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VITAMIN D AND RESPIRATORY TRACT INFECTIONS: A NARRATIVE REVIEW OF DEFICIENCY, SUPPLEMENTATION STRATEGIES, AND CLINICAL OUTCOMES

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ABSTRACT

Vitamin D is widely recognised for its role in calcium homeostasis and skeletal health, yet its biological relevance extends beyond the musculoskeletal system to immune regulation and host defence. Over the past decade, the relationship between vitamin D status and respiratory tract infections (RTIs) has attracted increasing scientific interest, particularly in the context of the widespread prevalence of vitamin D deficiency and the global impact of the COVID-19 pandemic. This narrative review synthesises evidence on vitamin D deficiency, supplementation strategies, and respiratory clinical outcomes, drawing on randomised controlled trials, systematic reviews, meta-analyses, observational studies, and selected mechanistic publications. The reviewed literature consistently suggests that low serum 25-hydroxyvitamin D [25(OH)D] concentrations are associated with increased susceptibility to RTIs and, in many settings, with poorer respiratory outcomes. However, evidence regarding the benefits of supplementation remains heterogeneous. Earlier meta-analyses suggested modest protective effects, particularly among individuals with lower baseline vitamin D status and in studies using daily or weekly standard-dose regimens, whereas more recent large randomised trials and updated meta-analyses have reported smaller, inconsistent, or statistically non-significant overall effects. These discrepancies likely reflect variation in study population, baseline deficiency, supplementation regimen, trial duration, and outcome definition. Current evidence does not support a universal preventive or therapeutic role of vitamin D supplementation for all RTIs, but it strongly supports the importance of identifying and correcting deficiency, particularly in high-risk groups. From a wider perspective, vitamin D deficiency should also be understood as a socially patterned and potentially modifiable determinant of health, with relevance to prevention, health equity, and public health planning.

KEYWORDS

Vitamin D; Respiratory Tract Infections; Deficiency; Supplementation; Clinical Outcomes; Public Health

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1. Introduction

Vitamin D is a fat-soluble secosteroid that has long held a central place in medicine because of its essential role in calcium regulation, phosphate homeostasis, and maintenance of skeletal integrity. Traditionally, the clinical significance of vitamin D was discussed mainly in relation to disorders such as rickets, osteomalacia, and osteoporosis. In recent decades, however, the scientific understanding of vitamin D has expanded considerably. It is now increasingly recognised that vitamin D has functions extending beyond the musculoskeletal system and may influence a wide range of biological processes, including immune regulation, inflammatory signalling, oxidative stress modulation, and epithelial barrier function. This broader perspective has generated sustained interest in the possibility that vitamin D status may be relevant to the risk, severity, and clinical course of respiratory tract infections (RTIs).

RTIs remain among the most common causes of acute morbidity worldwide and represent a significant burden for both individuals and healthcare systems. They encompass a broad clinical spectrum, from mild, self-limiting upper respiratory tract infections—such as the common cold, pharyngitis, sinusitis, and influenza-like illness—to more serious lower respiratory tract infections, including bronchitis and pneumonia. Although upper RTIs are often regarded as benign, their cumulative social and economic burden is substantial because of their high incidence, associated absenteeism, repeated healthcare visits, and frequent overuse of antibiotics. Lower RTIs are of even greater concern because they account for a considerable proportion of hospital admissions, complications, and deaths, especially in young children, older adults, and those with chronic cardiopulmonary conditions or broader physiological vulnerability.

At the same time, vitamin D deficiency remains highly prevalent in many regions of the world. Low serum 25-hydroxyvitamin D [25(OH)D] concentrations are common among individuals with limited sunlight

exposure, obesity, malabsorption syndromes, advanced age, darker skin pigmentation at higher latitudes, institutionalisation, chronic illness, and poor dietary intake. This widespread prevalence of deficiency has led to growing concern in both clinical and public health circles. The issue is particularly relevant in the context of respiratory infection because the same groups most vulnerable to severe deficiency are often those at increased risk of poor respiratory outcomes.

Several biological mechanisms support the plausibility of a relationship between vitamin D and respiratory health. Vitamin D receptors (VDRs) are expressed in a range of immune and epithelial cells, including macrophages, dendritic cells, neutrophils, and activated T lymphocytes. Through these receptors, vitamin D can influence both innate and adaptive immune responses. Experimental work has shown that vitamin D may promote the expression of antimicrobial peptides such as cathelicidin and defensins, both of which are relevant to host defence against respiratory pathogens. Vitamin D has also been implicated in the modulation of inflammatory cytokines, the maintenance of epithelial barrier integrity, and the control of excessive inflammatory responses that may contribute to tissue damage during infection.

One of the most important mechanistic observations in this field is that respiratory epithelial cells are capable of converting inactive vitamin D into its active form. This suggests that vitamin D may contribute directly to airway host defence at the local tissue level rather than only through systemic endocrine pathways. In addition, broader mechanistic literature has linked vitamin D deficiency to oxidative stress, mitochondrial dysfunction, and chronic low-grade inflammation, all of which may compromise resilience during acute illness.

The COVID-19 pandemic brought these issues into particularly sharp focus. During the pandemic, vitamin D became one of the most widely discussed micronutrients in relation to infection risk and severity. This was driven by several factors. First, populations at highest risk of severe COVID-19—older adults, individuals with obesity, institutionalised populations, and people with chronic cardiometabolic disease—also tend to be at increased risk of vitamin D deficiency. Second, vitamin D is widely available, relatively inexpensive, and familiar to both clinicians and the public, making it an attractive candidate for preventive or adjunctive intervention. Third, a large number of observational studies reported associations between low vitamin D status and adverse COVID-19 outcomes, including greater risks of hospitalisation, severe disease, and death. At the same time, the findings of randomised controlled trials and later meta-analyses did not consistently support a clear overall protective effect of supplementation, which made interpretation more complex.

The resulting literature is substantial but not uniform. Some trials and earlier pooled analyses suggested that vitamin D supplementation may provide modest protection against RTIs, particularly in people with low baseline vitamin D status and in studies using daily or weekly standard-dose regimens. However, more recent large randomised trials and updated meta-analyses have often reported smaller effects or statistically non-significant overall results.

This inconsistency has practical implications. It raises important questions about how supplementation should be recommended in clinical practice, whether vitamin D deficiency should be approached as a public health priority, how evidence should be communicated to the public, and how the broader issue intersects with social determinants of health.

This last point is particularly important for the present manuscript. Vitamin D deficiency is not distributed randomly within the population. It is shaped not only by biology but also by everyday living conditions. Urban indoor lifestyles, reduced mobility, occupational patterns, food access, chronic disease burden, environmental exposure, poverty, and social isolation can all influence whether individuals are able to maintain adequate vitamin D levels.

Deficiency can therefore be understood not only as a biomedical phenomenon but also as a socially patterned vulnerability that intersects with health equity, preventive care, and wider public health planning.

For this reason, the topic is relevant not only to clinical medicine but also to the aims and scope of the *International Journal of Innovative Technologies in Social Science*. The issue extends naturally into questions of health education, communication, prevention, inequality, implementation, and policy.

The aim of this narrative review is to synthesise current evidence on the relationship between vitamin D and respiratory tract infections, with particular emphasis on three interrelated themes: deficiency, supplementation strategies, and clinical outcomes. In addition, the review considers the implications of this evidence for public health, preventive healthcare, health

education, and health equity. Rather than asking simply whether vitamin D "works," the review seeks to examine for whom it may matter most, under what circumstances supplementation may be justified, and how the present evidence should be interpreted responsibly.

2. Methodology

This study was conducted as a narrative literature review. A narrative approach was chosen because the literature on vitamin D and respiratory tract infections spans several different forms of evidence, including mechanistic studies, observational analyses, randomised controlled trials, and evidence syntheses such as systematic reviews and meta-analyses.

These bodies of literature differ not only in methodology but also in populations studied, baseline vitamin D status, dosing strategies, study duration, and outcome definitions. Because of this substantial heterogeneity, a descriptive and critical synthesis was considered more appropriate than an attempt to generate a new pooled quantitative estimate.

The main literature search was carried out using PubMed and Google Scholar. The review focused primarily on studies published between January 2015 and February 2025, although selected earlier studies were also included when they represented landmark randomised trials, foundational mechanistic investigations, or key observational studies central to understanding the topic. Search terms included combinations of "vitamin D," "25-hydroxyvitamin D," "respiratory tract infection," "acute respiratory infection," "upper respiratory tract infection," "lower respiratory tract infection," "influenza," "COVID-19," "deficiency," "supplementation," "immunity," "meta-analysis," and "public health."

Only peer-reviewed English-language studies were included. Priority was given to randomised controlled trials, systematic reviews, meta-analyses, and major observational studies with clear clinical or epidemiological relevance. Mechanistic and broader biological reviews were also included when they contributed substantially to the biological plausibility of the vitamin D–RTI relationship, especially in relation to epithelial host defence, local vitamin D activation, antimicrobial peptide expression, oxidative stress, and immune signalling.

Studies were considered eligible if they examined the association between vitamin D status and the risk or severity of respiratory tract infections, the preventive effect of vitamin D supplementation on RTIs, or the role of supplementation during active respiratory infection. Particular attention was also given to studies exploring whether outcomes differed according to baseline vitamin D deficiency, age, dose, supplementation regimen, or specific clinical population, as well as to papers discussing the broader public health and social implications of vitamin D deficiency in respiratory disease. Titles and abstracts were screened for relevance, and the full texts of major studies were subsequently reviewed in detail. Additional references were identified through manual screening of the bibliographies of key meta-analyses, reviews, and randomized controlled trials. For each included study, information was extracted on study design, participant characteristics, sample size, baseline serum 25(OH)D concentrations where available, intervention type and dose, frequency and duration of supplementation, respiratory outcomes assessed, safety findings, and major methodological limitations.

The findings were synthesised narratively rather than quantitatively. This was necessary because studies differed substantially in their populations, interventions, and endpoints. For example, some focused on upper RTIs, others on influenza or acute respiratory infection more broadly, and still others on COVID-19-specific outcomes. Likewise, some interventions used daily physiological supplementation, while others used large intermittent bolus regimens. Such differences limit the interpretability of direct pooled comparison beyond what has already been reported in published meta-analyses.

Because this review was based exclusively on previously published material, ethical approval was not required.

3. Results

3.1. Global prevalence and determinants of vitamin D deficiency

Vitamin D deficiency is a global issue rather than a problem confined to specific climates or healthcare settings. It is often discussed in relation to winter months and higher-latitude populations, but low serum 25(OH)D concentrations are also common in regions with abundant sunlight. This apparent paradox reflects the fact that vitamin D status is determined by more than geography alone.

One of the most important contributors to low vitamin D status is reduced sunlight exposure. Indoor work, prolonged screen-based or sedentary lifestyles, urban environments, reduced mobility, and institutionalisation all decrease the opportunity for endogenous vitamin D synthesis. In older adults, this is compounded by age-related declines in cutaneous vitamin D production. In many cases, lower levels of outdoor activity coexist with poorer nutritional status and chronic disease, further increasing the likelihood of deficiency.

Obesity is another key determinant. People with obesity often have lower circulating vitamin D levels, possibly because vitamin D is sequestered in adipose tissue and becomes less bioavailable. In addition, dark skin pigmentation may reduce the efficiency of ultraviolet-mediated vitamin D synthesis in higher-latitude environments, increasing the risk of deficiency in specific ethnic groups. Malabsorption, liver disease, and other chronic illnesses can further impair vitamin D status.

Diet also plays a role. Natural food sources of vitamin D are relatively limited, and many populations depend on fortified foods or supplements to maintain adequate intake. Where food fortification is absent or limited, and where dietary quality is poor, deficiency becomes more likely. These issues often intersect with food insecurity, poverty, and low health literacy.

From a public health perspective, deficiency is therefore not merely a biochemical finding; it is socially patterned. It is more common in populations already burdened by frailty, chronic disease, reduced healthcare access, poor diet quality, environmental disadvantage, or limited mobility. This is particularly relevant to respiratory health because these same groups are often those most vulnerable to complications of respiratory tract infection.

Understanding this distribution matters. It means that vitamin D deficiency is relevant not only as an individual clinical issue but also as a broader public health concern connected with inequality, prevention, and health system planning.

3.2. Mechanistic evidence supporting a role of vitamin D in respiratory defence

The biological plausibility of a relationship between vitamin D and respiratory tract infections is supported by a substantial body of mechanistic literature. These studies suggest that vitamin D may influence host defence through multiple pathways relevant to airway immunity, epithelial integrity, and inflammatory regulation.

A landmark contribution in this area came from **Hansdottir et al. (2008)**, who demonstrated that respiratory epithelial cells are able to convert inactive vitamin D into its active form. This was an important finding because it indicated that vitamin D might act locally within the respiratory tract and not only through systemic endocrine mechanisms. In their study, active vitamin D increased expression of host-defence genes, including cathelicidin and CD14, supporting the idea that vitamin D may contribute directly to local airway immunity.

The review by **Greiller and Martineau (2015)** further synthesised evidence from in vitro studies examining how vitamin D metabolites influence the epithelial response to respiratory viruses. The authors reported that vitamin D does not consistently reduce viral replication in experimental models of rhinovirus, respiratory syncytial virus, or influenza. However, it does modulate the expression and secretion of cytokines, chemokines, and antimicrobial peptides in infected epithelial cells. This suggests that vitamin D's importance may lie less in direct antiviral action and more in its ability to shape host defence and inflammatory responses.

Broader biological literature offers a complementary perspective. **Wimalawansa (2019)** linked vitamin D deficiency with oxidative stress, mitochondrial dysfunction, and inflammatory dysregulation. While not specific to respiratory infection, these mechanisms are highly relevant in acute illness, especially where immune and metabolic demands are high.

Biesalski (2020) similarly discussed the possible role of vitamin D in the context of COVID-19, with particular focus on inflammatory pathways, epithelial vulnerability, and the renin-angiotensin system.

The broader review by **Gombart et al. (2020)** also placed vitamin D within the wider framework of micronutrient-dependent immunity. Their work emphasised that immune competence depends on several nutrients acting together, and that vitamin D contributes to epithelial barriers, innate immune signalling, and inflammatory control within this broader network.

Taken together, the mechanistic evidence supports several important concepts. Respiratory epithelial cells can locally activate vitamin D; vitamin D can promote antimicrobial peptide expression; it may help regulate excessive inflammatory responses; and deficiency may worsen oxidative and inflammatory injury. These mechanisms make the vitamin D–RTI relationship biologically credible even when the clinical trial evidence is mixed.

3.3. Observational evidence: low vitamin D status and respiratory vulnerability

A substantial observational literature has linked low vitamin D status with increased respiratory risk. One of the earliest and most widely cited population-based studies in this field is **Ginde et al. (2009)**, who analysed data from the Third National Health and Nutrition Examination Survey in the United States. They found that lower serum 25(OH)D concentrations were independently associated with recent upper respiratory tract infection.

The association appeared particularly strong in participants with underlying respiratory diseases such as asthma and chronic obstructive pulmonary disease.

This study was important because it demonstrated the vitamin D–URTI relationship at the population level rather than only in selected clinical subgroups. It suggested that low vitamin D status may reflect increased respiratory vulnerability more broadly across the community.

Subsequent observational work has generally pointed in a similar direction. Lower vitamin D levels have repeatedly been associated with increased risk of respiratory symptoms, more frequent infections, or worse respiratory outcomes. During the COVID-19 era, numerous studies also reported that lower 25(OH)D concentrations were associated with more severe disease, higher hospitalisation rates, or higher mortality.

A particularly important contemporary contribution is the large UK Biobank analysis by **Sha et al. (2023)**. In that cohort, vitamin D deficiency and insufficiency were associated with increased all-cause mortality and respiratory disease mortality. Self-reported vitamin D supplement use was associated with lower all-cause mortality and lower respiratory mortality. Although this study did not measure acute RTI prevention directly, it strengthens the broader argument that vitamin D status has meaningful relevance to respiratory health outcomes.

The major limitation of observational evidence is confounding. Low vitamin D status tends to coexist with multiple other adverse factors, including aging, obesity, sedentary behaviour, frailty, poor diet, chronic inflammation, lower socioeconomic position, and reduced access to healthcare. These same factors may independently increase the risk of respiratory infection and poorer recovery. Therefore, vitamin D deficiency may at times function more as a marker of vulnerability than as a direct causal exposure.

Even so, the consistency of observational findings remains notable. At a minimum, the evidence indicates that low vitamin D status is clinically relevant and identifies groups in whom respiratory risk is elevated.

3.4. Early randomised controlled trials: positive and negative primary evidence

Primary randomised controlled trials conducted before the most recent wave of large meta-analyses offer useful insight into why the literature remains difficult to interpret. Urashima et al. (2010)

Urashima et al. conducted a randomised, double-blind, placebo-controlled trial in schoolchildren and found that daily vitamin D3 supplementation at 1200 IU reduced the incidence of seasonal influenza A. The authors also reported fewer asthma attacks in children with previous asthma. This trial remains important because it suggested that vitamin D may have a protective effect in a paediatric viral respiratory setting. Camargo et al. (2012)

Camargo et al. studied Mongolian schoolchildren during winter, a setting characterised by very low baseline vitamin D levels. Vitamin D supplementation in fortified milk significantly reduced the rate of acute respiratory infection. This trial is often cited as one of the clearest examples of benefit in a highly deficient paediatric population and strongly supports the possibility that deficiency correction may matter most where baseline levels are very low. Bergman et al. (2012)

Bergman et al. examined vitamin D3 supplementation in patients with frequent respiratory tract infections, including those with antibody deficiency or increased respiratory susceptibility. Over one year, supplementation reduced infectious burden and antibiotic use. This trial is particularly relevant because it focused on a clinically vulnerable population rather than on healthy volunteers and suggests that supplementation may have value in selected high-risk groups. Murdoch et al. (2012)

In the VIDARIS trial, Murdoch et al. administered monthly high-dose vitamin D3 to healthy adults and found no reduction in the incidence or severity of upper respiratory tract infections. This trial has become one of the most important negative studies in the field and is often cited in discussions about the limitations of broad supplementation strategies, especially those using intermittent high-dose regimens. Goodall et al. (2014)

Goodall et al. randomised university students to vitamin D3 or placebo and did not observe a significant reduction in symptomatic clinical URTI. However, laboratory-confirmed URTI and viral load appeared lower in the vitamin D group. This study is valuable because it highlights the importance of endpoint selection.

Clinical symptoms and virological outcomes may not always move in parallel, and this may partly explain why some trials appear negative while still suggesting biologically relevant effects.

Taken together, these early trials suggest that supplementation may be more promising in children, in clearly deficient populations, and in selected recurrent RTI groups than in healthy adults or in studies using intermittent high-dose schedules.

3.5. Systematic reviews and meta-analyses: shifting evidence over time

The interpretation of vitamin D's effects on RTIs has evolved considerably as more studies have been completed. Vuichard Gysin et al. (2016)

This systematic review and meta-analysis found a small but statistically non-significant reduction in clinical RTI among healthy individuals. The authors noted high heterogeneity and concluded that the evidence did not support a clear preventive effect in healthy populations. Martineau et al. (2017)

The individual participant data meta-analysis by Martineau et al. was a major development in the field. It found an overall protective effect of vitamin D supplementation against acute respiratory tract infection. The benefit appeared strongest in participants with profound vitamin D deficiency and in those receiving daily or weekly non-bolus regimens. This study strongly shaped subsequent scientific discussion and supported the idea that benefit may be concentrated in selected contexts. Jolliffe et al. (2021)

This aggregate-data meta-analysis still found a modest overall preventive effect. More favourable results were observed in trials using daily dosing, standard-dose regimens, shorter duration, and paediatric populations. However, baseline vitamin D deficiency did not emerge as a uniformly strong or consistent effect modifier across all subgroup analyses. Wang et al. (2024)

Wang et al. reported no significant overall preventive effect in the main pairwise analysis, although their dose-response modelling suggested that daily doses in the range of 400–1200 IU may be more favourable and that winter-related settings might be particularly relevant. Their interpretation was clearly more cautious than earlier pooled analyses. Jolliffe et al. (2025)

The latest update found that the overall point estimate remained slightly favourable, but the confidence interval included the null value and the overall result was no longer statistically significant. Although some subgroup trends remained suggestive, meta-regression did not confirm strong or consistent modification by age, dose, frequency, or baseline vitamin D status.

Overall, these updates indicate that the evidence has shifted from cautious optimism towards a more restrained and nuanced interpretation. If supplementation is beneficial, the effect appears modest and not consistently demonstrable across all populations and study designs.

3.6. Regimen matters: dose, frequency, and duration

The reviewed literature repeatedly suggests that the way vitamin D is administered may influence outcomes. Daily or weekly dosing generally appears more favourable than large monthly or intermittent bolus administration. The dose range most often linked to more favourable trends is 400 to 1000 IU/day, or modestly above that range in some analyses.

Large intermittent bolus regimens have often yielded null findings. The Murdoch trial is one notable example. A biologically plausible explanation is that daily replacement may create a more stable physiological environment for local tissue activation and immune regulation, whereas bolus regimens may not sustain the same pattern of availability.

Trial duration is also relevant. Studies lasting up to one year and overlapping with high-risk seasonal periods have sometimes shown more favourable results than longer or more diffuse interventions. These observations suggest that the question is not simply whether supplementation is given, but how it is delivered and to whom.

3.7. Population-specific findings Children

Children have shown some of the clearest positive results, particularly in trials of influenza or deficiency-focused RTIs. Meta-analyses also suggest that younger populations may derive more benefit than adults under some conditions. This may reflect both biological responsiveness and higher exposure to circulating respiratory viruses in school settings.

Healthy adults

Healthy adults have generally shown weaker or null effects in randomised trials. This suggests that supplementation may have little effect on RTIs in populations with relatively adequate baseline status or low event rates, especially when interventions are not targeted to deficiency.

Older adults

The 2024 meta-analysis by Jia et al. found that supplementation probably results in little or no difference in acute respiratory infection incidence among older adults. This is one of the strongest recent null findings and weakens the argument for broad RTI-focused supplementation in this age group, although it does not diminish the relevance of correcting deficiency for other health reasons.

Selected recurrent RTI populations

Patients with recurrent respiratory infections may still be among the most relevant groups for future research. The findings of Bergman et al. suggest that recurrent infection history and clinical vulnerability may define a subgroup more likely to benefit than the general population.

3.8. Vitamin D and COVID-19

COVID-19 brought vitamin D into the centre of public and scientific attention. Mechanistic and observational evidence often suggested that low vitamin D status was associated with greater disease severity or mortality. However, randomised trial evidence remained mixed.

The CORONAVIT trial is particularly important because it tested a realistic population-level “test-and-treat” strategy. Even though vitamin D levels improved, the study found no reduction in the risk of all-cause acute respiratory infection or COVID-19. This is highly relevant for implementation and policy, because it suggests that biochemical improvement alone does not necessarily translate into measurable short-term respiratory protection in broad populations.

At the same time, strongly pro-causality interpretations, such as those presented by Wimalawansa (2025), continue to argue that the totality of epidemiological and mechanistic data points to a causal role of deficiency. These arguments highlight the broader scientific debate but go further than the evidence from the most recent large randomised studies allows.

3.9. Vitamin D as treatment during active respiratory infection

Treatment evidence remains limited. The meta-analysis by Cho et al. found no clinically meaningful benefit when higher-quality studies were considered. This suggests that vitamin D supplementation may not function as an effective stand-alone treatment once an acute respiratory infection is established.

3.10. Safety of supplementation

Across the reviewed literature, vitamin D supplementation appears generally safe within conventional dose ranges. Major trials and meta-analyses have not shown major increases in serious adverse events, and hypercalcaemia and kidney stones have been uncommon. This supports the use of vitamin D for deficiency correction and targeted preventive care.

4. Discussion

4.1. Overall interpretation of the evidence

The current evidence suggests that vitamin D is relevant to respiratory health, but not in a simple or universally predictive way. Deficiency is consistently associated with increased respiratory vulnerability, but supplementation does not appear to exert a strong or reliable preventive or therapeutic effect across all populations and clinical contexts.

This distinction is central to an evidence-based interpretation of the field. It is appropriate to conclude that low vitamin D status identifies people at increased risk of poor respiratory outcomes. It is less appropriate to conclude that supplementation will uniformly reduce that risk in all groups. The totality of the literature suggests that if supplementation is beneficial, it is likely to be modest, selective, and dependent on baseline status, dose, and population.

4.2. Heterogeneity and why it matters

The literature is highly heterogeneous. This heterogeneity is not a nuisance detail but one of the key findings in itself. It arises from variable baseline deficiency levels, different supplementation regimens, different age groups and clinical populations, diverse endpoint definitions, and adherence and crossover issues.

Because of this, apparently conflicting results may reflect genuine contextual differences rather than simple contradiction. It also explains why broad universal claims about vitamin D and RTIs are difficult to justify. In some cases, true biological effects may be diluted by trial design; in others, positive early signals may have been amplified by small-study effects or selective populations.

4.3. Clinical implications

The most practical implication is that vitamin D deficiency should be identified and corrected, especially in older adults, people with obesity, individuals with chronic disease, institutionalised populations, and those with recurrent respiratory problems or low sunlight exposure.

At the same time, supplementation should not be presented as a universally effective stand-alone strategy for RTI prevention or treatment. Its role is better understood as supportive, targeted, and integrated into broader preventive care. For clinicians, this means that vitamin D is relevant in risk reduction and deficiency correction, but should not be overstated as a guaranteed anti-infective intervention.

4.4. Public health and social relevance

Vitamin D deficiency is a public health issue as much as a clinical one. It is common, relatively inexpensive to address, and socially patterned. This means it intersects with inequality, frailty, chronic disease burden, and access to preventive healthcare.

This broader relevance supports targeted public health strategies such as food fortification, risk-based supplementation, preventive outreach, and improved public health education.

These approaches may be worthwhile even if supplementation does not dramatically reduce RTI incidence at a universal population level. Correcting deficiency may still improve health resilience and reduce broader vulnerability among groups already burdened by poorer outcomes.

4.5. Strengths and limitations

This review integrates evidence from multiple domains—mechanistic, observational, randomised, and meta-analytic—while also addressing social and public health implications. It includes both positive and negative findings and avoids one-sided interpretation.

Its limitations include the narrative design and the fact that it does not provide a new pooled estimate. Interpretation also necessarily depends on the strengths and weaknesses of the available literature. In addition, some areas of the evidence base remain more extensive for biological plausibility than for definitive clinical efficacy.

4.6. Methodological considerations in interpreting the evidence

One of the main reasons why this literature remains difficult to interpret is the large variation in study design and methodological approach. Several trials included participants whose average baseline vitamin D levels were not clearly deficient. From a biological standpoint, supplementation is more likely to affect outcomes when it corrects a meaningful deficiency than when it is given to people who already have near-sufficient levels. This issue may partly explain why deficiency-focused paediatric trials appeared more favourable than broad adult trials.

Another major concern is supplementation strategy. Daily or weekly regimens may differ substantially from monthly high-dose regimens in their physiological effects. This means that studies cannot always be meaningfully pooled without attention to regimen differences. The fact that several null trials used intermittent high-dose administration further supports the idea that physiological replacement and bolus therapy should not be treated as equivalent interventions.

Outcome definition is also highly variable. Studies differ in whether they assess self-reported colds, physician-diagnosed infections, laboratory-confirmed viral illness, or hospitalisation. These are not equivalent outcomes and likely differ in both sensitivity and specificity to any potential effect of vitamin D. This may partly explain why some trials report no benefit on symptom-defined outcomes but still suggest effects on laboratory-confirmed infection or viral load.

Finally, crossover supplementation and imperfect adherence are especially relevant in vitamin D trials because supplements are widely available without prescription. These issues can reduce the difference between intervention and control groups, particularly in pragmatic designs. This was an important consideration in CORONAVIT and in other real-world trials in which control participants may independently initiate supplementation during follow-up.

These methodological considerations are not minor technical limitations. They are central to understanding why the evidence remains heterogeneous and why strong general conclusions should be avoided. A more precise interpretation of the literature requires careful attention to deficiency status, intervention strategy, population selection, and endpoint definition.

4.7. Future directions

Future work should focus on clearly deficient participants, achieved 25(OH)D concentrations rather than assigned dose alone, direct comparison of daily and bolus regimens, standardised clinically meaningful endpoints, and implementation strategies relevant to real-world high-risk populations.

There is also a need for more studies examining selected vulnerable groups rather than broadly mixed populations, since targeted interventions may be more informative than universal designs. In addition, implementation science approaches may be particularly useful in understanding whether deficiency correction can be integrated effectively into routine care and public health systems.

4.8. Implications for health education, communication, and preventive healthcare systems

The findings reviewed in this paper also have implications beyond clinical interpretation of trial results. One of the most important lessons from the vitamin D literature is that scientific uncertainty does not eliminate the public health relevance of deficiency. Rather, it shifts attention towards how evidence is communicated, how deficiency is identified in routine practice, and how preventive strategies are implemented at population level. This is particularly important in the case of respiratory tract infections, where prevention depends not only on medications or vaccines but also on broader health behaviour, educational access, and system-level support.

A recurring challenge in this field is the gap between scientific evidence and public understanding. Vitamin D is often discussed in oversimplified terms, either as a “natural immune booster” that can prevent infection in all circumstances or, conversely, as an ineffective intervention because some trials have failed to show significant benefit. Neither position accurately reflects the evidence. The available literature suggests that vitamin D deficiency is clinically meaningful, but that supplementation is not equally effective across all populations or settings. Public communication that ignores this distinction may contribute to confusion, inappropriate self-medication, or scepticism towards evidence-based prevention strategies.

This has important implications for health education. Educational interventions related to vitamin D should not focus exclusively on supplementation as a cure or universal protective measure. Instead, they should promote a broader understanding of deficiency risk, including factors such as limited sunlight exposure, low dietary intake, ageing, obesity, chronic illness, and social or environmental barriers to healthy behaviours. Education should also emphasise that vitamin D is one component of overall immune resilience and preventive health, rather than a substitute for vaccination, medical consultation, or treatment of acute illness.

In this context, digital health communication may play an increasingly important role. Public access to health information now occurs largely through online sources, social media, mobile applications, and digital campaigns. These tools can increase awareness but can also spread misleading or exaggerated claims, especially for low-cost and widely available interventions such as vitamin D. This creates an important opportunity for preventive healthcare systems to use digital platforms more effectively. Clear, accessible, and evidence-based communication about vitamin D could improve public understanding of who may be at risk of deficiency, what constitutes reasonable supplementation, and why deficiency correction is relevant even when the evidence for universal infection prevention remains mixed.

The reviewed studies also raise questions about screening and implementation in routine care. Since the strongest evidence concerns the risks associated with low vitamin D status rather than the universal effectiveness of supplementation, healthcare systems may benefit more from a targeted approach than from broad untailored supplementation campaigns. Such an approach would focus on groups known to be at increased risk of deficiency, including older adults, institutionalised individuals, people with limited mobility, populations living at higher latitudes, people with darker skin pigmentation in low-sunlight settings, and

individuals with obesity, malabsorption, or chronic disease. In these groups, assessment of vitamin D status and correction of deficiency may be more clinically meaningful than universal, non-selective preventive advice.

From a health systems perspective, this targeted strategy may also be more cost-effective. Respiratory tract infections generate a large burden through outpatient consultations, antibiotic prescriptions, sick leave, emergency visits, and hospital admissions. Even if vitamin D supplementation does not produce a dramatic reduction in RTI incidence across the general population, identifying and correcting deficiency in high-risk groups could still contribute to improved health outcomes and reduced downstream healthcare burden. This is particularly relevant where deficiency overlaps with frailty, chronic disease, and limited access to preventive services. In such cases, vitamin D deficiency correction may function as a low-cost adjunct within a broader package of preventive care.

The issue is also relevant to social determinants of health. Vitamin D deficiency is not distributed randomly across society. It is shaped by structural factors such as housing conditions, occupational patterns, food access, environmental exposure, poverty, urban design, and chronic disease burden. People living in densely populated urban areas, working indoors, or experiencing food insecurity may be less able to maintain adequate vitamin D status through lifestyle alone. Likewise, older adults and socially isolated individuals may have reduced access to both nutritional guidance and routine preventive assessment. In this sense, vitamin D deficiency can be viewed not only as a nutritional issue, but also as an indicator of broader social and environmental disadvantage.

For this reason, discussions of vitamin D and RTIs should not be limited to the language of micronutrient supplementation alone. They should also consider equity-oriented public health strategies, including food fortification, preventive primary care outreach, health literacy initiatives, and context-sensitive supplementation guidance. This broader perspective aligns particularly well with journals and readers interested in the interaction between health, society, and policy.

Another practical implication concerns the design of preventive recommendations. The reviewed evidence repeatedly suggests that supplementation effects may vary according to dose and frequency. Daily or weekly physiological regimens appear more promising than large intermittent bolus doses, yet public messaging rarely reflects this distinction. Better communication of such nuances could improve adherence, reduce misuse of excessive dosing, and align community-level behaviour more closely with the available evidence. This is especially relevant in the digital era, where people often self-manage supplementation without professional guidance.

Finally, the vitamin D literature illustrates a broader challenge in modern preventive medicine: how to act responsibly when biological plausibility is strong, observational evidence is consistent, but randomised intervention data remain heterogeneous. In such situations, healthcare systems and policymakers must often decide whether to wait for perfect evidence or to implement proportionate, low-risk preventive measures in the meantime. With vitamin D, the strongest justification lies not in framing supplementation as a universal anti-infective intervention, but in recognising deficiency as a common and remediable condition with potential consequences for respiratory and general health.

In summary, the social and public health significance of vitamin D in respiratory infection lies in three areas: first, the need for better health education and more accurate communication; second, the importance of targeted prevention in groups at high risk of deficiency; and third, the opportunity to integrate deficiency correction into broader preventive healthcare and equity-oriented policy approaches. These implications do not depend on proving that vitamin D supplementation prevents every respiratory infection.

Rather, they arise from the broader reality that maintaining nutritional adequacy is a fundamental part of resilient and preventive health systems.

5. Conclusions

Vitamin D deficiency is consistently associated with increased susceptibility to respiratory tract infections and with less favourable respiratory outcomes. Mechanistic studies strongly support a biologically plausible role for vitamin D in airway host defence, immune regulation, and inflammatory control. However, randomised evidence regarding supplementation remains heterogeneous. Earlier meta-analyses suggested modest protective effects, particularly in deficient populations and with daily standard-dose regimens, whereas more recent large trials and updated meta-analyses have shown smaller, inconsistent, or statistically non-significant overall effects.

Current evidence therefore does not support a universal claim that vitamin D supplementation prevents or treats respiratory tract infections in all individuals. It does, however, support the clinical importance of

identifying and correcting vitamin D deficiency, particularly in high-risk populations. From a broader perspective, vitamin D deficiency should also be understood as a socially patterned and potentially modifiable determinant of health, with relevance to prevention, health equity, and public health planning.

In summary, vitamin D should not be overstated as a universal respiratory intervention, but neither should its importance be underestimated. The most evidence-based position is that maintaining adequate vitamin D status is a reasonable component of preventive healthcare and may contribute to respiratory resilience, especially where deficiency is common and vulnerability is high.

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