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Parkinson's Disease

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January 2026

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1. **Clinical, Biological, and Functional Connectivity Profile of Patients With De Novo Parkinson Disease Who Are APOE epsilon4 Carriers.**

Authors: Conti, Matteo;Mascioli, Davide;Simonetta, Clara;Ferrari, Valerio;Bissacco, Jacopo;Bagetta, Silvio;Carparelli, Federico;Bernardini, Sergio;Di Giuliano, Francesca;Marchionni, Enrica;Pierantozzi, Mariangela;Mercuri, Nicola Biagio;Schirinzi, Tommaso and Stefani, Alessandro

Publication Date: Jan 13 ,2026

Journal: Neurology 106(1), pp. e214449

Abstract: BACKGROUND AND OBJECTIVES: Growing evidence suggests that the APOE epsilon4 allele, a genetic risk factor for Alzheimer disease (AD), influences the clinical-pathologic features of Parkinson disease (PD). APOE epsilon4 promotes brain amyloid accumulation, indicating a PD subtype more susceptible to late copathology. However, the early correlates of APOE epsilon4 carriers in PD are not known. In this study, we used a multimodal approach to define the clinical, neurochemical, and neurophysiologic profiles of APOE epsilon4 carriers in PD at onset. METHODS: We conducted a single-center, cross-sectional study at Tor Vergata Hospital (Rome, Italy), enrolling newly diagnosed, drug-naive PD participants and age-matched/sex-matched healthy controls (HCs). Patients with PD were stratified by APOE genotype into epsilon4 and non-epsilon4 carriers and evaluated through a comprehensive clinical assessment and the measurement of CSF amyloid peptides and tau protein levels. Group differences in high-density EEG-based functional connectivity (FC) were analyzed using network-based statistics to identify APOE epsilon4-modulated patterns. Clinical and biomarker associations with network metrics were tested using analysis of covariance and

correlation analyses. RESULTS: The study included 66 PD participants (mean age 63.2 [10.1] years, 35% female, 52 epsilon4 noncarriers, 14 epsilon4 carriers) and 55 HCs (mean age 62.0 [15.2] years, 42% female). PD epsilon4, compared with PD non-epsilon4, demonstrated higher motor impairment, especially in bradykinesia (16.4 [7.6] vs 11.0 [5.6], p = 0.02) and gait disturbances (3.46 [2.23] vs 1.94 [1.46], p = 0.003) Movement Disorder Society-sponsored Unified Parkinson's Disease Rating Scale part III scores, and reduced CSF amyloid-beta42 (Abeta42)/amyloid-beta40 (Abeta40) ratio (0.09 [0.03] vs 0.13 [0.03], p F = 3.9, p = 0.034) and increased beta-band connectivity (F = 9.8, p r = -0.62, p = 0.02) and positively with Montreal Cognitive Assessment (r = 0.57, p = 0.03) and CSF Abeta42/Abeta40 (r = 0.54, p = 0.04). beta-FC correlated with bradykinesia in both groups, with stronger associations in epsilon4 carriers (r = 0.54, p = 0.04) than in non-epsilon4 (r = 0.28, p = 0.04). DISCUSSION: APOE epsilon4 defines a PD subtype characterized by greater motor impairment, reduced CSF Abeta42/Abeta40, and distinct FC abnormalities since the onset. An early amyloid-mediated network disruption thus emerges as the potential biological signature of epsilon4 carriers. Although limited by single-center and cross-sectional design, this study supports APOE epsilon4 as a stratification marker for early diagnostic and therapeutic strategies in PD.

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2. **Association between cognitive adverse effects of anticholinergic medication and development of dementia in Parkinson's disease.**

Authors: Ha S.H.;Kim S.;Lee S.;Jin B.;Woo K.A.;Shin J.H. and Kim, H. J.

Publication Date: 2026

Journal: Parkinsonism and Related Disorders 142(pagination), pp. Article Number: 108136. Date of Publication: 01 Jan 2026

Abstract: Introduction: Approximately one-third of patients with Parkinson's disease (PD) develop dementia, and anticholinergic use has been implicated as a risk factor, particularly with prolonged exposure. This study examined whether short-term anticholinergic use was associated with differing dementia incidence between cognitive and non-cognitive adverse effects groups. Method(s): We retrospectively reviewed records of 209 PD patients prescribed anticholinergics (trihexyphenidyl, benztropine, or amantadine) for the first time at Seoul National University Hospital between 2011 and 2020. Patients were classified into three groups: those who discontinued due to cognitive or non-cognitive adverse effects, and those who continued long-term use without adverse effects. Dementia incidence was compared across groups using Kaplan-Meier analysis, and multivariable logistic regression adjusted for age, sex, and disease duration. Result(s): Of the 155 patients analyzed, 62 continued long-term use, whereas 12 and 81 discontinued due to cognitive and non-cognitive adverse effects, respectively. Baseline characteristics and anticholinergic dosages were comparable among groups. After covariate adjustment, dementia incidence did not differ between cognitive and non-cognitive adverse effects groups (adjusted OR = 1.17, 95 % CI 0.13-10.22, p = 0.890). Excluding those who discontinued due to lack of effect yielded similar results (adjusted OR = 0.68, 95 % CI 0.10-4.59, p = 0.690). No significant difference was observed between the long-term use and cognitive adverse effects group (adjusted OR = 1.57, 95 % CI 0.23-10.89, p = 0.646). Conclusion(s): The cognitive adverse effects of anticholinergics were not associated with increased dementia risk. Prospective studies assessing individual variability in anticholinergic sensitivity and cognitive outcomes in PD are warranted.

3. **Association between cognitive adverse effects of anticholinergic medication and development of dementia in Parkinson's disease.**

Authors: Ha, Su Hyeon;Kim, Seoyeon;Lee, Seungmin;Jin, Bora;Woo, Kyung Ah;Shin, Jung Hwan and Kim, Han-Joon

Publication Date: Jan ,2026

Journal: Parkinsonism & Related Disorders 142, pp. 108136

Abstract: INTRODUCTION: Approximately one-third of patients with Parkinson's disease (PD) develop dementia, and anticholinergic use has been implicated as a risk factor, particularly with prolonged exposure. This study examined whether short-term anticholinergic use was associated with differing dementia incidence between cognitive and non-cognitive adverse effects groups. METHODS: We retrospectively reviewed records of 209 PD patients prescribed anticholinergics (trihexyphenidyl, benztropine, or amantadine) for the first time at Seoul National University Hospital between 2011 and 2020. Patients were classified into three groups: those who discontinued due to cognitive or non-cognitive adverse effects, and those who continued long-term use without adverse effects. Dementia incidence was compared across groups using Kaplan-Meier analysis, and multivariable logistic regression adjusted for age, sex, and disease duration. RESULTS: Of the 155 patients analyzed, 62 continued long-term use, whereas 12 and 81 discontinued due to cognitive and non-cognitive adverse effects, respectively. Baseline characteristics and anticholinergic dosages were comparable among groups. After covariate adjustment, dementia incidence did not differ between cognitive and non-cognitive adverse effects groups (adjusted OR = 1.17, 95 % CI 0.13-10.22, p = 0.890). Excluding those who discontinued due to lack of effect yielded similar results (adjusted OR = 0.68, 95 % CI 0.10-4.59, p = 0.690). No significant difference was observed between the long-term use and cognitive adverse effects group (adjusted OR = 1.57, 95 % CI 0.23-10.89, p = 0.646). CONCLUSIONS: The cognitive adverse effects of anticholinergics were not associated with increased dementia risk. Prospective studies assessing individual variability in anticholinergic sensitivity and cognitive outcomes in PD are warranted.

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4. **Macronutrient content and quality, and risk of multimorbidity in the UK Biobank.**

Authors: Vazquez-Fernandez, Aitana;Yevenes-Briones, Humberto;Baylin, Ana;Caballero, Francisco F. and Lopez-Garcia, Esther

Publication Date: Jan 12 ,2026

Journal: Journals of Gerontology Series A-Biological Sciences & Medical Sciences 81(2)

Abstract: BACKGROUND: Multimorbidity is a major determinant of lifespan in older adults. We aimed to examine the association between overall, healthy and unhealthy low-carbohydrate diets (LCD) and low-fat diets (LFD) with the incidence of multimorbidity. METHODS: 112 710 individuals (40-70 years) from the UK Biobank were included. Food consumption was assessed using up to five 24-h dietary recalls. LCD and LFD scores were calculated based on macronutrient quality. We calculated three versions of each score-overall,

healthy and unhealthy. Multimorbidity was defined as the coexistence of >=2 of nine chronic diseases, including cancer, chronic obstructive pulmonary disease, dementia, Parkinson's disease, stroke, depression, osteoarthritis, diabetes, and coronary heart disease. RESULTS: There were 8387 individuals with multimorbidity during a median follow-up of 10.7 years. Overall, LCD and LFD scores were not associated with higher multimorbidity risk. There was a higher multimorbidity risk for individuals in the highest quintile (Q5) of unhealthy LCD vs. lowest quintile (Q1) [fully adjusted hazard ratio (HR): 1.07, 95%CI: 1.01, 1.15, p-trend = 0.16] overall as well as among non-tobacco smokers [1.11 (1.00, 1.23), p-trend = 0.09]. The unhealthy LFD score was associated with multimorbidity overall [1.07 (1.00, 1.14), p-trend = 0.07] and never-smokers [1.12 (1.01, 1.24); p-trend = 0.01]. Healthy score results were less consistent. The plant protein component had an inverse association with incident multimorbidity risk, whereas the low-quality-fat and animal protein components were each associated with a higher risk of multimorbidity. CONCLUSION: Diet scores defined only by the total amount of carbohydrates or fat were not associated with risk of multimorbidity. Unhealthy diet scores, including low-quality macronutrients and animal protein, were associated with increased risk of multimorbidity.

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5. **Impact of best practice advisory on reducing contraindicated medications in hospitalized patients with Parkinson's disease.**

Authors: Xu Z.;Jiang A.;Bujala N.;Sackonvitz A.;Bond C.;Dohle C. and Amodeo, K.

Publication Date: 2026

Journal: Parkinsonism and Related Disorders 142(pagination), pp. Article Number: 108129. Date of Publication: 01 Jan 2026

Abstract: Background: Patients with Parkinson's disease (PD) face heightened risks during hospitalization, including prolonged hospital stay and discharge to higher levels of care. Possible contributing factors include non-adherence to home medication regimens and administration of contraindicated medications. Objective(s): To evaluate the impact of Best Practice Advisory (BPA), integration into Electronic Medical Records (EMRs) aimed at minimizing the prescription of contraindicated dopamine blocking agents (DBA) in hospitalized PD patients. Method(s): This is a single center, retrospective, cohort study comparing frequency of administration of contraindicated medications before and after implementation of a BPA at Westchester Medical Center (WMC) between January 2023 and July 2024. The primary outcome is the prescription of DBA. Secondary outcomes included discharge level of care, and hospital length of stay. Result(s): Two-hundred and eleven charts were reviewed, and patients with confirmed diagnosis of PD or related Parkinsonism, who were prescribed dopaminergic medications at the time of admission were included. After BPA implementation, there was a statistically significant drop in rates of contraindicated prescriptions for psychosis and antiemetics, 33.33 %-2.86 % (p Result(s): Two-hundred and eleven charts were reviewed, and patients with confirmed diagnosis of PD or related Parkinsonism, who were prescribed

dopaminergic medications at the time of admission were included. After BPA implementation, there was a statistically significant drop in rates of contraindicated prescriptions for psychosis and antiemetics, 33.33 %-2.86 % (p Result(s): Two-hundred and eleven charts were reviewed, and patients with confirmed diagnosis of PD or related Parkinsonism, who were prescribed dopaminergic medications at the time of admission were included. After BPA implementation, there was a statistically significant drop in rates of contraindicated prescriptions for psychosis and antiemetics, 33.33 %-2.86 % (p Conclusion(s): Implementing a BPA effectively reduced the prescription of contraindicated medications for PD patients. This highlights the value of targeted BPAs in improving PD patient safety and lays the groundwork for further medication quality improvement initiatives aimed at optimizing inpatient care for this vulnerable population.

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6. **Impact of best practice advisory on reducing contraindicated medications in hospitalized patients with Parkinson's disease.**

Authors: Xu, Zhimin;Jiang, Andy;Bujala, Nishitha;Sackonvitz, Ariel;Bond, Colleen;Dohle, Carolin and Amodeo, Katherine

Publication Date: Jan ,2026

Journal: Parkinsonism & Related Disorders 142, pp. 108129

Abstract: BACKGROUND: Patients with Parkinson's disease (PD) face heightened risks during hospitalization, including prolonged hospital stay and discharge to higher levels of care. Possible contributing factors include non-adherence to home medication regimens and administration of contraindicated medications. OBJECTIVE: To evaluate the impact of Best Practice Advisory (BPA), integration into Electronic Medical Records (EMRs) aimed at minimizing the prescription of contraindicated dopamine blocking agents (DBA) in hospitalized PD patients. METHODS: This is a single center, retrospective, cohort study comparing frequency of administration of contraindicated medications before and after implementation of a BPA at Westchester Medical Center (WMC) between January 2023 and July 2024. The primary outcome is the prescription of DBA. Secondary outcomes included discharge level of care, and hospital length of stay. RESULTS: Two-hundred and eleven charts were reviewed, and patients with confirmed diagnosis of PD or related Parkinsonism, who were prescribed dopaminergic medications at the time of admission were included. After BPA implementation, there was a statistically significant drop in rates of contraindicated prescriptions for psychosis and antiemetics, 33.33 %-2.86 % (p : Two-hundred and eleven charts were reviewed, and patients with confirmed diagnosis of PD or related Parkinsonism, who were prescribed dopaminergic medications at the time of admission were included. After BPA implementation, there was a statistically significant drop in rates of contraindicated prescriptions for psychosis and antiemetics, 33.33 %-2.86 % (p : Two-hundred and eleven charts were reviewed, and patients with confirmed diagnosis of PD or related Parkinsonism, who were prescribed dopaminergic medications at the time of admission were included. After BPA implementation, there was a statistically significant drop in rates of contraindicated prescriptions for psychosis and antiemetics, 33.33 %-2.86 % (p CONCLUSION: Implementing a BPA effectively reduced the prescription of contraindicated medications for PD patients. This highlights the value of targeted BPAs in improving PD patient safety and lays the groundwork for further medication quality improvement initiatives aimed at optimizing inpatient care for this vulnerable population.

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7. **Automated synthetic contrast-enhanced MRI improves choroid plexus segmentation in Parkinsonian syndromes.**

Authors: Ambaye, Dagnachew Tessema;Jo, Sungyang;Enes Candan, Huseyin;Tessema, Abel Worku;Myratgeldiyev, Nepes;Suh, Chong Hyun;Ryu, Jihong;Chung, Sun Ju;Lee, Hansol;Lee, Jae-Hyeok;Lee, Eun-Jae and Cho, HyungJoon

Publication Date: Nov ,2025

Journal: Radiology Advances 2(6), pp. umaf042

Abstract: Background: Choroid plexus (ChP) has gained attention as a potential biomarker in neurodegenerative diseases, yet its segmentation remains challenging. Gadolinium-based contrast-enhanced MRI (CE-MRI) is the reference standard, as non-contrast MRI images lack sufficient contrast. However, gadolinium deposition, risk of nephrogenic system fibrosis in renally impaired patients, and patient discomfort limit its repeated administration. Purpose: To develop deep learning-based synthetic-contrast-enhanced MRI (SynCE-MRI) using T1-weighted images to improve ChP visualization and evaluate its ability to detect morphological changes in Parkinsonian syndromes. Materials and methods: This retrospective study included 265 (mean age = 65.7 +/- 7.00 years, males/females: 120/145) consecutive patients in the internal cohort (174 with Parkinson's disease [PD], 46 with essential tremor, and 45 with atypical Parkinsonian disorder [APD]) who underwent T1W and CE-MRI at 3T from Asan Medical Center (June 2021-December 2023), and an external cohort of 58 (mean age = 60.7 +/- 7.8 years, males/females: 40/18) patients (29/29 PD/APD) from Pusan National University, Yangsan Hospital (April 2011-December 2014). Nested-UNet was used for SynCE-MRI synthesis from T1W images. The 3D-UNet ChP segmentation model was trained by CE-MRI and tested using SynCE-MRI. Kruskal-Wallis and Bonferroni-corrected Mann-Whitney U tests assessed image synthesis, segmentation, and ChP morphometry (P Results: SynCE-MRI achieved high-fidelity images with peak signal-to-noise ratio (PSNR) 35.37 +/- 1.32 and structural similarity index measure (SSIM) 0.970+/-0.0054. Segmentation accuracy for SynCE-MRI (dice score = 0.803 +/- 0.029, 95% CI: 0.797-0.810) significantly outperformed manual (dice score = 0.59 +/- 0.057, 95% CI: 0.578-0.603; P P P = .04) and external cohort (APD: 2.81 +/- 0.48 mL, 95% CI: 2.60-3.02 vs PD: 2.52 +/- 0.45 mL, 95% CI: 2.36-2.69; P = .03). Conclusion: SynCE-MRI accurately replicates CE-MRI for ChP imaging and morphometry, outperforms T1W imaging in segmentation, and detects ChP enlargement in APD versus PD across internal and external cohorts, consistent with CE-MRI findings. Copyright © The Author(s) 2025. Published by Oxford University Press on behalf of the Radiological Society of North America.

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8. **The relationship between neuropsychiatric dimensions and markers of Parkinson's disease risk in the UK Biobank.**

Authors: Attaallah, Bahaaeddin;Waters, Sheena;Marshall, Charles and Noyce, Alastair

Publication Date: Dec 01 ,2025

Journal: Npj Parkinsons Disease 11(1), pp. 344

Abstract: Neuropsychiatric symptoms are a significant yet often overlooked aspect of Parkinson's disease (PD). Using UK Biobank data, we examined associations between neuropsychiatric dimensions and PD risk markers. Factor analysis identified four dimensions-Depression, Anxiety, Adult Stress-Adversity, and Alcohol- and Substance-Related Behaviours (ASRB) -across three groups: PD, healthy controls, and cerebrovascular disease (CVD) as neurological controls. These dimensions showed distinct patterns in PD. Depression scores were significantly elevated, while ASRB scores were consistently lower. Neuroimaging linked ASRB to subcortical changes specific to PD, particularly quantitative susceptibility mapping in the substantia nigra, consistent with the dopaminergic system's role in goal-directed behaviour. GBA1 carrier status was linked to age-related changes in this dimension. Furthermore, PD patients with higher ASRB showed greater volatility in cognitive and motor function, with worsening before diagnosis and subsequent improvement. These findings highlight the complex interplay between psychiatric symptoms, neurobiological changes, and genetic factors in PD, suggesting that specific neuropsychiatric profiles may serve as early indicators of disease risk and progression.

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9. **Whole-exome sequencing and burden analysis identify six novel candidate risk genes and expand the genetic landscape of Parkinson's disease.**

Authors: Fan, Yu;Hu, Zhen;Yan, Qin-Qin;Wan, Jing-Jin and Liu, Jun

Publication Date: Dec 03 ,2025

Journal: Npj Parkinsons Disease 11(1), pp. 347

Abstract: Parkinson's Disease (PD) is a complex neurodegenerative disorder with a largely undefined genetic architecture, particularly regarding the role of rare coding variants. We performed a large-scale exome-wide association study to systematically identify rare genetic risk factors for PD. We analyzed whole-exome sequencing (WES) data from 3,602 PD patients and a strictly defined control group of 145,496 individuals of European ancestry from the UK Biobank. We focused on identifying high-confidence protein-truncating variants (PTVs) and used a rigorous gene-based association analysis to find genes significantly associated with PD risk. Our analysis identified PTVs in nine genes that were significantly more frequent in PD cases. These include three previously reported genes for PD/parkinsonism (ATP5F1C, COMMD9, and OPA1) and six novel genes (RGMB, SNX13, MGST2, NMBR, RCBTB1, and JAG1). Following sensitivity analyses, eight genes remained significant. Functional enrichment analysis highlighted pathways related to Notch binding and glutathione transferase activity. This study significantly expands the known genetic landscape of PD by identifying six novel candidate risk genes. Our findings underscore the importance of rare, high-impact PTVs in PD pathogenesis and provide new avenues for mechanistic research and the development of targeted therapeutics.

10. **Distinct serum micronutrient metabolic profiles in Parkinson's disease patients with diabetes mellitus: associations with motor and non-motor symptoms.**

Authors: Feng T.;Tuersong T.;Wang X.;Li P.;Shang S.;Yang P.;Pan Y. and Yang, X.

Publication Date: 2025

Journal: Nutritional Neuroscience (pagination), pp. Date of Publication: 2025

Abstract: Background: Parkinson's disease (PD) is a common neurodegenerative disease, and its pathogenesis may be related to abnormal metabolism of micronutrients. Method(s): This study included 316 PD patients who visited the Second Affiliated Hospital of Xinjiang Medical University from January 2021 to December 2023. Patients were divided into two groups: those with both PD and diabetes mellitus(PD-DM group), and those with PD without DM(PD-NDM group). Inductively coupled plasma-mass spectrometry was employed to determine the levels of micronutrients, including calcium (Ca), magnesium (Mg), and iron (Fe), in serum samples. Next, demographic characteristics, clinical parameters, and micronutrient differences were compared between the two groups. Furthermore, the correlation between micronutrients and the progression of PD, as well as motor and non-motor symptoms, was analyzed. Finally, logistic regression was used to investigate the factors influencing PD with DM. Result(s): The PD-DM group had higher serum Ca(2.27 +/- 0.14 vs 2.22 +/- 0.12) and lower Mg (0.83 +/- 0.08 vs 0.89 +/- 0.06) and Fe (14.28 +/- 5.13 vs 16.45 +/- 6.81) than the PD-NDM group (P Result(s): The PD-DM group had higher serum Ca(2.27 +/- 0.14 vs 2.22 +/- 0.12) and lower Mg (0.83 +/- 0.08 vs 0.89 +/- 0.06) and Fe (14.28 +/- 5.13 vs 16.45 +/- 6.81) than the PD-NDM group (P Result(s): The PD-DM group had higher serum Ca(2.27 +/- 0.14 vs 2.22 +/- 0.12) and lower Mg (0.83 +/- 0.08 vs 0.89 +/- 0.06) and Fe (14.28 +/- 5.13 vs 16.45 +/- 6.81) than the PD-NDM group (P Result(s): The PD-DM group had higher serum Ca(2.27 +/- 0.14 vs 2.22 +/- 0.12) and lower Mg (0.83 +/- 0.08 vs 0.89 +/- 0.06) and Fe (14.28 +/- 5.13 vs 16.45 +/- 6.81) than the PD-NDM group (P Conclusion(s): Patients with PD and DM exhibit distinct micronutrient metabolic abnormalities, notably higher Ca and lower Mg and Fe levels.Copyright © 2025 Informa UK Limited, trading as Taylor & Francis Group.

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11. **Impact of type 2 diabetes mellitus on severity of Parkinson's disease: a cross-sectional study.**

Authors: Hamdy A.;Elawady A.;Nowara A. and Elshafei, O.

Publication Date: 2025

Journal: Romanian Journal of Neurology/ Revista Romana De Neurologie 24(3), pp. 287–294

Abstract: Background and objectives. Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms that significantly impact quality of life. This study aimed to investigate whether the presence of type 2 diabetes mellitus (T2DM) influences the clinical severity and manifestations of PD across motor and non-motor domains. Materials and methods. This cross-sectional study compared 80 PD patients (40 with T2DM and 40 without) at the Neurology Department of Mansoura University Hospital, Egypt. Demographic and clinical characteristics were documented. The Unified

Parkinson's Disease Rating Scale (UPDRS), Montreal Cognitive Assessment (MoCA), Hamilton Anxiety and Depression Scales, and Schwab and England Activities of Daily Living Scale were assessed in all participants. Results. PD patients with T2DM exhibited significantly more severe motor impairments, including substantial gait problems (p = 0.003) and reduced independence (p

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12. **Cognitive reserve, frailty status, and risk of neurodegenerative diseases: a prospective cohort study.**

Authors: Huang, Xiaxuan;Ling, Yitong;Tan, Shanyuan;Bai, Zihong;Shen, Si;Wang, Hao and Lyu, Jun

Publication Date: Dec 10 ,2025

Journal: Npj Parkinsons Disease 12(1), pp. 20

Abstract: Cognitive frailty has emerged as an important concept in research and clinical practice, yet the combined effect of cognitive reserve and frailty on neurodegenerative disease risk remains unexplored. This study included 346,025 UK Biobank participants followed for up to 15 years. Cognitive reserve indicators were generated using latent class analysis based on educational level, occupational achievement, confiding in others, social contact, leisure activities, and television viewing time. The primary outcome was neurodegenerative disease, with secondary outcomes including Parkinson's disease, Alzheimer's disease, and all-cause dementia. During a median follow-up of 13.7 years, 5,590 new cases of neurodegenerative diseases were diagnosed. Compared to non-frail individuals, pre-frail and frail individuals had 1.47-fold (95% CI: 1.39-1.55) and 2.74-fold (95% CI: 2.46-3.06) increased risk, respectively, while high cognitive reserve conferred protection (HR = 0.82, 95% CI: 0.76-0.87). In joint effect analysis, individuals with low levels of cognitive reserve and frailty had the highest risk (HR = 3.13, 95% CI: 2.70-3.63), demonstrating significant additive interaction. Cross-sectional neuroimaging analyses showed that lower cognitive reserve levels was associated with reduced total brain volume (beta = -0.161), reduced hippocampal volumes (betaleft = -0.085, betaright = -0.097), and increased white matter hyperintensities (beta = 0.045). These findings emphasize maintaining cognitive reserve and managing frailty as modifiable factors for preventing neurodegenerative diseases. Copyright © 2025. The Author(s).

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13. **Perspectives on digital health and advanced treatment referral in Parkinson's care among Danish neurologists: a mixed methods study.**

Authors: Karottki, N. L. C.;Thomsen, T. H.;Jennum, P. J.;Bibi, S.;Sharifi, M.;Coskun, O. and Biering-Sorensen, B.

Publication Date: 2025

Journal: Frontiers in Neurology [Electronic Resource] 16, pp. 1618348

Abstract: Introduction: Advanced treatments such as infusion therapies and deep brain stimulation can improve symptoms in Parkinson's disease, but identifying the right patients at the right time remains challenging. Digital health technologies offer objective, continuous, and

remote symptom tracking, making them increasingly relevant in Parkinson's management. This study examines Danish neurologists' perspectives on current referral practices for advanced Parkinson's treatment and explores the perceived advantages and barriers of digital health technologies use in clinical decision-making. Methods: Using a mixed methods approach, we surveyed neurologists involved in Parkinson's management across outpatient hospital settings and private practices. Results: Nineteen neurologists completed the survey, and six participated in semi-structured interviews. Most neurologists (15/19, 79%) believe current referral criteria for advanced treatment need improvement, and only (5/19, 26%) regularly use available decision-support tools. Discussion: The perceived advantages of digital health technologies include improved treatment optimization, real-world symptom tracking, and enhanced patient health literacy. However, concerns include uncertainty about the clinical relevance of measurements, resource constraints, and lack of supporting evidence. Neurologists also expressed reservations about reduced patient interaction and the insufficient tracking of non-motor symptoms in current digital health technologies. Our findings should be considered exploratory but highlight the limitations of current referral strategies for advanced treatment and neurologists' mixed perspectives on digital health technologies, with qualitative insights revealing both optimism and concerns about implementation. Digital health technologies have the potential to aid in identifying people with Parkinson's who may benefit from advanced treatment, and future referral criteria may benefit from incorporating objective digital measurements.

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14. **Association between motor symptom severity and urinary dysfunction in Parkinson's disease: a retrospective study.**

Authors: Lee, Jun Seok;Yoo, Joonsang;Son, Nak-Hoon;Byun, Hye Jin and You, Sooyeoun

Publication Date: 2025

Journal: Frontiers in Aging Neuroscience 17, pp. 1688656

Abstract: Introduction: Urinary dysfunction is a common non-motor symptom in patients with Parkinson's disease (PD) and is often associated with greater motor disability and reduced quality of life. Despite its clinical relevance, the association between motor symptom severity and urinary dysfunction remains poorly understood. This study aimed to elucidate this relationship using validated clinical questionnaires to assess urinary symptoms. Methods: We conducted a single-center, retrospective cross-sectional study including 223 patients with PD who visited a university hospital between September 2023 and February 2024. Urinary dysfunction was evaluated using the Overactive Bladder Symptom Score (OABSS) and International Prostate Symptom Score (IPSS), comprising the symptom (IPSS-symptom score; Q1-7) and satisfaction (IPSS-satisfaction score; Q8) scores. We analyzed the changes in urinary symptoms, overall satisfaction, and prodromal symptoms across the Hoehn and Yahr (HY) stages. Patients were divided into early (HY 2) groups to assess early urinary symptom changes. Results: The OABSS, IPSS-symptom score, and IPSS-satisfaction score significantly increased with advancing HY stage. Compared to the early group, the late group exhibited significantly higher OABSS ($p = 0.015$), IPSS-symptom scores ($p = 0.002$), and IPSS-satisfaction scores (p Conclusion: Our study provides evidence that urinary dysfunction intensifies with motor symptom progression in PD. These findings highlight the importance of

early detection and proactive management of urinary symptoms in patients with PD to enhance their overall quality of life. Copyright © 2025 Lee, Yoo, Son, Byun and You.

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15. **Adverse experiences in childhood and young adulthood, genetic susceptibility, and neurodegenerative disease incidence: a lifespan analysis.**

Authors: Li, Jie;Xu, Xiaoqin;Sun, Ying;Fu, Yanqi;Tan, Xiao;Wang, Ningjian;Lu, Yingli;Li, Jiang and Wang, Bin

Publication Date: Dec ,2025

Journal: European Journal of Psychotraumatology 16(1), pp. 2599612

Abstract: Background: Much remains unknown about the associations between adverse childhood experiences (ACEs), adverse adulthood experiences (AAEs) and the risk of neurodegenerative diseases, including dementia and Parkinson's disease (PD). Purpose: To examine the associations of ACEs and AAEs with incident dementia and PD, and to evaluate their interactions with genetic risk. Methods: We included 147,942 participants (mean [SD]: 55.9 [7.7] years) without dementia and PD at baseline from UK Biobank. ACEs and AAEs were assessed through an online mental health questionnaire, including emotional neglect, physical abuse, emotional abuse, sexual abuse, and physical neglect. Polygenic risk scores (PRS) were constructed for dementia and PD. Replication analysis was conducted in the China Health and Retirement Longitudinal Study (CHARLS) cohort. Results: During a median follow-up of 15.1 years, 851 incident dementia and 729 PD cases occurred. A greater number of ACEs was associated with increased risks of dementia (HR, 1.14, 95% CI: 1.08-1.21, per additional ACE) and PD (1.11, 1.04-1.18). Similarly, a higher number of AAEs was linked to elevated risks of dementia (1.16, 1.09-1.24) and PD (1.02, 0.95-1.10), though the latter was not statistically significant. Moreover, significant additive interactions between ACEs, AAEs, and genetic risk were observed for dementia, which accounted for an additional 13% to 19% of dementia cases. Results from the CHARLS confirmed the associations of ACEs and AAEs with dementia and PD. Conclusions: Exposure to ACEs or AAEs was associated with increased risks of dementia and PD. The dementia risk associated with ACEs was amplified in individuals with AAEs or high genetic susceptibility. These findings highlight the importance of life-course prevention targeting both ACEs and AAEs in mitigating dementia and PD risks, particularly among individuals with high genetic susceptibility. These findings should be interpreted with caution due to potential recall bias, self-reported assessments, and selection bias.; plain-language-summary Exposure to adverse childhood experiences (ACEs) was associated with dementia and Parkinson's disease (PD).ACEs could additively interact with adverse adulthood experiences (AAEs) and genetic susceptibility to escalate dementia risk. Language: English

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16. **Life-Space Movement Capture: Rethinking Passive Sensor Measures for Assessing Parkinson's At Home.**

Authors: Margariti E.K.;Czech E.;Morgan C.;Whone A.;O'Kane A.A.;O'Hara K.;Durrant A.;Kirk D. and Craddock, I.

Publication Date: 2025

Journal: SSRN (pagination), pp. Date of Publication: 09 Dec 2025

Abstract: Clinical drug trials for Parkinson's currently require the routine measurement of movement-related symptoms in controlled clinical settings. For patients (and clinicians) in such trials, there are potential advantages in moving towards long-term free-living and unobtrusive activity monitoring at home. However, home environments create additional complexities for developing sufficiently rigorous sensor-based metrics to monitor Parkinson's progression. To unpack these complexities, we conducted an interview-based study with 18 people (14 Parkinson's patients and 4 carers) in the UK, to better understand their symptoms' expression and coping, and explore what sensory measures and technologies would meaningfully capture their experiences at home. Through a thematic analysis of the interview data, we illustrate how anticipation of symptoms shape their daily activities and space-use patterns at different spatio-temporal levels at home. We draw upon this analysis to inform patient-centred recommendations and implications for the design of sensor-based measures and systems for monitoring chronic condition symptoms at home.

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17. **Impact of Electronic Prescribing on Parkinson's Disease Medication Management: A Retrospective Before-and-After Audit at a UK Teaching Hospital.**

Authors: Omer, Yad Z.;Chakraborty, Mayurika;Phillips, Katie;Ponniah, Gobeka and Strens, Lucy

Publication Date: Nov ,2025

Journal: Cureus 17(11), pp. e97619

Abstract: BACKGROUND: Parkinson's disease (PD) medications are classified as time-critical, with delays or omissions potentially leading to increased morbidity, prolonged admissions, and worsened clinical outcomes. The introduction of electronic prescribing (EPR) has shown potential to reduce prescribing errors, but its impact on PD-specific medication safety remains unclear. This audit aimed to evaluate the accuracy and timeliness of PD medication prescribing and administration before and after the implementation of EPR at a UK teaching hospital. METHODS: A retrospective clinical audit was conducted at University Hospitals Coventry and Warwickshire NHS Trust, Coventry, England. Records from adult inpatient admissions with a confirmed diagnosis of PD were reviewed over two six-month periods: July-December 2023 (pre-EPR) and July-December 2024 (post-EPR). A total of 100 randomly selected admissions (50 from each period) were analysed. Data were collected on prescribing accuracy (dose and formulation), administration timing, missed/delayed doses, and use of dopamine-blocking medications. The audit was assessed against the National Institute for Health and Care Excellence (NICE) QS164, NG71, and QS120 standards, which expect 100% accurate prescribing and administration of time-critical PD medicines within +/-30 minutes. Data were analysed using descriptive statistics in Microsoft Excel (Microsoft Corporation, Redmond, WA). RESULTS: Prescription of the correct PD dose decreased from 48/50 (96%) in 2023 to 45/50 (90%) in 2024, and correct formulation from 48/50 (96%) to 44/50 (88%). Correct administration times fell from 39/50 (78%) to 33/50 (66%). In both years, 36/50 (72%) of patients received their first dose on time. Full adherence to all prescribed doses declined from 28/50 (56%) to 24/50 (48%) post-EPR. Dopamine-blocking medication

use increased from 1/50 (2%) to 2/50 (4%). Discharge to care homes increased in 2024 (17/50 (34%) vs. 10/50 (20%)), while in-hospital deaths rose slightly (4/50 (8%) vs. 3/50 (6%)). CONCLUSION: Following the implementation of EPR, reductions were observed across several PD medication safety metrics; however, these findings represent observational associations and do not imply direct causation. The results highlight the importance of targeted staff training, early recognition of PD during clerking, and the use of clinical decision-support tools to optimise the safe and effective use of EPR systems in this patient group.

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18. **Exploring the relationship between epilepsy and neurodegenerative diseases.**

Authors: Rivera S.L.R.;Martinez H.R.;Cantu J.A.I. and Osorio, E. C.

Publication Date: 2025

Journal: Romanian Journal of Neurology/ Revista Romana De Neurologie 24(3), pp. 295–301

Abstract: Background. Epilepsy is frequently observed as a comorbid condition across a broad spectrum of neurological disorders, including various neurodegenerative diseases. Aims. To explore the relationship between epilepsy and neurodegenerative diseases. Methods. This was an analytical, retrospective, observational, and longitudinal study. Inclusion criteria: patients with epilepsy and neurodegenerative diseases (Alzheimer disease, Down syndrome, dementia with Lewy bodies, Parkinson disease, Lafora disease, neuronal ceroid lipofuscinosis) from June to December 2024 at a tertiary private hospital. Study variables: age, gender, grade of dementia (Global Deterioration Scale), type of epilepsy, electroencephalogram abnormalities, alterations in magnetic resonance imaging, treatment, and evolution of epilepsy. Information was analyzed in SPSS software. Results. We selected 50 patients with epilepsy and neurodegenerative diseases. An association was found between severe grades of dementia and drug-resistant epilepsy, with statistical significance (p

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19. **Depression preceding and following the diagnosis of Parkinson's disease and Lewy body dementia.**

Authors: Rohde C.;LangeskovChristensen M.;Jorgensen L.B.;Borghammer P. and Ostergaard, S. D.

Publication Date: 2025

Journal: General Psychiatry 38(6) (pagination), pp. Article Number: e102405. Date of Publication: 03 Dec 2025

Abstract: Background Depression is a common comorbidity in Parkinson's disease (PD) and Lewy body dementia (LBD). However, studies examining the rate of incident depression in the period preceding and following the diagnosis of PD and LBD are lacking in the literature. Aims To quantify the incidence of depression in the period preceding and following the diagnosis of PD and LBD. Methods We conducted a retrospective case-control study. Specifically, we used Danish registers to identify all patients with a diagnosis of PD or LBD in the period from 2007

to 2019. These patients were matched by age, calendar year of diagnosis and sex with up to three patients diagnosed with rheumatoid arthritis (RA), chronic kidney disease (CKD) or osteoporosis, respectively. The outcome was incident depression. The incidence of depression was assessed for up to 10 years before and up to 10 years after the diagnosis of PD or LBD. Hazard rates of incident depression for patients with PD or LBD, both before and after diagnosis, were compared with those for patients with RA, CKD or osteoporosis using a Cox-proportional hazards model. Results We identified 17 711 patients with PD or LBD. Their median age was 74.98 (68.10-80.85) years, and 39.92% were females. These patients were matched to 19 556, 40 842 and 47 809 patients with RA, CKD and osteoporosis, respectively. From 7 to 8 years before diagnosis to 5 years after diagnosis, patients with PD and LBD consistently had higher hazard rates of incident depression than all comparator groups. Conclusions These findings are compatible with depression being an early manifestation of the neurodegenerative changes eventually leading to PD and LBD and imply that incident depression at a late age should raise awareness of potential PD and LBD.

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20. **A mixed-methods study to explore the modifiable aspects of treatment burden in Parkinson's disease and develop recommendations for improvement.**

Authors: Tan Q.Y.;Ibrahim K.;Roberts H.C.;Amar K. and Fraser, S. D. S.

Publication Date: 2025

Journal: Plos One 20(12 December) (pagination), pp. Article Number: e0338620. Date of Publication: 01 Dec 2025

Abstract: Background People with Parkinson's (PwP) and their caregivers have to manage multiple daily healthcare tasks (treatment burden). This can be challenging and may lead to poor health outcomes. Objective To assess the extent of treatment burden in Parkinson's disease(PD), identify key modifiable factors, and develop recommendations to improve treatment burden. Methods A mixed-methods study was conducted consisting of: 1) a UK-wide cross-sectional survey for PwP and caregivers using the Multimorbidity Treatment Burden Questionnaire (MTBQ) to measure treatment burden levels and associated factors and 2) focus groups with key stakeholders to discuss survey findings and develop recommendations. Results 160 PwP (mean age = 68 years) and 30 caregivers (mean age = 69 years) completed the surveys. High treatment burden was reported by 21% (N = 34) of PwP and 50% (N = 15) of caregivers using the MTBQ. Amongst PwP, higher treatment burden was significantly associated with advancing PD severity, frailty, a higher number of non-motor symptoms, and more frequent medication timings (>3 times/day). Caregivers reporting higher treatment burden were more likely to care for someone with memory issues, had lower mental well-being scores and higher caregiver burden. Three online focus groups involved 11 participants (3 PwP, 1 caregiver and 7 healthcare professionals) recruited from the South of England. Recommendations to reduce treatment burden that were discussed in the focus groups include improving communication. clear expectation setting, and better signposting from healthcare professionals, increasing education and awareness of PD complexity, flexibility of appointment structures, increasing access to healthcare professionals, and embracing the supportive role of technology. Conclusions Treatment burden is common amongst PwP and

caregivers and could be identified in clinical practice using the MTBQ. There is a need for change at individual provider and system levels to recognise and minimise treatment burden to improve health outcomes in PD.

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21. **A mixed-methods study to explore the modifiable aspects of treatment burden in Parkinson's disease and develop recommendations for improvement.**

Authors: Tan, Qian Yue;Ibrahim, Kinda;Roberts, Helen C.;Amar, Khaled and Fraser, Simon D. S.

Publication Date: 2025

Journal: PLoS ONE [Electronic Resource] 20(12), pp. e0338620

Abstract: BACKGROUND: People with Parkinson's (PwP) and their caregivers have to manage multiple daily healthcare tasks (treatment burden). This can be challenging and may lead to poor health outcomes. OBJECTIVE: To assess the extent of treatment burden in Parkinson's disease(PD), identify key modifiable factors, and develop recommendations to improve treatment burden. METHODS: A mixed-methods study was conducted consisting of: 1) a UK-wide cross-sectional survey for PwP and caregivers using the Multimorbidity Treatment Burden Questionnaire (MTBQ) to measure treatment burden levels and associated factors and 2) focus groups with key stakeholders to discuss survey findings and develop recommendations. RESULTS: 160 PwP (mean age = 68 years) and 30 caregivers (mean age = 69 years) completed the surveys. High treatment burden was reported by 21% (N = 34) of PwP and 50% (N = 15) of caregivers using the MTBQ. Amongst PwP, higher treatment burden was significantly associated with advancing PD severity, frailty, a higher number of non-motor symptoms, and more frequent medication timings (>3 times/day). Caregivers reporting higher treatment burden were more likely to care for someone with memory issues, had lower mental well-being scores and higher caregiver burden. Three online focus groups involved 11 participants (3 PwP, 1 caregiver and 7 healthcare professionals) recruited from the South of England. Recommendations to reduce treatment burden that were discussed in the focus groups include improving communication. clear expectation setting, and better signposting from healthcare professionals, increasing education and awareness of PD complexity, flexibility of appointment structures, increasing access to healthcare professionals, and embracing the supportive role of technology. CONCLUSIONS: Treatment burden is common amongst PwP and caregivers and could be identified in clinical practice using the MTBQ. There is a need for change at individual provider and system levels to recognise and minimise treatment burden to improve health outcomes in PD. Copyright: © 2025 Tan et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

22. **Group singing through the lens of polyvagal theory: A pilot study in patients with Parkinson's disease.**

Authors: Wunnenberg, Elke and Baumann, Nicola

Publication Date: 2025

Journal: PLoS ONE [Electronic Resource] 20(12), pp. e0337210

Abstract: There is a need to counteract the chronic progression of Parkinson's disease (PD). This complex challenge requires new theoretical frameworks and practical strategies. In this study, we implemented group singing in line with the Singing Hospitals format and examined it through the lens of Polyvagal Theory to evaluate its potential benefits for people with PD. According to Polyvagal Theory, facilitating a shift in autonomic states from defense to safety and social engagement may enhance physiological regulation and thereby promote well-being across physical, mental, emotional, and social dimensions. In a pilot study, we recruited patients with PD and examined their responses to two group singing formats (weekly sessions: N1 = 13, one-day-workshop: N2 = 14) and a non-singing control group (N3 = 22). We designed scales of physical, mental, emotional, and social states that PD patients rated before and after eight one-hour singing sessions (N1) or an eight-hour singing workshop (N2). Findings show that PD patients benefited from group singing across both settings (large effect size: d = 2.43). Furthermore, self-reported interoceptive sensibility, used as a proxy for polyvagal autonomic reactivity, showed a substantial reduction in discomfort after weekly singing, while remaining constant in the control group (large effect size: d = 0.94). We observed the predicted singing-dependent effects and interpreted them as a shift in autonomic regulation consistent with Polyvagal Theory. Singing may represent a feasible, low-threshold resource for coping. Furthermore, Polyvagal Theory may provide an innovative framework for PD and help to bridge motor and non-motor symptoms.

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23. **Delayed Disease Onset Report in UK Biobank: Implications for Prodromal Studies in Parkinson's Disease.**

Authors: Zolfaghari S.;Kouchache T.;Delva A.;Bouhadoun S.;Kuhlencord M.;Pelletier A.;Noyce A.J.;Waters S.;Belete D.;Wilkinson T.;Bush K.;Morys F.;Vo A.;Rannikmae K.;Dagher A. and Postuma, R. B.

Publication Date: 2025

Journal: Movement Disorders (pagination), pp. Date of Publication: 2025

Abstract: Background: UK Biobank (UKBB) provides extensive genetic, imaging, and health data for ~500,000 participants, enabling studies of prodromal phases of diseases like Parkinson's disease (PD). However, during analysis, we became concerned about the accuracy of diagnosis timing. Objective(s): To evaluate the accuracy of PD diagnosis timing in UKBB. Method(s): We examined PD diagnosis timing using hospital, primary care, death

records, and self-reported data. We assessed discrepancies between sources and identified co-occurring diagnoses recorded on the same date as PD. Result(s): Among 3979 PD cases, 97% of the 786 participants with both self-reported and electronic health records (EHRs) reported their diagnosis earlier than recorded in the EHR, with a typical delay of 5 to 7 years. Multiple codiagnoses were often logged on the same date, suggesting retrospective or batch data entry. Conclusion(s): Substantial delays in PD documentation may misclassify already diagnosed individuals as prodromal. This introduces significant bias into studies of early disease markers and distorts the timing between risk factors and clinical onset.

Sources Used:

The following databases are used in the creation of this bulletin: EMBASE and Medline.

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