

# THE EFFECTS OF VITAMIN D LEVELS AND SUPPLEMENTATION ON ORAL HEALTH - REVIEW

Wpływ stężenia witaminy D i jej suplementacji na stan zdrowia jamy ustnej – przegląd literatury



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#### **Abstract**

Introduction: Vitamin D plays a crucial role in many biological processes, such as regulating calcium-phosphate metabolism, enhancing immune response, and stimulating the mineralization of hard tissues. Vitamin D deficiency affects up to 30% of children in developed countries, especially during the autumn-winter period. In the context of dentistry, reduced vitamin D levels are associated with increased caries activity, including severe early childhood caries. Materials and methods: A literature review was conducted using the PubMed database. The analysed studies assessed diverse populations in terms of age, geographical location, and socioeconomic status. Results: The optimal level of vitamin D is considered to be at least 75 nmol/L. Vitamin D deficiency is associated with various systemic diseases, including dental caries. Children with severe early childhood caries have lower levels of vitamin D, which increases their susceptibility to caries. Adequate vitamin D levels promote enamel mineralization, increase salivary flow, and salivary calcium content, which protect against cariogenic microorganisms. There is also evidence linking maternal vitamin D levels and the risk of caries in their children. Conclusions: Vitamin D plays a crucial role in the prevention and treatment of dental caries, especially in children. Promoting vitamin D supplementation, according to Polish guidelines, can significantly reduce the risk of caries. Research on genetic polymorphisms opens new perspectives for the individualization of caries prevention strategies. Monitoring vitamin D levels in expectant mothers can also contribute to reducing the risk of caries in their offspring. Further research is needed to better understand the mechanisms of vitamin D impact on oral health and to develop detailed recommendations for supplementation.

## Streszczenie

Wstep: Witamina D odgrywa główną role w wielu procesach biologicznych, w tym w regulacji gospodarki wapniowofosforanowej, wzmacnianiu odpowiedzi immunologicznej i stymulacji mineralizacji tkanek twardych. Niedobór witaminy D dotyczy nawet 30% dzieci w krajach rozwiniętych i występuje zwłaszcza w okresie jesienno-zimowym. Obniżone stężenie witaminy D jest powiązane m.in. ze zwiększoną aktywnością próchnicy, w tym ciężką postacią próchnicy wczesnego dzieciństwa. Materiały i metody: Przegląd literatury przeprowadzono z wykorzystaniem bazy danych PubMed. Analizowane prace obejmowały badania różnych pod względem wieku, szerokości geograficznej i statusu socjoekonomicznego grup. Wyniki: Za optymalne steżenie witaminy D uznaje się co najmniej 75 nmol/l. Jej niedobory są powiązane z wieloma schorzeniami ogólnoustrojowymi, w tym z próchnicą zębów. U dzieci z próchnicą wczesnego dzieciństwa obserwuje się niższe stężenie witaminy D, co zwiększa ich podatność na próchnice. Odpowiednie stężenie witaminy D wpływa korzystnie na mineralizacje szkliwa oraz zwieksza wydzielanie śliny i zawartość wapnia, co chroni przed działaniem kariogennych mikroorganizmów. Istnieją również dowody na wpływ stężenia witaminy D u matek na ryzyko wystąpienia próchnicy u ich dzieci. Wnioski: Witamina D odgrywa kluczową role w prewencji i leczeniu próchnicy zębów, zwłaszcza u dzieci. Promowanie suplementacji witaminy D, zgodnie z polskimi wytycznymi, może znacząco zmniejszyć ryzyko wystąpienia tej choroby. Badania nad polimorfizmami genowymi otwierają nowe perspektywy dla indywidualizacji profilaktyki próchnicy. Monitorowanie stężenia witaminy D u przyszłych matek może również przyczynić się do zmniejszenia ryzyka rozwoju próchnicy u ich potomstwa. Konieczne są dalsze badania, aby lepiej zrozumieć mechanizmy wpływu witaminy D na zdrowie jamy ustnej i opracować szczegółowe rekomendacje dotyczące suplementacji.

Keywords: dental caries; vitamin D; calcitriol; supplementation; early childhood caries

Słowa kluczowe: próchnica zębów; witamina D; kalcytriol; suplementacja; próchnica wczesnego dzieciństwa

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# Introduction

It is estimated that vitamin D deficiency may affect up to 30% of children in developed countries (depending on the definition), especially during the autumn/winter period [1]. 25OHD (25-hydroxycholecalciferol) is the main circulating vitamin D metabolite [2], whose serum level is the best indicator of vitamin D deficiency [3]. In the kidneys, it undergoes hydroxylation to the active form of vitamin D, i.e. 1,25-dihydroxycholecalciferol (calcitriol) [3]. Vitamin D receptors are expressed across many tissues, which translates into a wide variety of functions of this compound [1].

Known properties of vitamin D include enhancing the antimicrobial response of the body [4], regulating calcium-phosphate metabolism by increasing calcium uptake in the small bowel [5], protecting against autoimmune disorders and even malignancies through antiproliferative properties [6], and stimulating mineralisation of hard tissues [5]. It has been shown that calcitriol deficiency can lead, among other things, to cardiovascular, respiratory and nervous system disorders.

Many studies indicate a link between reduced vitamin D levels in children and increased activity of dental caries [1,2,4], including severe early childhood caries (SECC) [4], defined as any sign of smooth-surface caries in a child younger than three years of age [4]. SECC is estimated to affect up to 621 million children worldwide, ranging from 11.7% in the UK to 41.1% in Poland, and up to 46.8% in the US [4].

The aim of this study was to explore and discuss the problem and to shed a broader light on the abundant evidence linking tooth decay with reduced vitamin D levels in order to raise awareness among dentists and the public.

### Materials and methods

The data presented were obtained from the PubMed database. The cited papers discuss studies conducted in different countries on several continents in populations that varied in terms of age, latitude inhabited and socioeconomic status.

### **Results**

The impact of vitamin D on the human body

A vitamin D level of  $\geq$ 75 nmol/L is most often considered optimal [2, 5, 7,]. Some authors propose a broader classification, distinguishing insufficiency (50–74.9 nmol/L), deficiency (25–49.9 nmol/L) and severe deficiency ( $\geq$ 5 nmol/L) in addition to normal levels ( $\geq$ 75 nmol/L) [8]. Vitamin D deficiency is also classified as low ( $\leq$ 50 nmol/L),

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moderate (<25 nmol/L) and severe (<12.5 nmol/L), with the latter two groups considered by the authors to be the cause of rickets, osteoporosis and osteomalacia [9]. Up to one billion people, both children and adults, have vitamin D deficiency defined as <25 nmol/L [10]. The terminology and classification of vitamin D deficiency is presented in table 1 [7].

# Vitamin D deficiency and oral health

In addition to systemic conditions, many papers point out that vitamin D deficiency is highly related to dental caries [1–4].

Early childhood caries (ECC), defined as presence of one or more decayed (non-cavitated or cavitated lesions). missing (due to caries) or filled tooth surfaces in any primary tooth in a child 71 months of age or younger, has been particularly linked to vitamin D deficiency [11]. Severe early childhood caries (SECC) is defined as any sign of smooth-surface caries in a child younger than three years of age [4]. Children with SECC have lower vitamin D levels [2, 8, 12] and are twice as likely to have vitamin D values <75 nmol/L [2]. Statistically, caries-free children are twice as likely to have normal calcidiol levels, whereas children with SECC are three times more likely to present with levels <35 nmol/L. Increased salivary flow and high salivary calcium content [2], as well as increased mineralisation of enamel and dentin, protection against hypoplasia and hypomineralisation leading to reduced teeth susceptibility to cariogenic microorganisms, are known mechanisms of action of vitamin D [5, 13]. Additionally, adequate vitamin D levels have a positive impact on salivary cathelicidin LL-37 [14]. Cathelicidin LL-37 is an antimicrobial peptide composed of 37 amino acids, produced via proteolytic degradation of the extracellular domain of hCAP-18, a protein expressed in epithelial cells and neutrophils [14], which shows activity against S. mutans [4]. Furthermore, calcitriol increases the intestinal uptake of calcium (by 40%) and phosphate (by up to 80%) [15]. It was also shown that ECC children are more likely to develop malnutrition and anaemia [15]. while SECC children have higher parathyroid hormone levels and lower serum calcium levels [12].

**Table 1.** Classification of vitamin D deficiency [7]

Plasma vitamin D level [nmol/L]	Grade
<25	Severe deficiency
25-50	Moderate deficiency
50-75	Sufficient level
75-200	Normal level

There also appears to be a link between maternal prenatal vitamin D levels and the risk of caries in the child [16–19]. Mineralisation of deciduous and permanent enamel occurs at 4 months gestation and after birth, respectively [16]. Alaskan researchers, Singleton et al. [17], demonstrated a 40% increase in DMFT (number of decayed, missing or filled teeth) in 12-35-month-old children whose mothers had low vitamin D levels at 36 weeks gestation compared to children whose mothers had normal vitamin D levels. Beckett et al. [16] found an increased risk of caries in 6-vear-old children whose mothers had vitamin D levels at third trimester of <50 nmol/L. Additionally, based on dental reviews of 1210 mother-child pairs, Tanaka et al. [20] found a negative correlation between the incidence of caries in the child and maternal intake of vitamin D. There is also evidence of an association between maternal calcidiol levels in the second trimester and the incidence of molar incisor hypomineralisation (MIH) in the child at the age of 7-9 years [18]. Lower vitamin D levels were also observed in mothers of children with deciduous molar hypomineralisation (DMH), diagnosed by digital microscopy [19]. Furthermore, it was shown that high-dose vitamin D supplementation in pregnancy can reduce the child's risk of enamel defects, such as opacity and chipping, by up to 50% [21].

A reference should be also made to studies that do not confirm the correlation between calcidiol levels and the risk of ECC [21-23], but indicate a relationship between salivary and serum levels of vitamin D [22], as well as papers presenting inconclusive results and suggesting the need for further research [24]. There have also been reports that negate the association with maternal vitamin D levels, while confirming that there is a twofold decrease in DMF in children with normal calcidiol levels compared to those with deficiency [25].

The impact of geographical latitude on vitamin D levels and the need for supplementation

Inhabitants of regions above the 37th parallel (including Poland), where the efficiency of endogenous vitamin D synthesis decreases between November and February due to lower UVB exposure, are at risk of vitamin D deficiency, and therefore the importance of vitamin D supplementation throughout the year is emphasised in this group [26]. Kuciński et al. [26] developed guidelines for vitamin D supplementation in the Polish population at different life stages. They suggested vitamin D supplementation at a dose of 400 IU per day from birth to 6 months of age, and then at 600 IU per day to 12 months of age. The dose is 600 IU per day for children from

1 to 3 years of age and 600–1000 IU per day from 4 to 10 years. Sunlight exposure for 30–45 minutes per day between 10 a.m. and 3 p.m., between the beginning of May and the end of September, is also recommended in this age group. Adolescents and adults up to 65 years of age should receive a daily dose of 1000 to 2000 IU, with sunlight exposure for 15–30 minutes. Individuals up to 75 years of age are recommended to continue the same dose throughout the year without additional exposure to sunlight. Due to their reduced ability to synthesise cholecalciferol in the skin, seniors >75 years of age should supplement vitamin D at a daily dose of 2000-4000 IU throughout the year. It is suggested that cholecalciferol be first choice, with calcifediol used as the second choice [26] (tab. 2).

As pointed out by Sobiech et al. [2], vitamin D supplementation during the autumn-winter period in Poland is associated with a twofold reduction in the risk of caries exacerbation in children ≥12 years of age. Hujoel et al. [27] have shown that supplementation reduced the risk of caries in children by 47%, but that this effect was no longer evident after the age of 13 years, especially in girls, which the authors explain by an increase in body fat. In their study in a population of 10-year-olds in Germany, Kühnisch et al. [28] showed a twofold decrease in the incidence of dental caries in children supplemented with vitamin D in their first year of life. However, these preparations were less effective than fluoride-containing supplements (OR = 2.08 for vitamin D and 2.47 for fluoride).

Obviously, dental caries is not the only problem against which vitamin D offers potential protection [10, 13]. Daily supplementation continued for 3 years can reduce the risk of tooth loss due to periodontitis by 60% [29]. As shown by Zhan et al. [23] in their study conducted among 1904 Germans over a 5-year period, a 10  $\mu$ g/L increase in calcidiol reduced the risk of tooth loss by 13%. However, this issue remains open as not all studies have confirmed such a relationship [30].

# Vitamin D and genetic predispositions

The influence of genetic factors on the action of vitamin D in the body is an interesting aspect. Gene polymorphisms are defined as variants of a given gene occurring in the population with a frequency greater than 1%, which distinguishes them from genetic mutations [31]. Rapid advances in knowledge and technology have allowed scientists to identify a clear link between active caries and the T allele of rs2228570 (Fokl) polymorphism related to one of the nucleotides that make up the vitamin D receptor

Table 2. Vitamin D supplementation guidelines by Kuciński et al. [26]

Population	Recommended vitamin D supplementation (IU/day)
Newborns and infants up to 6 months of age	400
Infants 6–12 months of age	400-600
Children 4–10 years of age	600-1000
Adolescents	1000-2000
Adults 19–65 years of age and younger seniors 66–75 years of age	1000-2000
Seniors >75 years of age	2000-4000

gene. In contrast, subjects with the C allele were more likely to be caries-free [31, 32]. However, this issue is not clear as Cogulu et al. [33] obtained a statistically significant correlation only for the Taql polymorphism, while they found no significant difference in the prevalence of Apal, Fokl and Cdx2 polymorphisms between cariesand caries-free population. Izakovicova Holla et al. [34], on the other hand, showed no link between caries and Taql polymorphisms, but observed a significant correlation between Taql and gingivitis.

#### Discussion

The research presented here indicates an indisputable role of vitamin D in the prevention and treatment of dental caries, including SECC. Findings on the relationship between vitamin D deficiency and increased dental caries highlight the importance of vitamin D levels for oral health. The cited research indicates that SECC children have lower vitamin D levels compared to their caries-free peers, suggesting that adequate vitamin D levels may protect against the development of this disorder [1, 2, 4].

It is also worth mentioning about the mechanisms by which vitamin D exerts its beneficial effects on oral health. These include increasing salivary flow and salivary calcium content, which promotes enamel and dentin mineralisation. Additionally, by improving gastrointestinal uptake of calcium and phosphate, calcitriol reinforces tooth structure and contributes to better protection against cariogenic bacteria [2, 8, 13–15].

Also of interest is the evidence for the association between maternal prenatal vitamin D levels and the risk of caries in the child. Research highlights the importance of adequate vitamin D levels from the earliest stages of life, pointing to the possibility of preventing dental disease through dietary interventions and supplementation in pregnancy [16–19].

Despite this considerable evidence, there are also studies that do not support the direct relationship between vitamin D levels and the risk of ECC [21, 22, 32]. This indicates the complexity of dental caries and the need for further research to better understand the role of vitamin D in the prevention of this disease.

When discussing supplementation guidelines, it is important to emphasise that adequate vitamin D intake is important not only for caries prevention, but also for overall health. Recommendations for supplementation, especially in regions with limited sunlight, are crucial to improve vitamin D status in the population, which may help reduce the incidence of caries, especially among children [26].

Research on gene polymorphisms affecting calcitriol activity in the body is also important. These findings open up new perspectives for the individualisation of preventive and therapeutic approaches to dental caries, based on the genetic predisposition of patients [31, 32].

The analysis of the cited studies indicates that further research is needed to better understand the impact of vitamin D on oral health, so that specific recommendations for

its supplementation can be made. Although maintaining optimal vitamin D levels can significantly contribute to oral health and caries prevention, individual needs and genetic differences in the population need to be considered.

#### Conclusions

In conclusion, vitamin D plays an important role in the prevention of caries, including severe early childhood caries. The association between low vitamin D levels and increased caries activity indicates the need to promote vitamin D supplementation as an effective form of prophylaxis. Polish guidelines on vitamin D supplementation emphasise its important role at different stages of life, which may be crucial in reducing the risk of caries.

Additionally, research on gene polymorphisms indicates that an individualised approach to caries prevention taking into account the genetic determinants of the body's response to vitamin D may be possible. It is likely that such an approach will increase the efficacy of caries prevention, particularly in individuals with specific genetic factors.

Attention has also been drawn to the importance of monitoring vitamin D levels in expectant mothers, which can reduce the risk of their offspring developing caries, pointing to the importance of maintaining adequate levels of this vitamin already from the prenatal period.

#### References

- Cetrelli L, Bletsa A, Lundestad A, et al. Vitamin D, oral health, and disease characteristics in juvenile idiopathic arthritis: a multicenter cross-sectional study. BMC Oral Health. 2022: 22: 333. doi: 10.1186/s12903-022-02349-1
- Sobiech P, Olczak-Kowalczyk D, Hosey MT, et al. Vitamin D supplementation, characteristics of mastication, and parent-supervised toothbrushing as crucial factors in the prevention of caries in 12- to 36-month-old children. Nutrients, 2022; 14: 4358. doi: 10.3390/nu14204358
- 3. Pfotenhauer KM, Shubrook JH. Vitamin D deficiency, its role in health and disease, and current supplementation recommendations. J Am Osteopath Assoc, 2017; 117: 301–305. doi: 10.7556/jaoa.2017.055
- 4. White JH. Emerging roles of vitamin D-induced antimicrobial peptides in antiviral innate immunity. Nutrients, 2022; 14: 284. doi: 10.3390/nu14020284
- Herzog K, Scott JM, Hujoel P, et al. Association of vitamin D and dental caries in children: findings from the National Health and Nutrition Examination Survey, 2005–2006.
  J Am Dent Assoc, 2016; 147: 413–420. doi: 10.1016/j. adaj.2015.12.013
- Ślebioda Z, Szponar E, Dorocka-Bobkowska B. Vitamin D and its relevance in the etiopathogenesis of oral cavity diseases. Arch Immunol Ther Exp (Warsz) 2016; 64: 385–397. doi: 10.1007/s00005-016-0384-z
- 7. Navarro CLA, Grgic O, Trajanoska K, et al. Associations between prenatal, perinatal, and early childhood vitamin D status and risk of dental caries at 6 years. J Nutr, 2021; 151: 1993–2000. doi: 10.1093/jn/nxab075
- 8. Zhou F, Zhou Y, Shi J. The association between serum 25-hydroxyvitamin D levels and dental caries in US adults. Oral Dis, 2020; 26: 1537–1547. doi: 10.1111/odi.13360

- Davit-Béal T, Gabay J, Antoniolli P, et al. Dental complications of rickets in early childhood: case report on 2 young girls. Pediatrics, 2014; 133: e1077-e1081. doi: 10.1542/ peds.2013-0733
- Holick MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord, 2017; 18:153–165. doi: 10.1007/s11154-017-9424-1
- Folayan M, Olatubosun S. Early childhood caries a diagnostic enigma. Eur J Paediatr Dent, 2018; 19: 88. doi: 10.23804/ejpd.2018.19.02.00
- 12. Williams TL, Boyle J, Mittermuller BA, et al. Association between Vitamin D and dental caries in a sample of Canadian and American preschool-aged children. Nutrients, 2021; 13: 4465. doi: 10.3390/nu13124465
- 13. Botelho J, Machado V, Proença L, et al. Vitamin D deficiency and oral health: a comprehensive review. Nutrients, 2020; 12: 1471. doi: 10.3390/nu12051471
- 14. Gyll J, Ridell K, Öhlund I, et al. Vitamin D status and dental caries in healthy Swedish children. Nutr J 2018; 17: 11. doi: 10.1186/s12937-018-0318-1
- 15. Almoudi MM, Hussein AS, Abu Hassan MI, et al. Dental caries and vitamin D status in children in Asia. Pediatr Int, 2019; 61: 327–338. doi: 10.1111/ped.13801
- 16. Beckett DM, Broadbent JM, Loch C, et al. Dental consequences of vitamin D Deficiency during pregnancy and early infancy an observational study. Int J Environ Res Public Health, 2022; 19: 1932. doi: 10.3390/ijerph19041932
- 17. Singleton RJ, Day GM, Thomas TK, et al. Impact of a prenatal vitamin D supplementation program on vitamin D deficiency, rickets and early childhood caries in an Alaska Native population. Nutrients, 2022; 14: 3935. doi: 10.3390/nu14193935
- 18. Børsting T, Schuller A, van Dommelen P, et al. Maternal vitamin D status in pregnancy and molar incisor hypomineralisation and hypomineralised second primary molars in the offspring at 7–9 years of age: a longitudinal study. Eur Arch Paediatr Dent, 2022; 23: 557–566. doi: 10.1007/s40368-022-00712-y
- 19. Reed SG, Voronca D, Wingate JS, et al. Prenatal vitamin D and enamel hypoplasia in human primary maxillary central incisors: a pilot study. Pediatr Dent J, 2017; 27: 21–28. doi: 10.1016/j.pdj.2016.08.001
- 20. Tanaka K, Hitsumoto S, Miyake Y, et al. Higher vitamin D intake during pregnancy is associated with reduced risk of dental caries in young Japanese children. Ann Epidemiol, 2015; 25: 620–625. doi: 10.1016/j.annepidem.2015.03.020
- 21. Nørrisgaard PE, Haubek D, Kühnisch J, et al. Association of high-dose vitamin D supplementation during pregnancy with the risk of enamel defects in offspring: a 6-year follow-up of a randomized clinical trial. JAMA Pediatr, 2019; 173: 924–930. doi: 10.1001/jamapediatrics.2019.2545

- 22. Hussein AS, Almoudi MM, Abu-Hassan MI, et al. Serum and saliva 25(OH)D levels in relation to dental caries in young children. J Clin Pediatr Dent, 2021; 45: 414–420. doi: 10.17796/1053-4625-45.6.8
- 23. Zhan Y, Samietz S, Holtfreter B, et al. Prospective study of serum 25-hydroxy vitamin D and tooth loss. J Dent Res, 2014; 93: 639–644. doi: 10.1177/0022034514534985
- 24. Rogalnikovaite K, Bendoraitiene E, Andruskeviciene V. Associations of prenatal vitamin D status with oral health in offspring: a systematic review. Oral Health Prev Dent, 2022; 20: 393–400. doi: 10.3290/j.ohpd.b3505831
- 25. Singleton R, Day G, Thomas T, et al. Association of maternal vitamin D deficiency with early childhood caries. J Dent Res, 2019; 98: 549–555. doi: 10.1177/0022034519834518
- Kuciński J, Fryska Z, Wołejko A, et al. Aktualne zalecenia w Polsce dotyczące suplementacji witaminy D. Med Og Nauk Zdr, 2023; 29: 277–282. doi: 10.26444/monz/176079
- 27. Hujoel PP. Vitamin D and dental caries in controlled clinical trials: systematic review and meta-analysis. Nutr Rev, 2013; 71: 88–97. doi: 10.1111/j.1753-4887.2012.00544.x
- 28. Kühnisch J, Thiering E, Heinrich-Weltzien R, et al. Fluoride/vitamin D tablet supplementation in infants-effects on dental health after 10 years. Clin Oral Investig, 2017; 21: 2283–2290. doi: 10.1007/s00784-016-2021-y
- 29. Uwitonze AM, Rahman S, Ojeh N, et al. Oral manifestations of magnesium and vitamin D inadequacy. J Steroid Biochem Mol Biol, 2020; 200: 105636. doi: 10.1016/j. jsbmb.2020.105636
- Pavlesen S, Mai X, Wactawski-Wende J, et al. vitamin D status and tooth loss in postmenopausal females: The Buffalo Osteoporosis and Periodontal Disease (OsteoPerio) Study. J Periodontol, 2016; 87: 852–863. doi: 10.1902/jop.2016.150733
- 31. Nireeksha N, Hegde MN, Shetty SS, et al. FOK I vitamin D receptor gene polymorphism and risk of dental caries: a case-control study. Int J Dent, 2022; 2022: 6601566. doi: 10.1155/2022/6601566
- 32. Qin X, Shao L, Zhang L, et al. Investigation of interaction between vitamin D receptor gene polymorphisms and environmental factors in early childhood caries in Chinese children. Biomed Res Int, 2019; 2019: 4315839. doi: 10.1155/2019/4315839.
- Cogulu D, Onay H, Ozdemir Y, et al. The role of vitamin D receptor polymorphisms on dental caries. J Clin Pediatr Dent, 2016; 40: 211–214. doi: 10.17796/1053-4628-40.3.211
- 34. Izakovicova Holla L, Borilova Linhartova P, Kastovsky J, et al. Vitamin D receptor Taql gene polymorphism and dental caries in Czech children. Caries Res, 2017; 51: 7–11. doi: 10.1159/000452635