

Review

Future Challenges of Vitamin D Deficiency: The Impact of Systemic Vitamin D Therapy on Serum Levels and Skin Diseases

T. Štrbac¹, V. Stojić², S. Frkanec³ and A. Stanimirović^{4,5}

¹University Eye Department, University Hospital “Sveti Duh”, Zagreb, Croatia; ²Department of Plastic and Reconstructive Surgery, University Hospital “Sveti Duh”, Zagreb, Croatia; ³University Department of ENT and Head and Neck Surgery, University Hospital Center, Zagreb, Croatia; ⁴School of Medicine, European University Cyprus, Cyprus; ⁵Dermatology & Venereology, University of Applied Health Sciences, Zagreb, Croatia

Corresponding author:

Dr. Tea Štrbac
University Eye Department,
University Hospital “Sveti Duh”,
Zagreb, Croatia
email: strbac27@gmail.com
tel: +385 99 691 03000

Keywords: *vitamin D, systemic therapy, skin diseases*

Received: 01 April 2025
Accepted: 09 June 2025

Copyright:
Journal of Applied Cosmetology ©2025
www.journalofappliedcosmetology.com
Copyright © by Journal of Applied Cosmetology

ISSN 2974-6140 (online) ISSN 0392-8543 (print).

This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder. Unauthorised reproduction may result in financial and other penalties
DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

ABSTRACT

In recent years, research on the role of vitamin D in skin diseases has grown, revealing its dose-dependent effects on cell function and its immunomodulatory, antioxidative, and cytoprotective properties. These findings have expanded their use in dermatology. However, the rising incidence of deficiency, linked to reduced sun exposure from indoor lifestyles and cultural practices, underscores the need for further investigation and therapeutic strategies. To review key insights on the systemic use of vitamin D in common immunomodulatory skin diseases, beyond its well-established topical applications. The electronic research of the literature included three databases: MEDLINE, Cochrane, and Google Scholar, as well as other available literature sources. Decreased serum vitamin D levels are observed in psoriasis, vitiligo, and alopecia areata. Systemic vitamin D therapy has shown clinical improvement in psoriasis, vitiligo, and atopic dermatitis, with limited but promising evidence in alopecia areata. It may play a role in managing acne vulgaris, though long-term data remain insufficient. The effects of systemic vitamin D analogs in the clinical treatment of many skin diseases are promising, but further clinical studies are needed.

INTRODUCTION

Vitamin D is a fat-soluble vitamin that plays an important role in several physiological functions. Previtamin D₃, produced in the skin and combined with UV, undergoes a rearrangement to one of the primary forms, which can be used - D₃ (cholecalciferol). Ergocalciferol, i.e., vitamin D₂, is another inactive form that is taken in with food, nutritional supplements, and medicines (1). Interestingly, these controlled processes prevent vitamin D intoxication due to the existing negative feedback loop (2). Numerous laboratory studies have demonstrated the dose-dependent molecular effects of this vitamin and its analogs on cell proliferation, differentiation, and apoptosis, where vitamin D promotes the differentiation and inhibits proliferation of the most prominent cells of epidermis, keratinocytes (3). Recent studies have highlighted its immunomodulatory effects, including the suppression of in vitro immunoglobulin IgE function, modulation of CD4⁺/CD8⁺ T-cells, and enhancement of IL-10 activity (4). Moreover, it has been noted for its antioxidative and cytoprotective effects (5). Recent scientific advances have expanded our understanding of its role beyond bone health, highlighting its significance in both nutrition and disease. Observational studies point to the broad, pleiotropic effects of maintaining optimal vitamin D levels, including benefits for immune function, reduced risk of type 2 diabetes, and potential improvements in cardiovascular outcomes and mortality. Findings from large-scale trials further support these extraskeletal roles. These advances in knowledge reinforce its classification as a modern hormone (6). Despite various sources contributing to vitamin D intake, including diet and UV radiation exposure, modern indoor lifestyles and cultural practices that limit sun exposure have led to widespread vitamin D deficiency, not only among the elderly, but increasingly across all age groups. This trend has become both a dermatological and broader public health concern, particularly in light of the rising prevalence of autoimmune diseases. Specifically, 40% of Europeans are affected by hypovitaminosis of vitamin D (7). The commonly acknowledged ranges for serum vitamin D levels are shown in Table I.

Table I. *The commonly acknowledged ranges for serum vitamin D levels.*

<i>Vitamin D status</i>	<i>25(OH)D serum concentration</i>
Deficiency	< 20ng/mL (50 nmol/L)
Insufficiency	20-29,9 ng/mL (50-74,9 nmol/L)
Normal	30-100 ng/mL (75-250 nmol/L)

We provide an overview of the pivotal information about the effect of systemic treatment with vitamin D, along with other therapies in patients with skin diseases (Table II). The electronic research of the literature included three databases: MEDLINE, Cochrane, and Google Scholar, along with other available literature data. This review encompasses a thorough examination of literature from 1986 to 2024, which included randomized controlled trials (RCTs), cohort studies, case-control studies, as well as previous systematic and narrative literature reviews and meta-analyses. Studies describing the impact of oral intake of vitamin D on each of the listed diseases individually, as well as studies describing the impact on the listed diseases collectively, were searched. Papers emphasizing topical vitamin D therapy were excluded.

Table II. *Correlation between efficacy of using per-oral vitamin D in specific dermatological diagnoses, Levels of Evidence, and Grading of Recommendation.*

<i>Diagnosis</i>	<i>Vitamin D oral supplementation</i>
Psoriasis	Grade B recommendation with IIa level of evidence
Vitiligo	Grade B recommendation with IIa level of evidence
Alopecia Areata	Grade B recommendation with IIb level of evidence
Atopic Dermatitis	Grade B recommendation with IIa level of evidence
Acne Vulgaris	Grade B recommendation with IIb level of evidence

Note: Adapted from Navarro-Triviño FJ, Arias-Santiago S, Gilaberte-Calzada Y. Vitamin D and the Skin: A Review for Dermatologists. *Actas Dermo-Sifiliográficas Engl Ed.* 2019 May;110(4):262–72.

Vitamin D and Psoriasis

In the 1980s, Morimoto and Kumahara reported significant improvement in psoriatic lesions in a patient treated orally with 25(OH)D for osteoporosis. In a subsequent study, 80% of 17 patients with psoriasis who received 40 IU of oral 25(OH)D daily for up to 6 months showed clinically significant improvement (8). Since then, various studies have reported that numerous vitamin D analogues are effective and safe for the topical treatment of psoriasis; however, the safety of oral administration remains questionable. In a 1996 long-term study, it was found that 88.0% of psoriasis patients with vitamin D deficiency noticed an improvement in their condition with oral calcitriol treatment at a dosage of 2-4 mcg per night for 36 months. Although serum

calcium levels and 24-hour urinary calcium excretion increased, they remained within normal ranges (9). Barrea et al. proposed that oral vitamin D intake of up to 10,000 IU daily showed no harmful effects. This dosage aligns with maximum cutaneous vitamin D production, and no cases of vitamin D intoxication solely from skin synthesis have been reported (10). Finamor et al. demonstrated a significant improvement in psoriasis severity, as indicated by a lower PASI score in patients receiving a dose of 35,000 IU of cholecalciferol for 6 months, accompanied by a notable increase in their serum vitamin D levels (11). Mahtani and Nair treated 6 psoriasis cases with daily oral Vitamin D3, ranging from 30,000 IU to 60,000 IU for 2 to 6 months, followed by a lower maintenance dose. All patients achieved complete disease control, as indicated by PASI and VAS scores (12). In another study, it was shown that a vitamin D3 dose higher than 40,000 IU was associated with hypercalcemia toxicity. Most studies reported no side effects within a narrow dose range of 0.25 to 2 mcg/day (13,14).

Vitamin D and Vitiligo

Akpolat et al. discovered that individuals with vitiligo consistently experienced lower levels of vitamin D in their serum, regardless of the season or the clinical type of vitiligo (15). A few years ago, meta-analysis showed that the VDR Apal polymorphism increased susceptibility to vitiligo, and their results led to a positive correlation between low serum vitamin D concentration and vitiligo incidence (16). Another study found no decrease in serum vitamin D levels in children with vitiligo ($p > 0.05$). However, they demonstrated that combining oral vitamin D with topical tacrolimus is more effective for achieving repigmentation compared to using topical tacrolimus alone. A dose of 1500 IU/day vitamin D was given if the serum vitamin D levels were less than 20 ng/ml, and 3000 IU/day was given if the serum vitamin D levels were less than 10 ng/ml for six months. Lesion size decreased after the end of the treatment in patients who received combination treatment ($p < 0.001$) (17). One pilot study assessed the efficacy and safety of prolonged high-dose vitamin D3 treatment of patients with psoriasis and vitiligo. Sixteen vitiligo patients with low baseline vitamin D levels (≤ 30 ng/mL) received daily vitamin D3 (35,000 IU) for six months alongside a low-calcium diet. Post-treatment, 25(OH)D3 levels significantly increased, and PTH levels decreased. In fourteen patients, 25-75% repigmentation has been observed. This suggests potential consideration for high-dose vitamin D3 therapy in vitiligo patients (11).

Vitamin D and Alopecia Areata

Alopecia areata (AA) is a T-cell-mediated autoimmune disease linked to other autoimmune conditions. The hair follicle is normally an immune-privileged site. Still, in AA, this privilege is compromised due to increased MHC I/II expression, reduced immunosuppressive signals, and elevated adhesion molecules, such as ICAM-2 and ELAM-1, leading to perifollicular inflammation and hair miniaturization. It has been demonstrated that Vitamin D receptors (VDRs) are strongly expressed in hair follicles, and a lack of VDRs reduces epidermal differentiation and growth of hair follicles (18).

A meta-analysis conducted before May 15, 2017, found that patients with alopecia areata (AA) had a higher prevalence of 25-hydroxyvitamin D deficiency compared to the control group. This suggests an autoimmunity role for vitamin D in the organism mediated by the immune system (19). Bakry et al. also found that alopecia totalis/universalis had significantly lower vitamin D levels compared to patchy AA ($P < 0.001$) and ophiasis ($P = 0.04$). Severe AA demonstrated significantly lower vitamin D levels compared to mild ($P = 0.002$) and moderate disease ($P = 0.03$) (20).

Although topical administration of vitamin D in AA is widespread, data on oral administration are missing. Papadimitriou et al. reported three pediatric cases using calcitriol and paricalcitol for the treatment of alopecia areata (AA). Hair regrowth was observed in all cases, though one patient experienced hypercalcemia, which

resolved by switching to paricalcitol. Results suggest a vitamin D immunomodulatory role in AA, highlighting potential for more effective, less calcemic calcitriol analogs in future therapies (21).

Vitamin D and Atopic Dermatitis

It has been identified that vitamin D analogues suppress in vitro immunoglobulin E (IgE) production and IgE-mediated cutaneous reactions as well (22). Samochoki et al. (2013) studied the effect of vitamin D supplementation on atopic dermatitis (AD). While serum vitamin D levels were similar between AD patients and controls, lower vitamin D levels were associated with more frequent bacterial skin infections in AD patients. After supplementation, the SCORAD index significantly decreased ($P < 0.05$) (23). A systematic review and meta-analysis by MJ Kim et al. in 2016 summarized all the evidence discovered so far about the function of vitamin D in atopic dermatitis. Compared to healthy controls, patients with AD had lower levels of the researched vitamin, particularly in the subgroup of pediatric population. Oral vitamin D supplementation has been associated with reductions in both SCORAD and Eczema Area and Severity Index (EASI) score in pediatric patients, so they believe that vitamin D supplementation should be considered as an adjuvant treatment in AD patients with moderate deficiency (levels below 20 ng/mL) (24). Regardless of the above results, several authors have obtained opposing results. For instance, it was observed that a positive correlation exists between vitamin D supplementation during infancy and a higher risk of developing eczema in preschool age. Another study demonstrated that patients with low vitamin D (<10 ng/mL) or with very high vitamin D serum levels (>54 ng/mL) had significantly higher IgE levels than healthy individuals with normal vitamin D serum levels (40–50 ng/mL). Correction of serum concentrations of vitamin D reduced IgE levels significantly. The findings suggest that there may be a threshold effect, where both very low and very high vitamin D levels are associated with increased IgE concentrations, indicating a potential U-shaped relationship. This means that either a deficiency or excess of vitamin D might contribute to elevated IgE, but other factors could also influence these results (25). A 2020 study assessed the impact of vitamin D supplementation on the response to standard treatment in pediatric patients with severe atopic dermatitis (AD). Patients receiving 1600 IU/day of vitamin D₃, along with topical hydrocortisone, showed significantly higher vitamin D levels ($P < 0.001$) and a marked reduction in EASI scores ($P = 0.035$) compared to the placebo group. Vitamin D also reduced *Staphylococcus aureus* colonization and improved clinical outcomes in children with moderate eczema (26).

Vitamin D and Acne Vulgaris

Oral vitamin D may help improve acne through several proposed mechanisms, like reducing inflammation by downregulating pro-inflammatory cytokines such as IL-6 and IL-8, by decreasing Toll-like receptor expression, and inhibiting the proliferation of *Propionibacterium acnes* in vitro (27).

In 2016, Lim et al. studied vitamin D levels in 80 acne patients and 80 healthy controls, finding a higher prevalence of deficiency in acne patients (48.8%) compared to controls (22.5%, $P=0.019$). Patients with deficiency were treated with either vitamin D₃ (1000 IU/day) or a placebo for 2 months. Vitamin D supplementation significantly increased 25(OH)D₃ levels ($P < 0.001$) and improved acne, with inflammatory lesions decreasing by 34.6% in the treatment group compared to 5.8% in the placebo group ($P < 0.05$) (28). Alhetheli et al. reported that lower values of serum vitamin D are more frequent in patients with acne, with P -value = 0.003; however, there was no significant association between the serum level of 25-hydroxyvitamin D [25 (OH) D] and the severity of acne vulgaris (29). Mohamed et al. studied the effect of alfacalcidol in 100 acne patients, who were randomized to receive either 0.25 µg daily or a placebo for three months, with 100 healthy controls. Acne patients had significantly lower 25-hydroxyvitamin D levels, which were inversely

correlated with the severity of their acne. After alfacalcidol treatment, the study group showed significantly higher vitamin D levels ($P < 0.05$) and a notable reduction in IL-6 and TNF α levels ($P < 0.05$), suggesting an anti-inflammatory effect of vitamin D (30).

Although evidence is still lacking, it is important to note that vitamin D supplementation is being encouraged in conjunction with standard acne treatments, such as retinoids, benzoyl peroxide, or antibiotics.

Beyond the Threshold: Rethinking Vitamin D Safety

Determining a definitive serum 25(OH)D concentration at which vitamin D toxicity reliably occurs remains challenging, as some individuals tolerate levels above 80 ng/mL (200 nmol/L) without developing hypercalcemia or hypercalciuria (30). In the context of psoriasis, the efficacy of high-dose systemic vitamin D therapy remains uncertain, with no clear evidence supporting its benefit at the upper dosing ranges; however, most studies have not reported significant adverse effects (13). Generally, vitamin D-induced hypercalcemia is rare and typically arises only with the ingestion of extremely high doses, often several hundred times the recommended intake. When present, diagnosis relies on detecting hypercalcemia in conjunction with elevated vitamin D metabolites and suppressed parathyroid hormone (PTH) levels, performing a set of biochemical tests sufficient to establish the condition (31). Given the variability in individual response and the limited data on long-term safety and therapeutic value in dermatological conditions, larger, well-controlled clinical trials are essential to determine optimal dosing strategies, efficacy, and potential adverse effects of vitamin D supplementation in this patient population.

Limitations of Review - Room for Improvement

Despite promising findings, several limitations make it difficult to apply current evidence in dermatology widely. A major challenge here lies in the heterogeneity of existing studies, which vary significantly in design, ranging from randomized controlled trials (RCTs) to observational studies and case series. Also, dosing regimens, supplementation forms, and patient populations, including differences between adults and children, limit the comparability of outcomes. Furthermore, publication bias remains a concern, with a tendency for studies reporting positive results to be published more readily than those with neutral or negative findings. Looking ahead, there is a critical need for large-scale, high-quality randomized controlled trials (RCTs) to establish standardized dosing protocols and to evaluate the long-term efficacy and safety of vitamin D supplementation, particularly in the aforementioned conditions, where the incidence is increasing rapidly. To make it more useful in practice, it's important to create clear, evidence-based guidelines.

CONCLUSION

Integrating vitamin D into the treatment of various skin conditions can enhance symptom management, support immune function, and promote overall skin health. A well-established relationship exists between serum vitamin D levels and skin diseases, indicating that deficiency is associated with the severity of conditions such as psoriasis, vitiligo, alopecia areata, atopic dermatitis, and acne vulgaris. This issue may become more prevalent in the future, as individuals with limited sun exposure, due to indoor work environments, home offices, or urban living, are at an increased risk of deficiency. Modern lifestyles, characterized by reduced sun exposure, particularly in regions with limited winter sunlight, have further exacerbated this trend. Ongoing research is essential to develop clear and evidence-based guidelines for vitamin D supplementation in dermatological practice.

Patient consent:

This review does not contain any personal information that could lead to the identification of the patients.

Acknowledgment and disclosures:

None.

Funding:

No funding or grant support.

Conflict of interest:

None.

REFERENCES

- Office of Dietary Supplements - Vitamin D [Internet]. [cited 2024 Apr 13]. Available from: <https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/>
- Bergqvist C, Ezzedine K. Vitamin D and the skin: what should a dermatologist know? *G Ital Dermatol Venereol* [Internet]. 2019 Dec [cited 2022 Apr 16];154(6). Available from: <https://www.minervamedica.it/index2.php?show=R23Y2019N06A0669>
- Wadhwa B, Relhan V, Goel K, Kochhar AM, Garg VK. Vitamin D and skin diseases: A review. *Indian J Dermatol Venereol Leprol*. 2015;81:344.
- Bizzaro G, Antico A, Fortunato A, Bizzaro N. Vitamin D and Autoimmune Diseases: Is Vitamin D Receptor (VDR) Polymorphism the Culprit? *Isr Med Assoc J*. 2017;19(7):438-443.
- Ellison DL, Moran HR. Vitamin D: Vitamin or Hormone? *Nurs Clin North Am*. 2021 Mar 1;56(1):47-57.
- Giustina A, Bilezikian JP, Adler RA, Banfi G, Bikle DD, Binkley NC, et al. Consensus Statement on Vitamin D Status Assessment and Supplementation: Whys, Whens, and Hows. *Endocr Rev*. 2024;45(5):625-54.
- Cashman KD, Dowling KG, Škrabáková Z, Gonzalez-Gross M, Valtueña J, De Henauw S, et al. Vitamin D deficiency in Europe: pandemic? *Am J Clin Nutr*. 2016;103(4):1033-44.
- Morimoto S, Yoshikawa K, Kozuka T, Kitano Y, Imanaka S, Fukuo K, et al. An open study of vitamin D3 treatment in psoriasis vulgaris. *Br J Dermatol*. 1986;115(4):421-9.
- Perez A, Raab R, Chen TC, Turner A, Holick MF. Safety and efficacy of oral calcitriol (1,25-dihydroxyvitamin D3) for the treatment of psoriasis. *Br J Dermatol*. 1996;134(6):1070-8.
- Barrea L, Savanelli MC, Di Somma C, Napolitano M, Megna M, Colao A, et al. Vitamin D and its role in psoriasis: An overview of the dermatologist and nutritionist. *Rev Endocr Metab Disord*. 2017;18(2):195-205.
- Finamor DC, Sinigaglia-Coimbra R, Neves LCM, Gutierrez M, Silva JJ, Torres LD, et al. A pilot study assessing the effect of prolonged administration of high daily doses of vitamin D on the clinical course of vitiligo and psoriasis. *Dermatoendocrinol*. 2013 Jan;5(1):222-34.
- Mahtani R, Nair PMK. Daily oral vitamin D3 without concomitant therapy in the management of psoriasis: A case series. *Clin Immunol Commun*. 2022;2:17-22.
- Stanescu AMA, Simionescu AA, Diaconu CC. Oral Vitamin D Therapy in Patients with Psoriasis. *Nutrients*. 2021;13(1):163.
- Fu LW, Vender R. Systemic Role for Vitamin D in the Treatment of Psoriasis and Metabolic Syndrome. *Dermatol Res Pract*. 2011;2011:1-4.
- Akpolat ND, Metin A. Plasma vitamin D levels in patients with vitiligo. *Bosphorus Med J*. 2022;9(1):0-0.
- Zhang JZ, Wang M, Ding Y, Gao F, Feng YY, Yakeya B, et al. Vitamin D receptor gene polymorphism, serum 25-hydroxyvitamin D levels, and risk of vitiligo: A meta-analysis. *Medicine (Baltimore)*. 2018;97(29):e11506.
- Karagüzel G, Sakarya NP, Bahadır S, Yaman S, Ökten A. Vitamin D status and the effects of oral vitamin D treatment in children with vitiligo: A prospective study. *Clin Nutr ESPEN*. 2016;15:28-31.
- Bhat YJ, Latif I, Malik R, Hassan I, Sheikh G, Lone KS, Majeed S, Sajad P. Vitamin D Level in Alopecia Areata. *Indian J Dermatol*. 2017 Jul-Aug;62(4):407-410. doi: 10.4103/ijd.IJD_677_16
- Tsai TY, Huang YC. Vitamin D deficiency in patients with alopecia areata: A systematic review and meta-analysis. *J Am Acad Dermatol*. 2018;78(1):207-9.

20. Bakry O, El Farargy S, El Shafiee M, Soliman A. Serum Vitamin D in patients with alopecia areata. *Indian Dermatol Online J.* 2016;7(5):371.
21. Papadimitriou DT, Bothou C, Dermitzaki E, Alexopoulos A, Mastorakos G. Treatment of alopecia totalis/universalis/focalis with vitamin D and analogs: Three case reports and a literature review. *World J Clin Pediatr.* 2021;10(6):192–9.
22. Relhan V, Goel K, Kochhar A, Garg V, Wadhwa B. Vitamin D and skin diseases: A review. *Indian J Dermatol Venereol Leprol.* 2015;81(4):344.
23. Samochocki Z, Bogaczewicz J, Jeziorkowska R, Sysa-Jędrzejowska A, Glińska O, Karczmarewicz E, et al. Vitamin D effects in atopic dermatitis. *J Am Acad Dermatol.* 2013;69(2):238–44.
24. Kim M, Kim SN, Lee Y, Choe Y, Ahn K. Vitamin D Status and Efficacy of Vitamin D Supplementation in Atopic Dermatitis: A Systematic Review and Meta-Analysis. *Nutrients.* 2016;8(12):789.
25. Vestita M, Filoni A, Congedo M, Foti C, Bonamonte D. Vitamin D and Atopic Dermatitis in Childhood. *J Immunol Res.* 2015;2015:1–7.
26. Mansour NO, Mohamed AA, Hussein M, Eldemiry E, Daifalla A, Hassanin S, et al. The impact of vitamin D supplementation as an adjuvant therapy on clinical outcomes in patients with severe atopic dermatitis: A randomized controlled trial. *Pharmacol Res Perspect [Internet].* 2020 Dec [cited 2022 Apr 16];8(6). Available from: <https://onlinelibrary.wiley.com/doi/10.1002/prp2.679>
27. Bhat Y, Latief I, Hassan I. Update on etiopathogenesis and treatment of Acne. *Indian J Dermatol Venereol Leprol.* 2017;83(3):298.
28. Lim SK, Ha JM, Lee YH, Lee Y, Seo YJ, Kim CD, et al. Comparison of Vitamin D Levels in Patients with and without Acne: A Case-Control Study Combined with a Randomized Controlled Trial. *Shellman YG, editor. PLOS ONE.* 2016;11(8):e0161162.
29. Alhetheli G, Elneam AIA, Alsenaid A, Al-Dhubaibi M. Vitamin D Levels in Patients with and without Acne and Its Relation to Acne Severity: A Case-Control Study. *Clin Cosmet Investig Dermatol.* 2020;13:759–65.
30. Ahmed Mohamed A, Salah Ahmed EM, Abdel-Aziz RTA, Eldeeb Abdallah HH, El-Hanafy H, Hussein G, et al. The impact of active vitamin D administration on the clinical outcomes of acne vulgaris. *J Dermatol Treat.* 2021;32(7):756–61.
31. Tebben PJ, Singh RJ, Kumar R. Vitamin D-Mediated Hypercalcemia: Mechanisms, Diagnosis, and Treatment. *Endocr Rev.* 2016;37(5):521–547. doi: 10.1210/er.2016-1070