



International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE VITAMIN D3 DEFICIENCY AND THE EFFECTIVENESS OF SUBLINGUAL SUPPLEMENTATION – A REVIEW OF CLINICAL STUDIES

DOI [https://doi.org/10.31435/ijitss.4\(48\).2025.4215](https://doi.org/10.31435/ijitss.4(48).2025.4215)

RECEIVED 19 October 2025

ACCEPTED 14 December 2025

PUBLISHED 20 December 2025



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VITAMIN D3 DEFICIENCY AND THE EFFECTIVENESS OF SUBLINGUAL SUPPLEMENTATION – A REVIEW OF CLINICAL STUDIES

Illia Koval (Corresponding Author, Email: illiakoval.pl@gmail.com)

Provincial Hospital in Poznań, Poznań, Poland

ORCID ID: 0009-0002-1109-6354

Wiktor Kubik

5th Military Clinical Hospital in Kraków, Kraków, Poland

ORCID ID: 0009-0000-4041-0846

Bartłomiej Czarnecki

Provincial Specialist Hospital No. 5 named after St. Barbara in Sosnowiec, Sosnowiec, Poland

ORCID ID: 0009-0006-8960-5760

Jan Nowak

Dr. Emil Warmiński Clinical Hospital of the Bydgoszcz University of Technology – Independent Public Health Care Facility, Bydgoszcz, Poland

ORCID ID: 0009-0006-8145-8647

Bartosz Zwoliński

Central Clinical Hospital of the Medical University of Warsaw, Warsaw, Poland

ORCID ID: 0009-0000-8675-3828

Kacper Sukiennicki

District Hospital in Chrzanów, Chrzanów, Poland

ORCID ID: 0009-0003-6864-4996

Wirginia Bertman

Stefan Żeromski Specialist Hospital, Kraków, Poland

ORCID ID: 0009-0002-9166-8681

Natalia Kołdej

District Hospital in Ilża, Ilża, Poland

ORCID ID: 0009-0004-3203-8019

Zuzanna Kępczyńska

St. Anne's Hospital in Piaseczno, Piaseczno, Poland

ORCID ID: 0009-0005-2360-854X

Katarzyna Szewczyk

L. Rydygier Specialist Hospital in Kraków, Kraków, Poland

ORCID ID: 0009-0008-7451-3091

Kamil Borysewicz

Municipal Specialist Hospital in Toruń, Toruń, Poland

ORCID ID: 0000-0003-4510-2759

Klaudia Romejko

Provincial Hospital in Poznań, Poznań, Poland

ORCID ID: 0009-0003-6452-1323

Barbara Kujawa

Provincial Hospital in Poznań, Poznań, Poland

ORCID ID: 0009-0000-3951-965X

ABSTRACT

Introduction and Aim: Vitamin D3 plays a crucial role in numerous metabolic processes, and its deficiency remains a global public health concern, particularly among children, the elderly, pregnant women, and individuals with obesity or chronic diseases. Limited sunlight exposure and inadequate dietary intake contribute to this deficiency. Traditional oral forms of supplementation (capsules, drops) may lead to variable absorption and reduced adherence, especially in populations with swallowing difficulties. The aim of this review was to assess the effectiveness of sublingual vitamin D3 supplementation compared with conventional oral formulations.

Materials and Methods: A review of randomized and controlled clinical trials published between 2015 and 2021 was conducted. Studies comparing sublingual (buccal) spray with oral capsules or drops in adults and children were analyzed for serum 25-hydroxyvitamin D [25(OH)D] levels, bioavailability, and patient acceptability.

Results: Clinical evidence indicates that sublingual vitamin D3 spray demonstrates comparable or greater efficacy in increasing serum 25(OH)D concentrations relative to oral capsules. In adults, sublingual administration provided faster absorption and improved bioavailability, especially in patients with intestinal malabsorption. In pediatric populations, sprays were equally effective as oral drops and showed higher acceptance due to ease of use. Improved compliance was observed across studies.

Conclusions: Sublingual vitamin D3 supplementation is an effective and well-tolerated alternative to traditional oral administration, particularly beneficial for individuals with absorption disorders or swallowing difficulties. Further research is needed to optimize dosage and duration in different risk groups.

KEYWORDS

Policy Development, School Management, Indiscipline, Leadership, Challenges and Strategies

CITATION

Illia Koval, Wiktor Kubik, Bartłomiej Czarnecki, Jan Nowak, Bartosz Zwoliński, Kacper Sukiennicki, Wirginia Bertman, Natalia Kołdej, Zuzanna Kępczyńska, Katarzyna Szewczyk, Kamil Borysewicz, Klaudia Romejko, Barbara Kujawa. (2025) Vitamin D3 Deficiency and the Effectiveness of Sublingual Supplementation – A Review of Clinical Studies. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4215

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Introduction

Vitamin D3 is a key fat-soluble compound involved in multiple metabolic reactions [1–7]. When consumed in recommended amounts, it exerts multidirectional effects on human physiology [2,4,6]. In addition to dietary sources, a substantial portion of vitamin D3 is synthesized in the skin through a non-enzymatic reaction triggered by UVB radiation acting on 7-dehydrocholesterol [3,5,6,8].

Despite the existence of natural regulatory mechanisms maintaining serum 25-hydroxycholecalciferol (25(OH)D) levels, vitamin D deficiency remains a significant public health issue [9–12]. Particularly vulnerable groups include children and the elderly [13,14], pregnant women [10,11,15], individuals with obesity [16–19], patients with infertility, musculoskeletal disorders, diabetes [20], lipid metabolism disorders, cardiovascular disease, autoimmune disorders, and liver disease.

The optimal serum level of vitamin D remains a matter of debate [7]. Some experts indicate that concentrations ≥ 75 nmol/L ensure sufficient vitamin D3 status, while others recommend >50 nmol/L [11,17]. Maintaining serum 25(OH)D above 50 nmol/L is generally considered optimal.

Due to the widespread prevalence of vitamin D3 deficiency, including in Poland's climate conditions, supplementation is recommended. Breastfed infants should receive 400 IU of vitamin D daily, while adults should take 400–800 IU daily throughout life [19,20]. Maintaining adequate vitamin D3 levels is particularly important during pregnancy and lactation.

The effectiveness of supplementation depends on the frequency of administration, route of delivery, bioavailability, intestinal absorption, and vitamin D metabolism [12]. In addition to traditional capsules, various supplement forms are available, such as gels, oral drops, soluble tablets, and the relatively new sublingual sprays.

Review of Clinical Studies

Randomized clinical trials in adults indicate that the sublingual form of vitamin D3 may be as effective or even more effective than traditional oral supplementation methods [12–16].

Satia et al. [12] conducted a randomized cross-over study involving 40 healthy adults and 20 patients with malabsorption syndrome. The study compared a sublingual spray (2×500 IU daily) with capsules (1000 IU daily) over 30 days. The results showed that the sublingual form was more effective in rapidly increasing plasma 25(OH)D levels, particularly among patients with intestinal absorption disorders, suggesting that bypassing part of the gastrointestinal tract may enhance vitamin D3 bioavailability.

Joshua J. Todd et al. [13] conducted a double-blind trial in 60 healthy adults who received either a sublingual spray or capsules (1000 IU daily) for four weeks. Both forms were equally effective in increasing serum 25(OH)D, but participants preferred the spray due to ease of use.

Williams et al. [15] performed a parallel-group randomized trial assessing high-dose supplementation (3000 IU daily for six weeks). Both spray and capsule forms significantly increased serum 25(OH)D levels. Participants reported greater satisfaction and convenience with the spray, which may play a crucial role in maintaining long-term adherence.

In children, short-term studies demonstrated comparable efficacy between sublingual sprays and oral drops in treating vitamin D3 deficiency [14,16]. The sublingual form is particularly advantageous in pediatrics due to easy dosing, higher acceptance, and suitability for children with swallowing difficulties. Absorption rates also depend on factors such as dark skin pigmentation, limited sunlight exposure, cultural or religious clothing practices, chronic diseases, obesity, malabsorption syndromes, and the use of certain medications (antiepileptics, glucocorticoids, antiretrovirals, antifungals) [18,19]. Obese individuals require higher doses of vitamin D3 to achieve adequate serum levels [18].

Penagini et al. [14] studied 50 children with neurological disorders, comparing a sublingual spray (800 IU) and oral drops (750 IU) over three months. Both groups achieved similar increases in serum 25(OH)D, but the spray was better accepted by children with swallowing difficulties.

Nalbantoglu et al. [16] examined children and adolescents aged 3–18 years, comparing the efficacy of spray and oral drops (2000 IU daily) over six weeks. Both forms showed comparable effectiveness in correcting vitamin D3 deficiency, with the spray being more convenient for pediatric use.

Table 1. Comparison of the effectiveness of different forms of vitamin D3 supplementation

Study	Study Type	Population	Form of Supplementation	Dose	Duration	Main Outcome
Satia et al., 2015 [12]	Randomized, cross-over	Healthy adults and malabsorption patients	Sublingual spray / capsule	2×500 IU spray / 1000 IU capsule	30 days	Spray superior in increasing 25(OH)D levels
Joshua J. Todd et al., 2019 [13]	Double-blind trial	Healthy adults	Spray / capsule	1000 IU	4 weeks	Both forms equally effective
Penagini et al., 2018 [14]	Randomized, placebo-controlled	Children with neurological disorders	Spray / oral drops	800 IU spray / 750 IU drops	3 months	Comparable efficacy in correcting deficiency
Williams et al., 2020 [15]	Randomized, parallel-group	Healthy adults	Spray / capsule	3000 IU	6 weeks	Both forms effective in raising 25(OH)D
Nalbantoglu et al., 2021 [16]	Randomized	Children and adolescents (3–18 years)	Spray / drops	2000 IU spray / 2000 IU drops	6 weeks	Comparable efficacy; better convenience with spray

Conclusions

The sublingual form of vitamin D3 represents an effective method for the prevention and treatment of vitamin D3 deficiency in both adults and children. The sublingual spray offers easy dosing, user convenience, and improved adherence—particularly valuable in pediatric populations and among individuals with swallowing difficulties. It also provides a valuable alternative for those unable to tolerate capsules or oral drops. Further research is warranted to determine the optimal dosage, duration, and efficacy of sublingual supplementation across different risk groups [12–16].

Disclosures

Author's contribution:

Illia Koval: Conceptualization; Investigation; Writing – Original Draft

Bartłomiej Czarnecki: Methodology; Formal Analysis; Project Administration

Jan Nowak: Methodology; Formal Analysis

Wiktor Kubik: Methodology; Formal Analysis

Bartosz Zwoliński: Software; Validation/Check; Data Curation

Kacper Sukiennicki: Resources; Writing – Original Draft

Virginia Bertman: Investigation; Writing – Review & Editing

Natalia Koldej: Investigation; Writing – Review & Editing

Klaudia Romejko: Investigation; Writing – Original Draft

Kamil Borysewicz: Data Curation; Writing – Original Draft

Zuzanna Kępczyńska: Data Curation; Supervision

Katarzyna Szewczyk: Validation/Check; Supervision

Barbara Kujawa: Project Administration

Supplementary Materials: They haven't been provided.

Funding Statement: This research received no funding

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflict of Interest: The authors declare no conflict of interest.

All authors have read and agreed with the published version of the manuscript.

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