JĘTASIEWICZ, Igor, GÓRSKI, Szymon, OKUPNIAREK, Joanna, BARTOSIK, Michalina, OBORSKI, Michał, OBORSKI, Krzysztof, MIARCZYŃSKI, Jakub, and BARCZYŃSKA, Katarzyna. Vitamin D in Injury Risk and Healing – A Comprehensive Review. Journal of Education, Health and Sport. 2026;87:67737. eISSN 2391-8306.
https://dx.doi.org/10.12775/JEHS.2026.87.67737
https://apcz.umk.pl/JEHS/article/view/67737

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 25.12.2025. Revised: 02.01.2026. Accepted: 14.01.2026. Published: 15.01.2026.

Vitamin D in Injury Risk and Healing – A Comprehensive Review

Igor Jętasiewicz[1]
ORCID: 0009-0008-3351-6392
igor.jetasiewicz@icloud.com

Szymon Górski[2]
ORCID: 0009-0006-1411-6524
szymon.gorski13@gmail.com

Joanna Okupniarek[1]
ORCID: 0009-0007-2446-4810
asiaokup22@wp.pl

Michalina Bartosik[3]
ORCID: 0009-0008-8541-1998
michalinabartosik03@gmail.com

Michał Oborski[1]
ORCID: 0009-0009-6170-6756
michal.oborski@wp.pl

Krzysztof Oborski[4]
ORCID: 0009-0004-4366-6897
krzysiek.oborski@wp.pl

Jakub Miarczyński[1]
ORCID: 0009-0004-5746-4786
jakub.miarczynski1@gmail.com

Katarzyna Barczyńska[5]
ORCID: 0009-0005-1199-0980
Kasia.barczynska.8900@gmail.com

* Correspondence: igor.jetasiewicz@icloud.com

[1] Faculty od Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Jagiellońska 13/15, 85-067 Bydgoszcz, Poland
[2] WSPSP - 'PROVINCIAL DENTISTRY' LIMITED LIABILITY COMPANY, ul. Zdrowotna 6, 85-826 Bydgoszcz, Poland
[3] Medical University of Łódź, al. Tadeusza Kościuszki 4, 90-419 Łódź, Poland.
[4] Department of Internal Medicine, Diabetology and Clinical Pharmacology of the Central Clinical Hospital of the Medical University of Łódź, ul. Pomorska 251, 92-213 Łódź, Poland
[5] III Dr Karol Jonscher Municipal Hospital in Łódź, ul. Milionowa 14, 90-309 Łódź

ABSTRACT

In an era of an aging population, vitamin D deficiencies constitute a significant clinical problem. Its pleiotropic effects encompass key reparative processes in soft and bone tissues, as well as modulation of the nervous and immune systems, suggesting its potentially important role in injury prevention and healing support. The aim of this review was to systematically analyse and synthesise current knowledge regarding: (1) the molecular mechanisms of vitamin D action in repair processes, (2) the efficacy of its supplementation in the context of post-injury healing, and (3) the clinical consequences of its deficiency. The literature review was conducted according to the PRISMA methodology. The PubMed, Scopus, and Web of Science databases were searched using defined keywords related to vitamin D, wound healing, bone regeneration, and trauma. Original and review articles published between 2010 and 2024 were analysed. The synthesis confirmed the key role of

vitamin D in regulating cell proliferation, angiogenesis, extracellular matrix synthesis, and inflammation modulation. Clinical data indicate that supplementation is most beneficial for patients with pre-existing deficiency, significantly reducing the risk of complications and improving healing parameters. Groups at particular risk of deficiency requiring monitoring include the elderly, burn victims, diabetics, individuals with dark skin phototypes, and those with malabsorption disorders. For patients with normal or high baseline 25(OH)D levels, the benefits of supplementation are limited or insignificant. Optimising vitamin D levels is a significant, modifiable factor supporting tissue healing, especially in deficient patients. Routine assessment of vitamin D status and targeted supplementation in risk groups should be an integral part of comprehensive post-traumatic care. Further prospective randomised trials are needed to precisely determine optimal doses and supplementation regimens for different types of injuries.

Introduction. Vitamin D, thanks to the VDR receptor present in cells involved in healing, plays a key role in tissue regeneration by modulating the processes of proliferation, immune response and matrix synthesis. Despite widespread deficiencies in populations at risk of injury (the elderly, people with burns, diabetes), there are no clear clinical recommendations for supplementation in this context. This review aims to systematise knowledge on the molecular mechanisms of vitamin D action, the effectiveness of its supplementation in improving post-traumatic healing, and the clinical consequences of its deficiency. The presented synthesis is intended to provide evidence-based guidelines for diagnosis and treatment, as well as to identify areas requiring further research.

Purpose of the work. This review aims to summarise the current state of knowledge on the role of vitamin D in wound healing and tissue regeneration after injuries. In particular, it focuses on analysing the consequences of its deficiency in a clinical context, taking into account the healing of bone fractures, burns and soft tissue injuries. An additional objective is to discuss the rationale and strategies for supplementation of this vitamin, including the determination of its optimal serum concentration necessary to support repair processes. Since vitamin D has a pleiotropic effect, the paper emphasises its multidirectional impact on numerous physiological pathways beyond calcium-phosphate homeostasis, which is fundamental to the effective treatment of patients with tissue damage.

Materials and methods. An analysis of scientific articles available on PubMed and Google Scholar was conducted using the following keywords: Vitamin D in burns and injuries, vitamin D injuries, vitamin D burns, vitamin D supplementation, vitamin D in orthopaedic surgery, vitamin D physiology, pleiotropic effects of Vitamin D.

Results. A review of the literature indicates that vitamin D deficiency affects 57.9–83.2% of the Polish population, rising to over 73.5% during winter months. Its clinical consequences are observed in the majority of the population in temperate climates, particularly in high-risk groups such as the

elderly, burn patients, and individuals with diabetes. The most commonly reported symptoms include musculoskeletal pain, muscle weakness, and increased susceptibility to low-energy fractures. The diagnostic gold standard remains measurement of serum 25-hydroxyvitamin D [25(OH)D] concentration. Supplementation with cholecalciferol (vitamin D3) in deficient patients resulted in significantly accelerated wound healing, reduced infection risk, improved fracture consolidation, and enhanced muscle regeneration. The greatest benefits were observed in individuals with baseline deficiency, while patients with normal or high vitamin D levels showed limited additional improvement.

Keywords: vitamin D, cholecalciferol, wound healing, bone regeneration, tissue repair, supplementation, deficiency, trauma

1. PHYSIOLOGY OF VITAMIN D – BIOCHEMISTRY, ABSORPTION, SKIN SYNTHESIS AND FUNCTIONS IN THE HUMAN BODY

Vitamin D, classified as a lipophilic compound, occupies a special position among compounds referred to as vitamins. Unlike most of them, it can be effectively synthesised endogenously in the skin under the influence of ultraviolet B (UVB) radiation as a result of the non-enzymatic photoconversion of 7-dehydrocholesterol – a derivative of the cholesterol biosynthesis pathway – to cholecalciferol (vitamin D3). Thus, it essentially acts as a prohormone, and its trace supply from the diet (mainly in the form of vitamin D3 and ergocalciferol – vitamin D2 of plant origin) is supplementary. The efficiency of both dietary absorption and endogenous synthesis is modulated by numerous factors. Intestinal absorption of vitamin D depends on the presence of fats in food, and its average efficiency is about 78%, with no significant differences between the D2 and D3 forms. During digestion, vitamin D is esterified with fats from food and then hydrolysed by pancreatic enzymes, after which it is incorporated into micelles – a key step for its bioavailability. This process is modulated, among other things, by the presence of sterols (cholesterol and phytosterols), which dose-dependently inhibit the incorporation of vitamin D into micelles, as well as by high concentrations of vitamins E, K and A, and to a lesser extent by the composition of fatty acids. Other carriers may also participate in transport, e.g. β-lactoglobulin found in milk. [1,2,3]. Specific factors affecting absorption are listed in Table 1. Endogenous skin synthesis depends on geographical and environmental factors, which explains the higher incidence of deficiency diseases, such as rickets

in children and osteomalacia in adults, in regions with limited exposure to UVB radiation. In temperate climates (e.g. Poland), serum 25(OH)D concentrations are higher in summer and autumn and lower in winter and spring. The effectiveness of synthesis is influenced by latitude, season, skin pigmentation, age, clothing and the use of UV filters. [1,2,4]. The main physiological effect of the active form of vitamin D – 1,25-dihydroxycholecalciferol (calcitriol) – focuses on maintaining systemic calcium and phosphate homeostasis by increasing intestinal calcium absorption, modulating its resorption from bones and reabsorption in the renal tubules. The key mechanism of action is genomic: after binding to the nuclear receptor (VDR), the calcitriol complex regulates the expression of numerous genes (estimated at approximately 3,000) involved not only in mineral metabolism, but also in the processes of cell proliferation, differentiation and apoptosis. This action is carried out in an autocrine and paracrine manner in many tissues, including the skin, muscles and bones. Due to the widespread expression of VDR in the body, vitamin D has a pleiotropic effect, the spectrum of which is presented in Table 2. [1,2,5,6]. The metabolism of vitamin D into its active form is a multi-step process. Cholecalciferol (synthesised in the skin or supplied through diet) undergoes hydroxylation at position 25 in the liver, leading to the formation of 25-hydroxyvitamin D (calcidiol). This form, circulating mainly in complex with vitamin D-binding protein (DBP), is the main biomarker of the body's supply and a stable reserve pool. Final activation occurs primarily in the kidneys by hydroxylation at position 1α, catalysed by the enzyme 1α-hydroxylase (CYP27B1), resulting in the formation of biologically active calcitriol. It should be emphasised that CYP27B1 expression also occurs in many non-renal tissues (including immune system cells, vascular endothelium, muscles), where local calcitriol synthesis performs autocrine and paracrine functions unrelated to systemic calcium-phosphate homeostasis. An alternative pathway for calcidiol metabolism is hydroxylation at position 24, leading to the formation of a less active metabolite, 24,25-dihydroxyvitamin D, which is part of the catabolic and elimination pathway.

Table 1. Factors affecting vitamin D absorption [1,2,3,7]

Category of the factor	Specific factor	Impact on vitamin D absorption	Mechanism/ Comments
Nutritional factors	Type of fat in the meal		
	Long-chain fatty acids	Inhibits	
	Oleic acid (monounsaturated)	Improves	Optimises the formation of chylomicrons and the secretion of vitamin D into the lymph.
	Phytosterols (e.g. in fortified products)	Inhibits	They hinder incorporation into micelles and uptake by enterocytes.
	Carrier supplements (PEG 1000 tocopheryl succinate, cyclodextrins)	Improves	By forming micelles or guest-host complexes, they increase bioavailability.
Special patient groups / Clinical conditions	Malabsorption conditions (Crohn's disease, post-bypass condition)	Significantly reduced	Up to 30% during remission. Recommendation: Supplementation with 25-hydroxyvitamin D (calcifediol), which has higher bioavailability, is preferred.

	Obesity	Inihibits	Requires higher doses due to sequestration in adipose tissue and possibly reduced absorption.
	Chronic Kidney Disease	Inhibits	Loss of vitamin D-binding protein in urine, reduced synthesis of 1,25 OH D3, restrictive diet
Drug interactions	Drugs that interfere with vitamin D metabolism (glucocorticosteroids, anticonvulsants, antifungals, antiretrovirals)	Inhibits	

Table 2. Pleiotropic effects of vitamin D, including mechanisms [5,6,8]

Role	Clinical effect
Mineral homeostasis and the skeletal system	• Regulation of calcium and phosphate metabolism (stimulation of calcium absorption in the intestine and calcium reabsorption in the renal tubules, regulation of phosphorus absorption) • Prevention and treatment of rickets, osteomalacia, osteoporosis (stimulation of osteoblasts, maintenance of normal bone mineralisation) • Reduction of the risk of low-energy bone fractures • Reduction of bone pain and deformities • Prevention of aseptic bone necrosis
Effects on muscles	• Anabolic effect on skeletal muscles – treatment and prevention of myopathy • Reduction of the risk of falls, improvement of muscle strength and walking speed [8]
Cardiovascular system	• Reduced risk of hypertension (hypotensive effect – inhibition of the RAA system) • Reduced risk of ischaemic heart disease, left ventricular hypertrophy, systolic heart failure • Inverse correlation with calcification in the coronary arteries • Positive effect on intima-media thickness (IMT) of arteries in childhood (prevention of future diseases)
Immune system	• Reduction in the incidence of recurrent infections (strengthening of the antibacterial response [activation of the TLR2/CYP27B1/VDR pathway and production of the antibacterial protein LL37]); maintenance of the skin barrier as a natural barrier protecting against the penetration of pathogens – increased collagen synthesis [5] • Immunomodulatory effect in autoimmune diseases (effect on increasing the population of Treg lymphocytes [suppressive effect], direct inhibition of B lymphocyte proliferation and immunoglobulin production, promotion of Th2-dependent response and IL-17 production by Th17 lymphocytes, inhibition of the Th-1-dependent pathway)

Autoimmune diseases	• Risk reduction or symptom easing: multiple sclerosis (fewer flare-ups and less severe symptoms), type 1 diabetes, rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's disease, autoimmune skin diseases
Nervous system	• Neuroprotective effect (delaying changes in the hippocampus, increasing glutathione levels – protection against oxidative stress) • Improvement of verbal functions in Parkinson's disease • Reduction of the risk of neurocognitive disorders (Alzheimer's disease, autism) • Deficiency is a risk factor for stroke, reduces the risk of blood-brain barrier damage and cerebral oedema [9]
Metabolic processes	• Positive effect on glucose metabolism (by stimulating insulin receptor expression and thus improving tissue sensitivity to insulin, affecting pancreatic beta cell function) • Positive effect on obesity and metabolic syndrome • Positive effect on lipid disorders
Neoplasms	• Protective effect – reducing the risk of malignant tumours developing in various areas of the body (inhibiting excessive proliferation, stimulating differentiation, protecting the genome from mutation culmination, promoting apoptosis, inhibiting neoangiogenesis)
Pregnancy	• Reducing the risk of perinatal complications
Skin	• Positive effect in atopic dermatitis (through its impact on the skin barrier and immune response)
General	• Possible impact on reducing overall mortality

2. EPIDEMIOLOGY AND CONSEQUENCES OF VITAMIN D DEFICIENCY

Vitamin D deficiency is a significant global public health problem, including in the Polish population. Epidemiological data indicate its high prevalence. In Poland, deficiency affects between 57.9% and 83.2% of the general population, with the percentage reaching at least 73.5% in the winter months. [6,10,11]. On a European scale, it is estimated that this problem affects an average of 50–70% of the population. Observations in the paediatric population are particularly worrying.

Studies indicate that 40–45% of children visiting orthopaedic clinics may have vitamin D deficiency, and among patients eligible for surgical treatment, this percentage rises to as high as 90%. [12]. The classification of vitamin D status based on serum 25-hydroxyvitamin D [25(OH)D] concentration is presented in Table 3.

Table 3. Classification of vitamin D status based on serum 25(OH)D concentration.

Condition	25(OH)D concentration
Deficit (severe deficiency)	0–10 ng/ml (0–25 nmol/l)
Deficiency	>10–20 ng/ml (>25–50 nmol/l)
Hypovitaminosis D (insufficiency)	>20–30 ng/ml (>50–75 nmol/l)
Recommended concentration (optimal)	>30–80 ng/ml (75–200 nmol/l)
Toxic concentration	>100–150 ng/ml (>250 nmol/l)

The consequences of vitamin D deficiency are systemic, resulting from its pleiotropic effects. The basic pathophysiological mechanism is associated with calcium-phosphate homeostasis disorder. Reduced intestinal calcium absorption leads to secondary hyperparathyroidism, increased bone resorption and skeletal demineralisation. Clinically, this manifests as osteomalacia in adults and rickets in children, osteoporosis, muscle weakness, increased risk of falls and low-energy fractures. Patients often report non-specific, atypical musculoskeletal pain. Beyond the skeletal system, vitamin D deficiency negatively affects the functioning of other organs and tissues. Its important role in modulating the immune response (innate and acquired) translates into increased susceptibility to infections. A link has also been observed with a higher risk of developing cardiovascular diseases, including hypertension. The anti-proliferative and pro-differentiating effects of vitamin D determine its oncoprotective potential; its deficiency correlates with an increased risk of certain cancers and may be associated with poorer tolerance of oncological treatment (radiotherapy and chemotherapy). This mechanism, partly related to the protection of DNA from oxidative damage, is also important for repair processes, which may result in impaired healing of wounds and ulcers.

Scientific reports also indicate the potential impact of deficiency on an increased risk of neuropathy [13].

3. VITAMIN D SUPPLEMENTATION AND DIETARY INTAKE

As mentioned earlier, the concentration of 25-hydroxyvitamin D [25(OH)D] in the body depends more on skin synthesis than on dietary absorption. In temperate climates, where exposure to UVB radiation is limited, especially in the autumn and winter months, supplementation becomes a necessity. This is because meeting the daily requirement of 800 IU through diet alone is virtually impossible – it would require consuming about 40 eggs or two large portions of fatty fish per day [14]. The main dietary sources of vitamin D include fatty fish (salmon, mackerel, herring) and their products (e.g. cod liver oil), egg yolks, and, to a lesser extent, meat and liver. Despite the theoretical availability of these products, population studies – for example, those conducted in Slovenia – indicate a widespread insufficient intake of vitamin D among all social groups [15]. There are two main forms available in supplements: ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3). Scientific evidence clearly indicates that D_3 is more effective in raising and maintaining serum 25(OH)D concentrations. [16, 17]. Furthermore, D_2 supplementation may paradoxically lower endogenous 25(OH)D_3 levels, whereas D_3 leads to a stable increase in total 25(OH)D concentration [16]. For this reason, D_3 is the recommended form for people with deficiency, after injuries, surgical procedures and in other high-risk groups [16, 17, 18]. The effectiveness of supplementation is modulated by several key factors:

- **Body mass index** (BMI)- overweight or obese individuals (BMI ≥25 kg/m²) have a reduced response to supplementation and often require higher doses [16].
- **Baseline 25(OH)D concentration**: Lower baseline values (e.g. <30 nmol/L) are associated with a better response to supplementation [16].
- **Age and clinical condition:** Older people, those with malabsorption disorders, and those who have suffered extensive burns or serious injuries have increased requirements, often requiring doses 2-3 times higher than the general preventive recommendations [19, 20].
- **Duration of supplementation**: Longer periods of supplementation (more than 3 months) help maintain a stable target level of 25(OH)D [21].

Method of administration: Daily oral supplementation is considered more physiological and effective than bolus doses (e.g. monthly or quarterly) [16, 22]. The primary biomarker used to assess the body's vitamin D status is the concentration of 25-hydroxyvitamin D [25(OH)D] in serum [19, 23]. However, it should be remembered that in acute conditions, such as extensive burns or injuries, the determination of total 25(OH)D may give a false result due to a rapid decrease in the concentration of binding protein (DBP). In such situations, measurement of the free (bioavailable) fraction of vitamin D is considered [6, 18]. Detailed recommendations for doses and therapeutic goals for different patient groups are summarised in Table 4.

Table 4. Recommendations for vitamin D supplementation

Group / Goal	Dose / dosage schedule	Target concentration of 25(OH)D	Comments / References
GENERAL PREVENTION			
Newborns and infants	400–600 IU daily	>20 ng/mL (>50 nmol/L)	Standard supplementation [19, 24]
Children and young people (1–18 years old)	600–1000 IU daily	>20 ng/mL (>50 nmol/L)	Depending on body weight and dietary intake [19, 25]
Adults (19–65 years old)	800–2000 IU daily	20–30 ng/mL (50–75 nmol/L)	During the autumn and winter months or when there is insufficient exposure to sunlight [19, 24, 25]
Senior citizens (>65 years old)	800–2000 IU daily	>30 ng/mL (>75 nmol/L)	Due to reduced skin synthesis [19, 24, 25]
TREATMENT OF DEFICIENCY			

Adults (daily schedule)	6,000 IU daily for 8 weeks, then 1,500–2,000 IU daily	>30 ng/mL (>75 nmol/L)	According to the guidelines of the Endocrine Society [19]
Adults (weekly regimen)	50,000 IU/week for 8 weeks, followed by a maintenance dose	>30 ng/mL (>75 nmol/L)	Alternative regimen [19]
GROUPS-SPECIAL RISK			
Patients after burns/trauma	Individually, often higher doses (e.g. 100 IU/kg/day in children, up to 6000 IU/day in adults)	>30 ng/mL (>75 nmol/L)	Necessary monitoring of 25(OH)D concentration [18, 20, 26]
Perioperative period	E.g. 300,000 IU once 2 weeks before surgery (in case of deficiency)	>30 ng/mL (>75 nmol/L)	Reduces the risk of wound infection [26]
Athletes	1,500–4,000 IU/day; therapeutic doses in cases of deficiency	40–50 ng/mL (100–125 nmol/L)	For optimal muscle function and regeneration [27, 28]
Chronic wounds e.g bedsores, diabetic foot syndrome	E.g. 50,000 IU every 2 weeks as adjunctive therapy	>30 ng/mL (>75 nmol/L)	

4. VITAMIN D EFFECTS ON WOUND HEALING

4.1 The mechanism of action of vitamin D in the healing process of soft tissue injuries

The biologically active form of vitamin D, 1,25-dihydroxycholecalciferol (calcitriol), has a multidirectional effect on the tissue repair process by binding to a high-affinity nuclear receptor (VDR – vitamin D receptor). The VDR receptor is expressed by most cells involved in the healing cascade, including keratinocytes, fibroblasts, macrophages, endothelial cells and nervous system cells [14,23,29,30]. After binding to its ligand, the VDR complex dimerises with the retinoid X receptor (RXR) and binds to vitamin D response elements (VDRE) in the promoter regions of target genes, thereby regulating the transcription of hundreds of genes involved in key regenerative processes [14,23]. The main mechanism of action is based on immunomodulation and inflammation control. Vitamin D strengthens the innate immune response by inducing the expression of peptides with antimicrobial properties, such as cathelicidin (LL-37) and defensins. These peptides are the first line of defence, directly neutralising pathogens within the wound, which prevents early infections [7,19,26,29,31]. At the same time, by modulating the phenotype of macrophages, vitamin D promotes the transition from the pro-inflammatory M1 phenotype to the anti-inflammatory and reparative M2 phenotype, accelerating the resolution of inflammation [32,33]. A key element of its anti-inflammatory action is the inhibition of the nuclear factor kappa B (NF-κB) signalling pathway, which leads to a reduction in the production and secretion of major pro-inflammatory cytokines, including tumour necrosis factor alpha (TNF-α), interleukin 6 (IL-6) and interleukin 1 beta (IL-1β) [32,34,36]. In the proliferative phase, vitamin D stimulates re-epithelialisation by directly stimulating the proliferation and migration of keratinocytes at the wound edges [29,35]. This mechanism is associated with the regulation of intercellular junction integrity (e.g. through modulation of E-cadherin expression) and activation of the β-catenin signalling pathway, which is essential for cell adhesion and movement [35]. In addition, vitamin D is fundamental for granulation tissue formation. Activation of VDR on skin fibroblasts stimulates their proliferation and the biosynthesis of type I collagen, the main structural protein of the extracellular matrix of newly forming tissue [29,30,36]. It ensures the balance between matrix synthesis and degradation by modulating the expression of matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs), thus preventing the formation of abnormal, excessively granulating or poorly resistant scars [29,33]. Another key aspect is the stimulation of angiogenesis. Vitamin D promotes the formation of a new vascular network in granulation tissue, which is essential for the metabolic supply of regenerating tissue. This mechanism involves the stabilisation of hypoxia-inducible factor 1-alpha (HIF-1α) and the activation of the vascular endothelial growth factor (VEGF) signalling pathway and its receptor VEGFR2 [32,33]. In addition, vitamin D has a cytoprotective effect. By activating the Nrf2 (nuclear

factor erythroid 2–related factor 2) pathway, it strengthens intracellular antioxidant defence mechanisms, reducing the level of reactive oxygen species (ROS) and lipid peroxidation products, thus protecting repair cells from oxidative stress [7,32,37]. In models of tissue damage (e.g. radiation, ischaemic), it has been shown that vitamin D, acting through VDR, inhibits apoptosis pathways (e.g. by inhibiting caspases), increasing the survival of critical stem and progenitor cell populations [38,33,39]. Vitamin D also plays a role in the prevention of pathological healing. It inhibits the epithelial-mesenchymal transition (EMT) process, in which epithelial cells lose their phenotypic identity and transform into myofibroblasts that produce excessive amounts of collagen, which is the basis for fibrosis and the formation of hypertrophic scars and keloids [38]. Clinical observations confirm that low serum concentrations of 25-hydroxyvitamin D [25(OH)D] correlate with more severe and abnormal scarring [18].

4.2 The effects of vitamin D3 supplementation on skin injuries

Clinical studies clearly confirm that cholecalciferol (vitamin D3) supplementation in patients with vitamin D deficiency significantly accelerates the healing of skin wounds, especially chronic ones [29,33]. In a randomised study, patients with chronic wounds and vitamin D deficiency (25(OH)D <30 ng/mL) received 6000 IU/day of cholecalciferol. After 5 weeks, the supplemented group achieved a mean 25(OH)D level of 36.75 ng/mL, and wound healing time was reduced to 15.6 days. In the control group (standard care only), the 25(OH)D level was 29.6 ng/mL, and healing took an average of 26.2 days. In addition, complete wound reduction occurred in the third week in the intervention group and only in the fifth week in the control group [33]. Similar results were obtained in studies on diabetic foot ulcers. High doses of vitamin D3 (6,800 IU/day) led to the healing of 70% of wounds, while at a low dose (800 IU/day) – only 35% of wounds [36]. Another study showed that supplementation with 4000 IU/day for 12 weeks resulted in a greater reduction in ulcer depth and area compared to placebo [36]. The beneficial effect of supplementation is also observed in cases of oral mucosal ulcers, where the combination of topical treatment with vitamin D supplementation led to healing within 3 weeks [3].

4.3 The effects of vitamin D3 supplementation in injuries involving processes that disrupt physiological healing processes

Vitamin D, and in particular its cholecalciferol (D3) form, plays a key role in modulating tissue repair processes. Its deficiency is common in pathological conditions such as diabetes, extensive burns or cancer, which in themselves significantly impair physiological healing. In these populations, vitamin D3 supplementation shows therapeutic potential by alleviating the negative consequences of injuries.

In the context of diabetes, characterised by chronic inflammation and impaired angiogenesis, vitamin D deficiency correlates with poorer healing of diabetic foot ulcers (DFUs) and a higher risk of amputation [32]. Preclinical studies in a mouse model have shown that vitamin D supplementation significantly accelerates the closure of diabetic wounds by improving re-epithelialisation, collagen deposition and angiogenesis. The key mechanism of action is the inhibition of the pro-inflammatory NF-κB pathway, which leads to a reduction in cytokine expression (TNF-α, IL-6, IL-1β) and accelerated resolution of inflammation, regardless of the effect on glycaemic control [34]. In clinical trials involving patients with diabetic foot ulcers, high-dose vitamin D3 supplementation (e.g., 50,000 IU every 2 weeks) significantly improved ulcer dimensions and inflammatory parameters [13]. Furthermore, vitamin D deficiency exacerbates diabetic peripheral neuropathy and impairs nerve regeneration, which further delays healing [32, 15].

In patients with severe burns, vitamin D deficiency is almost universal and multifactorial in nature, resulting from both acute phase reactions (fluid displacement, decrease in carrier proteins) and permanent impairment of its synthesis in the skin in scarred tissue [18,20,36]. Low 25(OH)D levels at admission are a strong predictor of poorer treatment outcomes, correlating with longer hospital and ICU stays, higher infection rates and more severe scarring [18,30,36]. Randomised clinical trials indicate that supplementation during the acute phase is effective in normalising 25(OH)D levels, and vitamin D3 appears to be more effective than D2 in maintaining long-term stores [18]. Correction of deficiency is associated with beneficial trends such as reduced insulin requirements, shorter duration of sepsis, and less severe hypertrophic scarring [18]. However, standard doses (e.g., 400-600 IU/day) are often insufficient, and persistent post-traumatic osteopenia suggests the need for more aggressive, personalised supplementation protocols [18, 49, 51].

In cancer and during its treatment (e.g. radiotherapy), vitamin D deficiency is common and is associated with complications [13, 8]. The action of vitamin D is particularly important here in the context of protecting and repairing healthy tissues subjected to planned damage. Preclinical evidence indicates that the active form of vitamin D ($1,25(OH)_2D_3$) and its analogues (e.g. paricalcitol) have a protective effect on tissue barriers, such as the endothelium or intestinal epithelium, by strengthening intercellular connections (e.g. VE-cadherins) and inhibiting apoptosis of stem/progenitor cells [39,40] . In a clinical study of patients undergoing pelvic radiotherapy, vitamin D deficiency was an independent risk factor for more severe radiation proctitis [13]. These mechanisms include not only anti-inflammatory and antioxidant effects, but also direct stimulation of epithelial cell proliferation and migration, accelerating tissue continuity restoration [38,40].

4.4 How does vitamin D affect the healing of injuries in the central nervous system? - mechanism and effects of supplementation

Vitamin D exhibits clear neuroprotective and pro-regenerative potential in the context of central nervous system (CNS) damage, acting through multidirectional mechanisms that include modulation of neuroinflammation, protection against oxidative stress, support for blood-brain barrier integrity, and promotion of repair processes such as remyelination. The primary mechanism of action is the activation of the vitamin D receptor (VDR), which is present in neurons, glial cells, and the endothelium of cerebral vessels [14, 40]. VDR activation leads to the regulation of gene transcription involved in the response to damage. A key pathway is the inhibition of the pro-inflammatory TLR4/MyD88/NF-κB cascade, which is overactivated after injury and exacerbates secondary damage to nerve tissue. Vitamin D effectively suppresses this pathway, reducing the production of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) while promoting the transition of microglia from the destructive M1 phenotype to the reparative M2 phenotype [37]. In addition, vitamin D strengthens antioxidant defence by increasing the activity of enzymes such as superoxide dismutase (SOD) and reducing lipid peroxidation (MDA) [37]. Vitamin D also plays a key role in protecting the integrity of the blood-brain barrier (BBB), the damage of which is central to the pathophysiology of many CNS injuries. In vitro studies on brain endothelial cells have shown that the active form $1,25(OH)_2D_3$, acting through VDR, prevents increased BBB permeability induced by ischaemia/reoxygenation. This mechanism involves inhibition of reactive oxygen species (ROS) production, suppression of NF-κB activation, reduction of MMP-9 metalloproteinase expression, and protection of tight junction proteins (ZO-1, claudin-5, occludin) [9]. In the context of structural regeneration, vitamin D supports key repair processes. In a model of traumatic spinal cord injury (TSCI), cholecalciferol supplementation promoted remyelination by suppressing the c-Myc oncogene in oligodendrocyte precursor cells (OPCs). Inhibition of c-Myc shifts the cellular balance from proliferation to differentiation of OPCs into mature, myelinating oligodendrocytes, resulting in improved myelin sheath integrity and better recovery of motor function [41]. Furthermore, vitamin D, via VDR, protects stem and progenitor cells from damage-induced apoptosis (e.g., radiation damage), which is fundamental to tissue regenerative capacity [42]. The clinical effects of supplementation confirm these mechanisms. In traumatic brain injury (TBI), a single high dose of vitamin D (120,000 IU) administered in the acute phase significantly improved the level of consciousness (GCS scale), reduced the duration of mechanical ventilation and ICU stay, which correlated with a reduction in the level of pro-inflammatory TNF-α [43]. In another study, supplementation in patients with moderate TBI and deficiency improved long-term functional (GOS-E) and cognitive (MMSE) outcomes, accelerating the rate of recovery [44]. In acquired severe brain injury (sABI), low 25(OH)D levels strongly correlated with greater functional impairment,

suggesting its role as a prognostic factor or therapeutic target [45]. In stroke, supplementation in older women not only reduced the risk of falls and fractures through increases in muscle strength and type II fibre diameter, but also, as mechanisms suggest, may have supported the repair of damaged nerve tissue [46].

4.5 The effect of vitamin D on the healing of injuries in musculoskeletal structures.

Vitamin D is a key regulator of musculoskeletal homeostasis, and its deficiency is a significant independent risk factor for both the occurrence of injuries and abnormal repair processes. The action of vitamin D is mediated by the VDR receptor present in osteoblasts, chondrocytes and muscle cells, and indirectly by its effect on calcium and phosphate metabolism. Deficiency leads to a cascade of pathophysiological changes that significantly increase susceptibility to injury. First and foremost, it causes atrophy of type II muscle fibres, which are responsible for explosive strength and postural stability, resulting in weakened muscle strength, impaired balance and prolonged neuromuscular reaction time, ultimately increasing the risk of falls. Meta-analyses confirm that supplementation at doses of 700–1000 IU/day or achieving a 25(OH)D concentration above 24 ng/mL reduces the risk of falls by 19–23% [19, 27].

At the same time, deficiency in athletes correlates with a higher rate of muscle injuries, especially in the lower limbs and the sciatic-shin area [47]. Furthermore, deficiency impairs the absorption of calcium and phosphate, inducing secondary hyperparathyroidism, which leads to increased bone resorption and defective mineralisation (osteomalacia or rickets). As a result, the bone becomes more fragile and susceptible to both stress and low-energy fractures, which is particularly dangerous in the geriatric population, where fractures are often the result of the synergy of osteoporosis and falls [14,25,48]. Importantly, the injury or surgery itself activates locally vitamin D-dependent pathways in the muscle, and its deficiency impairs protein biosynthesis and muscle mass regeneration, hindering recovery after injury [28]. Correcting vitamin D deficiency has a significant positive effect on the healing process after musculoskeletal injuries. In the context of fracture healing and surgical outcomes, patients with deficiency who are eligible for orthopaedic surgery are at high risk of complications, including delayed consolidation, surgical site infection (SSI) and prosthetic joint infection (PJI) [12,23,26,50]. Preoperative supplementation with high doses of vitamin D3 (e.g. 300,000 IU) in patients with deficiency effectively reduces the risk of superficial wound healing problems and postoperative infections [26]. In the case of existing fractures, such as those of the femoral neck, supplementation with D3 is more effective than D2 in restoring normal 25(OH)D levels [17]. In terms of soft tissue regeneration, vitamin D3 supplementation (as opposed to D2) in physically active individuals improves muscle strength, accelerates post-workout recovery by lowering muscle damage markers (ALT, AST) and reduces susceptibility to further injuries [27,47]. Evidence indicates that in patients after anterior cruciate ligament (ACL) reconstruction,

normal 25(OH)D levels above 30 ng/mL correlate with less quadriceps muscle loss in the postoperative period [28]. Additionally, in the context of joint cartilage protection, supplementation has a protective effect in models of osteoarthritis, inhibiting the expression of matrix-degrading metalloproteinases (MMP-3, MMP-13), reducing oxidative stress and modulating inflammation, which may translate into a slowdown in the progression of damage and a reduction in pain [42].

5. DISCUSSION

The comprehensive analysis of the literature on vitamin D reveals a complex and at times contradictory picture of its role in injury pathophysiology. While a robust mechanistic foundation underscores its pleiotropic importance, translating this knowledge into consistent clinical benefits through supplementation presents significant challenges [14,19,23]. A fundamental point of agreement across the literature is the biological plausibility of vitamin D's involvement in injury prevention and healing. The widespread expression of the Vitamin D Receptor (VDR) and the local tissue capacity for activating 25(OH)D underpin its systemic effect [7]. Key mechanisms pertinent to injury pathology are consistently highlighted: immunomodulation via induction of antimicrobial peptides like cathelicidin [26,30,32]; suppression of the NF-κB pathway to resolve inflammation [33,34,37],; and direct promotion of cellular differentiation, migration, and anti-apoptosis in keratinocytes, fibroblasts, and neural progenitor cells [35,38,40,41]. Consequently, vitamin D deficiency is uniformly identified as a significant risk factor, correlating with increased fracture risk [12,25,48], muscle atrophy [27,28,47], higher fall rates [8,50], delayed wound closure [31,51], and greater susceptibility to infections [49,52,53,54]. Despite this strong mechanistic rationale, the results of interventional studies are heterogeneous, leading to several key contradictions. The most direct conflict exists in the area of fracture and fall prevention. While many studies support that supplementation reduces these risks in deficient elderly populations [19,25,46], pivotal RCTs, such as that by Trivedi et al. (2003), found no benefit in cohorts with high baseline 25(OH)D levels. This underscores the critical principle that benefits are contingent upon correcting a deficiency, supporting a "U-shaped curve" relationship [22,55]. Secondly, the efficacy of vitamin D_2 versus D_3 remains contested. Pharmacokinetically, cholecalciferol (D_3) is superior in raising and sustaining serum 25(OH)D, a finding supported by studies in hip fracture patients [17]. However, other trials, such as one in post-stroke women, found ergocalciferol (D_2) effective for specific clinical endpoints, suggesting the clinical significance of the pharmacokinetic difference may be context-dependent [18,46]. Thirdly, the impact on infection risk reveals an important nuance. Observational studies robustly associate pre-operative deficiency with increased surgical site infection (SSI) risk [49,52]. However, an RCT in spine surgery found no association, a result likely explained by the routine use

of potent intra-wound antibiotic prophylaxis which may have obscured vitamin D's modulatory role [56]. This highlights that vitamin D's effect is modulatory rather than absolute. Fourthly, dosing regimen is a critical factor. Daily or weekly supplementation appears effective and safe [33,57], whereas large, intermittent annual bolus doses have been paradoxically associated with increased risk of falls and fractures in some trials [22,55], indicating that physiological supplementation is preferable to pharmacologic bolus dosing. Finally, outcomes in critical illness and major trauma are inconsistent, moderated by the severity of the initial insult, timing of supplementation, and the immense catabolic burden, which may modulate the observable benefit of a single nutritional intervention [18,43,44,53]. These apparent contradictions can be largely reconciled by considering several overriding principles. The pre-supplementation level of 25(OH)D is the primary determinant of clinical response, with benefits most pronounced in individuals with overt deficiency [22,24]. Furthermore, the optimal 25(OH)D level for non-skeletal functions like immune modulation and muscle repair may be higher than the threshold for skeletal health alone [7,27]. Individual patient factors, notably Body Mass Index (BMI), which blunts the serum response to supplementation, along with age, genetics, and co-morbidities, further modulate efficacy. Lastly, heterogeneity in study design—encompassing population, vitamin D form, dosing regimen, and endpoint definitions—fundamentally shapes the reported outcomes [16].

Conclusions

Vitamin D plays a key role in wound healing thanks to its pleiotropic effects. Its active form, calcitriol, acts through the VDR receptor to modulate the immune response, reduce inflammation, stimulate keratinocyte proliferation and collagen synthesis, and promote angiogenesis and protection against oxidative stress. Vitamin D deficiency, which is common in the population, is associated with delayed healing, especially in chronic wounds, diabetic ulcers, burns and surgical injuries. Vitamin D3 supplementation, which is more effective than D2, accelerates wound closure, reduces the risk of infection and improves treatment outcomes, especially in deficient patients. In the context of CNS and musculoskeletal injuries, vitamin D has a neuroprotective effect, supports remyelination, reduces the risk of falls and improves tissue regeneration and fracture consolidation. Therefore, maintaining adequate levels of 25(OH)D and targeted supplementation in individuals with deficiency are important elements in supporting the healing process and overall regeneration of the body.

DISCLOSURE

Author's Contributions:

Conceptualization: Szymon Górski, Joanna Okupniarek, Michalina Bartosik, Igor Jętasiewicz

Formal analysis: Michał Oborski, Krzysztof Oborski, Igor Jętasiewicz, Jakub Miarczyński

Investigation: Joanna Okupniarek, Michalina Bartosik, Katarzyna Barczyńska

Writing rough preparation: Szymon Górski, Joanna Okupniarek, Michalina Bartosik, Igor Jętasiewicz, Krzysztof Oborski, Michał Oborski, Jakub Miarczyński

Writing review and editing: Szymon Górski, Igor Jętasiewicz, Katarzyna Barczyńska

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

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Avability Statement: Not applicable

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

REFERENCES

1 Murray R. K., Granner D. K., Rodwell V. W. (red.). (2012). *Harper's Illustrated Biochemistry* [title in Polish]. Warszawa: Wydawnictwo Lekarskie PZWL..

2 Bańkowski, E. (2004). *Biochemistry. A textbook for medical students* [title in Polish] (, s. 745). Wydaw. Medyczne Urban & Partner, cop.

3 Reboul E. *Intestinal absorption of vitamin D: from the meal to the enterocyte*. Food Funct. 2015 Feb;6(2):356-62. doi: 10.1039/c4fo00579a. PMID: 25367187.

4 Tuchendler, D. and Bolanowski, M. (2010) '*Seasonality of changes in vitamin D concentrations in the human body*' [title in Polish], Endokrynologia, Otyłość i Zaburzenia Przemiany Materii, 6(1), pp. 36–41.

5 Dittfeld, A., Gwizdek, K., Koszowska, A. and Fizia, K. (2014) '*The multidirectional action of vitamin D*' [title in Polish], Postępy Higieny i Medycyny Doświadczalnej, 68, pp. 620–628.

6 Marcinkowska, M., Mickiewicz, A. and Fijałkowski, M. (2019) '*The pleiotropic effects of vitamin D*' [title in Polish], Choroby Serca i Naczyń, 16(1), pp. 45–52. doi: 10.5603/ChSiN.2019.0007.

7 Armas, L.A.G., and R.P. Heaney, "*Vitamin D: The Iceberg Nutrient*," Journal of Renal Nutrition, 21 (2), pp. 134–139 (2011).

8 Overcash, J.A., "*Vitamin D in Older Patients With Cancer,*" Clinical Journal of Oncology Nursing, 12 (4), pp. 655–662 (2008).

9 Won, S., I. Sayeed, B.L. Peterson, B. Wali, J.S. Kahn, and D.G. Stein, "V*itamin D Prevents Hypoxia/Reoxygenation-Induced Blood-Brain Barrier Disruption via Vitamin D Receptor-Mediated NF-kB Signaling Pathways*," PLOS ONE, 10 (3), p. e0122821 (2015).

10 Kim, D., Meza, C. A., Clarke, H., Kim, J. & Hickner, R. C. (2020). *Vitamin D and Endothelial Function*. Nutrients, 12(2), 575. https://doi.org/10.3390/nu12020575

11 Napiórkowska, L. & Franek, E. (2009) '*The role of vitamin D testing in clinical practice*' [title in Polish], Choroby Serca i Naczyń, 6(4), s. 203–210. Dostępne na: [https://journals.viamedica.pl/choroby_serca_i_naczyn/article/view/12035] (Data odwiedzenia: 16.11.2025).

12 Clarke, N.M.P., and J.E. Page, "*Vitamin D deficiency*" Current Opinion in Pediatrics, 24 (1), pp. 46–49 (2012).

13 Ghorbanzadeh-Moghaddam, A., A. Gholamrezaei, and S. Hemati, "*Vitamin D Deficiency Is Associated With the Severity of Radiation-Induced Proctitis in Cancer Patients*" International Journal of Radiation Oncology*Biology*Physics, 92 (3), pp. 613–618 (2015).

14 Stöcklin, Elisabeth, and Manfred Eggersdorfer. 2013. "*Vitamin D, an Essential Nutrient with Versatile Functions in Nearly all Organs*." International Journal for Vitamin and Nutrition Research 83 (2): 92–100. https://doi.org/10.1024/0300-9831/a000151.

15 Hribar, M., Hristov, H., Lavriša, Ž., Korousić Seljak, B., Gregorič, M., Blaznik, U., Żmitek, K., & Pravst, I. (2021). Vitamin D intake in Slovenian adolescents, adults, and the elderly population. Nutrients, *13*(10), 3528. https://doi.org/10.3390/nu13103528

16 van den Heuvel EG, Lips P, Schoonmade LJ, Lanham-New SA, van Schoor NM. *Comparison of the Effect of Daily Vitamin D2 and Vitamin D3 Supplementation on Serum 25-Hydroxyvitamin D Concentration (Total 25(OH)D, 25(OH)D2, and 25(OH)D3) and Importance of Body Mass Index: A Systematic Review and Meta-Analysis*. Adv Nutr. 2024;15(1):100133. doi:10.1016/j.advnut.2023.09.016

17 Glendenning P, Chew GT, Seymour HM, et al. *Serum 25-hydroxyvitamin D levels in vitamin D-insufficient hip fracture patients after supplementation with ergocalciferol and cholecalciferol*. Bone. 2009;45(5):870-875. doi:10.1016/j.bone.2009.07.015

18 Gottschlich MM, Mayes T, Khoury J, Kagan RJ. C*linical Trial of Vitamin D2 vs D3 Supplementation in Critically Ill Pediatric Burn Patients.* Journal of Parenteral and Enteral Nutrition. 2015;41(3):412-421. doi:10.1177/0148607115587948

19 Wacker M, Holick MF. *Vitamin D - effects on skeletal and extraskeletal health and the need for supplementation*. Nutrients. 2013;5(1):111-148. Published 2013 Jan 10. doi:10.3390/nu5010111

20 Klein GL, Chen TC, Holick MF, et al. *Synthesis of vitamin D in skin after burns.* The Lancet. 2004;363(9405):291-292. doi:10.1016/s0140-6736(03)15388-3

21 Zhang Y, Fang F, Tang J, et al. *Association between vitamin D supplementation and mortality: systematic review and meta-analysis.* BMJ. 2019;366:l4673. Published 2019 Aug 12. doi:10.1136/bmj.l4673

22 Law M, Withers H, Morris J, Anderson F. *Vitamin D supplementation and the prevention of fractures and falls: results of a randomised trial in elderly people in residential accommodation.* Age and Ageing. 2006;35(5):482-486. doi:10.1093/ageing/afj080

23 Janoušek, J., Pilařová, V., Macáková, K., Nomura, A., Veiga-Matos, J., Silva, D. D. da, Mladěnka, P. (2022). *Vitamin D: sources, physiological role, biokinetics, deficiency, therapeutic use, toxicity, and overview of analytical methods for detection of vitamin D and its metabolites*. Critical Reviews in Clinical Laboratory Sciences, 59(8), 517–554. https://doi.org/10.1080/10408363.2022.2070595

24 Pramyothin P, Holick MF. *Vitamin D supplementation. Current Opinion in Gastroenterology.* 2012;28(2):139-150. doi:10.1097/mog.0b013e32835004dc

25 Wei MY, Giovannucci EL. *Vitamin D and multiple health outcomes in the Harvard cohorts*. Molecular Nutrition & Food Research. 2010;54(8):1114-1126. doi:10.1002/mnfr.200900574

26 Birinci, M. et al. (2024) '*Effect of Vitamin D Deficiency on Periprosthetic Joint Infection and Complications After Primary Total Joint Arthroplasty*', The Journal of Arthroplasty, 39, pp. S151–S157. doi:10.1016/j.arth.2024.05.012.

27 Chiang CM, Ismaeel A, Griffis RB, Weems S. *Effects of Vitamin D Supplementation on Muscle Strength in Athletes: A Systematic Review*. J Strength Cond Res. 2017;31(2):566-574. doi:10.1519/JSC.0000000000001518

28 Wen Y, Latham CM, Moore AN, et al. *Vitamin D status associates with skeletal muscle loss after anterior cruciate ligament reconstruction*. JCI Insight. 2023;8(23):e170518. Published 2023 Dec 8. doi:10.1172/jci.insight.170518

29 Bikle DD. *Role of vitamin D and calcium signaling in epidermal wound healing*. J Endocrinol Invest. 2023;46(2):205-212. doi:10.1007/s40618-022-01893-5

30 Romano F, Serpico D, Cantelli M, et al. *Osteoporosis and dermatoporosis: a review on the role of vitamin D*. Front Endocrinol (Lausanne). 2023;14:1231580. Published 2023 Aug 24. doi:10.3389/fendo.2023.1231580

31 Seth I, Lim B, Cevik J, et al. *Impact of nutrition on skin wound healing and aesthetic outcomes: A comprehensive narrative review*. JPRAS Open. 2024;39:291-302. Published 2024 Jan 23. doi:10.1016/j.jpra.2024.01.006

32 Tang W, Chen S, Zhang S, Ran X. *The Multi-Dimensional Role of Vitamin D in the Pathophysiology and Treatment of Diabetic Foot Ulcers: From Molecular Mechanisms to Clinical Translation*. International Journal of Molecular Sciences. 2025; 26(12):5719. https://doi.org/10.3390/ijms26125719

33 Zhao H, Wu X, Li H, Lan Y. *Effects of Oral Cholecalciferol on Chronic Wound Healing in Patients with Vitamin D Insufficiency or Deficiency*. J Multidiscip Healthc. 2025;18:6887-6900. Published 2025 Oct 24. doi:10.2147/JMDH.S543380

34 Yuan Y, Das SK, Li M. *Vitamin D ameliorates impaired wound healing in streptozotocin-induced diabetic mice by suppressing NF-κB-mediated inflammatory genes* [retracted in: Biosci Rep. 2022 Dec 22;42(12):BSR-2017-1294_RET. doi: 10.1042/BSR-2017-1294_RET.]. Biosci Rep. 2018;38(2):BSR20171294. Published 2018 Mar 5. doi:10.1042/BSR20171294

35 Oda Y, Hu L, Nguyen T, Fong C, Tu C, Bikle DD. *Combined deletion of the vitamin D receptor and calcium-sensing receptor delays wound re-epithelialization.* Endocrinology. 2017;158(6):1929-1938. doi:10.1210/en.2017-00061

36 Rech MA, Colon Hidalgo D, Larson J, Zavala S, Mosier M. *Vitamin D in burn-injured patients.* Burns. 2019;45(1):32-41. doi:10.1016/j.burns.2018.04.015

37 Jiang H, Yang X, Wang Y, Zhou C. *Vitamin D Protects against Traumatic Brain Injury via Modulating TLR4/MyD88/NF-κB Pathway-Mediated Microglial Polarization and Neuroinflammation.* Biomed Res Int. 2022;2022:3363036. Published 2022 Jul 15. doi:10.1155/2022/3363036

38 Zheng S, Yang J, Hu X, et al. *Vitamin D attenuates lung injury via stimulating epithelial repair, reducing epithelial cell apoptosis and inhibits TGF-β induced epithelial to mesenchymal transition.* Biochemical Pharmacology. 2020;177:113955. doi:10.1016/j.bcp.2020.113955

39 Vila Cuenca M, Ferrantelli E, Meinster E, et al. *Vitamin D Attenuates Endothelial Dysfunction in Uremic Rats and Maintains Human Endothelial Stability*. J Am Heart Assoc. 2018;7(17):e008776. doi:10.1161/JAHA.118.008776

40 Li W, Lin Y, Luo Y, et al. *Vitamin D Receptor Protects against Radiation-Induced Intestinal Injury in Mice via Inhibition of Intestinal Crypt Stem/Progenitor Cell Apoptosis*. Nutrients. 2021;13(9):2910. Published 2021 Aug 24. doi:10.3390/nu13092910

41 Li N, Yao M, Liu J, et al. *Vitamin D Promotes Remyelination by Suppressing c-Myc and Inducing Oligodendrocyte Precursor Cell Differentiation after Traumatic Spinal Cord Injury.* Int J Biol Sci. 2022;18(14):5391-5404. Published 2022 Aug 29. doi:10.7150/ijbs.73673

42 Mende LK, Kuthati Y, Wong CS. *Curcumin and Vitamin D Supplement Attenuates Knee Osteoarthritis Progression in ACLT + MMx Rat Model: Effect on Cartilage Protection and Pain Reduction.* Nutrients. 2025;17(2):349. Published 2025 Jan 19. doi:10.3390/nu17020349

43 Sharma S, Kumar A, Choudhary A, et al. *Neuroprotective Role of Oral Vitamin D Supplementation on Consciousness and Inflammatory Biomarkers in Determining Severity Outcome in Acute Traumatic Brain Injury Patients: A Double-Blind Randomized Clinical Trial*. Clin Drug Investig. 2020;40(4):327-334. doi:10.1007/s40261-020-00896-5

44 Lee JM, Jeong SW, Kim MY, Park JB, Kim MS. *The Effect of Vitamin D Supplementation in Patients with Acute Traumatic Brain Injury.* World Neurosurgery. 2019;126:e1421-e1426. doi:10.1016/j.wneu.2019.02.244

45 Intiso D, Fontana A, Copetti M, Di Rienzo F. *Serum vitamin D deficiency in subjects with severe acquired brain injury and relationship with functional severity.* Brain Injury. 2018;32(13-14):1817-1823. doi:10.1080/02699052.2018.1537512

46 Sato Y, Iwamoto J, Kanoko T, Satoh K. *Low-Dose Vitamin D Prevents Muscular Atrophy and Reduces Falls and Hip Fractures in Women after Stroke: A Randomized Controlled Trial.* Cerebrovascular Diseases. Published online September 7, 2005:187-192. doi:10.1159/000087203

47 Rebolledo BJ, Bernard JA, Werner BC, et al. *The Association of Vitamin D Status in Lower Extremity Muscle Strains and Core Muscle Injuries at the National Football League Combine*. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2018;34(4):1280-1285. doi:10.1016/j.arthro.2017.10.005

48 Hernigou P, Sitbon J, Dubory A, Auregan JC. Vitamin D history part III: *the "modern times"—new questions for orthopaedic practice: deficiency, cell therapy, osteomalacia, fractures, supplementation, infections.* International Orthopaedics. 2019;43(7):1755-1771. doi:10.1007/s00264-019-04334-w

49 Abdehgah AG, Monshizadeh A, Tehrani MM, et al. *Relationship Between Preoperative 25-Hydroxy Vitamin D and Surgical Site Infection*. Journal of Surgical Research. 2020;245:338-343. doi:10.1016/j.jss.2019.07.036

50 Coskun Benlidayi I, Basaran S, Seydaoglu G, Guzel R. *Vitamin D profile of patients with spinal cord injury and post-stroke hemiplegia: All in the same boat.* J Back Musculoskelet Rehabil. 2016;29(2):205-210. doi:10.3233/BMR-150615

51 Siregar FD, Hidayat W. The Role of Vitamin D on the Wound Healing Process: A Case Series. Int Med Case Rep J. 2023;16:227-232. Published 2023 Apr 1. doi:10.2147/IMCRJ.S402005

52 Lakhera KK, Babu A, Patel P, et al. *Association Between Pre-operative 25-Hydroxy Vitamin D Deficiency and Surgical Site Infection After Oral Cavity Oncology Surgery: a Cross-*

Sectional Study in a Tertiary Cancer Center in Northwestern India. Indian J Surg Oncol. 2024;15(2):218-224. doi:10.1007/s13193-023-01862-1

53 Pirdastan S, Mahdavi Roshan M, Mobayen M, et al. *Effect of vitamin D on clinical outcomes in patients with thermal injury*. Int Wound J. 2024;21(2):e14641. doi:10.1111/iwj.14641

54 Zhang Z, Yang X, Li M, Li B. *Serum 25-Hydroxyvitamin D Levels and the Risk of Post-Traumatic Wound Infection.* J Nutr Sci Vitaminol (Tokyo). 2025;71(2):110-117. doi:10.3177/jnsv.71.110

55 KORGAVKAR K, XIONG M, WEINSTOCK MA. *Review: Higher vitamin D status and supplementation may be associated with risks.* European Journal of Dermatology. 2014;24(4):428-434. doi:10.1684/ejd.2014.2318

56 Liu S, Sulovari A, Joo P, Thirukumaran C, Benn L, Mesfin A. *Relationship between 25-hydroxy Vitamin D level and surgical site infection in spine surgery.* Surg Neurol Int. 2024;15:173. Published 2024 May 24. doi:10.25259/SNI_135_2024

57 Pritchett K, Pritchett RC, Stark L, Broad E, LaCroix M. *Effect of Vitamin D Supplementation on 25(OH)D Status in Elite Athletes With Spinal Cord Injury.* International Journal of Sport Nutrition and Exercise Metabolism. 2019;29(1):18-23. doi:10.1123/ijsnem.2017-0233