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Role of vitamin D supplementation in the prevention of URTI (upper respiratory tract infections) among highly physically active individuals

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Abstract

Introduction: High-intensity physical exercise, characteristic of professional sports and military training, is associated with a significantly increased risk of upper respiratory tract infections (URTI). Such a phenomenon, described as the "J-curve", is explained by the post-exercise "open window" effect, which is effectively state of a transient immunosuppression. At the same time, vitamin D deficiency is particularly common among professional athletes, especially during winter at higher latitudes.

Methods: The aim of this narrative review was to assess the effectiveness of vitamin D interventions in the prevention of URTI based on randomized controlled trials and recent meta-analyses

Results: Despite a lack of evidence in general population meta-analyses for the effectiveness of vitamin D in preventing infections, some athlete-focused trials have confirmed measurable benefits in targeted high-risk groups. It is shown that a daily supply of vitamin D in athletes and recruits training in winter effectively corrects deficiencies, significantly shortens the duration and severity of URTI symptoms.

Conclusions: These observations suggest that maintaining adequate vitamin D status in athletes exposed to intense physical stress, particularly during winter months, may contribute to improved mucosal immune defence and reduced severity of URTI symptoms. Potential mechanisms may involve vitamin D receptor–mediated induction of antimicrobial peptides such as LL-37 and modulation of local inflammatory responses.

Key words: vitamin D, upper respiratory tract infections, immune system, professional sports, LL-37.

1. Introduction

In the demanding world of professional sports, as well as within rigorous tactical training environments, upper respiratory tract infections (URTI) are generally considered to be among the most common causes of training disruptions, prolonged absences, and a subsequent decrease in overall starting disposition and athletic performance [1]. Despite the widely acknowledged benefits associated with regular physical activity and its potentially beneficial influence on general immunity, this protective phenomenon appears to apply primarily to activities of moderate intensity. In the context of competitive sports, the correlation between cumulative training load and an individual's susceptibility to infections is frequently described using the so-called “J-curve” [2]. As suggested by classic observational studies, while moderate exercise may stimulate and seemingly strengthen immune responses, extreme and long-term physical exertion, such as participating in marathons, enduring multi-week training camps, or undergoing rigorous military conditioning, can potentially lead to a drastic decrease in immune function [2]. This physiological strain is hypothesized to lead to the creation of the so-called "open window" (often referred to as the Open Window Theory). This concept describes a state of transient immunosuppression, during which the functional capacity of lymphocytes and natural killer (NK) cells may be temporarily disturbed, a condition that potentially increases the organism's overall susceptibility to both viral and bacterial pathogens [3].

This apparent susceptibility to infections seems to drastically intensify during the autumn-winter period, a phenomenon that is inextricably linked to atmospheric physics and seasonal environmental conditions. At latitudes situated above the 35th parallel—a region encompassing the entirety of Central Europe—the specific angle of sunlight during the winter months may often prevent sufficient cutaneous synthesis of cholecalciferol via UVB radiation [4, 5]. Consequently, this environmental limitation is thought to lead to widespread vitamin D deficiencies among athletic populations. Epidemiological data suggest that during the demanding preparation period for the spring round, a substantial proportion 42.8% of elite athletes, such as football players training at higher latitudes, may exhibit suboptimal serum concentrations of 25(OH)D, frequently falling significantly below what are considered safe and optimal values [5, 6].

Even though vitamin D historically has been associated predominantly with the regulation of calcium-phosphate metabolism and bone health, the pivotal discovery in 1983 of the Vitamin D Receptor (VDR) on peripheral blood mononuclear cells fundamentally altered the paradigm of how this compound is perceived in the medical literature [7]. Since then, evidence has suggested that various cells of the immune system possess the ability for the intracellular expression of this receptor, as well as the capacity for the local conversion of circulating vitamin D into its biologically active form. This localized conversion is currently hypothesized to serve as an important, and perhaps crucial, cellular defence mechanism [7]. Consequently, maintaining an adequate vitamin D status, alongside carefully targeted supplementation strategies when appropriate, is now increasingly recognized as a potentially essential factor in modulating complex immune responses, supporting overall health care, and possibly sustaining athletic performance in highly demanding settings [8, 9, 10].

Given these complex physiological interactions, the primary aim of this narrative review is to offer a comprehensive summary and an objective analysis of the currently available clinical evidence regarding the potential effectiveness of vitamin D supplementation in individuals burdened with extreme physical effort. Furthermore, this work will attempt to provide a mechanistic explanation of the observed clinical effects, looking particularly through the prism of how vitamin D may potentially influence tissue antimicrobial peptide expression in these highly stressed populations.

2. Methodology

To ensure the methodological transparency of this narrative review, the electronic databases PubMed/MEDLINE and Google Scholar were searched. The literature retrieval process utilized specific keyword combinations linked by standard Boolean operators (AND, OR). The primary search string incorporated terms such as "vitamin D" OR "cholecalciferol", which were cross-referenced with "upper respiratory tract infections" OR "URTI", and specific target populations defined as "athletes" OR "military" OR "physical exertion". Furthermore, mechanistic terms like "LL-37" and "cathelicidin" were included to identify relevant molecular studies.

The search strategy was purposely narrowed down to full-text publications available in English and Polish. To ensure the inclusion of the most current clinical guidelines and updated systematic data, the selected literature originated mainly from the last 10 years. The main analysis included mostly large-scale meta-analyses and randomized double-blind controlled trials (RCTs), as these are generally considered to provide the most robust foundation for evaluating the effectiveness of clinical interventions.

PICO Criteria

In order to select high-reliability evidence, strict criteria based on the PICO scheme were applied:

- **P (Population):** Healthy adults burdened with high physical effort (elite athletes, martial arts competitors, military formation recruits).
- **I (Intervention):** Oral cholecalciferol (vitamin D3) supplementation, with a particular emphasis on dosage and intervention duration.
- **C (Comparison):** Control group receiving a placebo or sun-simulating intervention.

- **O (Outcomes):** Impact on the incidence, duration, and severity of URTI symptoms, as well as an assessment of mucosal mechanisms (changes in defence marker concentrations, such as LL-37 peptide or secretory IgA).

Table 1. Characteristics of selected, key studies and meta-analyses included in the review.

Author / Year (Type)	Studied population (P)	Applied intervention (I)	Main clinical observations (O)
Martineau et al. 2017 [11] (Meta-analysis)	General population, healthy adults.	Vitamin D supplementation (individual participant data from RCTs).	Shows a clear protective effect of supplementation against acute respiratory tract infections in a broad population approach.
Jolliffe et al. 2021 [12] & 2025 [13] (Meta-analyses)	General population, healthy adults (newest data update).	Vitamin D supplementation (various regimens from 44 RCTs).	In a mass approach, in the general population, supplementation no longer shows statistically significant protection against URTI (OR tends to 1.00).
Wang et al. 2024 [14] (Meta-analysis)	General population, with extraction of seasonality.	Verification of exact doses and season.	Shows effectiveness in winter months with daily doses; excludes shock megadoses.
Scott et al. 2019 [15] (RCT)	Military recruits (US Marine Corps).	Vitamin D supplementation during basic training.	Demonstrates the relationship between targeted supplementation and the modulation of mucosal salivary immune responses during severe physical stress.
Jung et al. 2018 [16] (RCT)	Taekwondo athletes during an exhausting winter period.	5000 IU/day for 4 weeks vs Placebo.	Supplementation corrected blood levels and reduced the nuisance of ongoing URTI symptoms; a smaller release

			of inflammatory lactoferrin was noted.
Vargas Buonfiglio et al. 2017 [17] (Mechanistic RCT)	Healthy adults.	1000 IU/day during a 90-day period.	Intervention precisely restored the drop in winter airway surface liquid (ASL) activity by stimulating LL-37 peptide production.

3. Results – Analysis of clinical evidence in a multilevel approach

3.1. The evolution of the population-based approach and the potential problem of data overinterpretation

The ongoing scientific debate concerning the potential effectiveness of vitamin D in the prevention of upper respiratory tract infections (URTI) necessitates a highly patient and nuanced assessment of the available data, as well as a strict avoidance of drawing hasty or overly generalized conclusions. Throughout the past decade, many global clinical guidelines have relied heavily upon the influential Martineau meta-analysis published in 2017. At the time, this comprehensive review appeared to demonstrate a relatively clear protective effect of vitamin D supplementation when evaluated through a broad, population-based approach [11].

However, as is the fundamental nature of evidence-based medicine (EBM), paradigms continuously evolve as new, larger datasets become available for critical review. This evolution is particularly evident in the newest large-scale meta-analysis from 2025, published in *The Lancet Diabetes & Endocrinology* (serving as an update to Jolliffe's extensive database [12]). This recent publication suggested that after meticulously aggregating data from subsequent, high-statistical-power studies, the previously observed general population effect of routine supplementation appears to become significantly blurred, if not entirely attenuated [13]. When applying a mass, undifferentiated approach to the data, the calculated Odds Ratio (OR) was reported at 0.96, with a confidence interval that unfortunately crossed the critical value of 1.00. From a purely mathematical perspective, this finding essentially abolishes the statistical significance of widespread anti-infective protection when applied to a general, largely well-nourished population [13].

The potential solution to this apparent statistical paradox, and arguably a key element to properly understanding the nuances of sports medicine immunology, may lie in the careful extraction and analysis of highly specific clinical subgroups. Supporting this hypothesis, a detailed dose-response meta-analysis conducted in 2024 indicated that the prophylactic effectiveness of the intervention seemingly grows at a rapid pace when researchers narrow their analysis to interventions implemented strictly during the winter months—a period when natural, sun-induced cutaneous synthesis virtually stops. Furthermore, this beneficial effect was observed to be most pronounced when moderate, consistent daily doses were utilized, as opposed to the administration of artificial, high-dose boluses [14].

Within these carefully targeted and seasonally adjusted subgroups, the incidence risk of URTI appeared to drop quite significantly (RR = 0.79) [14]. Ultimately, these evolving datasets lead researchers to formulate an important, though cautious, conclusion: vitamin D does not appear to act as a universal prophylactic antimicrobial applicable to every human subject regardless of their baseline status. Rather, it may act more accurately as a targeted physiological corrector, exerting its most significant clinical benefits primarily in states characterized by a deep depletion of its physiological precursors.

3.2. Evidence from high-load environments (Competitive sports and military training)

The unique and highly demanding environments characteristic of both military training grounds and intensive winter sports camps appear to serve as highly representative models of the physiological state described by the aforementioned "J-curve" hypothesis.

These specific settings tend to combine several potentially detrimental factors, including elevated oxidative stress, cumulative tissue microdamages, transient periods of exercise-induced immunosuppression, and a notable, season-dependent lack of adequate sunlight exposure.

Within this specific context, the research conducted by Scott et al. (2019) on cohorts of US Marine Corps recruits undergoing physically strenuous basic training provides potentially valuable insights into the suggested importance of maintaining an optimal vitamin D status for the preservation of mucosal immunity [15]. In their study, the authors systematically investigated the potential effects of targeted vitamin D supplementation on various parameters of salivary immune responses. Based on their findings, they cautiously established that securing and maintaining adequate circulating levels of 25(OH)D appears to play a functional role in modulating the first line of mucosal defence against common respiratory pathogens, particularly when individuals are operating within such severe, high-load military environments [15].

Furthermore, these military-based reports seem to closely correspond with the clinical observations presented in the work of Jung et al. (2018), who focused their examinations on a specialized population of elite academic taekwondo athletes [16]. In this particular model, a four-week, physically exhausting indoor training camp was observed to result in a seemingly significant increase in the athletes' general susceptibility to infections. A subsequent double-blind intervention, utilizing a relatively high daily supply of cholecalciferol (5000 IU/day), was reported to quickly and effectively saturate the organism with the necessary precursor [16]. Crucially, the authors demonstrated the presence of a strong negative statistical correlation within their dataset. Specifically, their analysis suggested that the higher the documented increase in circulating 25(OH)D concentration in response to the applied treatment, the more notably the total health complaints and specific respiratory symptoms reported by the athletes appeared to drop ($r = -0.435$) [16]. This observed correlation tentatively supports the hypothesis that aggressively correcting underlying seasonal deficiencies might translate directly into beneficial clinical outcomes in highly stressed, competitive populations.

3.3 Molecular mechanisms of protection: Role of ASL fluid and Cathelicidin

To understand the potential link between systemic vitamin D levels and localized mucosal protection, researchers usually look at the specific microenvironment of the respiratory tract. The cells lining the respiratory epithelium are naturally separated from the outside air by a thin, specialized layer of fluid, commonly referred to as Airway Surface Liquid (ASL). This layer appears to do more than simply keep the epithelial cilia lubricated; current physiological models describe it as a primary chemical defence zone capable of neutralizing a variety of incoming pathogens [17, 18].

Experimental observations, particularly those derived from *in vitro* and *ex vivo* models such as the work conducted by Vargas Buonfiglio et al. (2017), suggest that the inherent biocidal capacity of this fluid might decline noticeably during the winter and early spring months [17]. Within this context, the active metabolite of vitamin D is thought to upregulate the expression of the *CAMP* gene directly within the respiratory epithelial cells. This specific gene is largely responsible for directing the local synthesis of cathelicidin (LL-37), an endogenous antimicrobial peptide [17].

In laboratory models, LL-37 is described as having a relatively broad spectrum of action against various bacterial and viral agents. The proposed mechanism of action involves the physical disruption of bacterial lipid membranes. Additionally, experimental data indicate it might possess targeted antiviral properties; for instance, exposure to LL-37 seems to effectively neutralize the Respiratory Syncytial Virus (RSV), which in turn may help limit the subsequent apoptosis and necrosis of human epithelial tissue following an infection [19].

A particularly notable detail regarding this pathway comes from Vargas Buonfiglio's 2017 experiments involving an LL-37 neutralizing antibody. When researchers introduced this specific antibody into the isolated ASL samples, the pathogen-killing capacity—which had been previously restored by the addition of vitamin D—appeared to be largely blocked [17]. Such laboratory observations offer a plausible biological explanation for how circulating precursors might eventually translate into an enhanced antimicrobial defence directly on the surface of the airways.

3.4 Modulation and silencing of inflammation

Vitamin D also acts as an intelligent buffer preventing the destructive overreactivity of the immune system. In the mentioned Jung study (taekwondo), an elevated release of an acute-phase protein – lactoferrin – in saliva was observed in the placebo group [16]. This means that unprotected mucous membranes, facing pathogen invasion, had to resort to a significant inflammatory reaction. In athletes supplemented with vitamin D, possibly due to the constant presence of an early shield from the LL-37 peptide, this emergency inflammatory process did not take place, which probably prevented local tissue damage [16]. A critical warning for sports medicine, based on experimental models, is the mechanistic observation that exposing respiratory epithelial cells to cigarette smoke extract appears to significantly reduce the expression of the local 1-alpha hydroxylase enzyme (CYP27B1). This specific enzyme is directly responsible for the intracellular activation of vitamin D3. Consequently, it is hypothesized that such exposure could potentially undermine the overall supplementation effort, effectively impairing the epithelial cells' ability to upregulate the expression of antimicrobial peptides (like cathelicidin) into the surface fluid in response to the circulating vitamin [17].

Discussion

Cholecalciferol should not be classified in sports medicine as a "stimulating agent" acting regardless of the baseline organism status. As the newest meta-analytical summaries indicate, administering it preventively to general population, in whom deficits do not occur, misses the statistical point in the fight against the common cold [13].

However, the situation changes completely in elite athletes and military trainees. In these selected populations, severe oxidative stress combined with micro-injuries generates a huge tissue demand, secondarily activating the renal and local hydroxylation of circulating calcidiol [5, 6]. Overlapping this negative vector in the winter period is a lack of solar synthesis. In such specific conditions of deep drainage (when parameters drop <50 nmol/L), a targeted daily oral supply of 1000–5000 IU becomes a critical intervention, supplementing the missing substrate for the local production of antimicrobial proteins (LL-37) on the bronchial surface [15, 17, 19].

4.1. Current regional guidelines and sports-specific dosage

Determining the exact amount of cholecalciferol required by an actively training athlete remains a subject of ongoing clinical discussion. Moving from theoretical molecular models to practical application usually demands a firm foundation in current medical consensus. In this regard, the 2023 guidelines formulated for Poland and Central Europe, which were endorsed by the Polish Society of Endocrinology, offer a highly useful starting framework for sports clinicians [20]. According to these updated criteria, an absolute vitamin D deficiency is generally defined as a serum 25(OH)D concentration falling below the threshold of 20 ng/mL (50 nmol/L), while a suboptimal status is typically classified in the range between 20 and 30 ng/mL. For the average, healthy adult population, standard seasonal prophylaxis usually involves the administration of 1000 to 2000 IU per day throughout the darker autumn and winter months.

However, individuals engaged in competitive sports frequently do not align seamlessly with these standard population profiles. It is widely hypothesized that extreme and regular physical exertion leads to a noticeably higher metabolic turnover of circulating nutrients. Furthermore, athletes typically present with an altered physical composition, often characterized by a significantly greater overall muscle mass and total body volume. The authors of the 2023 Polish guidelines appear to account for such variables, formally noting that individuals presenting with a higher body mass, or those who simply might require enhanced physiological support, could potentially scale their daily preventive dosing up to 4000 IU while maintaining a safe profile [20]. When looking specifically through the lens of sports immunology, it is thought that aiming for the upper end of the established optimal reference range, usually cited as 30 to 50 ng/mL, might actually be necessary to fully support the broader pleiotropic effects of the vitamin, including the continuous, adequate activation of the *CAMP* gene for localized LL-37 peptide synthesis.

Following this line of reasoning, establishing a daily intake somewhere between 2000 and 4000 IU seems to be a biologically justifiable strategy for heavily burdened athletes participating in intensive winter training cycles. In certain instances where a profound baseline deficit is detected upon screening, a short-term, targeted therapeutic intervention utilizing up to 5000 IU per day might be considered to rapidly restore circulating levels, a protocol similar to what has been documented in cohorts of elite combat sports athletes [16]. Despite these physiological rationales, empirical or "blind" supplementation without prior laboratory assessment is generally discouraged in modern sports medicine. The routine biochemical monitoring of serum 25(OH)D concentrations continues to be viewed as the clinical gold standard. Such an individualized approach is believed to allow for a much more precise dose titration, which theoretically helps in mitigating the risks of both transient seasonal infection susceptibility and the admittedly rare, but possible, threat of hypervitaminosis.

4.2 Limitations

When interpreting the overall findings presented in this narrative review, several methodological and physiological aspects require careful consideration. Foremost, it must be acknowledged that the currently available clinical evidence focusing specifically on highly burdened athletic and military populations remains somewhat limited in scope and volume. Historically, the vast majority of large-scale randomized trials designed to investigate the relationship between vitamin D supplementation and respiratory tract infections have been conducted within much broader, general population cohorts. Because the average population does not typically endure the extreme physical stress and subsequent transient infection susceptibility characteristic of elite training environments, extrapolating these generalized data directly to high-performance groups usually requires a degree of scientific caution.

Additionally, the specific studies discussed in this analysis often differ considerably in their structural design. There is noticeable variability regarding the applied supplementation protocols, particularly concerning the exact dosages and the frequency of administration. Furthermore, the baseline vitamin D status of the enlisted participants frequently varies from study to study. This is generally considered a critical variable, as individuals starting an intervention with severe pre-existing deficits are logically more likely to demonstrate noticeable clinical improvements compared to subjects who already possess adequate serum levels prior to receiving the supplement. The distinct seasonal conditions under which these trials were performed also introduce another layer of complexity, often serving as a natural confounding variable depending on the potential for incidental, sun-induced cutaneous synthesis among the participants.

Collectively, these methodological differences are thought to contribute to a certain degree of statistical heterogeneity in the reported clinical outcomes, making it somewhat difficult to establish a single, universally applicable protective protocol. Finally, while numerous experimental models and mechanistic observations suggest that vitamin D appears to enhance local mucosal immunity—primarily through the targeted induction of antimicrobial peptides like LL-37—translating these isolated cellular mechanisms into guaranteed, observable clinical outcomes requires a measured approach. To fully understand and accurately quantify the true magnitude of this protective physiological effect in a living organism, the field would ultimately benefit from further, rigorously controlled clinical trials conducted strictly within environments characterized by high physical performance.

5. Conclusions

A critical assessment of the available evidence material allows for the following scientific conclusions. According to 2024-2025 analyses, population-wide routine supplementation does not exert a strong prophylactic effect in a healthy adult population. Nevertheless, this intervention may show clinically meaningful protective effects in selected subgroups exposed to extreme physical stress and seasonal vitamin D deficiency (e.g., in martial arts, military camps). Restoring and maintaining an optimal 25(OH)D concentration through continuous, precise dosing allows these groups to significantly reduce training absence caused by the duration of coughing and infectious upper respiratory tract symptoms. The physiological foundation of this phenomenon is not a systemic organism stimulation, but the highly targeted cellular ability of activated vitamin D to stimulate CAMP gene expression, which restores – impaired during a deficit and immunosuppression period – the secretory chemical mucosal barrier, including cathelicidin (LL-37 peptide) with a broad spectrum of antibacterial and antiviral activity. Targeted nutritional support, including adequate vitamin D intake during winter or in deficient athletes, may further enhance immune resilience and facilitate recovery from training-related stress and injuries [21].

Disclosure Section

Author Contribution:

Conceptualization, [J.M.]; methodology, [J.M., K.Ł., A.M., P.G., M.N., and M.R.]; formal analysis, [K.Ł., A.M., P.G., M.N., and M.R.]; investigation, [K.Ł., A.M., P.G., M.N., and M.R.]; writing—original draft preparation, [J.M.]; writing—review and editing, [K.Ł., A.M., P.G., M.N., and M.R.]. All of the authors have read and agreed to the published version of the manuscript.

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Declaration of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used Gemini (Google) for the purpose of translation of the original Polish text into English, grammar correction, and formatting. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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