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Research paper

Survey on vitamin D supplementation in children in France: Evaluation of real-life practices following the new 2022 French recommendations

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ABSTRACT

Background and objective: In 2022, recommendations for vitamin D supplementation in children were updated in France. The objective of this study was to assess real-life practices of vitamin D supplementation in children following these recommendations.
Methods: A thirty-three-question questionnaire was distributed to members of the scientific societies of paediatrics and general medicine via an online platform.
Results: There were 966 respondents, of whom 87 % were paediatricians and 13 % were general practitioners. About half of the physicians (47 %) were in private practice, 49 % worked in a hospital centre and 6 % worked in a maternal and child health centre. As recommended and regardless of the professional practice, vitamin D supplementation was almost systematically prescribed in all age groups (over 90 % of respondents), in daily doses up to 2 years of age (97 % of all respondents) and then every 3 months in older children (year-round in 38 % and winter/spring only in 40 %). Contrary to the new recommendations, loading doses of 200,000 units of vitamin D were prescribed by 5 % of respondents and non-pharmaceutical forms of vitamin D (*e.g.* unlicensed food supplements) were prescribed by 10 % of respondents. Although risk factors such as low sun exposure and dark skin were well known by respondents (75 % and 74 % respectively), obesity and veganism were only reported by half the respondents (40 % and 53 % respectively). Two-thirds (61 %) of respondents reported assessing calcium intakes when following children; however, only 10 % of them use specific questionnaires or calcium equivalence tables. Finally, the calcium content of foods and its bioavailability appeared to be poorly understood by health professionals.
Conclusion: This survey shows that the practice of paediatricians and general practitioners are in accordance with the new recommendations for vitamin D supplementation in very young children. The identification by this survey of knowledge gaps will allow targeted information campaigns.

1. Introduction

Vitamin D is one of the key hormones involved in regulating calcium and phosphate homeostasis and maintaining an optimal bone mineralisation throughout life [1,2]. In humans, the main sources of vitamin D are sunlight and diet. Indeed, vitamin D_3 is synthesised in the skin under the action of ultraviolet radiation or it can be found in oily fish and cod liver oil. Vitamin D_2 is found in yeast and mushrooms. To be effective, vitamin D is converted by 25-hydroxylase in the liver to 25-hydroxyvitamin D [25(OH)D], which is further converted by the

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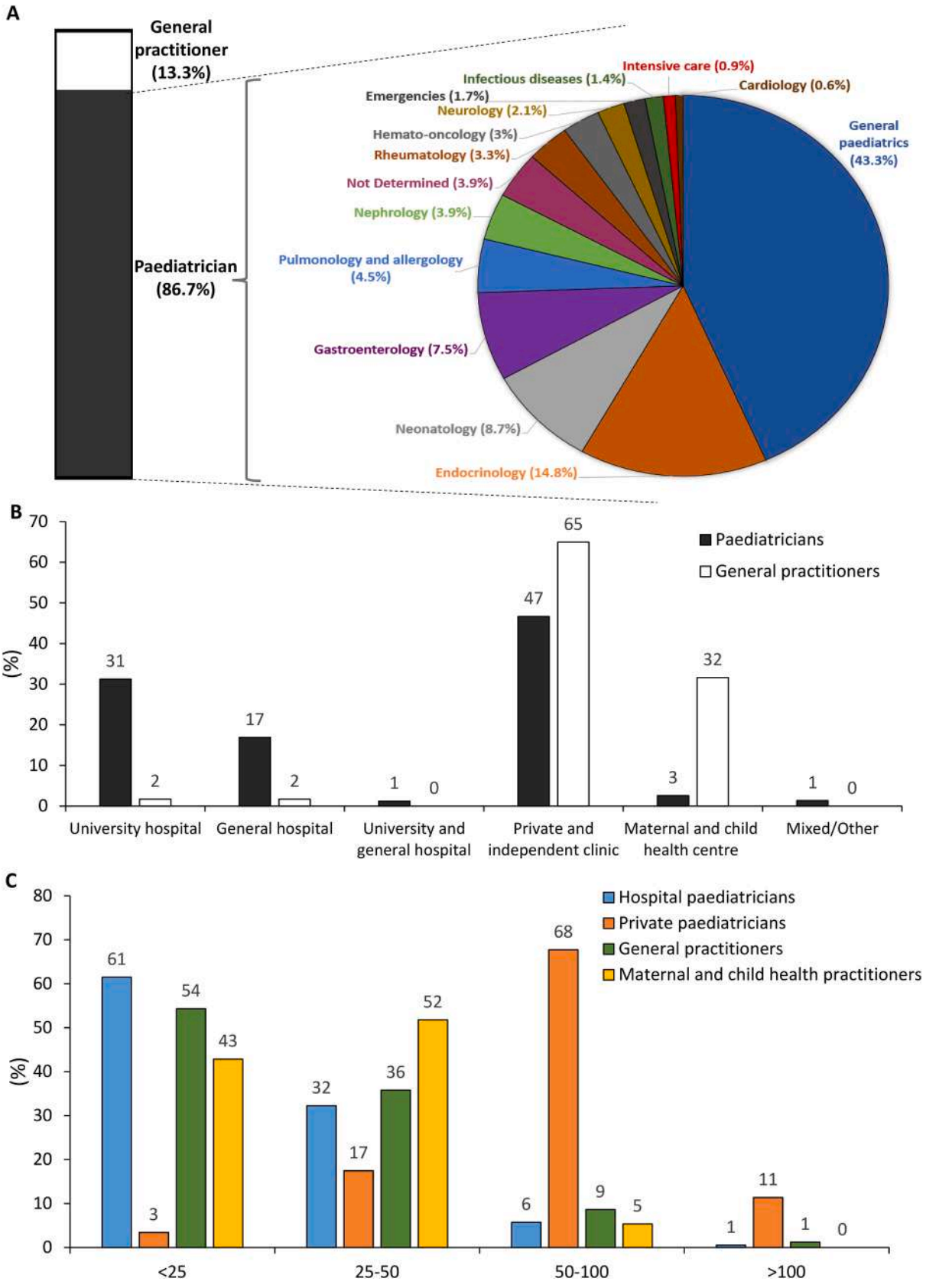

Fig. 1. Respondent demographics. A. Respondents specialities. B. Medical practice. C. Number of patients seen by week.

25-hydroxyvitamin D-1a-hydroxylase in the kidneys to the active form, 1,25-dihydroxyvitamin D [1,25(OH)$_2$D]. The 25(OH)D is considered to be the reserve form of vitamin D. Despite the absence of a definitive consensus on the normal range of serum 25(OH)D concentrations, the following cut-off points have been proposed: sufficiency 75–100 nmol/L (30–60 ng/ml), insufficiency 50–75 nmol/L (20–30 ng/ml), deficiency 25–50 nmol/L (10–20 ng/ml) and severe deficiency < 25 nmol/L (< 10 ng/ml) [3,4]. Vitamin D deficiency, frequently associated with inadequate calcium intake, is the primary cause of rickets and osteomalacia, which are characterized by abnormal growth plates and impaired bone mineralisation, respectively [1]. Rickets can be associated with hypocalcaemia, which can lead to life-threatening complications, including neurological (*e.g.* hypocalcaemic seizures), respiratory (*e.g.* laryngospasm) and cardiac (*e.g.* arrhythmias, dilated cardiomyopathy) issues [5]. Furthermore, vitamin D deficiency has been associated with extra-skeletal effects including the development of infectious and autoimmune diseases, some cancers, type 2 diabetes mellitus and cardiovascular disease [6]. In France and other industrialised countries, vitamin D supplementation policies in the 1960s and the infant formula fortification in the 1970s led to the near disappearance of rickets from the 1980s onwards. However, over the past 20 years, several studies have reported an increased incidence of vitamin D deficiency and rickets worldwide [7]. It has been estimated that approximately 1 billion people worldwide have vitamin D deficiency or insufficiency [8]. This pandemic, which is attributed to modern lifestyles and environmental factors that limit sunlight exposure, affects all countries and age groups. Children and adolescents are particularly at risk, as bone growth increases the need for calcium in this population. In the United States, despite the fortification of certain dairy products and cereals with vitamin D, 50 % of children aged 1–5 years and 70 % of children aged 6–11 years have vitamin D insufficiency or deficiency (defined as < 30 ng/ml) [9]. In England, the incidence of vitamin D deficiency in children increased from 3 per 100,000 person-years in 2000 to 261 per 100,000 person-years in 2014, and the number of diagnoses increased 15-fold between 2008 and 2014 [10]. In 2014, a multicenter French study reported the vitamin D status of 326 children aged 6 to 10 years: 3 % had severe deficiency and 34 % had vitamin D insufficiency or deficiency [11]. This vitamin D deficiency can occur as early as the foetal period and early infancy. For instance, in the USA, 73 % of the pregnant women and 80 % of their infants were found to be vitamin D deficient at the time of birth despite taking a daily prenatal multivitamin containing 400 IU of vitamin D [12]. In France, a recent prospective study showed that 46.5 %, 13.0 % and 68.5 % of pregnant women at the 1st trimester, pregnant women at the 3rd trimester and in cord blood show vitamin D deficiency, respectively [13]. Concomitantly to this increased incidence of vitamin D insufficiency and deficiency, studies have reported an increased incidence of rickets in Europe and North America, with a current annual incidence of approximately 3 / 100,000 children of all ages [14–16]. Infants are particularly at risk with an annual incidence of 6 / 100,000 in children under 3 years of age in a Danish study [14] and 7.5 / 100,000 in children under 5 years of age in a British study [17,18].

These data emphasise the importance of adequate vitamin D intake in children. In France, guidelines on vitamin D supplementation were first published by the Nutrition Committee of the French Society of Paediatrics in 2012 [19]. These guidelines were updated in 2022 with the objectives to prevent rickets, simplify the recommendations and be aligned with the European guidelines of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition [4,20]. The aim of this survey was to evaluate the extent to which the recently revised recommendations for vitamin D supplementation were being implemented in the French paediatric population by paediatricians from various specialties (*i.e.* paediatricians and general practitioners) and with diverse practice settings (*i.e.* hospital paediatricians, private paediatricians and general practitioners, maternal and child health practitioners).

2. Material and methods

2.1. Survey development

This survey was developed in December 2023 by a steering committee of experts from three clinical specialties (paediatric endocrinology, nephrology and nutrition) involved in the new 2022 recommendations on vitamin D supplementation. A 33-question clinical practice questionnaire was developed and validated by a group of general paediatricians and general practitioners. All questions included in the final version of the survey are provided in **Supplementary File S1**. The survey began by collecting demographic information about the respondent's location, clinical specialty, type of institution in which they were primarily employed, and the number of children they saw on a weekly basis. Subsequently, respondents were asked to provide responses to general questions regarding vitamin D supplementation and recommended calcium dietary intake.

2.2. Survey implementation and distribution

The survey was implemented for distribution via the online platform Google Form and doctors were invited to participate. Several paediatric and general medical societies were contacted to distribute a link to the survey to their members. A list of the societies that helped to distribute the survey is provided in the Acknowledgements. The survey was available for completion between January and March 2023. The first respondent completed the survey on 13 January 2023 and the last respondent completed the survey on 8 March 2023.

2.3. Statistical analysis

For the purposes of statistical analysis, the results were exported in Prism format from the Google Form survey platform.

Four groups were considered for comparisons based on type of professional practice: private paediatricians, hospital paediatricians, private general practitioners, and maternal and child health practitioners (paediatricians or general practitioners). The responses were also differentiated according to 4 age groups: infants (0 to 2 years), toddlers (2 to 5 years), children (5 years to adolescence) and adolescents. For maternal and child health practitioners who only followed children up to the age of 5, only responses for children under this age were included.

Differences between groups were assessed using contingency tables and the chi-squared test for independence.

All tests were two-tailed, and a p-value of <0.05 was considered significant throughout the study ($p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$). Statistical analyses were performed using Prism software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Demographics of respondents

A total of 966 respondents were included in the study, with 87 % being paediatricians and 13 % being general practitioners (Fig. 1**A**). Among the paediatricians, 43 % were general paediatricians and 57 % were specialist paediatricians. The most common paediatric specialties were endocrinology (15 %), followed by neonatology (9 %) and gastroenterology (8 %).

In terms of the type of practice, the majority of doctors (47 %) had a private practice (private clinic or independent practice). This was the case for 47 % of paediatricians and 65 % of general practitioners. 49 % of respondents worked in a hospital centre (university or general hospital or both). The majority of these were paediatricians (99 %) (Fig. 1**B**). In contrast, 6 % of respondents worked in a maternal and child health centre, the majority of whom (66 %) were general practitioners. The majority of respondents worked in urban or suburban areas (92 %)

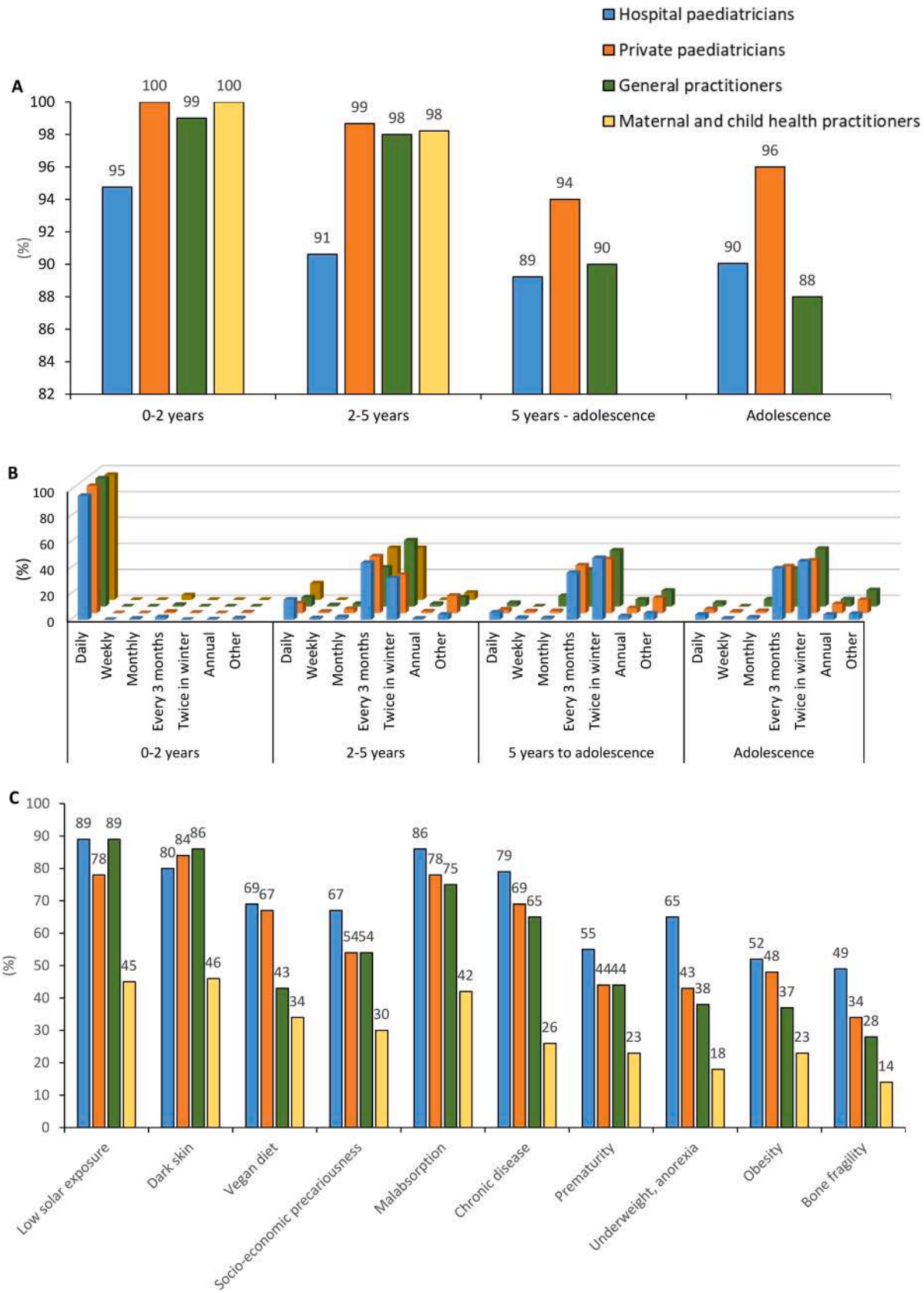

Fig. 2. Vitamin D supplementation. A. Prescription according to age groups. B. Frequency of administration according to age groups. C. Risk factors of vitamin D deficiency.

Table 1
Most frequently prescribed forms of vitamin D supplementation.

Vitamin D formulations	Number of respondents (n = 966)
Licensed vitamin D	
Oral solutions	
ZymaD 10 000 UI/mL ®	852 (88.2 %)
Adrigyl 10 000 UI/mL ®	554 (57.3 %)
Sterogyl 2 000 000/100 mL ®	13 (1.3 %)
Deltius 10 000 UI/mL ®	7 (0.7 %)
Ampoules	
Uvedose 100 000 UI ®	538 (55.7 %)
ZymaD 50 000 UI ®	413 (42.8 %)
ZymaD 80 000 UI ®	287 (29.7 %)
Uvedose 50 000 UI ®	268 (27.7 %)
ZymaD 200 000 UI ®	44 (4.6 %)
Unlicensed food supplements	
Pediakid D3 ®	55 (5.7 %)
ErgyD ®	23 (2.4 %)
Alvityl 2,5 µg/5 mL ®	10 (1.0 %)
Pediakid gums D3 ®	2 (0.2 %)
Alvityl 5 µg tablet ®	2 (0.2 %)
Pediakid 22 vitamins ®	1 (0.1 %)

compared with rural areas. A quarter of general practitioners worked in rural areas, in comparison to only 5 % of paediatricians.

The number of children seen per week varied widely by type of practice (Fig. 1**C**). The number of children seen per week by paediatricians in private practice was significantly higher than that seen by hospital paediatricians, general practitioners and maternal and child health professionals. In fact, 79 % of paediatricians in private practice saw >50 children per week, compared to <50 children per week for 93 %, 90 % and 95 % of hospital paediatricians, general practitioners and maternal and child health professionals, respectively.

3.2. Vitamin D supplementation

Although there was no statistical difference in the responses between paediatricians and general practitioners, significant differences were found according to professional practice.

Vitamin D supplementation was almost systematically prescribed in all age groups, regardless of the professional practice (Fig. 2**A**). It is noteworthy that 5–11 % of hospital paediatricians reported that they did not usually prescribe vitamin D.

With regard to frequency of administration, vitamin D supplementation was most commonly given daily up to 2 years of age (97 % of all respondents) and every 3 months in older children (year-round in 38 % and winter/spring only in 40 %) (Fig. 2**B**).

The most commonly prescribed forms of vitamin D supplementation were Zyma-D 10,000 IU/mL ® (88.2 %) and Adrigyl 10,000 IU/mL ® (57.3 %) as a drinkable suspension, and Uvedose 100,000 IU ® (55.7 %) and Zyma-D 50,000 IU ® (52,8 %) as a loading dose (Table 1). Despite the lack of recommendation for use in children, 5 % of respondents indicated that they had prescribed loading doses of 200,000 units of vitamin D, with 77 % of paediatricians reporting this practice. Furthermore, 10 % of respondents regularly prescribed non-drug forms of vitamin D, such as nutritional supplements (Pediakid® and ErgyD®), despite the recent pharmacovigilance alert [21]. Seventy percent of respondents did not consider the presence or absence of excipients in the different forms of vitamin D when choosing a prescription.

Among the risk factors for vitamin D deficiency, low sun exposure and dark skin were most commonly reported by respondents (75 % and 74 %, respectively), followed by vegan diet (53 %) and obesity (40 %) (Fig. 2**C**). These risk factors were less commonly reported by maternal and child health professionals. The majority of respondents (70 %) indicated that they had adjusted the dose of vitamin D in children with risk factors. This was most commonly done by increasing the dose in infants and by increasing the frequency in older children. However, half of respondents (52 %) did not change the vitamin D dose for children with dark skin. In line with the new recommendations, three-quarters of respondents (76 %) did not change vitamin D supplementation in children who were exclusively breastfed.

Half of the respondents (49 %) assessed serum vitamin D levels in the presence of risk factors. However, there were significant variations according to medical practice: 67 % of hospital paediatricians, 41 % of private paediatricians, 20 % of private general practitioners and 30 % of maternal and child health practitioners.

3.3. Calcium nutritional intakes

Most of the respondents (78 %) recommend consuming at least 3 dairy products per day. Despite the fact that 61 % of respondents reported that they assess calcium intakes when following up children (Fig. 3**A**), only 10 % of them regularly use specific questionnaires or calcium equivalence tables (Fig. 3**B**).

Almost three-quarters of respondents (73 %) stated that calcium-rich vegetables cannot replace dairy products. Conversely, three-quarters (71 %) were unaware that calcium-rich mineral water could be an adequate substitute to dairy products. Additionally, respondents were queried regarding the suitability of various products as substitutes for milk in order to ensure adequate calcium intake in children (Fig. 3**C**). While approximately half (52 %) of respondents were aware that cooked cheese (*e.g.* "gruyere") could be used as a substitute for milk, only 10 % were aware that calcium-rich mineral water (*e.g.* Contrex®) could also serve as a substitute for milk.

4. Discussion

This survey was the first to assess real-life practices following the new 2022 guidelines for vitamin D supplementation in the French paediatric population.

It is notable that the observed differences are more related to the type of practice than to the specialty. It is important to highlight that some recommendations appear to be applied with great efficacy by doctors who care for children. It is notable that the recommendation to supplement children from birth to the end of peak pubertal growth is followed by the majority of respondents (over 90 % of respondents). This is an important point, as in the previous 2012 guidelines, there was no specific recommendation for children aged 5–10 years [19]. However, it should be noted that the rate of vitamin D prescription is slightly lower among hospital paediatricians for all age groups. One hypothesis could be that hospital paediatricians are most likely to provide subspecialist consultations. They may not feel responsible for prescribing vitamin D, as this is most often done by the child's doctor (paediatrician or general practitioner). Similarly, daily supplements for children under 2 years of age are used by almost all respondents (97 %), regardless of their specialty or type of practice. After the age of two, prescriptions for vitamin D every three months appear to be the norm, likely to improve compliance. This aligns with the information leaflets distributed by the OSCAR rare disease health network and the 2022 guidelines [4].

With regard to the type of vitamin D prescribed, it is noteworthy that 10 % of respondents indicated the use of unlicensed food supplements, while 5 % of respondents prescribed loading doses of 200,000 units of vitamin D, which is contrary to recommendations. Indeed, there are considerable variations between the measured and declared vitamin D content in these supplements, which could potentially lead to the risk of vitamin D intoxication [22]. In France, an alert from the French Drug Agency (ANSM) in 2023 reported the occurrence of vitamin D intoxication (revealed by severe hypercalcemia associated with cardiac repolarisation disorder and nephrocalcinosis) in neonates receiving unlicensed food supplements. An English study demonstrated that unlicensed food supplements accounted for 40 % of vitamin D prescriptions in primary care in England in 2018 [23]. In this study, the mean (±SD) vitamin D content of the 11 food supplements tested ranged from 41.2 ± 10.6 % to 165.3 ± 17.8 % of the labelled claim, with eight

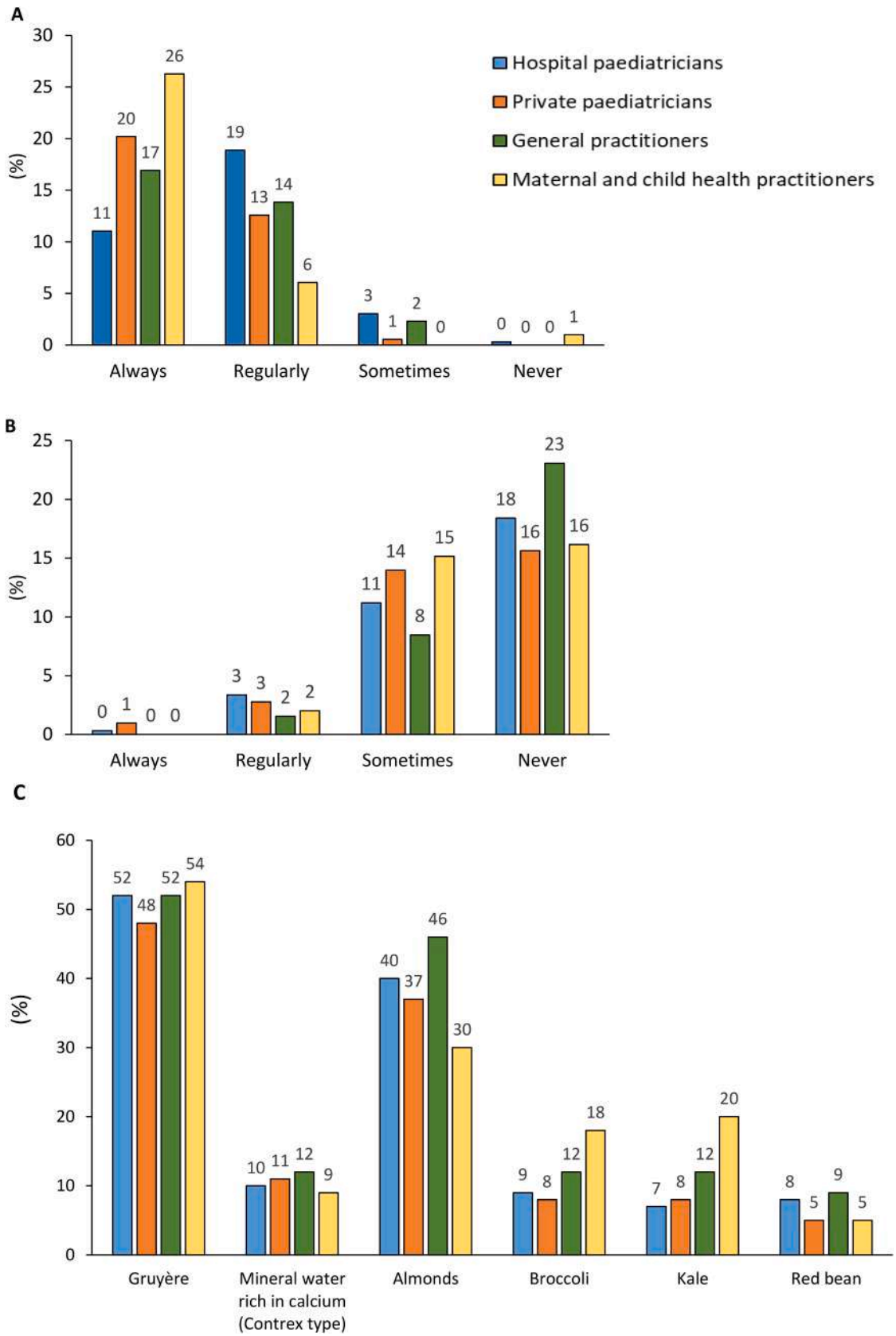

Fig. 3. Calcium intake. A. Assessment of calcium intake during follow-up of the child. B. Use of specific questionnaires or calcium equivalence tables. C. Knowledge of milk substitutes.

of the preparations not meeting the food supplement specification (80–150 % of the labelled claim). In contrast, the two licensed preparations exhibited vitamin D contents of 90.9 ± 0.7 % and 90.5 ± 3.9 % of the labelled amount, respectively, which met the British Pharmacopeia specification for licensed medicines (90–125 % of the labelled amount).

There was some variation in the respondents' knowledge of risk factors for vitamin D deficiency. In line with recent guidelines [4], three-quarters of respondents reported prescribing the same dose of vitamin D for infants, regardless of whether they were breastfed or formula-fed. This recommendation is justified by the study by Rosendhal et al., which demonstrated that a daily supplement of 400 IU was sufficient to ensure adequate vitamin D intake in children under 2 years of age, regardless of diet [24]. Similarly, three-quarters of respondents were aware of low sun exposure and dark skin as risk factors. However, despite this, only 50 % of respondents increased the dosage prescribed for dark-skinned children. Reduced exposure to sunlight, which is essential for the synthesis of vitamin D in the skin, is a major factor in vitamin D deficiency, particularly in children living in high-latitude countries. Indeed, in these countries, the oblique zenith angle of the sun and the wearing of covering clothing, especially in winter, interfere with the synthesis of vitamin D in the skin [25]. Among other risk factors, obesity and veganism are less well-known risk factors for vitamin D deficiency (40 % and 53 % of positive responses respectively). Several studies have shown that vitamin D levels are lower in obese children than in children of normal weight [26]. Moreover, higher doses of vitamin D are required to achieve satisfactory vitamin D levels in this population [27–29]. Given the high prevalence of obesity worldwide, particularly in children (around 5 % in France) [30], it is important to make physicians aware of the importance of vitamin D supplementation in this at-risk population. In contrast, certain restrictive diets, which are currently widespread such as vegan diets, can also lead to vitamin D deficiency. As dietary vitamin D is derived almost exclusively from oily fish and fortified dairy products, individuals on a vegan diet that excludes all animal products are at high risk of calcium and vitamin D deficiency and nutritional rickets [31]. Diseases associated with deficient intake or malabsorption of calcium and vitamin D (*i.e.* underweight, anorexia, malabsorption, chronic pathology) are also considered as risk situations by respondents. In this survey, half of the respondents assessed serum vitamin D levels in the presence of risk factors or chronic diseases, with significant discrepancies observed depending on the type of practice. For instance, 67 % of hospital paediatricians, 41 % of private paediatricians, 20 % of private general practitioners and 30 % of maternal and child health practitioners conducted such assessments. As anticipated, the high frequency of prescribing by hospital paediatricians is likely attributable to their role in monitoring children with chronic diseases.

With regards to calcium intake, although two-thirds (61 %) of respondents reported that they assess calcium intakes when following up children, only 10 % of them regularly use specific questionnaires or calcium equivalence tables. Furthermore, the calcium content of foods and its bioavailability appear to be poorly known by health professionals. Consequently, a significant proportion of respondents (71 %) were unaware that calcium-rich mineral water could be employed as a substitute for dairy products, at least in terms of calcium absorption. With regard to calcium intake, it is crucial to consider not only the calcium content of foods but also their bioavailability, particularly the efficiency of calcium absorption. Although certain vegetables contain calcium at levels comparable to or even higher than those found in dairy products, their absorption is significantly lower (approximately seven times less than that of dairy products). Consequently, these vegetables cannot provide an adequate calcium intake. Therefore, equivalence tables must be consulted [4], and a calcium supplement must be prescribed in cases of vegan diets.

Regarding the strengths and weaknesses of this study, it is important to emphasise that this is the first and only survey conducted one year after the update of the guidelines on vitamin D supplementation in children in France. Moreover, this survey includes responses from approximately a thousand doctors who care for children, with a good distribution between doctors working in hospitals and those working in private practice (49 *vs*. 47 % respectively) and between general and specialised paediatricians (43 *vs* 57 % respectively). However, it is important to highlight a number of significant biases. Firstly, although there was no difference in responses between these two groups, general practitioners were under-represented compared with paediatricians (13 % *vs* 87 %). In contrast, 85 % of children are followed by general practitioners in France [32]. The majority of doctors practise in urban and suburban areas (92 %), with a very low representation of doctors practising in rural areas. Finally, there may be a bias in the selection of participants due to the fact that the questionnaire was sent out by scientific societies. Doctors who responded were therefore likely to be better informed than those who did not belong to a learned society.

5. Conclusion

Overall, this survey shows that paediatricians and general practitioners are following the new recommendations for vitamin D supplementation in children. The identification by this survey of knowledge gaps (*i.e.* certain risk factors, contraindications to dietary supplements and lack of knowledge of the calcium equivalence of foods) will enable the implementation of targeted information campaigns.

Supplementary File S1: Thirty-three questions clinical practice questionnaire

Declaration of competing interest

The authors declare no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.arcped.2024.09.006.

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