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Parkinson's Disease

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March 2025

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Book a session today at https://forms.office.com/e/HyiSXfDaYV (these sessions will be held on a monthly basis)

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1. **Predicting Dementia in People with Parkinson's Disease.**

Authors: Aborageh M.;Hahnel T.;Conde P.M.;Klucken J. and Frohlich, H.

Publication Date: 2025

Journal: medRxiv (pagination), pp. Date of Publication: 28 Jan 2025

Abstract: Parkinson's disease (PD) exhibits a variety of symptoms, with approximately 25% of patients experiencing mild cognitive impairment and 45% developing dementia within ten years of diagnosis. Predicting this progression and identifying its causes remains challenging. Our study utilizes machine learning and multimodal data from the UK Biobank to explore the predictability of Parkinson's dementia (PDD) post-diagnosis, further validated by data from the Parkinson's Progression Markers Initiative (PPMI) cohort. Using Shapley Additive Explanation (SHAP) and Bayesian Network structure learning, we analyzed interactions among genetic predisposition, comorbidities, lifestyle, and environmental factors. We concluded that genetic predisposition is the dominant factor, with significant influence from comorbidities. Additionally, we employed Mendelian randomization (MR) to establish potential causal links between hypertension, type 2 diabetes, and PDD, suggesting that managing blood pressure and glucose levels in Parkinson's patients may serve as a preventive strategy. This study identifies risk factors for PDD and proposes avenues for prevention.

2. **Validating the Accuracy of Parkinson's Disease Clinical Diagnosis: A UK Brain Bank Case-Control Study.**

Authors: di Biase L.;Pecoraro P.M. and Di Lazzaro, V.

Publication Date: 2025

Journal: Annals of Neurology (pagination), pp. Date of Publication: 2025

Abstract: Objective: Despite diagnostic criteria refinements, Parkinson's disease (PD) clinical diagnosis still suffers from a not satisfying accuracy, with the post-mortem examination as the gold standard for diagnosis. Seminal clinicopathological series highlighted that a relevant number of patients alive-diagnosed with idiopathic PD have an alternative post-mortem diagnosis. We evaluated the diagnostic accuracy of PD comparing the in-vivo clinical diagnosis with the post-mortem diagnosis performed through the pathological examination in 2 groups. Method(s): In this retrospective case-control study, patients and healthy subjects who consented to the post-mortem pathological diagnosis at the UK Brain Bank were consecutively enrolled from the UK Brain Bank. Medical records were reviewed to classify participants and performance metrics were further calculated using neuropathological diagnosis as the gold standard. Result(s): Four thousand five hundred seventy one subjects were eligible for the study. The clinical diagnosis group was: 1,048 Parkinson's patients and 1,242 healthy subjects. Pathology diagnosis group were: 996 Parkinson's patients and 1,288 subjects with no post-mortem abnormality. For the group of clinical diagnosis, PD diagnosis showed: sensitivity of 99%, specificity of 86%, accuracy of 90.96%, F1-Score 0.89, and a receiver operating characteristics area under the curve (ROC AUC) 0.925 (SE +/- 0.006) [95% confidence interval [CI]: 0.913, 0.937], pResult(s): Four thousand five hundred seventy one subjects were eligible for the study. The clinical diagnosis group was: 1,048 Parkinson's patients and 1,242 healthy subjects. Pathology diagnosis group were: 996 Parkinson's patients and 1,288 subjects with no post-mortem abnormality. For the group of clinical diagnosis, PD diagnosis showed: sensitivity of 99%, specificity of 86%, accuracy of 90.96%, F1-Score 0.89, and a receiver operating characteristics area under the curve (ROC AUC) 0.925 (SE +/- 0.006) [95% confidence interval [CI]: 0.913, 0.937], pInterpretation(s): Our findings confirm a still significant diagnostic error and emphasize the need for more fine and homogeneous criteria to classify idiopathic Parkinson's patients correctly. ANN NEUROL 2025.Copyright © 2025 The Author(s). Annals of Neurology published by Wiley Periodicals LLC on behalf of American Neurological Association.

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3. **Leveraging Action Unit Derivatives for Early-Stage Parkinson's Disease Detection.**

Authors: Filali Razzouki A.;Jeancolas L.;Mangone G.;Sambin S.;Chalancon A.;Gomes M.;Lehericy S.;Corvol J.C.;Vidailhet M.;Arnulf I.;PetrovskaDelacretaz D. and ElYacoubi, M. A.

Publication Date: 2025

Journal: IRBM 46(1) (pagination), pp. Article Number: 100874. Date of Publication: 01 Feb 2025

Abstract: Objective: Hypomimia is a symptom of Parkinson's disease (PD), involving a

decrease in facial movements and a loss of emotional expressions on the face. The objective of this study is to identify hypomimia in individuals in the early stage of PD by analyzing facial action units (AUs). Method(s): Our study included video recordings from 109 PD subjects and 45 healthy control (HC) subjects with an average of two videos per person (294 videos in total). The participants were requested to perform rapid syllable repetitions. For the purpose of discriminating between normal facial muscle movements and those specific to PD subjects experiencing hypomimia, we calculate the derivatives of the AUs. We derive global features based on the AUs intensities and their derivatives, and utilize XGBoost and Random Forest to perform the classification between PD and HC. Result(s): We achieve subject-level classification scores of up to 73.7% for balanced accuracy (BA) and an area under the curve (AUC) of 81.39% using XGBoost, and a BA of 79.1% and an AUC of 83.7% with Random Forest. These findings show potential in identifying hypomimia during the early phases of PD. Moreover, this research could facilitate the continuous monitoring of hypomimia beyond hospital settings, enabled by telemedicine.

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4. **Cbt for Psychosis in Parkinson's Disease: A Framework for How and Why.**

Authors: Foley J.A. and Bell, V.

Publication Date: 2025

Journal: SSRN (pagination), pp. Date of Publication: 16 Jan 2025

Abstract: Psychosis is a serious comorbidity to Parkinson's disease associated with high levels of distress and disability but access to effective treatments remain limited, leading to high rates of emergency hospitalization. Here, we propose a new framework for how cognitive behavioural therapy (CBT) may be used to treat Parkinson's disease psychosis. We note specific adaptions, including aims that focus on reducing distress and disability and extending quality of life; tailored psychoeducation; assessment and formulation that additionally includes disease course, medication effects and side-effects, and Parkinson's specific social factors; addressing anxiety and depression alongside cognitive appraisals for the types of psychotic symptoms more common in Parkinson's disease; appropriate reality testing sensitive to disease progression; and trigger monitoring and management for hallucinations and delusions that carefully distinguishes this from avoidant coping. We review preliminary case study-level evidence for the successful use of CBT for Parkinson's disease psychosis and suggest a road map for its formal evaluation before integration into evidence-based healthcare.

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5. **Large-scale proteomic analyses of incident Parkinson's disease reveal new pathophysiological insights and potential biomarkers.**

Authors: Gan Y.H.;Ma L.Z.;Zhang Y.;You J.;Guo Y.;He Y.;Wang L.B.;He X.Y.;Li Y.Z.;Dong Q.;Feng J.F.;Cheng W. and Yu, J. T.

Publication Date: 2025

Journal: Nature Aging (pagination)

Abstract: The early pathophysiology of Parkinson's disease (PD) is poorly understood. We analyzed 2,920 Olink-measured plasma proteins in 51,804 UK Biobank participants, identifying 859 incident PD cases after 14.45 years. We found 38 PD-related proteins, with six of the top ten validated in the Parkinson's Progression Markers Initiative (PPMI) cohort. ITGAV, HNMT and ITGAM showed consistent significant association (hazard ratio: 0.11-0.57, P = 6.90 x 10-24 to 2.10 x 10-11). Lipid metabolism dysfunction was evident 15 years before PD onset, and levels of BAG3, HPGDS, ITGAV and PEPD continuously decreased before diagnosis. These proteins were linked to prodromal symptoms and brain measures. Mendelian randomization suggested ITGAM and EGFR as potential causes of PD. A predictive model using machine learning combined the top 16 proteins and demographics, achieving high accuracy for 5-year (area under the curve (AUC) = 0.887) and over-5-year PD prediction (AUC = 0.816), outperforming demographic-only models. It was externally validated in PPMI (AUC = 0.802). Our findings reveal early peripheral pathophysiological changes in PD crucial for developing early biomarkers and precision therapies.

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6. **Optic Disc Pallor in Parkinson's Disease: A UK Biobank Study.**

Authors: Gibbon S.;Breen D.P. and MacGillivray, T. J.

Publication Date: 2025

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

Abstract: Background: Recent studies have suggested that retinal changes measured with optical coherence tomography are detectable in early Parkinson's disease (PD), highlighting the potential of ophthalmic biomarkers for diagnosis and monitoring. Objective(s): We set out to investigate the relationship between optic disc pallor measured in fundoscopy images and both prevalent and incident PD. Method(s): We analyzed color fundus photographs from 787 UK Biobank participants: 89 with prevalent PD, 317 with incident PD, and 381 age- and sex-matched controls. Optic disc pallor in several zones was quantified using semi-automated software. We used logistic and linear regression, adjusted for relevant covariates, to test for associations between disc pallor and PD status and duration. Result(s): Participants with prevalent PD had significantly paler optic discs globally (OR per standard deviation [SD] increase = 1.39 [CI: 1.08-1.81], P = 0.012) and across several zones compared to controls. Each year since PD diagnosis was associated with a 1.37 SD increase in global pallor (standardized beta = 1.37 [SE = 0.61], P = 0.029), and a similar increase across several zones, however, this finding was sensitive to outliers with long disease duration. No significant associations were observed for the incident PD group. Conclusion(s): Optic disc pallor is significantly associated with PD and may become more pronounced with disease duration. This suggests that optic disc pallor, measured in routinely taken color fundus photographs, may serve as a biomarker for PD-related neurodegeneration. © 2025 The Author(s). Movement Disorders published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

7. **Penetrance of Parkinson's disease in GBA1 carriers is depending on the variant severity and polygenic background.**

Authors: Hassanin E.;Landoulsi Z.;Pachchek S.;Krawitz P.;Maj C.;Kruger R.;May P. and Bobbili, D. R.

Publication Date: 2025

Journal: medRxiv (pagination), pp. Date of Publication: 28 Jan 2025

Abstract: Background: Heterozygous variants in the GBA1 gene cause Parkinson's disease (PD) with variable penetrance and have been classified into severe, mild, and PD-specific risk variants based on their association with Gaucher's disease (GD; mild and severe) or PD (risk variants). Polygenic risk scores (PRS) further modify PD susceptibility and may influence the age of onset in GBA1 variant carriers. Our study investigates the interaction between a genome wide PRS and pathogenic GBA1 variants (GBA1PVs), focusing on how established combined PD risk polymorphisms may influence GBA1-related PD risk across different levels of GBA1-mediated pathogenicity. Method(s): GBA1 variants were identified from whole exome sequencing data in the UK Biobank (UKB) cohort and from GBA1-targeted PacBio sequencing in the Luxembourg Parkinson's Study (LuxPark). PRSs were calculated for all participants using established genome-wide significant SNPs, excluding variants within the GBA1 locus, and then categorized based on both PRS levels and GBA1PVs carrier status. Carriers of GBA1PVs were further divided into 'severe (Gaucher-related) +mild (PD-related)' and 'risk' groups. To evaluate the relationship between PRS, GBA1PVs carrier status or severity, and PD risk, logistic regression and Cox proportional hazards regression were conducted with disease presence as the dependent variable. Result(s): We identified GBA1PVs in 8.8% of PD patients in the UKB discovery cohort and 9.9% in the LuxPark replication cohort. GBA1PVs carriers had consistently higher PD risk compared to non-carriers across all PRS categories. In UKB, GBA1PVs carriers in the highest PRS category had a 2.3-fold increased risk of PD (OR: 2.34; 95% CI, 2.08-2.63) and cumulative incidence of 67% by the age of 75, while those in LuxPark had a 1.6-fold higher risk (OR: 1.64; 95% CI, 1.52-1.76), and cumulative incidence of 81% at the age of 75. Carriers of "severe+mild" GBA1 variants had nearly double the risk of PD compared to "risk" variant carriers, with ORs ranging from 2.05 to 3.69 in UKB and 1.73 to 1.98 in LuxPark. The interaction between the PRSs and GBA1PVs severity was similar in the two cohorts. Conclusion(s): Our findings demonstrate that GBA1PVs carrier status and severity significantly impact PD risk, with severe variants conferring higher risk than risk ones. Additionally, PRS consistently increases both PD risk and GBA1PVs penetrance in an additive manner across all variant types, defining a genetic background that influences PD penetrance in GBA1PVs carriers. The presence of additional PD-associated risk variants in GBA1 carriers defines new avenues to incorporate PRS and genetic risk data into future clinical trial design and genetic counselling in GBA1-associated PD.

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8. **Associations of physical activity, sedentary behavior, and sleep with risk of incident Parkinsona's disease: A prospective cohort study of 401,697 participants.**

Authors: Jiao H.;Huang S.;Cheng W.;Feng J. and Yu, J.

Publication Date: 2025

Journal: Chinese Medical Journal (pagination)

Abstract: Background: Physical activity, sedentary behavior (SB), and sleep duration are associated with brain health. Effects of those on developing Parkinsona's disease (PD) are poorly investigated. This study aimed to examine the independent and joint associations of physical activity, SB, sleep with PD risk. Method(s): We analyzed data on 401,697 participants from the UK Biobank cohort, which was enrolled in 2006-2010. Physical activities were measured based on a questionnaire. Sleep and SB time were defined through self-reported total number of hours. Models fitted with restricted cubic spline were conducted to test for linear and non-linear shapes of each association. Cox proportional hazards regression models were used to estimate the association of three modifiable behaviors. Result(s): Our analytic sample included 401,697 participants with 3030 identified cases of PD (mean age, 63 years; 62.9% male). PD risk was 18% lower in the high total physical activity group (95% CI, 0.75-0.90), 22% lower in the high leisure-time physical activity (LTPA) group (95% CI, 0.71-0.86) compared with the low level and 14% higher in the high sleep duration group (95% CI, 1.05-1.24) compared to moderate group. Total SB time was irrelevant with PD risk, while high TV viewing showed a 12% increase of PD risk compared to the low group (95% CI, 1.02-1.22). Low computer use (0 h/day) was associated with a 14% higher risk compared to 1 h/day use (95% CI, 1.04-1.26). Those associations were independent. A combination of 7 h/day sleep, moderate-to-high computer use, and moderate-to-vigorous intensity of LTPA showed lowest PD risk (HR, 0.70; 95% CI, 0.57-0.85). Conclusion(s): Physical activity, SB, and sleep were associated with PD risks separately. Our findings emphasize the possibility for changing these three daily activities concurrently to lower the risk of PD. These findings may promote an active lifestyle for PD prevention.

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9. **Joint effect of modifiable risk factors on Parkinson's disease: a large-scale longitudinal study.**

Authors: Li P.;Zhu X.;Liu M.;Wang Y.;Huang C.;Sun J.;Tian S.;Li Y.;Qiao Y.;Yang J.;Cao S.;Cong C.;Zhao L.;Su J. and Tian, D.

Publication Date: 2025

Journal: Frontiers in Human Neuroscience 19(pagination), pp. Article Number: 1525248. Date of Publication: 2025

Abstract: Introduction: Previous researches have often underestimated the diversity and combined effects of risk factors for Parkinson's disease (PD). This study aimed to identify how multiple modifiable risk factors collectively impact PD. Method(s): The study included 452,492 participants from the UK Biobank, utilizing genetic data and 255 phenotypic variables. A broad exposure association study was conducted across seven domains: socioeconomic status, medical history, psychosocial factors, physical measures, early life, local environment, and lifestyle. Risk scores of each domain for each participant were generated. The joint effects of modifiable and genetic risks assessed using Cox proportional hazards model. Population attributable fraction (PAF) was estimated to quantify contribution ratio of risk factors in different

domains to the occurrence of PD. Result(s): Multiple risk factors significantly (pResult(s): Multiple risk factors significantly (p-4) associated with PD was observed. The top 5 factors were hand grip strength (hazard ratio (HR)=0.98, p=1.59x10-24), long-standing illness (HR=1.38, p=3.63x10-20), self-reported nervousness (HR=1.56, p=5.9x10-20), ever suffered from mental health concerns (HR=1.42, p=5.48x10-18) and chest pain (HR=1.42, p=1.43x10-18). Individuals with unfavorable medical history, psychosocial factors, physical measures, and lifestyle had an increased risk of PD by 33 to 51% compared to those with favorable factors (p). Individuals with unfavorable medical history, psychosocial factors, physical measures, and lifestyle had an increased risk of PD by 33 to 51% compared to those with favorable factors (pDiscussion(s): Results indicated that addressing modifiable risk factors, especially in physical measures and psychological factors, could potentially prevent up to 33.87% of PD cases. In formulating prevention strategies, it is recommended to prioritize domains such as physical measures, psychosocial factors, lifestyle, and medical history.

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10. **Exploring how PRIME-Parkinson care is implemented and whether, how and why it produces change, for who and under what conditions: a protocol for an embedded process evaluation within the PRIME-UK randomised controlled trial.**

Authors: Lloyd K.;Tenison E.;Smith S.;Lithander F.;Kidger J.;Brant H.;Redwood S.;BenShlomo Y. and Henderson, E. J.

Publication Date: 2025

Journal: BMJ Open 15(1), pp. e086353

Abstract: INTRODUCTION: The PRIME-UK randomised controlled trial (RCT) aims to establish whether a model of care that seeks to be proactive, integrated and empower participants, caregivers and healthcare professionals can improve outcomes in people with parkinsonism. Given that this intervention is novel and complex, understanding whether and how the intervention will be acceptable, implementable, cost-effective and scalable across contexts are key questions beyond that of whether 'it works'. We describe an embedded process evaluation to answer these questions, which aims to support interpretation of the trial results, refinement of the intervention and support future scaling of the PRIME-Parkinson model of care. METHODS AND ANALYSIS: A mixed-methods approach will be used to collect data across four process evaluation domains: implementation, mechanism of change, acceptability and context. Quantitative data will be collected prospectively from all participants and analysed descriptively with exploratory tests of relationships as power allows. Qualitative data will be collected through semistructured interviews with a purposively sampled subpopulation of participants, caregivers and staff members as well as case studies where relevant. Interview transcripts will be analysed thematically using interpretive qualitative analysis. Synthesis of quantitative and qualitative data will also be performed to draw conclusions. ETHICS AND DISSEMINATION: The quantitative data will be collected as part of the main PRIME-UK RCT which was been granted NHS REC approval (21/LO/0387) on 27 July 2021. The qualitative data will be collected as part of a substudy, 'PRIME-Qual', which was granted NHS REC approval (21/LO/0388) on 14 July 2021. The mixed-methods process evaluation will be published after the conclusion of the trial in addition to the main trial findings. TRIAL REGISTRATION NUMBER: NCT05127057.

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11. **Machine learning prediction algorithms for 2-, 5- and 10-year risk of Alzheimer's, Parkinson's and dementia at age 65: a study using medical records from France and the UK General Practitioners.**

Authors: Nedelec T.;Zaidi K.;Montaud C.;Guinebretiere O.;Sipila P.;Wei D.;Yang F.;Freydenzon A.;Belloir A.;Fournier N.;Hamieh N.;Lekens B.;Slaouti Y.;McRae A.;CouvyDuchesne B.;Hswen Y.;Fang F.;Kivimaki M.;Ansart M. and Durrleman, S.

Publication Date: 2025

Journal: medRxiv (pagination), pp. Date of Publication: 25 Jan 2025

Abstract: Background: Leveraging machine learning on electronic health records offers a promising method for early identification of individuals at risk for dementia and neurodegenerative diseases. Current risk algorithms heavily rely on age, highlighting the need for alternative models with strong predictive power, especially at age 65, a crucial time for early screening and prevention. Method(s): This prospective study analyzed electronic health records (EHR) from 76,427 adults (age 65, 52.1% women) using the THIN database. A general risk algorithm for Alzheimer's disease, Parkinson's disease, and dementia was developed using machine learning to select predictors from diagnoses, and medications. Result(s): Medications (e.g., laxatives, urological drugs, antidepressants), along with sex, BMI, and comorbidities, were key predictors. The algorithm achieved a 38.4% detection rate at a 5% false-positive rate for 2-year dementia prediction. Conclusion(s): The validated prediction algorithms, easy to implement in primary care, identify high-risk 65-year-olds using medication records. Further refinement and broader validation are needed.Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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12. **Depression and incidence of inflammation-related physical health conditions: a cohort study in UK Biobank.**

Authors: Saha S.;Prigge R.;Jackson C.A.;Guthrie B. and Fleetwood, K. J.

Publication Date: 2025

Journal: medRxiv (pagination), pp. Date of Publication: 17 Jan 2025

Abstract: Background Depression is associated with multiple physical health conditions, and inflammation is a mechanism commonly proposed to explain this association. We aimed to investigate the association between depression and the incidence of physical health conditions thought to have an inflammatory etiological component, including coronary heart disease, peripheral arterial disease, type 2 diabetes, inflammatory bowel disease, inflammatory arthritis and Parkinson's Disease. Methods We conducted a cohort study using UK Biobank (UKB) data linked to primary care, hospital admission and death data. We ascertained depression at baseline using primary care and hospital records, and self-report at the UKB baseline

assessment. We identified incident physical health conditions during follow-up using primary care, hospital admission and death data. We used Cox proportional hazards models to determine hazard ratios of each incident inflammation-related condition in those with versus without depression at baseline, serially adjusting for sociodemographic factors, lifestyle factors and baseline count of morbidities. Result We included 172,556 UKB participants who had continuous primary care records. Of these, 30,770 (17.8%) had a history of depression at baseline. After excluding participants with missing data, 168,641 (98%) were included in analysis. Median follow-up was 7.1 years (IQR: 6.3, 8.0). In the model adjusted for age and sex, depression was significantly associated with a higher hazard of all inflammation-related conditions. After additionally accounting for differences in country, ethnicity and deprivation, the association between depression and each condition generally attenuated but remained statistically significant, with effect estimates ranging from a 30% increased hazard of inflammatory bowel disease (HR 1.30, 95% CI 1.06 to 1.58) to a 53% increased hazard of Parkinson's Disease (HR 1.53, 95% CI 1.25 to 1.87). After further adjusting for lifestyle factors and comorbidity count, the association persisted only for Parkinson's Disease (HR 1.45, 95% CI 1.18 to 1.79). Conclusions Our study found that depression is consistently associated with multiple inflammation-related physical health conditions, although associations did not persist after adjustment for lifestyle factors and baseline physical condition count. Further research is needed to explore underlying mechanisms, including inflammatory biomarkers and modifiable lifestyle factors on the causal pathway.

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13. **Chronic Musculoskeletal Pain and Risk of Incident Parkinson's Disease: A 13-Year Longitudinal Study.**

Authors: Vazirian F.;Tian J.;Jane A.;Aitken D.;Callisaya M.L.;Cicuttini F.;Jones G. and Pan, F.

Publication Date: 2025

Journal: Movement Disorders 40(1), pp. 87–96

Abstract: Background: Chronic musculoskeletal pain often co-occurs with Parkinson's disease (PD); however, whether individuals with chronic pain have a higher risk of developing PD is unclear. Objective(s): To investigate the associations between chronic pain and incident risk of three neurodegenerative parkinsonism categories including PD, multiple system atrophy (MSA), and progressive supranuclear palsy (PSP). Method(s): This study included 355,890 participants (mean [standard deviation] age, 56.51 [8.07] years, 48.40% male) who did not have parkinsonism at baseline from a population-based cohort. Musculoskeletal pain in the hip, neck/shoulder, back, knee, or "all over the body" was assessed. Chronic pain was defined if pain lasted >=3 months. Participants were categorized into four groups: no chronic pain, having one or two, three or four sites, and pain "all over the body." The diagnosis of PD, MSA, and PSP used self-reports, hospital records, and death registries. Multivariable-adjusted Cox regression was performed for the analyses. Result(s): Over a median follow-up of 13.0 years, 2044 participants developed PD, 77 participants developed MSA, and 126 participants developed PSP. In multivariable analyses, there was a dose-response relationship between number of chronic pain sites and incident risk of PD (hazard ratio, 1.15; 95% confidence interval, 1.07-1.23). Participants with one or two pain sites and three or four pain sites had an

11% and 49% increased risk of developing PD, respectively. There were no associations between chronic pain and MSA or PSP. Conclusion(s): Chronic musculoskeletal pain was independently associated with PD, suggesting that chronic pain could be used to identify individuals at risk of developing PD. © 2024 International Parkinson and Movement Disorder Society.

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14. **Exenatide once a week versus placebo as a potential disease-modifying treatment for people with Parkinson's disease in the UK: a phase 3, multicentre, double-blind, parallel-group, randomised, placebo-controlled trial.**

Authors: Vijiaratnam N.;Girges C.;Auld G.;McComish R.;King A.;Skene S.S.;Hibbert S.;Wong A.;Melander S.;Gibson R.;Matthews H.;Dickson J.;Carroll C.;Patrick A.;Inches J.;Silverdale M.;Blackledge B.;Whiston J.;Hu M.;Welch J., et al

Publication Date: 2025

Journal: The Lancet 405(10479), pp. 627–636

Abstract: Background: GLP-1 receptor agonists have neurotrophic properties in in-vitro and in-vivo models of Parkinson's disease and results of epidemiological studies and small randomised trials have suggested possible benefits for risk and progression of Parkinson's disease. We aimed to establish whether the GLP-1 receptor agonist, exenatide, could slow the rate of progression of Parkinson's disease. Method(s): We did a phase 3, multicentre, double-blind, parallel-group, randomised, placebo-controlled trial at six research hospitals in the UK. Participants were aged 25-80 years with a diagnosis of Parkinson's disease, were at Hoehn and Yahr stage 2.5 or less when on dopaminergic treatment, and were on dopaminergic treatment for at least 4 weeks before enrolment. Participants were randomly assigned (1:1) using a web-based system with minimisation according to Hoehn and Yahr stage and study site to receive extended-release exenatide 2 mg by subcutaneous pen injection once per week over 96 weeks, or visually identical placebo. All participants and all research team members at study sites were masked to randomisation allocation. The primary outcome was the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III score, off dopaminergic medication at 96 weeks, analysed in the intention-to-treat population using a linear mixed modelling approach. This study is registered with ISRCTN (14552789), EudraCT (2018-003028-35), and ClinicalTrials.gov (NCT04232969). Finding(s): Between Jan 23, 2020, and April 23, 2022, 215 participants were screened for eligibility, of whom 194 were randomly assigned to exenatide (n=97) or placebo (n=97). 56 (29%) participants were female and 138 (71%) were male. 92 participants in the exenatide group and 96 in the placebo group had at least one follow-up visit and were included in analyses. At 96 weeks, MDS-UPDRS III OFF-medication scores had increased (worsened) by a mean of 5.7 points (SD 11.2) in the exenatide group, and by 4.5 points (SD 11.4) points in the placebo group (adjusted coefficient for the effect of exenatide 0.92 [95% CI -1.56 to 3.39]; p=0.47). Nine (9%) participants in the exenatide group had at least one serious adverse event compared with 11 (11%) in the placebo group. Interpretation(s): Our findings suggest that exenatide is safe and well tolerated. We found no evidence to support exenatide as a disease-modifying treatment for people with Parkinson's disease. Studies with agents that show better target engagement or in specific subgroups of patients are needed to establish whether there is any support for the use of GLP-1 receptor agonists for Parkinson's disease. Funding(s):

National Institute for Health and Care Research and Cure Parkinson's.

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15. **Deep Learning Classification for Prodromal Parkinson's Disease Based on Spatiotemporal Features of Specific Finger Movements.**

Authors: Wang W.C.;Chiu C.C. and Yeh, S. J.

Publication Date: 2025

Journal: SSRN (pagination), pp. Date of Publication: 06 Jan 2025

Abstract: The finger-tapping test in the Unified Parkinson's Disease Rating Scale (UPDRS) primarily focuses on motor control changes between the thumb and index fingers. However, this approach may overlook functional impairments in other fingers and is often insufficient for detecting early symptoms of Parkinson's disease. To assist patients and physicians with early detection, this study aims to develop a classification method based on clinical practice with deep learning for prodromal Parkinson's disease by combining specific finger movements that involve consecutively tapping the thumb five times with the index, middle, ring, and little fingers in sequence with both hands performing the task simultaneously. Motion signals of finger movements were captured and transformed into normalized grayscale images reflecting spatial and temporal features. Forty-one prodromal Parkinson's disease patients and thirty non-prodromal Parkinson's disease subjects were recruited from Taichung Cheng-Ching General Hospital. Statistical and significance analyses of the feature parameters were conducted during the experiments. The results showed that the parameters, including total completion time, the average duration of single cycle tapping, and the enslavement index, all exhibited an increasing trend with disease progression (p

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16. **Using Healthcare Redesign to Identify Medication Management Issues in Parkinson's Disease.**

Authors: Williams, Susan;Iannuzzi, Marissa A. and Prior, Sarah J.

Publication Date: Jan 30 ,2025

Journal: Pharmacy : A Journal of Pharmacy Education and Practice 13(1)

Abstract: BACKGROUND: Parkinson's disease (PD) is a neurodegenerative disorder that is predominantly controlled through pharmacotherapy. People with PD have highly complex medication regimens that are often poorly managed during hospital admissions. This project aims to understand the issues experienced by patients with PD and healthcare staff that impacted their medication management during their hospital admission at a tertiary metropolitan hospital in New South Wales, Australia. METHODS: This project focuses on the mixed-methods diagnostics phase of the healthcare redesign approach to health service improvement, utilising organisational data, online surveys, interviews, and focus groups. RESULTS: The findings from this project highlight key areas to address to improve the medication management of patients with PD admitted to hospital. The organisational data (n =

222) showed that the identification of PD patients, untimely medication reviews, prescribing errors, and untimely medication administration all contributed to poor patient experience. The staff surveys (n = 81) highlighted that a lack of knowledge of PD medications and poor patient identification impacted patient experience. The patient surveys (n = 18) and patient interviews (n = 16) suggested that confidence around medication management and administration timing could be improved. CONCLUSIONS: Poor PD medication management in hospital impacts the patient experience and should be improved to ensure better outcomes for patients and the health services.

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17. **Causal relationship between B vitamins and neuropsychiatric disorders: A systematic review and meta-analysis.**

Authors: Ye M.;Yang X.;Yan J.;Yao Y.;Lv H.;Yue Z.;Lin X.;Qian C. and Liu, Z.

Publication Date: 2025

Journal: Neuroscience and Biobehavioral Reviews 170(pagination), pp. Article Number: 106068. Date of Publication: 01 Mar 2025

Abstract: Recently, there has been an increasing interest in how diet and nutrition influence both physical and mental health. Numerous studies have highlighted the potential role of B vitamins in neuropsychiatric disorders (NPDs), yet the exact causal relationship between these nutrients and NPDs remains unclear. In our Mendelian randomization (MR) meta-analysis, we examined the links between B vitamins (VB6, VB12, and folate) and NPDs, utilizing data from previous MR studies, the UK Biobank, and FinnGen databases. Our MR analysis revealed a complex, multifaceted association: VB6 appears to protect against Alzheimer's disease (AD) but may increase the risk for conditions such as major depressive disorder and post-traumatic stress disorder. VB12 seems protective against autism spectrum disorder (ASD) but may heighten the risk for bipolar disorder (BD). Folate has shown protective effects against AD and intellectual disability (ID). The meta-analysis suggests that B vitamins may protect against certain disorders like AD and Parkinson's disease, but they might also be risk factors for anxiety and other psychiatric conditions. Further subgroup analysis indicates that VB6 protects against epilepsy and schizophrenia but increases the risk of mania; VB12 protects against ID and ASD but raises the risk of schizophrenia and BD; folate protects against schizophrenia, AD, and ID. These findings reveal the intricate influence of B vitamins on mental health, emphasizing that different B vitamins have distinct impacts on various NPDs. This complexity underscores the importance of personalized supplementation in developing future therapeutic approaches for NPDs.

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18. **Neurotrophic factors for Parkinson's disease: Current status, progress, and remaining questions. Conclusions from a 2023 workshop**

Authors: Barker, Roger A.;Saarma, Mart;Svendsen, Clive N.;Morgan, Catherine;Whone, Alan;Fiandaca, Massimo S.;Luz, Matthias;Bankiewicz, Krystof S.;Fiske, Brian;Isaacs, Lyndsey;Roach, Arthur;Phipps, Thomas;Kordower, Jeffrey H.;Lane, Emma L.;Huttunen, Henri J.;Sullivan, Aideen;O'Keeffe, Gerard;Yartseva, Valeria and Federoff, Howard

Publication Date: Nov ,2024

Journal: Journal of Parkinsons Disease Print 14(8), pp. 1659–1676

Abstract: In 2023, a workshop was organized by the UK charity Cure Parkinson's with The Michael J Fox Foundation for Parkinson's Research and Parkinson's UK to review the field of growth factors (GFs) for Parkinson's disease (PD). This was a follow up to a previous meeting held in 2019.1 This 2023 workshop reviewed new relevant data that has emerged in the intervening 4 years around the development of new GFs and better models for studying them including the merit of combining treatments as well as therapies that can be modulated. We also discussed new insights into GF delivery and trial design that have emerged from the analyses of completed GDNF trials, including the patient voice, as well as the recently completed CDNF trial.2 We then concluded with our recommendations on how GF studies in PD should develop going forward.; plain-language-summary For many years, scientists have explored the idea of administering growth factors to the brain, thereby repairing the damage associated with neurodegenerative diseases like Parkinson's disease (PD). Growth factors like glial cell line-derived neurotrophic factor (GDNF) have shown promise in animal models of PD, and initial clinical trials suggested that this approach may be beneficial for patients. However, there has been some uncertainty in the field after a number of clinical trials did not reach their primary endpoints. Nevertheless, the development of growth factor therapies for PD has continued, with new trials underway. Recent developments in this scientific area were discussed at a workshop organized by a number of PD charities in 2023. The discussion and conclusions from that workshop are presented in this new paper. Language: English

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19. **Prospective Study of Lung Function with Prodromal, Clinical Parkinson's Disease, and Mortality.**

Authors: Chen X.;Zhang Z.;Tong L.;Wang H.;Xu X.;Sun L.;Li Y. and Gao, X.

Publication Date: 2024

Journal: Journal of Parkinson's Disease 14(7), pp. 1427–1439

Abstract: Background: The association of lung function with the risk of developing prodromal and clinical-diagnosed Parkinson's disease (PD) and with the risk of mortality among individuals with PD remains unknown. Objective(s): To prospectively examine the associations of lung function with the risk of prodromal, clinical-diagnosed PD, and PD-related mortality in participants of the UK Biobank. Method(s): Included were 452,518 participants free of PD at baseline. Baseline lung function, including forced expiratory volume in 1-s (FEV1), forced vital capacity (FVC), peak expiratory flow (PEF), and FEV1/FVC ratio, was assessed. Eight prodromal features were measured using self-reported diagnoses, hospital admission, and primary care data. Incident PD cases were identified using linkages with hospital admission, death register, and self-report. Vital status and date of death were provided by the UK National Health Service (NHS) and the NHS Central Register. We used Cox proportional hazard models to evaluate these associations. Result(s): Poor lung function was associated with higher risk of PD in a dose-response relationship: the adjusted hazard ratio comparing the lowest vs. the highest lung function quintile was 1.18 (95% CI, 1.02- 1.37) for FEV1, 1.14 (95% CI, 0.99- 1.29) for FVC, and 1.23 (95% CI, 1.08- 1.41) for PEF (p-trend Result(s): Poor lung function was associated with higher risk of PD in a dose-response relationship: the adjusted hazard ratio comparing the lowest vs. the highest lung function quintile was 1.18 (95% CI,

1.02- 1.37) for FEV1, 1.14 (95% CI, 0.99- 1.29) for FVC, and 1.23 (95% CI, 1.08- 1.41) for PEF (p-trend Conclusion(s): The current study showed that individuals with poor lung function had a high future risk of prodromal and clinical PD and a higher rate of PD-related mortality.

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20. **Exploring the Link between Periodontal Disease and Systemic Conditions: Implications for Alzheimer's, Parkinson's, and Rheumatoid Arthritis.**

Authors: Kanimozhi;Aishwarya K.;Yadav S.;Chandy A.A.;Muralikrishna R. and Shinkre, R.

Publication Date: 2024

Journal: Journal of Pharmacy and Bioallied Sciences 16(Suppl 4) (pp S3775-S3777), pp. Date of Publication: 01 Dec 2024

Abstract: Background: There is a growing correlation between periodontal disease, a common inflammatory disorder that affects the tissues supporting the teeth, and several systemic diseases. Material(s) and Method(s): Two hundred patients from a tertiary care hospital, ages 50-75, participated in this cross-sectional research. The subjects were split up into four groups: 50 individuals with rheumatoid arthritis, 50 with Alzheimer's disease, 50 with Parkinson's disease, and 50 with periodontal disease. To evaluate periodontal condition, including clinical attachment loss and pocket depth, thorough oral exams were performed. Measurements were made of serum biomarkers for inflammation, such as interleukin-6 (IL-6) and C-reactive protein (CRP). Multivariate regression models were used to examine correlations between the severity of periodontal disease and the underlying systemic diseases. Result(s): In all groups, there were significant relationships between higher levels of indicators of systemic inflammation and the severity of periodontal disease. In comparison to healthy controls (CRP mean value: 2.1 mg/L; IL-6 mean value: 6.4 pg/mL), participants with periodontal disease had higher mean levels of CRP (5.6 mg/L) and IL-6 (mean value: 12.8 pg/mL). Furthermore, compared to those with rheumatoid arthritis, those with Alzheimer's and Parkinson's disorders showed higher levels of pocket depth and periodontal attachment loss. Conclusion(s): In conclusion, the results point to a possible connection between systemic diseases such rheumatoid arthritis, Parkinson's disease, and Alzheimer's.

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21. **Commercial symptom monitoring devices in Parkinson's disease: benefits, limitations, and trends.**

Authors: RodriguezMartin D. and PerezLopez, C.

Publication Date: 2024

Journal: Frontiers in Neurology 15(pagination), pp. Article Number: 1470928. Date of Publication: 2024

Abstract: Parkinson's disease (PD) is a neurodegenerative disorder that significantly impacts patients' quality of life. Managing PD requires accurate assessment of motor and non-motor symptoms, often complicated by the subjectivity in symptom reporting and the limited

availability of neurologists. To address these challenges, commercial wearable devices have emerged to continuously monitor PD symptoms outside the clinical setting. The main devices include PKGTM, Kinesia 360TM, Kinesia UTM, PDMonitorTM, and STAT-ONTM. These devices utilize advanced technologies such as accelerometers, gyroscopes, and specific algorithms to provide objective data on motor symptoms like tremors, dyskinesia, and bradykinesia. Despite their potential, the adoption of these devices is limited due to concerns about their accuracy, complexity of use, and lack of independent validation. The correlation between these devices' measurements and traditional clinical observations varies, and patient usability and adherence remain critical areas for improvement. To optimize their utility and improve patient outcomes, it is essential to conduct validation and usability studies with a sufficient number of patients, develop standardized protocols, and ensure integration with hospital information systems.

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22. **Satisfaction and Preferences for Infusion Therapies in Advanced Parkinson's Disease-Patient Perspective.**

Authors: Wegrzynek-Gallina, Julia;Chmiela, Tomasz;Boronczyk, Michal;Buczek, Aleksandra;Hudzinska, Patrycja;Bigajski, Hubert;Waksmundzki, Damian;Gawryluk, Justyna and Siuda, Joanna

Publication Date: 2024

Journal: Medicina (Kaunas, Lithuania)

Abstract: Background and Objectives: The rapid growth of the number of advanced Parkinson's disease (PD) patients has caused a significant increase in the use of device-aided therapies (DATs), including levodopa-carbidopa intestinal gel (LCIG) and continuous subcutaneous apomorphine infusion (CSAI). The objective of this study was to evaluate patients' satisfaction and the factors influencing preferences for CSAI and LCIG. Materials and Methods: The research focused on individuals diagnosed with advanced PD undergoing DAT at the Neurology Department of the University Hospital in Katowice. A telephone survey conducted between June and July 2024 evaluated the experiences of patients with LCIG and CSAI. The Parkinson's Disease Questionnaire (PDQ-8) and the Stress Scale for Family Caregivers (BSFC-s) were applied. Based on medical record data comprising reasons for the exclusion of individuals, disease-related and treatment data were collected. Results: Among the original cohort of 64 patients, 50 completed the survey, including 31 who might choose between infusion therapies. The average patient ages were 70.6 +/- 4.7 (CSAI) and 71.2 +/- 7.2 years (LCIG), with disease durations of 15 (IQR: 12-19) and 18 (IQR: 13-19) years, respectively. LCIG patients presented higher PDQ-8 scores (20 (IQR: 13-27) vs. 13 (IQR: 6-19), p = 0.008), and higher BSFC-s scores (19 (IQR: 12-21) vs. 9 (IQR: 2.5-13), p = 0.011). Furthermore, significant factors influencing patient preferences included fear of surgery (75% vs. 36.8%, p = 0.043) and concerns about DAT safety (83.3% vs. 47.4%, p = 0.049). Conclusions: LCIG and CSAI therapies offer benefits and disadvantages, with safety concerns and fear of surgery seeming to be decisive in the decision-making process.

23. **The East London Parkinson's Disease Project - A case-control study in a diverse population.**

Authors: Zirra A.;Dey K.C.;Camboe E.;Waters S.;Haque T.;Huxford B.;Chohan H.;Donkor N.;Kahan J.;BenJoseph A.;Gallagher D.A.;Budu C.;Boyle T.;Simonet C.;Lees A.J.;Marshall C.R. and Noyce, A. J.

Publication Date: 2024

Journal: medRxiv (pagination), pp. Date of Publication: 26 Nov 2024

Abstract: Background: There is a relative dearth of research on patients with Parkinson's disease (PD) from under-represented ethnic groups in the United Kingdom. Objective(s): The East London Parkinson Disease project seeks to understand the clinical manifestations and determinants of PD in a diverse population. Method(s): Patients with PD were recruited from the Royal London Hospital. Healthy controls came from community engagement events and partners of patients. Data on clinical features assessed by motor and non-motor scales were collected between January 2019 and February 2024, and compared between groups. Parametric, non-parametric tests, and unmatched logistic models, adjusted for age, gender and duration of disease were used. Result(s): We assessed 218 patients with PD and 90 controls. Among them, 50% of patients and 64% controls identified as South Asian or Black. Males comprised 63% of patients and 70% of controls. After adjusting for age, gender, disease duration and treatment burden, South Asian and Black patients had significantly worse motor scores compared to White patients (mean [SD], 42.2 [18.8], and 47 [16.6] vs 35.2 [16.4], pResult(s): We assessed 218 patients with PD and 90 controls. Among them, 50% of patients and 64% controls identified as South Asian or Black. Males comprised 63% of patients and 70% of controls. After adjusting for age, gender, disease duration and treatment burden, South Asian and Black patients had significantly worse motor scores compared to White patients (mean [SD], 42.2 [18.8], and 47 [16.6] vs 35.2 [16.4], pResult(s): We assessed 218 patients with PD and 90 controls. Among them, 50% of patients and 64% controls identified as South Asian or Black. Males comprised 63% of patients and 70% of controls. After adjusting for age, gender, disease duration and treatment burden, South Asian and Black patients had significantly worse motor scores compared to White patients (mean [SD], 42.2 [18.8], and 47 [16.6] vs 35.2 [16.4], pConclusion(s): Our results suggest that patients with PD from South Asian and Black ethnic groups may have more severe motor and certain non-motor features, including cognitive impairment, compared to White patients.

Sources Used:

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

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