ 59\$) in Geneva's hospital. Costs were analysed per patient and per year. Indirect costs due to nurse care, blood draw, etc. were not considered. Number of "unnecessary" blood tests and supplementation was evaluated.

Data collection

We collected data in a protected and anonymous database. The ethics committee waived the need to collect individual patients' consent. This study was approved by the institutional ethics committee on January 24, 2019 (study number: ID 2016 - 01278).

Statistical analysis

We applied standard descriptive statistics. Groups were compared with χ^2 tests. Linear regression was used to study the relationship between age and 25(OH)D levels. P values < 0.05 were considered statistically significant. Data was analysed with SPSS statistical software (version 25.0; SPSS Inc., Chicago, IL).

Results

Between 2015 and 2018, 1246 children had a first encounter in Geneva's migrant consultation. 528 were included (Fig. 1). 388 (73%) were deficient and 146 (28%) presented severe deficit.

302 children were male (57%) and 226 female (43%). Females showed more deficit (77%) than males (71%), but no significant difference was found except for African girls ($p = 0.03$). Severe deficit was significantly higher in females (34%) than males (23%) ($p = 0.008$), in particular if older than 10 years old (53% versus 31% respectively) ($p = 0.01$).

The most represented geographic zones were the Eastern Mediterranean ($n = 295$), African ($n = 123$) and European regions ($n = 54$). The highest prevalence of deficit was found in the Eastern Mediterranean (80%) and African regions (75%). Severe deficit was mostly found in the South East Asian (39%) and Eastern Mediterranean regions (33%). Children from the region of the Americas had predominantly sufficient values (75%). Half of the European children were deficient (Table 3, Fig. 2a).

Table 3
Vitamin D status by origin

Origin (N)	25(OH)D \leq 50 nmol/L (%)	25(OH)D < 25 nmol/L (%)	25(OH)D 25–50 nmol/L (%)	25(OH)D > 50 nmol/L (%)
Eastern Mediterranean Region (295)	236 (80)	98 (33)	138 (47)	59 (20)
Syria (133)	98 (74)	26 (20)	72 (54)	35 (26)
Afghanistan (67)	57 (85)	31(46)	26 (39)	10 (15)
Iraq (66)	57 (86)	31 (47)	26 (39)	9 (14)
Palestine (15)	13 (87)	4 (27)	9 (60)	2 (13)
Others ^a (14)	11 (79)	6 (43)	5 (36)	3 (21)
African Region (123)	92 (75)	26 (21)	66 (54)	31 (25)
Eritrea (92)	73 (79)	20 (22)	53 (58)	19 (21)
Others ^b (31)	19 (61)	6 (19)	13 (42)	12 (39)
European Region (54)	27 (50)	5 (9)	22 (41)	27 (50)
Georgia (20)	9 (45)	2 (10)	7 (35)	11 (55)
Others ^c (34)	18 (53)	3 (9)	15 (44)	16 (47)
South East Asian region (33)	21 (64)	13 (39)	8 (24)	12 (36)
Sri-Lanka (32)	21 (66)	13 (41)	8 (25)	11 (34)
Others ^d (1)	0 (0)	0 (0)	0 (0)	1 (100)
Western Pacific Region (15)	10 (67)	3 (20)	7 (47)	5 (33)
Mongolia (14)	9 (64)	3 (21)	6 (43)	5 (36)
Others ^e (1)	1 (100)	0 (0)	1 (100)	0 (0)
Region of the Americas (8)	2 (25)	1 (13)	1 (13)	6 (75)
Others ^f (8)	2 (25)	1 (13)	1 (13)	6 (75)
Total (528)	388 (73)	146 (28)	242 (46)	140 (27)
^a Iran, Egypt, Pakistan, Sudan, Yemen				

Origin (N)	25(OH)D ≤ 50 nmol/L (%)	25(OH)D < 25 nmol/L (%)	25(OH)D 25–50 nmol/L (%)	25(OH)D > 50 nmol/L (%)
^b Algeria, Angola, Ethiopia, Somalia, Nigeria, Cameroon, Senegal, Burkina Faso, Ivory Coast, Guinea-Bissau, Uganda				
^c Turkey, Romania, Kosovo, Azerbaijan, Russia, Armenia, Macedonia, Serbia, Spain, Albania, Moldova, Portugal, Ukraine				
^d Bangladesh				
^e Philippines				
^f Bolivia, Salvador, Columbia, Honduras				

90 (17%) children were born out of their origin country. 21 (4%) were born out of their origin geographic zone, amongst which 13 (2%) were born in the European region.

The most represented countries of origin were Syria (n = 133), Eritrea (n = 92), Afghanistan (n = 67), Iraq (n = 66), Sri-Lanka (n = 32), Georgia (n = 20), Palestine (n = 15) and Mongolia (n = 14). Except for Georgia (45% of hypovitaminosis D), most children of the previously mentioned countries were deficient. Palestinian, Iraqi and Afghan children were the most deficient with more than 85% of insufficient values. Iraqi and Palestinian children showed the largest proportion of severe deficit (47% and 46% respectively) (Table 3).

The predominant age categories were 5 to < 10 years old (n = 237) and ≥ 10 years old (n = 131). Children aged 3 to < 5 years old (n = 99) and < 3 years old (n = 66) were slightly less represented. All age categories showed predominant deficit, increasing with age (p < 0.001) (Fig. 2b). Severe deficit also increased with age (p < 0.001) There was no significant difference in gender in the age categories.

On average, children consulted 4.7 months after arrival in Switzerland (IC 95% = 0.76). 25(OH)D levels were examined on average 1.4 months after first encounter (IC 95% = 0.11).

Seasons of vitamin D analysis were equally represented (103 measures in summer, 152 in spring, 139 in winter and 134 in autumn). There was a difference in deficit according to season (p < 0.001), with a predominance of insufficient values in winter (96%) and sufficient values in summer (56%). Severe deficit was high in winter (53%) and almost inexistent in summer (4%). (see Fig. 2c).

91(17%) children had hyperparathyroidism with 90% concomitant hypovitaminosis D. 28 (5%) had hypocalcaemia with 89% concomitant vitamin D deficiency. 42 (8%) presented with hypophosphatemia with 86% concomitant deficient cholecalciferol. 2 patients (0.4%) presented with biological rickets and both had concomitant severe vitamin D deficit.

The most cost-effective strategy over 10 years was strategy 2 (systematic arrival supplementation without vitamin D level check, followed by winter substitution) with a mean cost of 19 CHF per patient per year (~ 21\$ in February 2021). It was 25% cheaper than strategy 1 (vitamin D level-based supplementation followed by winter substitution for all), with a mean cost of 25 CHF per patient per year (~ 28\$).

With strategy 2, 140 (27%) children with sufficient 25(OH)D levels would have received unnecessary supplementation. With strategy 1, 388 (73%) children with insufficient 25(OH)D levels would have had an unnecessary blood sampling.

Discussion

Vitamin D levels

Two-thirds (73%) of migrant children are deficient in vitamin D at arrival in Switzerland, one-third (28%) of them severely. This is higher than the rate in Swiss children (40–50%) [12]. It is consistent with other studies, although reference values for deficit can vary between authors. For example, 72.3% of refugees in Canada were deficient (< 50 nmol/L) [29] and 77.4% in Italy (< 75 nmol/L) [30]. Supplementation is needed to prevent impact on bone health [1–4].

Besides the overall hypovitaminosis D, we found that the presence and severity of deficit varies according to origin, age and gender.

Even though hypovitaminosis D is classically associated with dark skin, a great majority of children with fairer complexion also presented with mild and severe deficit. For example, Eastern Mediterranean children were predominantly deficient (80%), a third of them (33%) severely. In particular, Palestinian, Iraqi and Afghan children showed a large proportion of deficit. This might be linked to cultural/religious practices associated with a more covering dress code. Another hypothesis may be related to the cause of migration (i.e armed conflict might be associated with more time spent indoors).

As expected, African children were largely deficient (75%), although slightly less severely (21%). Similarly to Switzerland, 50% of European children had vitamin D deficit [12]. We found 75% of sufficient values in children from the region of the Americas but had a limited number of patients (n = 8). Similar results for geographic distribution of hypovitaminosis D were found in a Canadian study [29]. Another Norwegian study [31] had comparable results, except for a lower prevalence of deficit in the East Asian region (approximately our Western Pacific region), but the analysed countries were different and they included adults. Close results were also found for African and Asian children in an Italian study, but they found a higher deficit in America and Europe [30]. These results are however difficult to compare as vitamin D ranges were different and geographic zones not clearly defined.

Hypovitaminosis D significantly increased with age. Highest prevalence of deficit (86%) and severe deficit (41%) were found in children older than 10 years old. Other studies found concordant results in Italy [30]

and Canada [29], with better vitamin D status in younger patients.

These results highlight the need for vitamin D prophylaxis for all migrants children and not only the young (< 3 years old) and dark-skinned children, as suggested in the current Swiss guidelines [11, 17].

Additionally, we found a significant difference in severe deficit linked to gender, which was more frequent in females (34%) than males (23%), especially if older than 10 years old. This result might be linked to cultural/religious dressing practices appearing with the first menstruations, limiting sun exposure. Gender differences in activities are also possible, with girls spending more time indoors than boys. Another Canadian study also found that Middle East, Asian and African female were particularly at risk of hypovitaminosis D [29]. Similar results were found in a Norwegian study, with a greater risk of hypovitaminosis D in females, especially if adolescent [31].

As expected due to the difference in sun exposure, vitamin D status largely varied between seasons, with a great majority of hypovitaminosis D in winter (96%) and a small majority of normal values in summer (56%). Half of the children (53%) were severely deficient in winter. These results, although consistent with current knowledge [3, 10] and several studies [30, 32, 33], emphasize the importance of wintertime supplementation, in particular in the migrant population. Although the specific impact of winter deficit is not yet clearly defined, it seems to negatively affect bone health [34].

Two children (0.4%) presented with biological rickets. Both had concomitant severe vitamin D deficit. Although rare in Europe, rickets is still present, especially in refugees and dark-skinned children and is mainly linked to vitamin D deficiency [35, 9].

Other biological manifestations related to vitamin D deficit were found (hyperparathyroidism 17%, hypocalcaemia 5% and hypophosphatemia 8%), all strongly correlated to hypovitaminosis D. These results were expected and emphasize the significant impact of decreased vitamin D levels and need for supplementation.

Moreover, it underlines the importance of vitamin D dosage and supplementation in case of musculoskeletal symptoms or more subtle symptoms (irritability, tiredness, weakness), in particular in teenagers (Table 1) [11, 9].

Cost analysis

Our data suggest that systematic vitamin D supplementation (three months at arrival followed by winter substitution) for all migrant children older than 3 years old without level check (strategy 2) is more cost-efficient than level-based supplementation, reducing costs by 25% over 10 years. As nurse care, number of appointments and blood draw costs associated to strategy 1 were not considered, the gap is presumably wider.

Being less discriminative, this strategy is nonetheless associated with a substantial number (27%) of unnecessary substitution. The supplementation with 600 IU per day of cholecalciferol should however not

induce toxicity in children with normal vitamin D status [12, 36, 37]. Winter substitution with two doses of 100'000 IU (corresponding approximately to 1100 IU/day) also stays below the safe upper intake concentrations [22, 11, 37, 38]. Moreover, it limits the need for an “unnecessary” blood drawn (vitamin D measure in deficient children, who will need supplementation anyway), which was a predominant drawback in the vitamin D level-based supplementation strategy (strategy 1).

However, unlike strategy 1, strategy 2 (systematic substitution) does not allow a control of the vitamin D correction in severely deficient children, as there is no base value. This might result in partial correction, especially if compliance is not adequate. It underlines the importance of symptom-based vitamin D level check, especially in high-risk groups, to avoid missing and under-treating cases of rickets. Indeed, severe or symptomatic deficit might needs higher doses for correction [9, 11].

Finally, there is a higher risk of loss of follow-up cases and thus lack of supplementation in strategy 1 due to the need for a second appointment to give the patient the vitamin D results before starting replacement therapy.

Limitations

This study is subject to various limitation. Although the number of patients in this study were relatively high, our population was heterogeneous and not all results were statistically significant. Some countries of origin and geographic zones were poorly represented. Furthermore, migrant population being subject to current refugee patterns, it might differ in other centres and change over time. Vitamin D levels might also vary according to type and duration of the refugee route taken or prior vitamin D substitution.

As our study was retrospective, we also lacked data about cultural/religious habits and outdoor time.

The nurse encounters in our consultation being subject to hourly rates regardless of exams performed, the costs of nurse care, number of appointments, blood draw and other collaterals were not considered, as not comparable. Newly arrived migrant children also often benefit from blood draws and follow-up appointments in other contexts, making the individual costs linked to vitamin D difficult to isolate. The price of vitamin D measuring and supplementation may also vary between centres and must be taken into account individually.

For these reasons, this study's results and the supplementation strategy proposed should be confirmed in a larger and if possible multicentred trial and adapted locally.

Conclusion

Two-thirds of migrant children arriving in Geneva are deficient in vitamin D and almost all of them have below-range levels in winter. Supplementation is needed to prevent hypovitaminosis D complications. Deficit varies according to origin country, geographic zone, age, gender and season of analysis but remains high in almost all categories. For this reason and due to a significant reduction in costs

compared to a vitamin D status-based supplementation, we suggest to systematically prescribe vitamin D for migrant children older than three years old at arrival and every winter.

Abbreviations

25(OH)D: 25-hydroxyvitamin D

PTH: parathyroid hormone

Declarations

Acknowledgments:

Dr Déborah Cisier, Department of Woman, Child and Adolescent, Geneva University Hospitals, Switzerland.

Authors' contributions:

All authors contributed to the study conception and design. Data collection and analysis were performed by OF. The first draft of the manuscript was written by OF and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflicts of interests:

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval:

This study was performed in line with the principles of the Declaration of Helsinki. Ethical approval was granted by the institutional ethics committee (Commission cantonale d'éthique de la recherche CCER) on January 24, 2019 (study number: ID 2016-01278).

References

1. Eugene J. Barrett, Paula Barrett (2012) The parathyroid glands and vitamin D. In: Walter F. Boron, Emile L. Boulpaep (eds) *Medical Physiology : a Cellular and Molecular Approach*. 2nd ed. edn. Saunders Elsevier, Philadelphia, pp 1094-1100
2. Chung M, Balk EM, Brendel M, Ip S, Lau J, Lee J, Lichtenstein A, Patel K, Raman G, Tatsioni A, Terasawa T, Trikalinos TA (2009) Vitamin D and calcium: a systematic review of health outcomes. *Evid Rep Technol Assess (Full Rep)* (183):1-420

3. Larry A. Greenbaum (2016) Rickets and Hypervitaminosis D. In: Robert M. Kliegman (ed) Nelson Textbook of Pediatrics. 20 edn. Elsevier, Philadelphia, pp 331-341
4. Pettifor JM (2004) Nutritional rickets: deficiency of vitamin D, calcium, or both? *Am J Clin Nutr* 80 (6 Suppl):1725S-1729S. doi:10.1093/ajcn/80.6.1725S
5. Schwalfenberg G (2007) Not enough vitamin D: health consequences for Canadians. *Can Fam Physician* 53 (5):841-854
6. Christakos S, DeLuca HF (2011) Minireview: Vitamin D: is there a role in extraskeletal health? *Endocrinology* 152 (8):2930-2936. doi:10.1210/en.2011-0243
7. Binkley N, Ramamurthy R, Krueger D (2012) Low vitamin D status: definition, prevalence, consequences, and correction. *Rheum Dis Clin North Am* 38 (1):45-59. doi:10.1016/j.rdc.2012.03.006
8. Bacchetta J, Ranchin B, Dubourg L, Cochat P (2010) [Vitamin D revisited: a cornerstone of health?]. *Arch Pediatr* 17 (12):1687-1695. doi:10.1016/j.arcped.2010.09.003
9. Gonzalez Nguyen-Tang E, Parvex P, Goischke A, Wilhelm-Bals A (2019) Carence en vitamine D et rachitisme : dépistage et traitement, aspects pratiques pour le clinicien. *Revue médicale Suisse*
10. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM, Endocrine S (2011) Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 96 (7):1911-1930. doi:10.1210/jc.2011-0385
11. Federal commission for nutrition (2012) Vitamin D deficiency: Evidence, safety, and recommendations for the Swiss Population. Federal Office for Public Health, Zurich
12. Federal commission for nutrition (2019) Prise de position concernant l'étude Bolland et al. de 2018 en relation au rapport d'experts de la CFN «Vitamin D deficiency: evidence, safety and recommendations for the Swiss population» de 2012. Federal Office for Public Health, Berne
13. Salerno G, Ceccarelli M, de Waure C, D'Andrea M, Buonsenso D, Faccia V, Pata D, Valentini P (2018) Epidemiology and risk factors of hypovitaminosis D in a cohort of internationally adopted children: a retrospective study. *Ital J Pediatr* 44 (1):86. doi:10.1186/s13052-018-0527-4
14. Baauw A, Kist-van Holthe J, Slattery B, Heymans M, Chinapaw M, van Goudoever H (2019) Health needs of refugee children identified on arrival in reception countries: a systematic review and meta-analysis. *BMJ Paediatr Open* 3 (1):e000516. doi:10.1136/bmjpo-2019-000516
15. Benson J, Skull S (2007) Hiding from the sun - vitamin D deficiency in refugees. *Aust Fam Physician* 36 (5):355-357
16. Erkal MZ, Wilde J, Bilgin Y, Akinci A, Demir E, Bodeker RH, Mann M, Bretzel RG, Stracke H, Holick MF (2006) High prevalence of vitamin D deficiency, secondary hyperparathyroidism and generalized bone pain in Turkish immigrants in Germany: identification of risk factors. *Osteoporos Int* 17 (8):1133-1140. doi:10.1007/s00198-006-0069-2
17. Office fédéral de la santé publique (2012) Apport en vitamine D : nouvelles recommandations de l'OFSP <https://www.admin.ch/gov/fr/accueil/documentation/communiques.msg-id-44932.html>. Accessed August 25, 2020

18. l'Allemand D, Neuhaus TJ, Janner M, Braegger C, Laimbacher J (2012) Recommandations de l'Office fédéral de la santé publique concernant l'apport en vitamine D en Suisse – quelle signification pour le pédiatre? *Paediatrica* 23
19. Grossman Z, Hadjipanayis A, Stiris T, Del Torso S, Mercier JC, Valiulis A, Shamir R (2017) Vitamin D in European children-statement from the European Academy of Paediatrics (EAP). *Eur J Pediatr* 176 (6):829-831. doi:10.1007/s00431-017-2903-2
20. IOM (Institute of Medicine) (2011) Dietary Reference Intakes for Calcium and Vitamin D. The National Academy of Sciences, Washington, DC
21. Wagner CL, Greer FR, American Academy of Pediatrics Section on B, American Academy of Pediatrics Committee on N (2008) Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Pediatrics* 122 (5):1142-1152. doi:10.1542/peds.2008-1862
22. Vidailhet M, Mallet E, Bocquet A, Bresson JL, Briend A, Chouraqui JP, Darmaun D, Dupont C, Frelut ML, Ghisolfi J, Girardet JP, Goulet O, Hankard R, Rieu D, Simeoni U, Turck D, Comité de nutrition de la Société française de p (2012) Vitamin D: still a topical matter in children and adolescents. A position paper by the Committee on Nutrition of the French Society of Paediatrics. *Arch Pediatr* 19 (3):316-328. doi:10.1016/j.arcped.2011.12.015
23. Scientific Advisory Committee on Nutrition (2016) Vitamin D and Health. Public Health England,
24. WHO regional offices. <http://www.who.int/about/regions/en/>. Accessed December 2, 2016
25. Hope Alberta Weiler (2017) Vitamin D Supplementation for Infants : Biological, behavioural and contextual rationale. https://www.who.int/elena/titles/bbc/vitamind_infants/en/. Accessed August 20, 2020
26. Estey MP, Cohen AH, Colantonio DA, Chan MK, Marvasti TB, Randell E, Delvin E, Cousineau J, Grey V, Greenway D, Meng QH, Jung B, Bhuiyan J, Secombe D, Adeli K (2013) CLSI-based transference of the CALIPER database of pediatric reference intervals from Abbott to Beckman, Ortho, Roche and Siemens Clinical Chemistry Assays: direct validation using reference samples from the CALIPER cohort. *Clin Biochem* 46 (13-14):1197-1219. doi:10.1016/j.clinbiochem.2013.04.001
27. Higgins V, Chan MK, Nieuwesteeg M, Hoffman BR, Bromberg IL, Gornall D, Randell E, Adeli K (2016) Transference of CALIPER pediatric reference intervals to biochemical assays on the Roche cobas 6000 and the Roche Modular P. *Clin Biochem* 49 (1-2):139-149. doi:10.1016/j.clinbiochem.2015.08.018
28. Dalle Carbonare L, Valenti MT, Del Forno F, Caneva E, Pietrobelli A (2017) Vitamin D: Daily vs. Monthly Use in Children and Elderly-What Is Going On? *Nutrients* 9 (7). doi:10.3390/nu9070652
29. Lane G, Nisbet C, Whiting SJ, Vatanparast H (2019) Canadian newcomer children's bone health and vitamin D status. *Appl Physiol Nutr Metab* 44 (7):796-803. doi:10.1139/apnm-2018-0705
30. Ceccarelli M, Chiappini E, Arancio R, Zaffaroni M, La Placa S, D'Andrea M, de Waure C, Da Riolo RM, Valentini P, on the behalf of National Working Group for the Migrant Children of the Italian Society of P (2020) Vitamin D deficiency in a population of migrant children: an Italian retrospective cross-sectional multicentric study. *Eur J Public Health* 30 (3):551-556. doi:10.1093/eurpub/ckz182

31. Eggemoen AR, Knutsen KV, Dalen I, Jenum AK (2013) Vitamin D status in recently arrived immigrants from Africa and Asia: a cross-sectional study from Norway of children, adolescents and adults. *BMJ Open* 3 (10):e003293. doi:10.1136/bmjopen-2013-003293
32. Aucoin M, Weaver R, Thomas R, Jones L (2013) Vitamin D status of refugees arriving in Canada: findings from the Calgary Refugee Health Program. *Can Fam Physician* 59 (4):e188-194
33. Guessous I, Dudler V, Glatz N, Theler JM, Zoller O, Paccaud F, Burnier M, Bochud M, Swiss Survey on Salt G (2012) Vitamin D levels and associated factors: a population-based study in Switzerland. *Swiss Med Wkly* 142:0. doi:10.4414/smw.2012.13719
34. Outila TA, Karkkainen MU, Lamberg-Allardt CJ (2001) Vitamin D status affects serum parathyroid hormone concentrations during winter in female adolescents: associations with forearm bone mineral density. *Am J Clin Nutr* 74 (2):206-210. doi:10.1093/ajcn/74.2.206
35. Creo AL, Thacher TD, Pettifor JM, Strand MA, Fischer PR (2017) Nutritional rickets around the world: an update. *Paediatr Int Child Health* 37 (2):84-98. doi:10.1080/20469047.2016.1248170
36. Office of Dietary Supplements Vitamin D - Fact Sheet for Health Professionals. <https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/>. Accessed August 20, 2020
37. Shroff R, Knott C, Rees L (2010) The virtues of vitamin D—but how much is too much? *Pediatr Nephrol* 25 (9):1607-1620. doi:10.1007/s00467-010-1499-9
38. Hamo S, Freychet C, Bertholet-Thomas A, Poulat AL, Cochat P, Vuillerot C, Bacchetta J (2015) [Vitamin D supplementation: not too much, not too little!]. *Arch Pediatr* 22 (8):868-871. doi:10.1016/j.arcped.2015.04.023

Figures

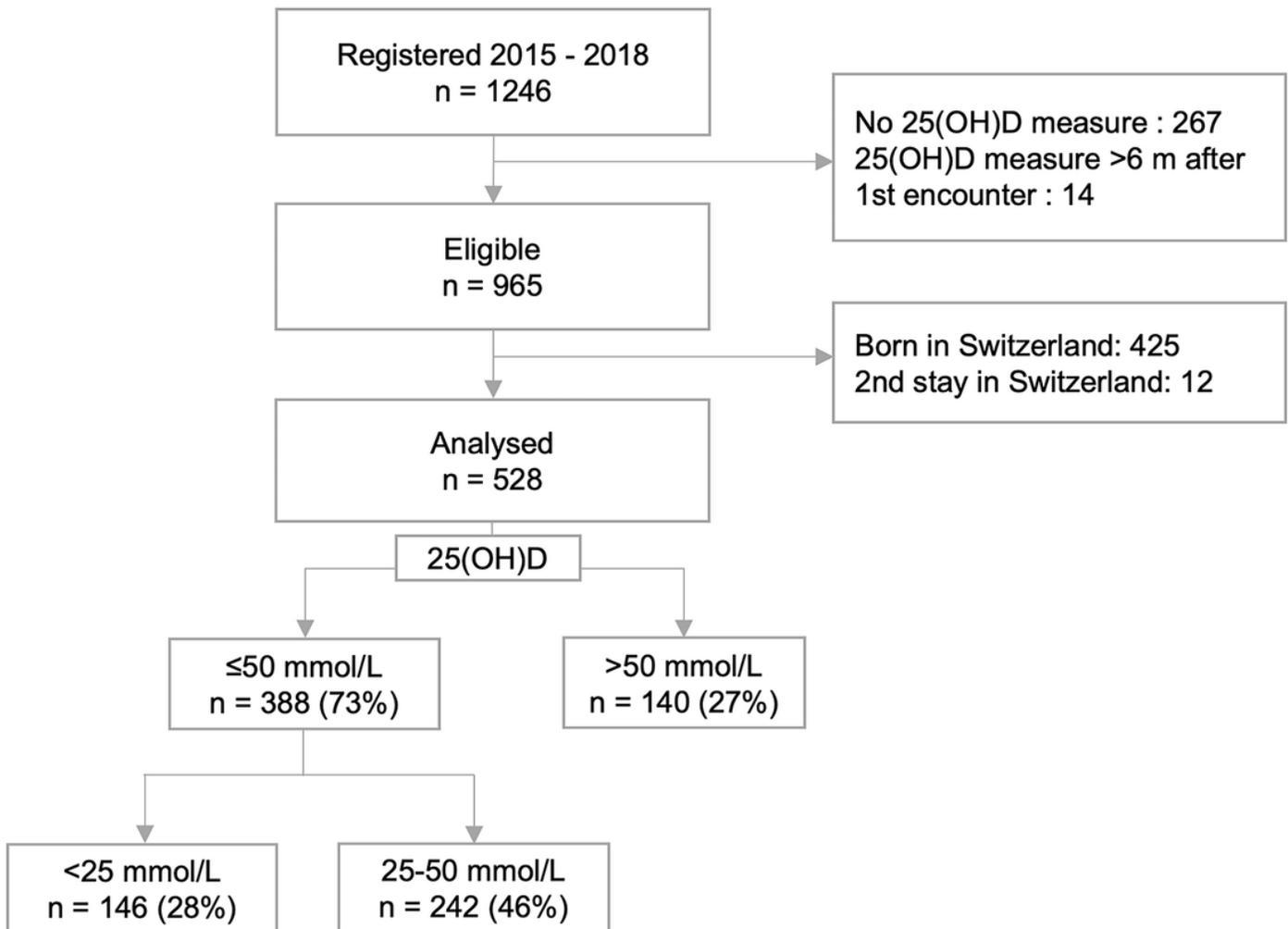


Figure 1

Flowchart showing excluded patients and vitamin D status of included children (25(OH)D levels <25 nmol/L, 25-50 nmol/L, >50 nmol/L)

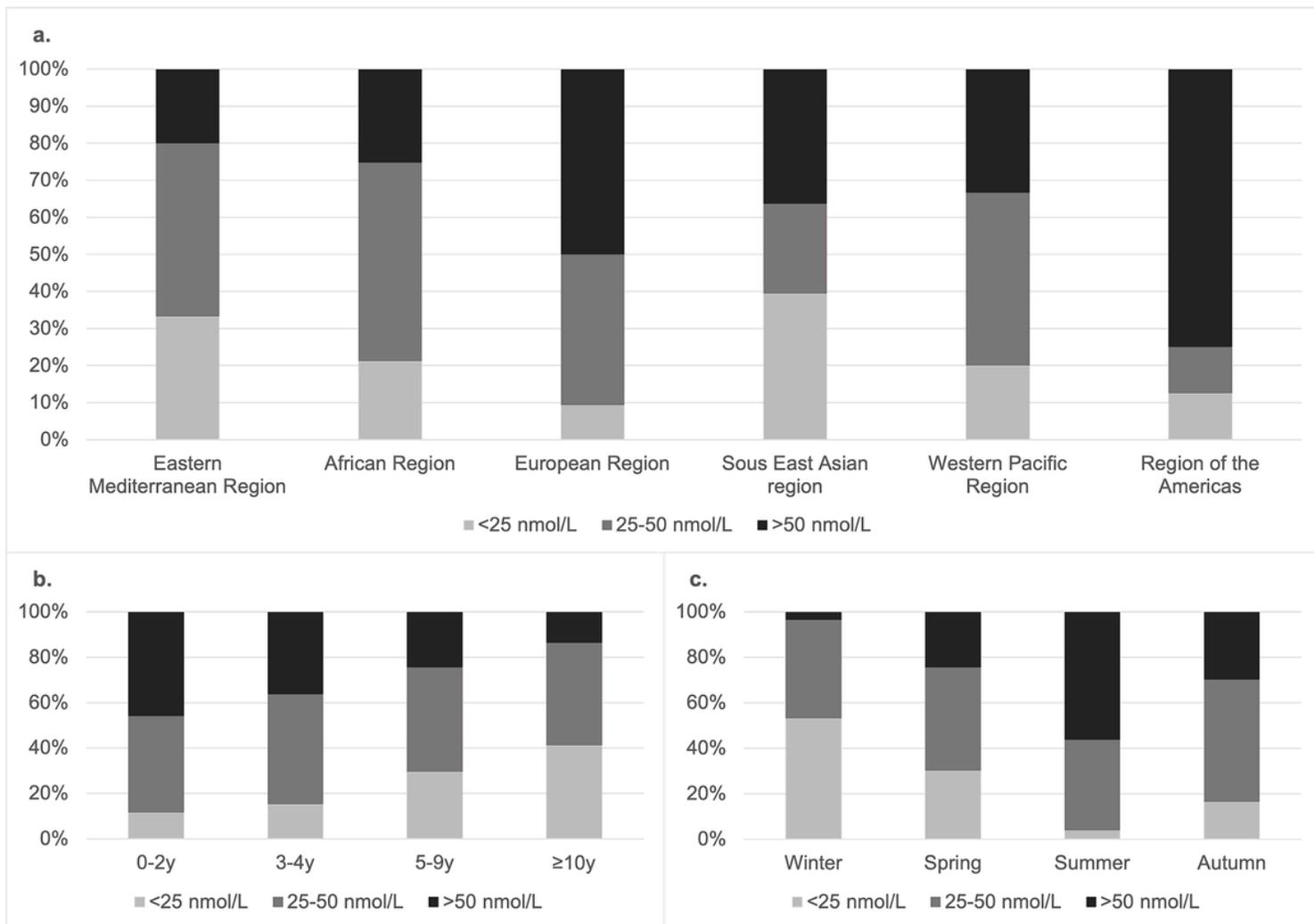


Figure 2

25(OH)D levels by geographic zones (a), age categories (b) and season of analysis (c)