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Dementia Risk in Psoriasis Patients Treated with Biologics: A Propensity Score-matched Population-based Cohort Study

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Translational research and animal models suggest that psoriasis treatments may have neuroprotective effects and reduce dementia risk. This study evaluates the association between biologic therapies for psoriasis and dementia incidence. A retrospective cohort included patients aged 65 or older with psoriasis, divided into 2 groups: those receiving biologic therapy following systemic treatment and those on systemic treatment alone. Patients with prior dementia were excluded. Dementia diagnosis was assessed at least 12 months after biologic initiation. Propensity score matching yielded 1,766 patients (883 per group). Biologic therapy was associated with a 53% reduced dementia risk (hazard ratio 0.47, 95% confidence interval 0.323–0.699), supported by a multivariate Cox model (adjusted hazard ratio 0.52, 95% confidence interval 0.392–0.699). These findings suggest that biologic therapies targeting tumour necrosis factor-alpha, interleukin-17, and interleukin-23 may reduce the risk of dementia, even after adjusting for age and other confounders.

Key words: psoriasis; dementia; biologic treatments; TNF-α; interleukin-17; interleukin-23.

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SIGNIFICANCE

Biologic treatments for psoriasis may significantly reduce dementia risk in patients aged 65 or older. This retrospective cohort study of 1,766 patients found a 53% lower incidence of dementia in those receiving biologic therapies compared with systemic treatments alone, suggesting potential neuroprotective benefits beyond skin disease management.

Psoriasis affects 0.5–11.4% of adults (1, 2) and is driven by cytokines including interleukin (IL)-12 and IL-23, which increase TH1, TH17, and TH22 cells. These cells secrete IL-22, INF-γ, TNF-α, and IL-17, promoting keratinocyte proliferation, inflammation, and angiogenesis, which characterize the psoriatic phenotype (3, 4). This understanding has led to the development of biological treatments for psoriasis.

Dementia involves progressive cognitive decline primarily due to degenerative diseases or vascular changes (5). The main subtypes of dementia are Alzheimer's disease, accounting for 60% of cases, and vascular dementia, making up 16% (6). Dementia prevalence above age 65 is 6.4–8.5%, with Alzheimer's and vascular dementia at 4.4% and 1.6%, respectively (6, 7). Alzheimer's incidence rises sharply with age, increasing from 2 per 1,000 individuals aged 65–74 to over 37 per 1,000 individuals over 85 (8). Advanced age, female gender, and genetics raise all-cause dementia risk, while cardiovascular factors specifically affect vascular dementia (6).

Research on the psoriasis–dementia relationship shows conflicting results. Some studies report no association or even a protective effect (9–11), while others suggest psoriasis may increase dementia risk by up to 49% (12–15). Although the pathogenesis of 2 of the diseases differs, evidence highlights common grounds through systemic inflammation, which is linked to neurodegeneration (15–18). Specifically, in Alzheimer's disease, impaired clearance of amyloid-β peptides can cause microbleeds and vascular distress, leading to cerebral amyloid angiopathy (CAA). This sequence of events increases inflammation, fibrinogenesis, and oxidative stress, thereby upregulating Th17 cells to produce IL-17, which exacerbates the inflammatory response (17, 19). TNF-α mediates chronic inflammation, activating the NF-κB pathway, contributing to brain damage via oxidative stress, neuroinflammation, and microglia activation (20–22). Supporting this, high serum TNF-α in those with mild cognitive impairment heightens Alzheimer's risk, and increased IL-12 levels are found in the brain tissues of individuals with Alzheimer's (16, 23). Additionally, elevated levels of IL-17, IL-8, and IL-23 are found in the serum of Alzheimer's patients compared with controls (18, 24); and a recent meta-analysis found that TNF-α inhibitors reduced dementia risk in psoriatic arthritis patients, while methotrexate did not (27).

Animal models corroborate these findings (17, 19), showing cognitive improvements with IL-17 inhibitors (25). In microglial/macrophage cultures, Aβ42 clearance was impaired by IL-18, IL-17, and IL-23, but this was reversible with their respective antibodies (26).

Despite this evidence, and even though non-biologic systemic treatments have been used for years, there still

are not enough reproducible data on the association between most systemic drugs and dementia. Considering the new generation of biologic treatments for psoriasis, there is an encouraging possibility of these treatments having a positive impact on slowing dementia and particularly Alzheimer's.

In this study, we aim to explore the impact of biologic treatments on dementia incidence in psoriasis patients, focusing on whether targeting cytokines involved in psoriasis and neuroinflammation can influence dementia occurrence.

MATERIALS AND METHODS

Study design and data source

This retrospective cohort study utilized data extracted from the Clalit Health Services (CHS) electronic database. Clalit Health Services, the largest public health provider in Israel, covers approximately 4.7 million people (28). The database includes comprehensive data from 14 hospitals and community dermatology clinics affiliated with Clalit.

Data were de-identified according to the standards of the institutional review board (IRB), extracted on June 2024, and mined between January 2000 and March 2023. The study cohort included all patients diagnosed with psoriasis (of any subtype) who were born before 1958, thus aged 65 years or older at the time of data extraction. The age of 65 was chosen as the cutoff since both the incidence and prevalence of dementia increase significantly above this age. Additionally, it is recognized as a common age for the onset of late-onset variant Alzheimer's disease.

All patients included in the study had moderate to severe disease, as evidenced by the need for systemic treatment.

Patients were divided into 2 groups based on their treatment regimen:

1. Study group:

- Patients who initiated biologic treatment after systemic treatment.
- Treatment lasted at least 1 year, as typical response time for skin and rheumatology conditions is usually 3–6 months, with an additional 6 months to ensure a sustained anti-inflammatory effect.
- Inclusion drugs: "TNF-α inhibitors (etanercept, adalimumab, infliximab, certolizumab pegol), interleukin (IL) inhibitors (ustekinumab, secukinumab, ixekizumab, guselkumab, risankizumab).

2. Control group:

- Patients treated with systemic drugs such as methotrexate, acitretin, apremilast, ciclosporin, and others for at least 90 days, the average time expected for a cutaneous response.
- Systemic treatment initiated after the diagnosis of psoriasis.
- No biologic treatment initiated for psoriasis.

Exclusion criteria included:

- Patients with a diagnosis of dementia prior to the diagnosis of psoriasis.
- Patients with a diagnosis of dementia prior to at least 12 months of treatment.
- A follow-up duration of less than 15 months.

The number of patients included in each group and the exclusions based on the inclusion and exclusion criteria are detailed in **Fig. 1**.

Data collection and definitions

Comprehensive patient data, including demographics (age at psoriasis diagnosis, gender, smoking status, BMI, socioeconomic status (SES), clinical data (time until systemic treatment onset, comorbidities, and treatment specifics), and dementia onset, were collected. Patients were classified into low, medium, and high-income SES based on residence, as per the Clalit Health database and Israeli Bureau of Statistics indicators (29). This enabled analysis of socioeconomic influences. Comorbidities were identified based on ICD-9 codes from the CHS database, covering specific and broader risk categories

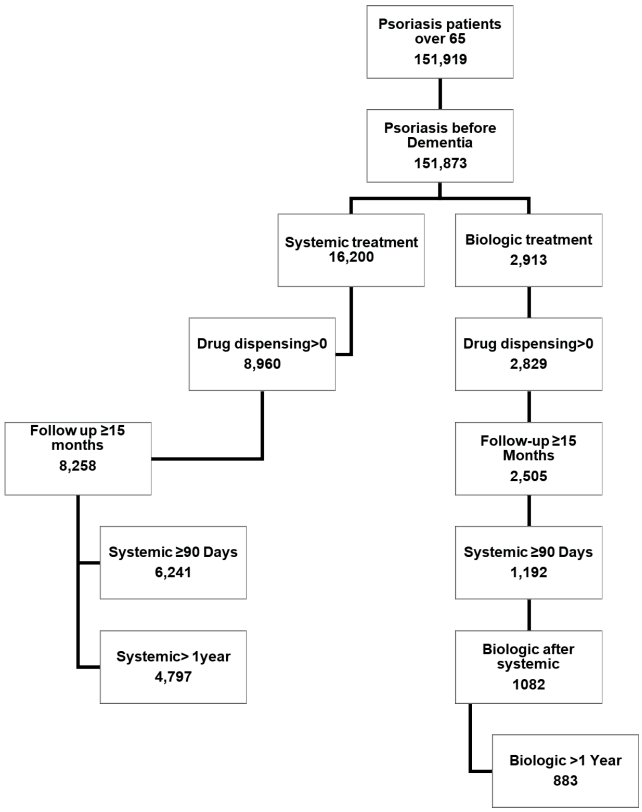

Fig. 1. Flow diagram of patient selection process. The initial cohort included 151,919 patients. After applying inclusion and exclusion criteria, 883 patients were retained in the study group, with 4,797 matched controls.

(e.g., peripheral vascular disease [PVD], cerebrovascular accident [CVA], mental illness, neoplasm). Dementia and its subtypes were defined according to ICD-9 codes, as provided in Table SI.

Outcome

The aim was to evaluate the reduction in the incidence of dementia among psoriasis patients receiving biologic therapy compared with those receiving only systemic treatment.

Statistical analysis

Descriptive statistics summarized patient demographics and clinical characteristics, with continuous variables expressed as means and standard deviations (SD) and categorical variables as frequencies and percentages. Independent *t*-tests and χ^2 tests were utilized to compare continuous and categorical variables, respectively.

Cox proportional hazards models were used to assess the relationship between biologic treatment duration and dementia risk. Both univariate and multivariate models were employed, with the latter adjusting for potential confounders such as age and depression. Hazard ratios (HR) and 95% confidence intervals (CI) were computed.

Propensity score matching (PSM)

To address potential selection biases and achieve balance between the treatment groups, we employed propensity score matching (PSM). Propensity scores were calculated using logistic regression, incorporating a comprehensive set of covariates. A total of 23 covariates were selected based on specific risk morbidities, clinical relevance derived from ICD-9 categories, their recognition in the literature as relevant in similar studies (6, 20), and statistical tests for differences between the groups. Examples of such covariates include demographic factors (age, gender, SES), comorbidities such as peripheral vascular disease (PVD), cerebrovascular accident (CVA), diabetes, and rheumatoid arthritis, as well as broad ICD-9 categories such as mental disorders and neoplasms. This extensive matching process utilized a 1:1 matching ratio, resulting in 893 matched pairs. Following the matching, the balance of covariates was rigorously assessed to ensure no significant differences remained between the groups.

Sensitivity analysis

Our study may be subject to *immortality bias*, occurring when patients must survive a certain period to qualify for a treatment group, thus skewing results. In our case, patients receiving biologic treatment had to survive the gap between starting systemic treatment and biologic therapy, creating an "immortal" period during which death could not occur. This might overestimate survival in the biologic group compared with systemic-only treatment. To address this, we conducted a sensitivity analysis to assess the bias's impact ensuring the robustness of our results.

Ethical considerations

The study protocol was reviewed and approved by the IRB, and informed consent was waived due to its retrospective design and use of de-identified data.

Software

All statistical analyses were performed using Enterprise Guide 8.3 software (SAS Institute Inc, Cary, NC, USA).

RESULTS

Propensity score matching (PSM) results

PSM resulted in 883 patients in the study group (treated with biologic treatment following systemic treatment) and 883 matching controls (treated with systemic treatment only). The mean age at psoriasis diagnosis was 56.2 years (SD = 7.8) in the study group and 57.7 years (SD = 9.2) in the control group. In both groups, 57% of participants were female. The demographic features and characteristics of psoriasis disease among participants as well as the comorbidities are detailed accordingly in **Tables I** and **II**. Owing to PSM, no significant between-group differences were observed in age at diagnosis of

Table I. Clinical background of propensity score matching (PSM) groups

Condition	Control *N* (%) 883 (50)	Study *N* (%) 883 (50)
Age at diagnosis, mean (SD)	57.7 (9.2)	56.2 (7.8)
40–50 years	197 (22.3)	206 (23.3)
50–60 years	424 (48.0)	417 (47.2)
>60 years	262 (29.7)	260 (29.4)
Gender (female)	505 (57.2)	507 (57.4)
SES category		
Low	171 (20.2)	154 (18.3)
Medium	299 (35.4)	294 (35.0)
High	373 (44.2)	390 (46.5)
Smoking status		
Yes, in the past	273 (30.9)	299 (33.9)
Yes, now	119 (13.5)	110 (12.5)
BMI category	29.5 (5.9)	29.4 (5.8)
<18 (underweight)	3 (0.3)	3 (0.3)
18–25 (normal weight)	192 (21.7)	157 (17.8)
25–30 (overweight)	322 (36.5)	385 (43.6)
30+ (obesity)	354 (40.1)	327 (37.0)
Psoriasis and systemic treatment		
Follow up time (years)	10.9 (5.2)	12.1 (4.8)
Time from diagnosis to systemic treatment	5.6 (4.8)	5.5 (4.4)
Years on systemic treatment	6.4 (5.6)	6.4 (5.1)
Number of systemic treatments	5.4 (5.6)	5 (4.4)
Biologic treatment		
Time from systemic to biologic treatment (years)		4.2 (3.7)
Years on biologic treatment		7.1 (4.6)
Number of biologic treatments		3.1 (3.1)

SD: standard deviation; SES: socioeconomic status; BMI: body mass index.

Table II. Prevalence of comorbidities in propensity score matching (PSM) groups

Condition	Control, *N* = 883 (50) *N* (%)	Study, *N* = 883 (50) *N* (%)
PVD	47 (5.3)	52 (5.9)
Atherosclerosis	164 (18.6)	169 (19.1)
CVA	86 (9.7)	96 (10.9)
Diabetes	400 (45.3)	396 (44.8)
Obesity	469 (53.1)	466 (52.8)
Hyperlipidaemia	745 (84.4)	758 (85.8)
Depression	136 (15.4)	142 (16.1)
Hypertension	570 (64.6)	561 (63.5)
Atopic dermatitis	26 (2.9)	28 (3.2)
Rheumatoid arthritis	244 (27.6)	263 (29.8)
Ischaemic heart disease	260 (29.4)	256 (29.0)
Alcoholic fatty liver	241 (27.3)	260 (29.4)
Psoriatic arthritis	615 (69.6)	617 (69.9)
Diseases of the circulatory system	803 (90.9)	795 (90.0)
Diseases of the nervous system	669 (75.8)	675 (76.4)
Neoplasms	687 (77.8)	690 (78.1)
Mental disorders	588 (66.6)	605 (68.5)

PVD: peripheral vascular disease; CVA: cerebrovascular accident.

psoriasis, sex, or comorbidities. The model demonstrated a 53% decrease in the risk of dementia within the study group (HR = 0.47, 95% CI: 0.323–0.699). This is illustrated in **Fig. 2**.

Methotrexate (75.8%) was the most frequently prescribed systemic drug, followed by acitretin (46.7%). As can be viewed in Table SII, patients in the study group used significantly more systemic agents compared with controls. Among biologic therapies, adalimumab was the most commonly prescribed (66%), followed by etanercept (54.1%) and secukinumab (27.4%). Details on biologic treatments are summarized in Table SIII.

In the PSM groups overall, 132 (7.5%) patients developed dementia. Dementia was more prevalent in the control group (8.8%) compared with the study group (6.1%) ($p < 0.03$). Alzheimer's disease was the most frequent type of dementia (4.1%). The rate of dementia types did not differ significantly between the groups. The prevalence of each type of dementia is presented in Table SIV.

Multivariate results

A total of 5,680 patients met the inclusion criteria, with 4,797 receiving only non-biologic systemic therapies. Significant differences were observed between the groups in terms of age: the control group had a mean age of 62.1 years (SD = 9.3), compared with 56.2 years (SD = 7.8) in the study group ($p < 0.001$). Patients in the study group also demonstrated longer treatment durations (mean: 6.4 years, SD = 5.1 vs 4.7 years, SD = 4.7; $p < 0.001$) and a higher number of treatments (mean: 5.0, SD = 4.4 vs 4.2, SD = 4.5; $p < 0.001$). SES categories did not significantly differ between the groups ($p = 0.4688$), as indicated by the χ^2 analysis. Comorbidities were distributed differently across groups. Rheumatoid arthritis ($p < 0.001$), psoriatic arthritis ($p < 0.001$), and alcoholic fatty liver disease ($p < 0.001$) were more prevalent in the study group. In contrast, peripheral vascular disease (PVD, $p = 0.002$), cerebrovascular accidents (CVA, $p < 0.001$), depression ($p = 0.047$), hypertension ($p < 0.001$), and atopic derma-

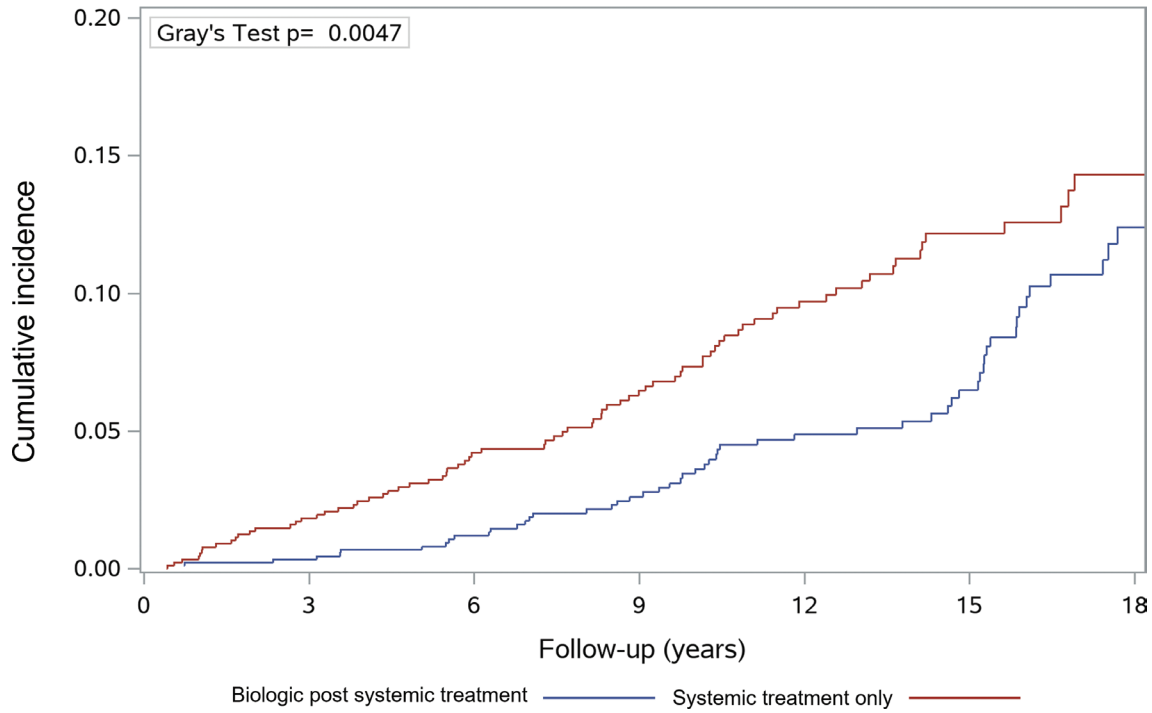

Fig. 2. Cumulative incidence of dementia in propensity score-matched patients with psoriasis. The blue curve represents patients treated with biologic therapies following systemic treatment, while the red curve represents patients treated with systemic therapy alone. Hazard ratio=2.11, 95% confidence interval 1.43–3.10.

titis ($p<0.001$) were more common in controls. Details of comorbidity prevalence are presented in Table SV.

12.6% of patients in the control group developed dementia. Application of a multivariate Cox proportional hazards model indicated that patients in the control group had a 98% increased risk of developing dementia compared with those in the biologic treatment group (adjusted HR = 1.98, 95% CI: 1.47–2.67). The covariates independently associated with increased dementia risk were: CVA (HR = 2.01, 95% CI: 1.70–2.39, depression (HR = 1.61, 95% CI: 1.37–1.90), diabetes (HR = 1.36, 95% CI: 1.15–1.61), and diseases of the nervous system (HR = 1.53, 95% CI: 1.18–1.98). Conversely, alcoholic fatty liver disease (HR = 0.77, 95% CI: 0.63–0.95) and neoplasms (HR = 0.73, 95% CI: 0.61–0.88) were associated with a reduced dementia risk. Mental disorders had the highest relative risk (HR = 5.58, 95% CI: 3.74–8.32).

Sensitivity analysis

To address potential immortal time bias, we conducted a sensitivity analysis. The immortality period was from the start of systemic treatment plus 90 days to the start of biologic therapy plus 90 days. The median immortality time before biologic treatment was 3 years (SD 3.7 years). Among 833 patients in the matched systemic treatment group, 13 (1.6%) died during this time, with 4 diagnosed with dementia before biologic treatment. Excluding these cases, our results remained statistically significant, reinforcing the study's validity and reliability.

DISCUSSION

Our study evaluated the impact of biologic treatments on the risk of developing dementia in psoriasis patients. We found that patients receiving biologic treatments had a lower prevalence of dementia (6.1%) compared with those treated with systemic therapies (12.6% in the raw data and 8.8% in the PSM group), corresponding to a 47–53% risk reduction. This surpasses the 17% reduction from cardiovascular and lifestyle management and the 19% reduction with hearing aids (31).

These findings highlight the potential of biologic treatments to target inflammation for dementia prevention, aligning with previous studies (12, 14, 20, 23, 24, 27, 32). Notably, etanercept and adalimumab use is associated with a 47% and 41% reduced Alzheimer's risk, respectively (23). Similar reductions appear with TNF-α inhibitors for psoriatic arthritis and rheumatoid arthritis (23, 24, 27, 32). Though lacking direct clinical studies of IL-17 and IL-23 inhibitors on dementia, laboratory findings and mouse models support a significant impact (17–19, 24, 25).

In our cohort, cardiovascular comorbidities were higher in moderate-to-severe psoriasis, compared with previous reports (33–35), likely due to older patient demographics. Differences existed between treatment groups: systemic-only had more cardiovascular risks while biologic had more inflammatory conditions. Despite this, dementia prevalence was lower in the study group, reinforcing the hypothesis that biologics reduce inflammation and dementia risk. No evidence showed that cardiovascular risk skewed the results toward higher dementia risk.

Our data also revealed a higher prevalence of depression and mental illness in the control group. Chronic skin diseases can contribute to depression by negatively affecting quality of life and self-esteem, while depression itself may promote neural inflammation and impair hippocampal neurogenesis (36, 37). This suggests that depression may play a role in the link between biologic therapy and reduced dementia risk. However, despite higher depression in the control group, the PSM model showed that this effect is independent of mental health (see Table II). Our study found no correlation between low SES and increased dementia prevalence, contrasting with previous findings (38, 39). SES distribution was comparable between the research groups, likely due to universal health coverage. Another study based on CHS database noted a high prevalence of biologic treatment among low to medium SES patients (40). Additionally, mandatory free public education and the absence of differences in smoking or other SES-related morbidities (39) between our study groups further contribute to SES parity in dementia prevalence.

Limitations

This study has several limitations. The retrospective design limits causal inference, and confounding factors, such as age and morbidities, may impact results. To mitigate this, we used PSM and a multivariate model, enhancing robustness, though some differences may persist. Immortality bias exists, as patients in the biologic group had to survive between systemic treatment and biologic therapy. While no retrospective design can entirely eliminate this bias, sensitivity analysis confirmed the statistical significance of our findings. Moreover, while a recorded psoriasis diagnosis was a defining inclusion criterion, it is possible that some patients received systemic or biologic therapies for conditions other than psoriasis, which could introduce variability in treatment interpretation. Despite this, the high quality of our database supports the reliability of our results. Future prospective studies are needed to validate these findings and explore mechanistic pathways, especially regarding the long-term cognitive outcomes of different psoriasis treatments.

Conclusion

Our study provides further evidence that biologic therapies, particularly TNF-α, IL-17, and IL-23 inhibitors,

may offer neuroprotective benefits by reducing the risk of dementia in psoriasis patients. These insights enhance our understanding of the role of systemic inflammation in neurodegenerative diseases.

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Data availability statement: The data supporting the findings of this study are not publicly available due to confidentiality restrictions. However, the data may be accessed upon reasonable request to the corresponding author and with permission from the appropriate authorities, where applicable.

IRB approval: Approved by the IRB of Emek Medical Center, Afula, Israel. Approval #EMC-0003-23.

Conflicts of interest: MZ has served as an investigator, speaker, and consultant for AbbVie, Sanofi, Novartis, Eli Lilly, Boehringer-Ingelheim, Janssen, Pfizer, DermAbio, and Neopharm. Dr Jen A. Barak Levitt has served as a speaker for Neopharm and Novartis, and as an investigator for DermAbio and Sanofi.

REFERENCES

1. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol 2017; 31: 205–212. https://doi.org/10.1111/jdv.13854
2. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. J Am Acad Dermatol 2014; 70: 512–516. https://doi.org/10.1016/j.jaad.2013.11.013
3. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. JAMA 2020; 323: 1945–1960. https://doi.org/10.1001/jama.2020.4006
4. Nestle FO, Kaplan DH, Barker J. Mechanisms of disease: psoriasis. N Engl J Med 2009; 361: 496–509. https://doi.org/10.1056/NEJMra0804595
5. Ferrari E, Cravello L, Bonacina M, Salmoiraghi F, Magri F. Stress and dementia. In: Steckler T, Kalin NH, Reul JMHM, eds. Techniques in the behavioral and neural sciences: Part 2: Stress: integrative and clinical aspects. Vol 15. Amsterdam: Elsevier, 2005: p. 357–370.https://doi.org/10.1016/S0921-0709(05)80064-1
6. Van der Flier WM, Scheltens P. Epidemiology and risk factors of dementia. J Neurol Neurosurg Psychiatry 2005; 76: v2–v7. https://doi.org/10.1136/jnnp.2005.082867
7. Hugo J, Ganguli M. Dementia and cognitive impairment: epidemiology, diagnosis, and treatment. Clin Geriatr Med 2014; 30: 421–442. https://doi.org/10.1016/j.cger.2014.04.001
8. Rabinovici GD. Late-onset Alzheimer disease. Continuum (Minneap Minn) 2019; 25: 14–33. https://doi.org/10.1212/CON.0000000000000700
9. Wu CY, Hu HY, Chou YJ, LI CP, Chang YT. Psoriasis is not a risk factor for dementia: a 12-year nationwide population-based cohort study. Arch Dermatol Res 2020; 312: 657–664. https://doi.org/10.1007/s00403-020-02057-2
10. Kridin K, Linder D, Shalom G, Piaserico S, Babaev M, Freud T, Comaneshter D, et al. Psoriasis and dementia: a cross-sectional study of 121801 patients. Acta Derm Venereol 2020; 100: 5844. https://doi.org/10.2340/00015555-3595
11. Pezzolo E, Mutlu U, Vernooij M, Dowlatshahi W, Gisondi EA, Girolomoni P, et al. Psoriasis is not associated with cognition, brain imaging markers, and risk for dementia: the Rotterdam Study. J Am Acad Dermatol 2021; 85: 671–680. https://doi.org/10.1016/j.jaad.2018.07.046
12. Kim M, Park HE, Lee SH, Han K, Lee JH. Increased risk of Alzheimer's disease in patients with psoriasis: a nationwide population-based cohort study. Sci Rep 2020; 10: 1–7. https://doi.org/10.1038/s41598-020-63550-2
13. Yen H, Yen H, Chi CC. Is psoriasis associated with dementia or cognitive impairment? A critically appraised topic. Br J Dermatol 2021; 184: 34–42. https://doi.org/10.1111/bjd.19025
14. Huang KL, Yeh CC, Wu SI, Huang KY, Yang YH, Kuo, TY, et al. Risk of dementia among individuals with psoriasis: a nationwide population-based cohort study in Taiwan. J Clin Psychiatry 2019; 80: 15854. https://doi.org/10.4088/JCP.18m12462
15. Lam M, Khorvash R, Drucker AM. Association between psoriasis and risk of dementia: a systematic review and meta-analysis. J Am Acad Dermatol 2021; 84: 790–792. https://doi.org/10.1016/j.jaad.2020.05.091
16. Heppner FL, Ransohoff RM, Becher B. Immune attack: the role of inflammation in Alzheimer disease. Nat Rev Neurosci 2015; 16: 358–372. https://doi.org/10.1038/nrn3880
17. Milovanovic J, Arsenijevic A, Stojanovic B, Kanjevac T, Arsenijevic, D, Radosavljevic G, et al. Interleukin-17 in chronic inflammatory neurological diseases. Front Immunol 2020; 11: 947. https://doi.org/10.3389/fimmu.2020.00947
18. Chen JM, Jiang GX, Li QW, Zhou ZM, Cheng Q. Increased serum levels of interleukin-18, -23, and -17 in Chinese patients with Alzheimer's disease. Dement Geriatr Cogn Disord 2014; 38: 321–329. https://doi.org/10.1159/000360606
19. Vellecco V, Saviano A, Raucci F, Casillo GM, Mansour AA, Panza E, et al. Interleukin-17 triggers systemic inflammation, peripheral vascular dysfunction, and related prothrombotic state in a mouse model of Alzheimer's disease. Pharmacol Res 2023; 187: 106595. https://doi.org/10.1016/j.phrs.2022.106595
20. Torres-Acosta N, O'Keefe JH, O'Keefe EL, Isaacson R, Small G. Therapeutic potential of TNF-α inhibition for Alzheimer's disease prevention. J Alzheimers Dis 2020; 78: 619–626. https://doi.org/10.3233/JAD-200711
21. Zheng Y, Zhang X, Zhang R, Wang Z, Gan J, Gao Q, et al. Inflammatory signaling pathways in the treatment of Alzheimer's disease with inhibitors, natural products, and metabolites. Int J Mol Med 2023; 52: 1–42. https://doi.org/10.3892/ijmm.2023.5314
22. Calsolaro V, Edison P. Neuroinflammation in Alzheimer's disease: current evidence and future directions. Alzheimers Dement 2016; 12: 719–732. https://doi.org/10.1016/j.jalz.2016.02.010
23. Mudrenko I, Chyniak O. Association between IL-17, IL-23 with neurocognitive scales in patients with Alzheimer's disease. Eur Psychiatry 2021; 64: S718–S719. https://doi.org/10.1192/j.eurpsy.2021.1903
24. Zhou M, Xu R, Kaelber DC, Gurney ME. Tumor necrosis factor blocking agents are associated with lower risk for Alzheimer's disease in patients with rheumatoid arthritis and psoriasis. PLoS One 2020; 15: e0229819. https://doi.org/10.1371/journal.pone.0229819
25. Cristiano C, Volpicelli F, Lippiello P, Buono B, Raucci F, Piccolo M, et al. Neutralization of IL-17 rescues amyloid-β-induced neuroinflammation and memory impairment. Br J Pharmacol 2019; 176: 3544–3557. https://doi.org/10.1111/bph.14586
26. Chen JM, Li QW, Jiang GX, Liu JS, Cheng Q. IL-18 induced IL-23/IL-17 expression impairs Aβ clearance in cultured THP-1 and BV2 cells. Cytokine 2019; 119: 113–118. https://doi.org/10.1016/j.cyto.2019.03.003
27. Xie W, Hou Y, Xiao S, Zhang X, Zhang Z. Association between disease-modifying antirheumatic drugs for rheumatoid arthritis and risk of incident dementia: a systematic review with meta-analysis. RMD Open 2024; 10: e004016. https://doi.org/10.1136/rmdopen-2023-004016
28. National Insurance Institute of Israel. Health insurance in Israel 2017 survey. [Accessed 25 Aug 2023] Available from: https://www.btl.gov.il/Publications/survey/Pages/seker_303.aspx.
29. Central Bureau of Statistics. Characterization and ranking of different geographical units in Israel. Available from: https://www.cbs.gov.il. Accessed Jan 2024.
30. Taquet M, Dercon Q, Todd JA, Harrison PJ. The recombinant shingles vaccine is associated with lower risk of dementia. Nat Med 2024; 30: 2777–2781. https://doi.org/10.1038/s41591-024-03201-5
31. Reuben DB, Kremen S, Maust DT. Dementia prevention

and treatment: a narrative review. JAMA Intern Med 2024; 184: 563–572. https://doi.org/10.1001/jamainternmed.2023.8522
32. Chou RC, Kane M, Ghimire S, Gautam, S, Gui J. Treatment for rheumatoid arthritis and risk of Alzheimer's disease: a nested case-control analysis. CNS Drugs 2016; 30: 1111–1120. https://doi.org/10.1007/s40263-016-0374-z
33. Feldman SR, Zhao Y, Shi L, Tran MH, Lu J. Economic and comorbidity burden among moderate-to-severe psoriasis patients with comorbid psoriatic arthritis. Arthritis Care Res 2015; 67: 708–717. https://doi.org/10.1002/acr.22492
34. Menter A, Korman NJ, Elmets CA, Van Voorhees AS, Leonardi CL, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol 2008; 58: 826–850. https://doi.org/10.1016/j.jaad.2008.02.039
35. Kampe T, Dorko E, Rimárová K, Houžvičková A, Baloghová J, Baranová, Z, et al. Prevalence of cardiovascular risk factors in patients with psoriasis. Cent Eur J Public Health 2022; 30: S05–S10. https://doi.org/10.21101/cejph.a6806
36. Katamanin OM, Tan IJ, Barry J, Jafferany M. Role of inflammation and cytokine dysregulation in depression in patients with inflammatory skin conditions. Am J Clin Dermatol 2024; 25: 1–9. https://doi.org/10.1007/s40257-024-00905-9
37. Dou Y, You J, Wang J, Li X, Lin Y, Liu B, et al. IL-17A mediates depressive-like symptoms by inducing microglia activation in psoriasiform dermatitis mice. Immun Inflamm Dis 2024; 12: e70092. https://doi.org/10.1002/iid3.70092
38. Wang K, Fang Y, Zheng R, Zhao X, Wang S, Lu J, et al. Associations of socioeconomic status and healthy lifestyle with incident dementia and cognitive decline: two prospective cohort studies. EClinicalMedicine 2024; 76: 102831. https://doi.org/10.1016/j.eclinm.2024.102831
39. Kalaria R, Maestre G, Mahinrad S, Acosta DM, Akinyemi RO, Alladi S, et al. The 2022 symposium on dementia and brain aging in low- and middle-income countries. Alzheimers Dement 2024; 20: 4290–4314. https://doi.org/10.1002/alz.13836
40. Shalom G, Zisman D, Bitterman H, Harman-Boehm I, Greenberg-Dotan S, Dreiher J, et al. Systemic therapy for psoriasis and the risk of herpes zoster: a 500000 person-year study. JAMA Dermatol 2015; 151: 533–538. https://doi.org/10.1001/jamadermatol.2014.4956