# Projections for prevalence of Parkinson's disease and its driving factors in 195 countries and territories to 2050: modelling study of Global Burden of Disease Study 2021

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## ABSTRACT

### OBJECTIVE
To predict the global, regional, and national prevalence of Parkinson's disease by age, sex, year, and Socio-demographic Index to 2050 and quantify the factors driving changes in Parkinson's disease cases.

### DESIGN
Modelling study.

### DATA SOURCE
Global Burden of Disease Study 2021.

### MAIN OUTCOME MEASURES
Prevalent number, all age prevalence and age standardised prevalence of Parkinson's disease in 2050, and average annual percentage change of prevalence from 2021 to 2050; contribution of population ageing, population growth, and changes in prevalence to the growth in Parkinson's disease cases; population attributable fractions for modifiable factors.

### RESULTS
25.2 (95% uncertainty interval 21.7 to 30.1) million people were projected to be living with Parkinson's disease worldwide in 2050, representing a 112% (95% uncertainty interval 71% to 152%) increase from 2021. Population ageing (89%) was predicted to be the primary contributor to the growth in cases from 2021 to 2050, followed by population growth (20%) and changes in prevalence (3%). The prevalence of Parkinson's disease was forecasted to be 267 (230 to 320) cases per 100 000 in 2050, indicating a significant increase of 76% (56% to 125%) from 2021, whereas the age standardised prevalence was predicted to be 216 (168 to 281) per 100 000, with an increase of 55% (50% to 60%) from 2021. Countries in the middle fifth of Socio-demographic Index were projected to have the highest percentage increase in the all age prevalence (144%, 87% to 183%) and age standardised prevalence (91%, 82% to 101%) of Parkinson's disease between 2021 and 2050. Among Global Burden of Disease regions, East Asia (10.9 (9.0 to 13.3) million) was projected to have the highest number of Parkinson's disease cases in 2050, with western Sub-Saharan Africa (292%, 266% to 362%) experiencing the most significant increase from 2021. The ≥80 years age group was projected to have the greatest increase in the number of Parkinson's disease cases (196%, 143% to 235%) from 2021 to 2050. The male-to-female ratios of age standardised prevalence of Parkinson's disease were projected to increase from 1.46 in 2021 to 1.64 in 2050 globally.

### CONCLUSIONS
By 2050 Parkinson's disease will have become a greater public health challenge for patients, their families, care givers, communities, and society. The upward trend is expected to be more pronounced among countries with middle Socio-demographic Index, in the Global Burden of Disease East Asia region, and among men. This projection could serve as an aid in promoting health research, informing policy decisions, and allocating resources.

### WHAT IS ALREADY KNOWN ON THIS TOPIC
Parkinson's disease is the neurological disease with the fastest growing prevalence and disability, as reported by the Global Burden of Disease (GDB) Study 2015

A study projecting the global number of Parkinson's disease cases in 2040 relied on worldwide prevalence data from a 2014 meta-analysis (12.9 million) and GBD 2015 (12.2 million)

Other investigations focused on forecasting prevalence and number of Parkinson's disease cases in specific regions and countries, including Europe, Canada, the US, China, and France

### WHAT THIS STUDY ADDS
From 2021 to 2050, the global number of Parkinson's disease cases was projected to increase by 112%, reaching 25.2 million in 2050

The age standardised prevalence was estimated to be 216 cases per 100 000 in 2050

The most substantial rise in both all age and age standardised prevalence of Parkinson's disease was projected to be in the middle fifth of Socio-demographic index

## Introduction
Parkinson's disease is the second most common neurodegenerative disease in the world.[1] The World Health Organization has estimated that neurodegenerative diseases including Parkinson's disease and Alzheimer's disease will become the second leading cause of death worldwide by 2040, surpassing cancer related deaths.[2] According to the Global Burden of Disease Study 2015, Parkinson's disease is the neurological disease with the fastest growing prevalence and disability.[3] The significance of a comprehensive forecast of future prevalence of Parkinson's disease is underscored by the substantial increasing trends in the disease burden of Parkinson's disease, as it plays a crucial role in gaining insights into future epidemic patterns, facilitating proactive management, enabling informed policy decisions,

and guiding public health interventions. To date, only one study has projected the future global number of patients with Parkinson's disease to 2040 on the basis of Global Burden of Disease 2015 and a 2014 meta-analysis, without projections for the global prevalence of Parkinson's disease.[4] Although other investigations have focused on forecasting the future prevalence of Parkinson's disease in the US and France,[5 6] as well as the future number of people with Parkinson's disease in Europe,[7] the US,[5 7] Canada,[7] China,[8] and France,[6] predictions of Parkinson's disease prevalence in most other countries and territories are still lacking. Previous investigations found great variations in prevalence estimates for Parkinson's disease across regions, age groups, sexes, and years, emphasising the complex nature of predicting future prevalence both temporally and spatially.[9] Therefore, to effectively target prevention and intervention, a comprehensive forecast and quantitative analysis of the future prevalence of Parkinson's disease at global, regional, and national levels by socioeconomic status, age, and sex is needed.

The prediction of future prevalence should be based on comprehensive, accurate, and updated historical data. Global Burden of Disease 2021 systematically quantifies the health loss caused by Parkinson's disease in terms of age, sex, year, and geographical location from 1990 to 2021. This provides a more recent and appropriate foundation for forecasting the future prevalence of Parkinson's disease than previous forecasts. The prevalence of Parkinson's disease is influenced by various factors, which in turn shape its future trajectory. Large scale epidemiological studies and meta-analyses have consistently shown that ageing is the primary risk factor for Parkinson's disease.[10 11] Extensive analyses from Global Burden of Disease 2019 indicated that the all age prevalence of Parkinson's disease increased more rapidly than the age standardised prevalence between 1990 and 2019, suggesting a significant impact of age structure on prevalence.[12] Furthermore, the increase in Parkinson's disease prevalence can be attributed to modifications in lifestyles, environmental factors, and healthcare provision resulting from industrialisation, urbanisation, and socioeconomic advancement. The Socio-demographic Index functions as a composite indicator for socioeconomic development, encompassing per capita average incomes, educational attainment, and fertility rates. Evidence has shown a significant association between age standardised prevalence of Parkinson's disease and Socio-demographic Index.[12] The Socio-demographic Index and its changes may influence the temporal and spatial pattern of Parkinson's disease prevalence. Global Burden of Disease non-fatal modelling, which incorporates Socio-demographic Index as a key indicator into the Poisson regression model for forecasting, has been used for projection of prevalence of various diseases, including dementia, diabetes, low back pain, rheumatoid arthritis, and osteoarthritis.[13-19] Therefore, population structure and Socio-demographic Index should be considered as crucial predictors for forecasting the prevalence of Parkinson's disease, which was not adequately taken into account by previous projections.

For trends unexplained by the above covariates, we should fit a random walk model to the residuals of regression framework and incorporate forecasts of these residuals to the estimated forecasts by using an autoregressive integrated moving average (ARIMA) approach. Furthermore, decomposition analysis is necessary to quantify the contribution of population ageing, population growth, and change in prevalence unrelated to demographic factors to the rising number of Parkinson's disease cases.[20]

Most previous studies have used a single model to project future prevalence of disease[13-16]; however, the results varied owing to uncertainty in model selection. The aim of this study was to provide projections of global, regional, and national prevalence of Parkinson's disease by age, sex, year, and Socio-demographic Index to 2050 by using a probabilistic bayesian model averaging approach, which would make prevalence predictions by considering an ensemble of models. In addition, this study sought to analyse the driving factors that influence the temporal and spatial patterns of predicted number of Parkinson's disease cases.

## Methods

### Overview

On the basis of Global Burden of Disease 2021,[21] we estimated the age, sex, and year specific prevalence of Parkinson's disease in 195 countries and territories from 2022 to 2050. We calculated the average annual percentage change to examine temporal trends in forecasted prevalence of Parkinson's disease. We did decomposition analysis to assess the relative contributions of population growth, population ageing, and changes in prevalence to changes in Parkinson's disease cases between 2021 and 2050. We used exposure levels and the prevalence ratio to estimate the population attributable fractions and potential impact fractions for modifiable factors of Parkinson's disease. This study adhered to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER), ensuring transparent reporting of health estimates (supplementary table S1).[19]

### Data sources and definitions

The case definition of Parkinson's disease in Global Burden of Disease 2021 was the presence of at least two of the four primary symptoms: rest tremor, bradykinesia, limb and trunk stiffness, and postural instability.[22] Alternative diagnostic criteria such as the UK Parkinson's Disease Society Brain Bank criteria and the Movement Disorder Society clinical diagnostic criteria for Parkinson's disease,[23 24] as well as ICD9 and ICD10 (international classification of disease, 9th and 10th revision) codes (ICD9: 332-332.0; ICD10: F02.3, G20-G20.9), diagnosis of Parkinson's disease by a medical professional, and prescription of Parkinson's disease specific medications were also accepted.[1] We used Global Burden of Disease 2021 to obtain the age, sex, year, and location specific prevalence data for Parkinson's disease from 1990 to 2021. We used Global Burden of Disease 2019 to obtain prevalence data for exposure factors such as current smoking and used the data for calculating Socio-demographic Index, including total fertility under 25 years old, mean education for individuals aged ≥15, and lag distributed income per capita. The prevalence of physical activity came from the WHO Global Health Observatory. We calculated the prevalence ratio for Parkinson's disease associated with physical activity on the basis of seven eligible studies included in the meta-analysis published in 2024.[25] We derived the prevalence ratio for Parkinson's disease associated with smoking from our updated meta-analysis, building on the previous meta-analysis published in 2012 (supplementary methods section 1.1).[26] The forecasted population data by age, sex, year, and location came from Global Burden of Disease 2017.[27]

The Global Burden of Disease Study 2021 used a bayesian meta-regression model (Disease Modelling Meta-Regression-2.1) to generate age, sex, year, and location specific prevalence rates for Parkinson's disease. The details of the general Global Burden of Disease Study methods are reported elsewhere and are in the supplementary methods (section 1.2).[1,21] We forecasted each of the component drivers, including total fertility under 25 years, education of people ≥15, and lag distributed income, separately by using a regression model combined with an ARIMA [0,1,0] model and combined them with the future Socio-demographic Index values from 2020 to 2050, based on estimates from Global Burden of Disease 2019.[28,29] The Global Burden of Disease Study 2017 projected the population from 2018 to 2100 for 195 countries and territories by using the standard cohort component method of projection.[27]

### Forecasting of Parkinson's disease prevalence to 2050 and decomposition analysis

We used a probabilistic bayesian model averaging approach and Poisson regression to estimate the location, age, and sex stratified prevalence of Parkinson's disease from 2022 to 2050.[30-32] Using an ensemble of models, the bayesian model averaging approach generated a posterior distribution for the prevalence of Parkinson's disease from each model, and we derived the final projections' posterior distribution by probabilistically combining these individual model distributions. We incorporated six prevalence projection models in this study, all of which used Poisson regression, and used Socio-demographic Index as a key predictor for projecting the prevalence of Parkinson's disease, a method widely used in non-fatal modelling for the Global Burden of Disease.[13-19]

We used three steps to project future prevalence. In step 1, we constructed three Poisson regression models. Model 1 accounted for the varying trends of Parkinson's disease prevalence across different locations, model 2 considered the distinct trends of Parkinson's disease prevalence among different age groups, and model 3 factored in the differences across both locations and age groups (fig 1, top). In step 2, we constructed three new prevalence models by fitting a random walk model (ARIMA [0,1,0]) to the residuals of the three aforementioned models and incorporated forecasts of these residuals into the estimated predictions.[18] We used the ARIMA to consider trends not elucidated by previous covariates. The details of the six models are described in supplementary methods section 1.3. In step 3, we incorporated the above six models into the bayesian model averaging framework and assessed the weighting assigned to each model by evaluating their performance in projecting withheld data. Firstly, we withheld the latest 11 years of data and measured the performance of each model by using the Global Burden of Disease prevalence results from 1990 to 2010 to project prevalence from 2011 to 2021 by age, sex, year, and location. To quantify the projection bias, we compared the projections with the withheld data and computed the summary root mean squared error. Secondly, we calculated the weights for each model by using the bayesian information criterion. This is a statistical criterion for model selection, which evaluates models on the basis of their likelihood while penalising them for their complexity. It balances model fit, as indicated by the maximised value of the likelihood function, against the model's complexity. This criterion helps in choosing the model that best balances goodness of fit and parsimony, thus avoiding overfitting. The model weights are shown in supplementary figure S1. Thirdly, we estimated the final projection by drawing simulations from the posterior distribution of Parkinson's disease prevalence for each model, in proportion to the weight calculated in step 2. We then combined these simulations to derive the posterior distribution of Parkinson's disease prevalence stratified by location, age, and sex under the bayesian model averaging approach, which formed the basis for calculating the prevalence projections. The formula that we used is shown in figure 1 (bottom). To obtain forecasted number of cases, we multiplied forecasted rates by forecasted population counts.

To measure the performance of the bayesian model averaging framework, we withheld 11 (2011-21) recent years of data to validate our approach. The period of 11 years is supported by findings in other studies and allowed sufficient remaining data to be used to generate the projections.[13,18] We used the remaining data to produce bayesian model averaging projections for this withheld period, and examined how well the projections reproduced the withheld data. We also compared the performance of the bayesian model averaging projection relative to the best model for each country and sex, with details shown in supplementary methods section 1.4.

We used Joinpoint regression analysis to examine the temporal trends in the prevalence of Parkinson's disease at the global, regional, and national levels by calculating average annual percentage change (supplementary methods section 1.5). We did a Das

**A**

Model 1:

$$E\left[\log\left(Y_{l,a,s,y}\right)\right] = \beta_l SDI_{l,y} + \alpha_{l,a,s}$$

Model 2:

$$E\left[\log\left(Y_{l,a,s,y}\right)\right] = \beta_l SDI_{y} + \sum_{a=1}^{16} \beta_a \text{ x age group}_a + \alpha_{l,a,s}$$

Model 3:

$$E\left[\log\left(Y_{l,a,s,y}\right)\right] = \beta_l SDI_{l,y} + \sum_{a=1}^{16} \beta_a \text{ x age group}_a + \alpha_{l,a,s}$$

**B**

BMA Model:

$$E\left(Y_{BMA}\right) = \sum_{M\epsilon\{\text{Model 1,......,Model 6}\}} \beta_{l,M}\, E\left(Y_M\right)$$

**Fig 1 | Equations used to construct models. Top: Poisson regression models. For each location (l), age group (a), sex (s), and year (y), Parkinson's disease prevalence estimates were log transformed: $\log(Y_{l,a,s,y})$. On right side of equation, $\beta_l$ was fixed coefficient on forecasted Socio-demographic Index, $\beta_a$ was fixed coefficient assigned to different age groups, and $\alpha_{l,a,s}$ was location, age, and sex specific random intercept. Bottom: bayesian model averaging (BMA) model. Y was prevalence of Parkinson's disease. For each model (M) and location (l), $\beta_{l,M}$ was fixed coefficient on prevalence of Parkinson's disease. $\beta_{l,M}$ for each model was calculated using bayesian information criterion**

Gupta decomposition analysis to determine the relative contributions of population growth, population ageing, and changes in prevalence rate unrelated to demographics to the change in prevalent cases at global, regional, and national levels between 2021 and 2050 (supplementary methods section 1.6).[20]

### Population attributable fractions and potential impact fractions of modifiable factors

In this study, two modifiable factors for Parkinson's disease were eligible according to the World Cancer Research Fund evidence grading criteria applied by Global Burden of Disease 2021: smoking and physical activity.[33] We used population attributable fractions to quantify the proportion of Parkinson's disease cases that would be changed if exposure to a given factor was entirely eliminated. We assumed that the association between modifiable factors and Parkinson's disease was constant worldwide. We estimated the total number of Parkinson's disease cases attributable to each modifiable factor by multiplying the population attributable fraction estimates by the number of Parkinson's disease cases. Moreover, to evaluate the potential impact of a partial increase or decrease in modifiable factors on the proportion of Parkinson's disease cases, we modelled the potential impact fractions resulting from a proportionate increase or decrease (20%) in prevalence of each factor. The detailed methods are described in supplementary methods sections 1.7 and 1.8.

### Compilation of results

We projected the prevalence of Parkinson's disease for both sexes, 16 age groups, and 195 countries and territories from 2022 to 2050. Additionally, we assigned countries to a fifth of Socio-demographic Index according to their estimated values on these indicators in 2021. The unit used in this study was per 100 000 population for both the all age and the age standardised prevalence of Parkinson's disease. For the age standardised prevalence, we used a standard population calculated as the non-weighted average across all countries of the percentage of the population in each five year age group from 2010 to 2035.[14] Uncertainty was propagated through all calculations by sampling 1000 draws at each step of the calculations, which enabled us to carry through uncertainty from multiple sources, including input data, corrections of measurement error, and estimates of residual non-sampling error. We determined the 95% uncertainty intervals for Parkinson's disease prevalence as the 2.5th and 97.5th centiles of the posterior distributions. Otherwise, we calculated 95% confidence intervals for the data pertaining to average annual percentage change, population attributable fractions, and potential impact fractions.

### Patient and public involvement

No patients or members of the public were invited to participate in determining the research question and outcomes, collecting and analysing the data, interpreting the results, or writing the manuscript. We invited two people with Parkinson's disease (one with de novo Parkinson's disease and one with advanced Parkinson's disease) and one care giver to assist in revising the plain English summary of the manuscript (supplementary methods section 1.9), as well as to read the full manuscript and provide their suggestions. The manuscript has been revised to optimise its readability, thereby facilitating the comprehension of its core content by the public. Furthermore, we will invite people with Parkinson's disease, their families, care givers, and other individuals involved in social welfare through outpatient recruitment and online channels to participate in the dissemination of our research. The invited individuals will be engaged in preparing comprehensible publicity materials (including a simple introduction, pictures, and multimedia content) and spreading information to the general public, policy makers, and scientists, as well as healthcare professionals through both social media platforms and traditional media outlets.

## Results

### Projected prevalence of Parkinson's disease from 2022 to 2050

Globally, we estimated that the number of people living with Parkinson's disease in 2050 would be 25.2 (95% uncertainty interval 21.7 to 30.1) million for all ages and both sexes combined, indicating an increase of 112% (95% uncertainty interval 71% to 152%) from 2021, with the number of cases estimated at 15.6

**Table 1 | Projected numbers, all age prevalence, and age standardised prevalence of Parkinson's disease in 2021 and 2050, as well as corresponding percentage changes globally, by Socio-demographic Index and Global Burden of Disease regions from 2021 to 2050. Values in parentheses are 95% uncertainty intervals**

| | No of cases (thousands) | | | All age prevalence (per 100 000) | | | Age standardised prevalence (per 100 000) | | |
|---|---|---|---|---|---|---|---|---|---|
| Location | 2021 | 2050 | Percentage change | 2021 | 2050 | Percentage change | 2021 | 2050 | Percentage change |
| Global | 11 894 (10 030 to 14 058) | 25 224 (21 678 to 30 112) | 112 (71 to 152) | 152 (130 to 181) | 267 (230 to 320) | 76 (56 to 125) | 140 (113 to 172) | 216 (168 to 281) | 55 (50 to 60) |
| **Socio-demographic Index** | | | | | | | | | |
| High | 2579 (2309 to 2945) | 3964 (3655 to 4664) | 54 (32 to 73) | 273 (245 to 313) | 406 (360 to 459) | 49 (31 to 69) | 125 (104 to 148) | 166 (136 to 206) | 33 (28 to 37) |
| High-middle | 1871 (1693 to 2429) | 3314 (3074 to 4399) | 77 (46 to 108) | 290 (234 to 335) | 518 (433 to 620) | 79 (59 to 117) | 174 (138 to 219) | 277 (213 to 365) | 59 (51 to 68) |
| Middle | 5240 (4213 to 6275) | 13 486 (10 214 to 14 886) | 157 (112 to 205) | 183 (148 to 221) | 448 (371 to 540) | 144 (87 to 183) | 155 (122 to 196) | 296 (225 to 395) | 91 (82 to 101) |
| Low-middle | 1487 (1203 to 1786) | 3735 (3065 to 4592) | 151 (121 to 220) | 65 (53 to 79) | 127 (104 to 155) | 96 (58 to 144) | 92 (73 to 116) | 129 (96 to 169) | 40 (32 to 49) |
| Low | 277 (222 to 335) | 906 (750 to 1120) | 227 (203 to 302) | 28 (23 to 35) | 52 (43 to 64) | 84 (66 to 141) | 74 (57 to 92) | 92 (70 to 122) | 26 (19 to 32) |
| **Global Burden of Disease regions** | | | | | | | | | |
| East Asia | 5312 (4240 to 6320) | 10 927 (9039 to 13 334) | 106 (94 to 176) | 357 (287 to 428) | 821 (674 to 995) | 130 (93 to 161) | 242 (189 to 312) | 593 (441 to 814) | 145 (132 to 159) |
| South East Asia | 506 (417 to 599) | 1346 (1144 to 1637) | 166 (141 to 200) | 75 (62 to 89) | 173 (147 to 211) | 131 (89 to 151) | 87 (68 to 107) | 112 (85 to 145) | 30 (24 to 35) |
| Oceania | 5 (4 to 6) | 11 (9 to 13) | 136 (90 to 169) | 34 (29 to 44) | 48 (42 to 61) | 42 (15 to 65) | 84 (63 to 105) | 91 (67 to 126) | 9 (5 to 12) |
| Central Asia | 59 (48 to 70) | 152 (130 to 189) | 157 (107 to 230) | 63 (52 to 75) | 127 (109 to 159) | 102 (62 to 132) | 86 (67 to 107) | 96 (71 to 126) | 11 (4 to 19) |
| Central Europe | 228 (203 to 262) | 291 (265 to 353) | 28 (11 to 48) | 202 (180 to 233) | 308 (279 to 372) | 52 (39 to 88) | 96 (78 to 115) | 103 (81 to 130) | 7 (2 to 13) |
| Eastern Europe | 337 (274 to 405) | 432 (387 to 554) | 28 (10 to 86) | 163 (132 to 196) | 239 (212 to 304) | 46 (19 to 89) | 91 (71 to 119) | 94 (65 to 124) | 3 (−5 to 10) |
| High income Asia Pacific | 296 (265 to 378) | 405 (336 to 519) | 37 (10 to 65) | 160 (143 to 204) | 252 (208 to 321) | 58 (22 to 75) | 64 (48 to 76) | 67 (51 to 90) | 5 (−1 to 11) |
| Australasia | 49 (41 to 58) | 86 (72 to 106) | 77 (44 to 97) | 166 (139 to 198) | 230 (193 to 283) | 39 (22 to 62) | 86 (68 to 113) | 117 (85 to 158) | 36 (28 to 44) |
| Western Europe | 1603 (1417 to 1832) | 2411 (2203 to 2814) | 50 (36 to 76) | 370 (328 to 423) | 550 (502 to 641) | 49 (32 to 66) | 152 (125 to 182) | 183 (148 to 226) | 20 (15 to 26) |
| Southern Latin America | 99 (86 to 119) | 196 (171 to 248) | 99 (70 to 125) | 148 (130 to 180) | 255 (223 to 323) | 73 (37 to 105) | 111 (85 to 139) | 133 (99 to 178) | 20 (12 to 28) |
| High income North America | 842 (752 to 957) | 1091 (1040 to 1320) | 30 (20 to 54) | 230 (207 to 263) | 271 (259 to 328) | 18 (10 to 50) | 121 (102 to 143) | 155 (126 to 193) | 28 (24 to 32) |
| Caribbean | 41 (33 to 48) | 88 (79 to 110) | 115 (97 to 169) | 87 (72 to 103) | 179 (160 to 224) | 105 (93 to 161) | 73 (59 to 92) | 95 (72 to 123) | 30 (26 to 34) |
| Andean Latin America | 95 (78 to 114) | 234 (202 to 286) | 145 (116 to 187) | 149 (124 to 180) | 266 (230 to 326) | 79 (66 to 130) | 158 (123 to 204) | 263 (193 to 363) | 67 (59 to 75) |
| Central Latin America | 253 (196 to 283) | 634 (545 to 759) | 151 (118 to 233) | 96 (76 to 110) | 194 (167 to 233) | 103 (97 to 139) | 95 (79 to 122) | 130 (101 to 169) | 38 (31 to 45) |
| Tropical Latin America | 231 (184 to 273) | 537 (455 to 673) | 133 (91 to 202) | 104 (83 to 123) | 222 (188 to 279) | 115 (89 to 160) | 89 (70 to 116) | 113 (82 to 157) | 27 (19 to 35) |
| North Africa and Middle East | 868 (584 to 891) | 3003 (2489 to 3608) | 246 (222 to 342) | 69 (56 to 83) | 169 (141 to 205) | 145 (99 to 190) | 103 (80 to 129) | 152 (116 to 203) | 49 (40 to 57) |
| South Asia | 2510 (1711 to 2662) | 6762 (5639 to 8664) | 169 (179 to 285) | 69 (57 to 85) | 161 (134 to 207) | 135 (122 to 194) | 92 (71 to 119) | 133 (97 to 180) | 44 (39 to 50) |
| Central Sub-Saharan Africa | 29 (24 to 36) | 96 (77 to 123) | 233 (166 to 342) | 22 (18 to 28) | 40 (33 to 51) | 81 (34 to 120) | 62 (46 to 80) | 72 (51 to 99) | 16 (8 to 25) |
| Eastern Sub-Saharan Africa | 90 (71 to 108) | 311 (252 to 389) | 246 (186 to 409) | 21 (17 to 26) | 39 (32 to 50) | 86 (62 to 144) | 59 (46 to 73) | 68 (52 to 88) | 15 (9 to 22) |
| Southern Sub-Saharan Africa | 37 (30 to 44) | 90 (75 to 115) | 141 (106 to 218) | 46 (38 to 56) | 81 (69 to 105) | 76 (39 to 128) | 67 (53 to 87) | 80 (58 to 108) | 20 (15 to 25) |
| Western Sub-Saharan Africa | 123 (102 to 149) | 483 (417 to 604) | 292 (266 to 362) | 26 (22 to 32) | 50 (44 to 64) | 92 (66 to 122) | 75 (58 to 93) | 91 (69 to 120) | 21 (15 to 27) |

(13.3 to 18.6) million in 2030 and 20.4 (17.5 to 24.3) million in 2040. We forecasted the all age prevalence of Parkinson's disease to be 267 (95% uncertainty interval 230 to 320) per 100 000 population in 2050 (243 (212 to 291) for women and 295 (260 to 355) for men), with an increase of 76% (56% to 125%) from 2021. We projected the age standardised prevalence to be 216 (168 to 281), representing a rise of 55% (50% to 60%) from 2021 (table 1; fig 2). Between 2021 and 2050, the number of Parkinson's disease cases (average annual percentage change 2.74%, 95% confidence interval 2.73% to 2.76%) and the all age prevalence of Parkinson's disease (average annual percentage change 2.10%, 2.09% to 2.11%) were projected to increase gradually, at a slower pace compared with the period from 1990 to 2021 (average annual percentage change 4.38% for the number of Parkinson's disease cases and 3.01% for all age prevalence). The age standardised prevalence of Parkinson's disease (average annual percentage change 1.52%, 1.51% to 1.53%) was projected to increase over the next 30 years at a pace similar to that observed from 1990 to 2021 average annual percentage change 1.50%, 1.39% to 1.62%) (supplementary table S3).

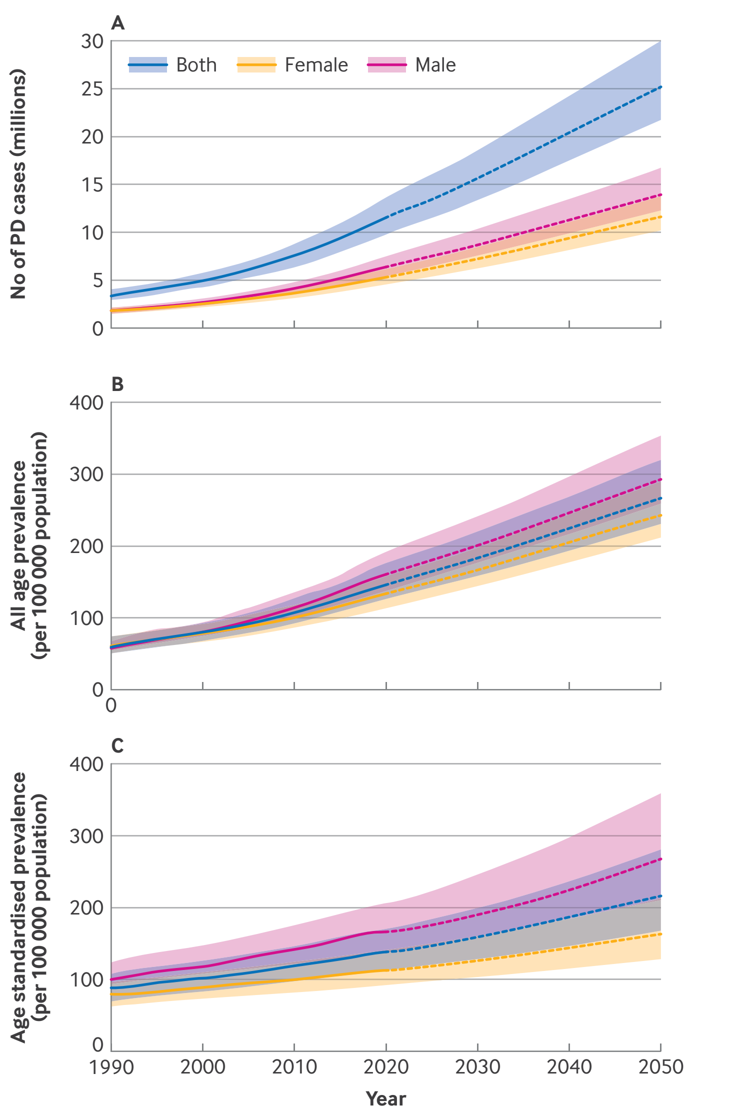


Fig 2 | Estimated trends in global number of Parkinson's disease (PD) cases (top), all age prevalence of PD (middle), and age standardised prevalence of PD (bottom), with 95% uncertainty intervals, 1990-2050. Solid lines represent values from Global Burden of Disease Study (1990-2021); dotted lines represent projected values (2022-50)

By 2050, the prevalence and prevalent cases of Parkinson's disease were projected to increase in all 21 Global Burden of Disease regions, with significant variations among them. The largest number of Parkinson's disease cases was projected to be in East Asia (10.9 (95% uncertainty interval 9.0 to 13.3) million) in 2050, followed by South Asia (6.8 (5.6 to 8.7) million), with the fewest number of cases estimated in Oceania (0.011 (0.009 to 0.013) million) and Australasia (0.086 (0.072 to 0.11) million) in 2050. The largest increases in number of Parkinson's disease cases were estimated to occur in western Sub-Saharan Africa (292%, 95% uncertainty interval 266% to 362%) and eastern Sub-Saharan Africa (246%, 186% to 409%) from 2021 to 2050, and the smallest increases in prevalent cases were projected in central Europe (28%, 11% to 48%) and eastern Europe (28%, 10% to 86%) (supplementary figure S2). The all age prevalence of Parkinson's disease was anticipated to be highest in East Asia (821, 95% uncertainty interval 674 to 995) in 2050, followed by western Europe (550, 502 to 641) and central Europe (308, 279 to 372), whereas the lowest was estimated to be in eastern Sub-Saharan Africa (39, 32 to 50) and central Sub-Saharan Africa (40, 33 to 51). The regions with the highest increase in all age prevalence were estimated to be North Africa and the Middle East (145%, 99% to 190%), South Asia (135%, 122% to 194%), and South East Asia (131%, 89% to 151%), whereas Australasia (39%, 22% to 62%) and high income North America (18%, 10% to 50%) were forecasted to have the lowest rise. In 2050, the highest age standardised prevalence for Parkinson's disease was projected to be in East Asia (593, 441 to 814), followed by Andean Latin America (263, 193 to 363), and western Europe (183, 148 to 226), with the lowest in high income Asia Pacific (67, 51 to 90), eastern Sub-Saharan Africa (68, 52 to 88) and central Sub-Saharan Africa (72, 51 to 99). We estimated that from 2021 to 2050, the age standardised prevalence of Parkinson's disease would increase with Socio-demographic Index across the 21 Global Burden of Disease regions, peak at a Socio-demographic Index of 0.8, and then decline (supplementary figure S3). We projected East Asia (145%,132% to 159%) and Andean Latin America (67%, 59% to 75%) to have the highest increase in age standardised prevalence of Parkinson's disease, with other Global Burden of Disease regions increasing at a lower rate than global growth after 2021 (table 1; supplementary table S3).

We projected that the high-middle Socio-demographic Index fifth would have the highest all age prevalence (518, 95% uncertainty interval 433 to 620) of Parkinson's disease in 2050, and we expected the lowest Socio-demographic Index fifth to have the lowest all age prevalence (52, 43 to 64). However, the


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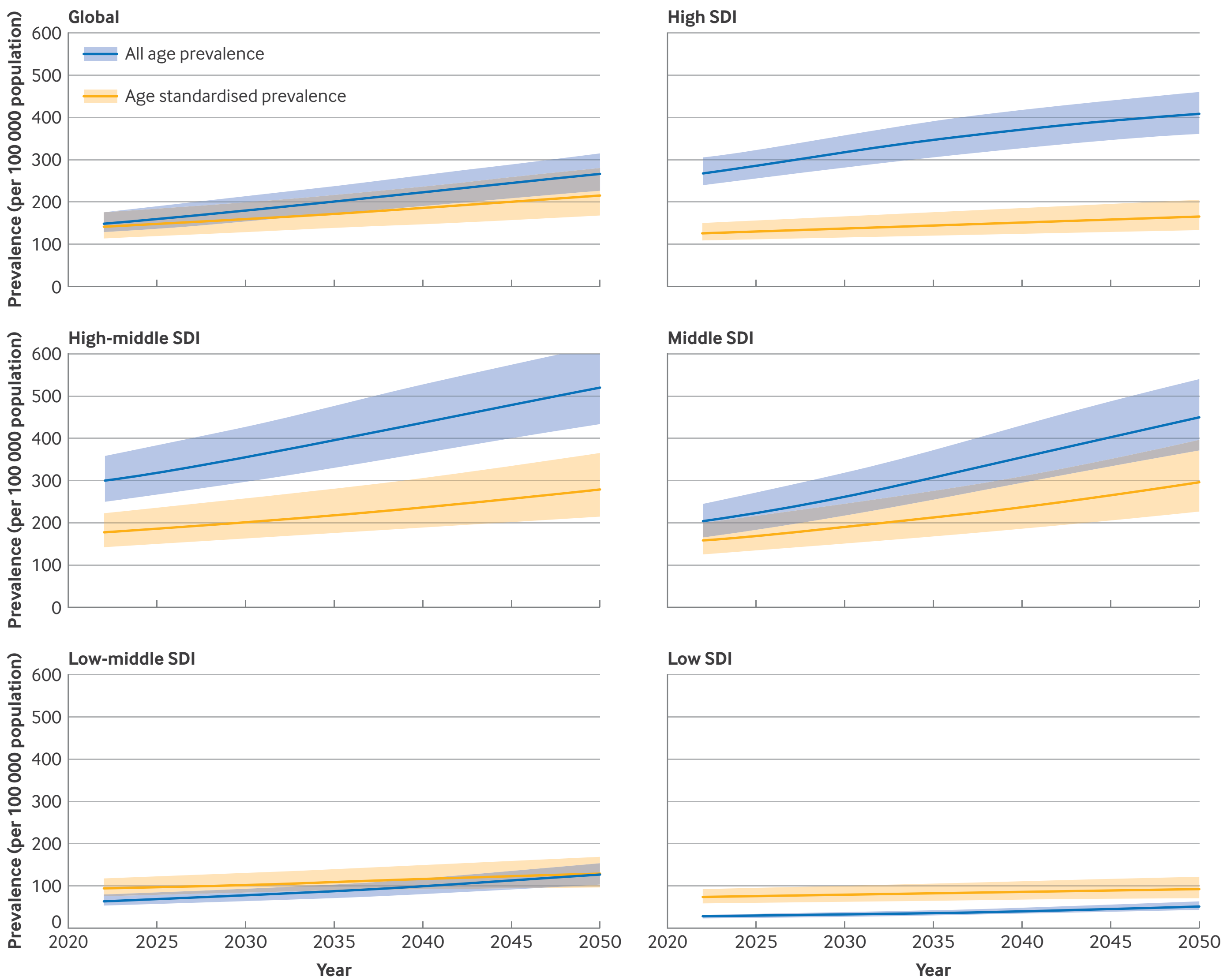


Fig 3 | Projected trends of all age prevalence and age standardized prevalence of Parkinson's disease from 2022 to 2050 globally and in locations grouped by Socio-demographic Index (SDI) fifths, with 95% uncertainty intervals

increase in all age prevalence of Parkinson's disease between 2021 and 2050 was forecasted to be highest in the middle Socio-demographic Index fifth (144%, 95% uncertainty interval 87% to 183%) and lowest in the highest fifth (49%, 31% to 69%). We projected that the middle Socio-demographic Index fifth (296, 95% uncertainty interval 225 to 395) would have the highest age standardised prevalence of Parkinson's disease in 2050, and the lowest would be observed in the lowest fifth (92, 70 to 122). Moreover, the growth in age standardised prevalence of Parkinson's disease would also be highest for the middle Socio-demographic Index fifth (91%, 82% to 101%) and lowest for the lowest fifth (26%, 19% to 32%) (table 1; fig 3). The increase in the total number of Parkinson's disease cases was expected to be highest in the lowest Socio-demographic Index fifth (227%, 203% to 302%), and lowest in the highest fifth (54%, 32% to 73%). Only the number of patients in low Socio-demographic Index regions was estimated to increase more rapidly from 2021 to 2050 than in the previous three decades (fig 4, top).

We projected that the all age prevalence of Parkinson's disease would increase in all countries and territories from 2021 to 2050, with 99% experiencing an increase in the number of cases and 94% experiencing an increase in age standardised prevalence (supplementary tables S4 and S5). However, we found evidence of great variation in the projected trend across countries and territories. Additionally, we forecasted the prevalence of Parkinson's disease to be highest in Spain (848, 95% uncertainty interval 728 to 1043), China (831, 724 to 1014), and Andorra (697, 588 to 873), whereas Somalia (20, 15 to 26), Niger (20, 16 to 26), and Chad (22, 19 to 30) would have the lowest. Qatar (1062%, 95% uncertainty interval 945% to 1726%) and Kuwait (425%, 389% to 549%) were projected to have the highest increase in prevalence, and Italy (3%, −25% to 34%) and Bulgaria (7%, −5% to 32%) were projected to have the lowest. Projected

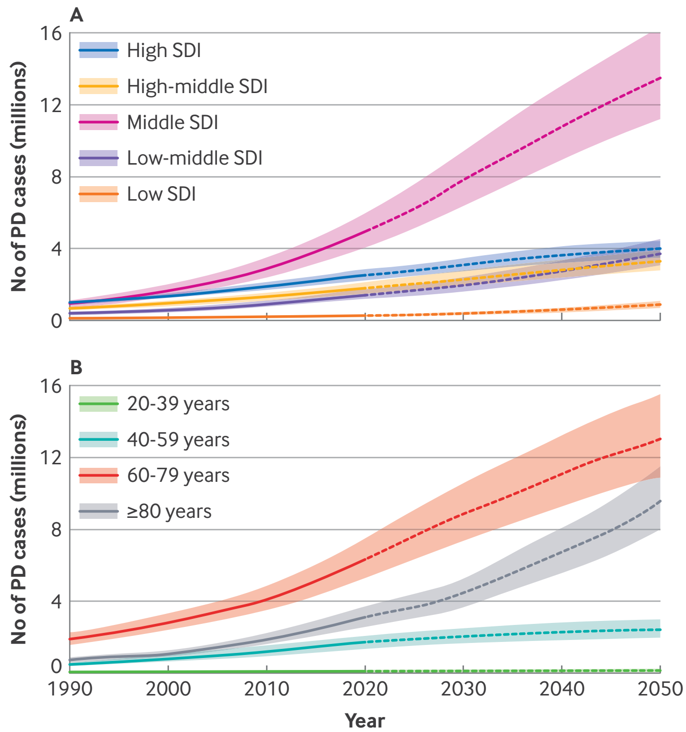


**Fig 4 | Estimated trends of numbers of Parkinson's disease (PD) cases by Socio-demographic Index (SDI) fifths (top) and age groups (bottom), for both sexes combined, with 95% uncertainty intervals, 1990-2050. Solid lines represent values from Global Burden of Disease (1990-2021); dotted lines represent projected values (2022-50)**

age standardised prevalence for 195 countries and territories in 2050 was estimated to range from 52 to 583. China was anticipated to have the highest age standardised prevalence (583, 449 to 822), and Norway was projected to have the largest increase in age standardised prevalence (292%, 273% to 311%) (fig 5; fig 6; supplementary figure S4). We estimated that approximately two thirds of global Parkinson's disease cases in 2050 would be found in the top 10 countries with the highest number of Parkinson's disease cases, with China having the highest number (10.5 (95% uncertainty interval 9.2 to 12.9) million), followed by India (2.8 (2.3 to 3.5) million) and the US (0.9 (0.8 to 1.1) million). Two countries projected to newly enter this top 10 ranking after 2021 were Indonesia and Mexico, both of which were middle Socio-demographic Index countries. Among the top 10 countries, we forecasted the largest increase in number of patients from 2021 to 2050 in Indonesia (184%, 163% to 301%), followed by Mexico (171%, 152% to 243%), and India (168%, 126% to 237%), with the smallest increases in the US (29%, 27% to 61%) and Germany (38%, 27% to 53%) (fig 7).

The projected prevalence of Parkinson's disease in 2050 showed an age dependent increase for both sexes, reaching its peak at age 85-89 before showing a slight decline, mirroring the observed trend in 2021 (supplementary figure S5). The global prevalence of Parkinson's disease in the >60 age group was expected to reach 1055 (95% uncertainty interval 923 to 1323) in 2050. Despite having the lowest prevalence (2, 95% uncertainty interval 1.7 to 4) and number of Parkinson's disease cases (0.12 (95% uncertainty interval 0.08 to 0.18) million) in 2050, people aged 20-40 years were projected to experience the greatest increase in prevalence of Parkinson's disease (average annual percentage change 1.21, 95% confidence interval 1.17 to 1.26), especially in countries with low (1.78, 1.73 to 1.83) or low-middle Socio-demographic Index (1.77, 1.71 to 1.82). People aged 40-59 years (average annual percentage change 0.24, 95% confidence interval 0.21 to 0.28) were expected to experience a similar increase in prevalence to the 60-79 years age group (0.28, 0.27 to 0.30) globally. The number of Parkinson's disease cases in 2050 was expected to be highest among people aged 60-79 years (13.0 (11.0 to 15.6) million), both globally and across four Socio-demographic Index regions, except for the high Socio-demographic Index region; this indicated a worldwide increase of 99% (54% to 122%) since 2021 (fig 4, bottom). We projected that people aged above 80 years would have the highest prevalence (2087, 1759 to 2540) in 2050 and the highest increase in the number of cases (196%, 143% to 235%) from 2021 to 2050, both globally and across all Socio-demographic Index regions (supplementary figures S6 and S7). Additionally, the average age of people with Parkinson's disease was projected to increase globally and across countries in various Socio-demographic Index fifths from 1990 to 2050, which was particularly pronounced in the middle Socio-demographic Index region (supplementary figure S8).

Of the total Parkinson's disease cases in 2050, we estimated that 46% would be female (11.5 (95% uncertainty interval 9.97 to 13.7) million). By 2050, the age standardised prevalence of Parkinson's disease in men (267, 95% uncertainty interval 209 to 360) was anticipated to remain higher than in women (163, 128 to 213). The male-to-female ratios of age standardised prevalence of Parkinson's disease were projected to increase from 1.46 in 2021 to 1.64 in 2050 globally, especially in the high-middle Socio-demographic Index (1.60 to 1.93) region. We projected that the age standardised prevalence in men would show a rapid increase (average annual percentage change 1.64%, 95% confidence interval 1.63% to 1.65%) compared with that in women (1.25%, 1.24% to 1.25%) globally. At the national level, 105 countries and territories would be anticipated to have an increase in the male-to-female ratio of age standardised prevalence of Parkinson's disease from 2021 to 2050. In 2050, the prevalence was projected to be higher in men than in women across all age groups (supplementary figure S9); however, the average age of people with Parkinson's disease was higher for women than for men (supplementary figure S8).

### Model validation

The bayesian model averaging approach had a smaller error than the best single models for different sex, country, and projection duration combinations

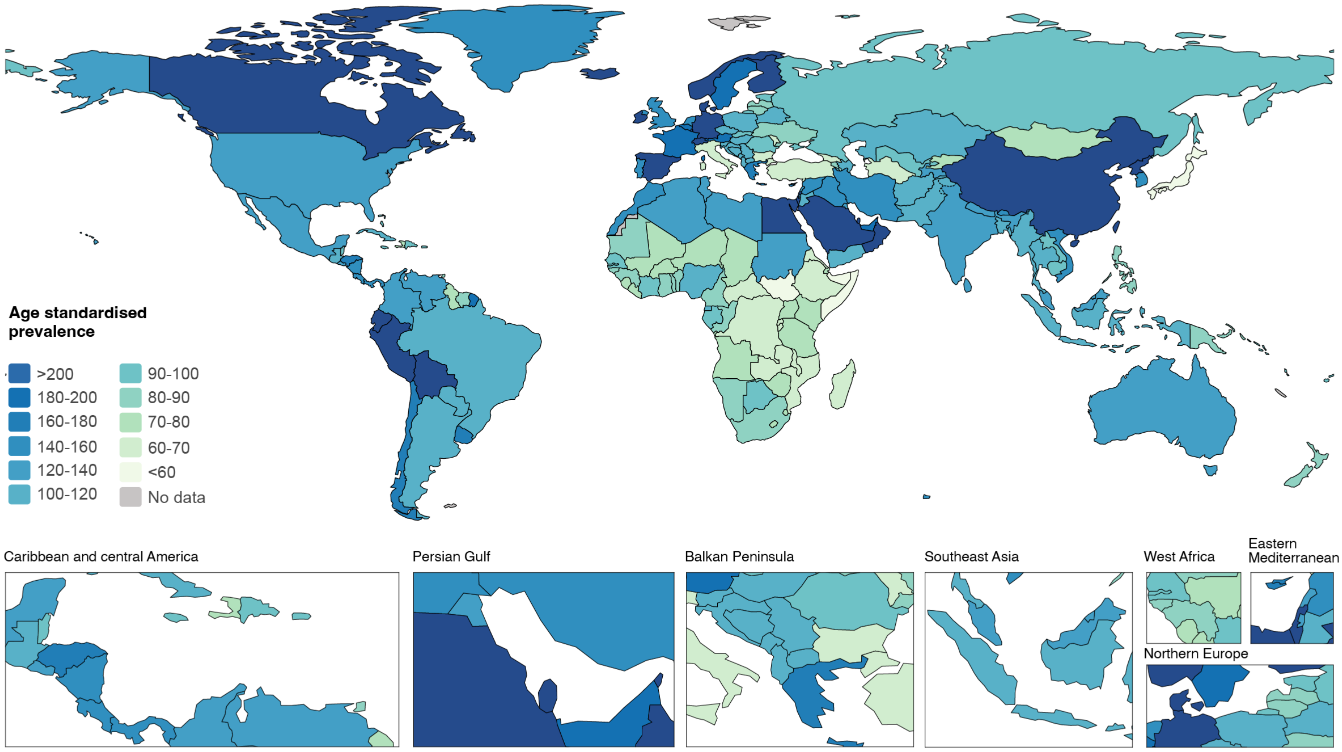


**Fig 5 | Projected age standardised prevalence (per 100 000) of Parkinson's disease in 2050, by country and territory for both sexes combined**

(supplementary figure S10). The comparison between the predicted Parkinson's disease prevalence and the results from Global Burden of Disease 2021 between 2011 and 2021 is shown in supplementary figure S11. Our models showed accurate predictions for the prevalence of Parkinson's disease in 195 countries and territories by age and sex from 2011 to 2021, with the root mean square error below 0.01 and bias less than 0.0001.

### Decomposition analysis

Between 2021 and 2050, our predictions indicated that population ageing, population growth, and changes in prevalence would contribute 89%, 20%, and 3%, respectively, to the increase in the number of Parkinson's disease cases globally, with different patterns at the regional and national levels. Population ageing was projected to be the predominant driver behind the increase in Parkinson's disease cases in all Socio-demographic Index regions after 2021. We estimated that the projected proportion of increase in cases attributed to population ageing would decrease consecutively from countries with low Socio-demographic Index to those with high Socio-demographic Index. Population growth was estimated to be the second factor driving the increase of Parkinson's disease patients globally and in countries with low Socio-demographic Index (78%). Conversely, the change in prevalence would be the second contributing factor to the increase in cases in countries with high (7%), high-middle (2%), middle (17%), and low-middle Socio-demographic Index (47%) (fig 8).

From 2021 to 2050, we projected that population ageing would be the leading driver of change in prevalent cases across all 21 Global Burden of Disease regions. The percentage of increase in Parkinson's disease cases attributed to population ageing was estimated to be highest in North Africa and the Middle East (197%), with the lowest in high income Asia Pacific (43%). Of the 21 Global Burden of Disease regions, change in prevalence was projected to be the second contributor to the increase in Parkinson's disease cases in four regions; however, it would contribute negatively to the increase in the number of cases in Oceania (−43%), high income North America (−26%), eastern Sub-Saharan Africa (−9%), central Europe (−8%), eastern Europe (−8%), and southern Sub-Saharan Africa (−1%) (fig 9). The percentage of increase in Parkinson's disease cases attributed to population growth was also estimated to be highest in western Sub-Saharan Africa (104%), with a negative contribution observed in central Europe (−16%), high income Asia Pacific (−13%), eastern Europe (−12%), and East Asia (−11%). The significant rise in projected Parkinson's disease cases in the western Sub-Saharan Africa region was attributed to a profound increase in population ageing, substantial population growth, and a notable rise in prevalence. The smallest forecasted increases in prevalent cases in central and eastern Europe since 2021 were expected to be attributed to the small change in population ageing, as well as a decrease in population and the prevalence of Parkinson's disease.

Population ageing was projected to be the primary contributing factor to the change in prevalent cases

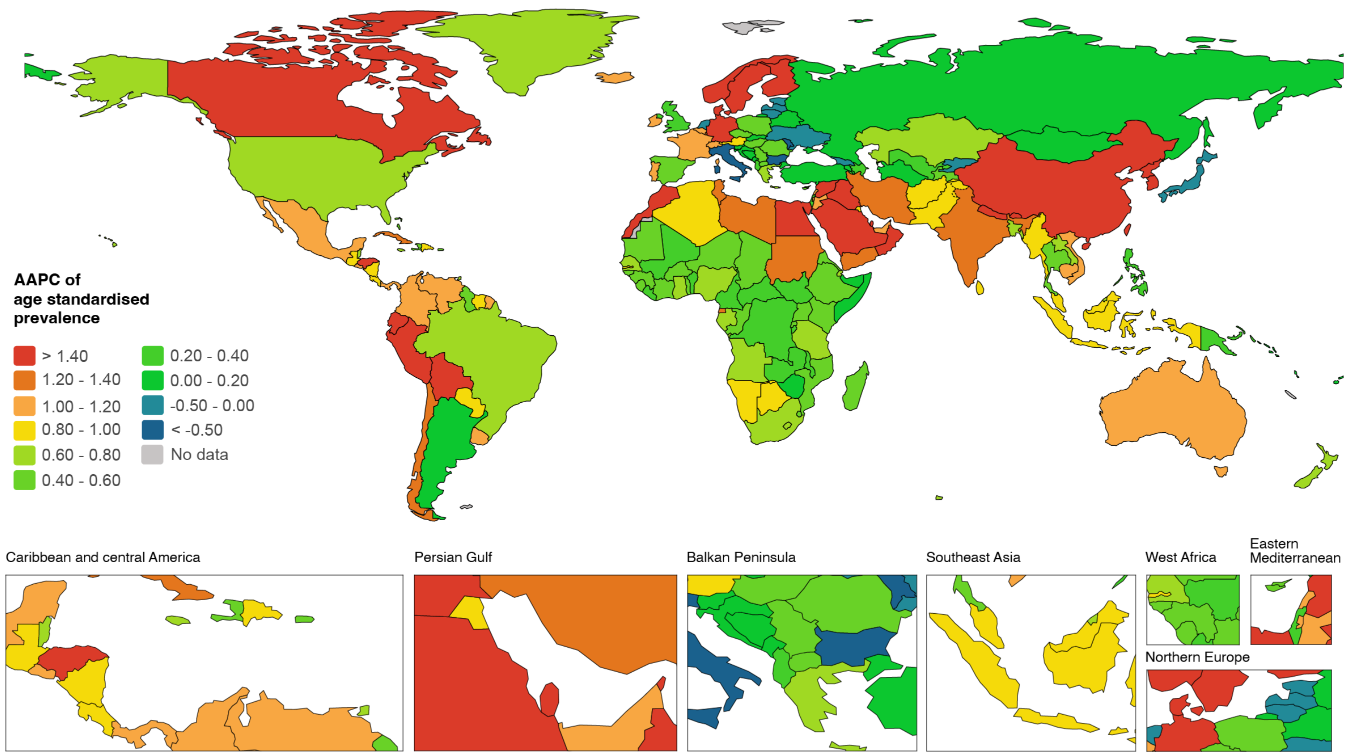


**Fig 6 | Projected average annual percentage change (AAPC) from 2021 to 2050, by country and territory for both sexes combined**

among the top 10 countries with the highest number of Parkinson's disease patients in 2050. The contribution of change in prevalence between 2021 and 2050 would be far below that observed during the period 1990-2021 in all the top 10 countries. From 2021 to 2050, the contribution of population growth in top 10 countries was projected to be negative in China (−11%), Spain (−10%), and Germany (−1%). In Indonesia, the country with the highest projected increase in Parkinson's disease cases from 2021 to 2050, the contribution of ageing (144%) to this increase was forecasted to be significantly higher than that in the previous three decades and would also be the highest among the top 10 countries. Negative contribution from changes in prevalence may be associated with the smallest increase in number of Parkinson's disease cases in the US.

### Population attributable fractions and potential impact fractions of modifiable factors

Globally, if all individuals adhered to regular physical activity, the projected number of Parkinson's disease cases would show a reduction of 4.9% (95% confidence interval 3.4% to 6.4%) compared with the initial forecast for 2050. Assuming a 20% increase in prevalence of physical activity in 2050, the future number of Parkinson's disease cases would decrease by 2.6% (1.8% to 3.4%), equating to 0.65 (95% confidence interval 0.45 to 0.86) million prevalent cases. If all individuals stopped smoking, the number of Parkinson's disease cases would show an increase of 10.6% (9.5% to 11.7%) in 2050 compared with the initial forecast. Assuming a 20% decrease in smoking prevalence in 2050, the future number of cases would increase by 2.1% (1.9% to 2.3%), equating to 0.53 (0.48 to 0.59) million prevalent cases.

## Discussion

### Principal findings

To the best of our knowledge, this study provides the first comprehensive projections of the global, regional, and national prevalence of Parkinson's disease until 2050. These projections indicate a universal increase in prevalence of Parkinson's disease worldwide; however, we would expect significant heterogeneity by location, age, sex, and socioeconomic status. The global number of cases of Parkinson's disease was forecasted to be 25.2 million in 2050. Furthermore, the all age prevalence of Parkinson's disease was projected to reach 267 cases per 100 000 population, indicating a growth of 76% from 2021, whereas the age standardised prevalence was expected to rise by 55%. The age standardised prevalence of Parkinson's disease generally was forecasted to show an upward trend with higher Socio-demographic Index across all 21 Global Burden of Disease regions. The greatest increase in age standardised rate would be observed in East Asia and countries with middle Socio-demographic Index. Meanwhile, the most pronounced increase in the number of Parkinson's disease cases was expected to occur in western Sub-Saharan Africa. The prevalence of Parkinson's disease in 2050 was



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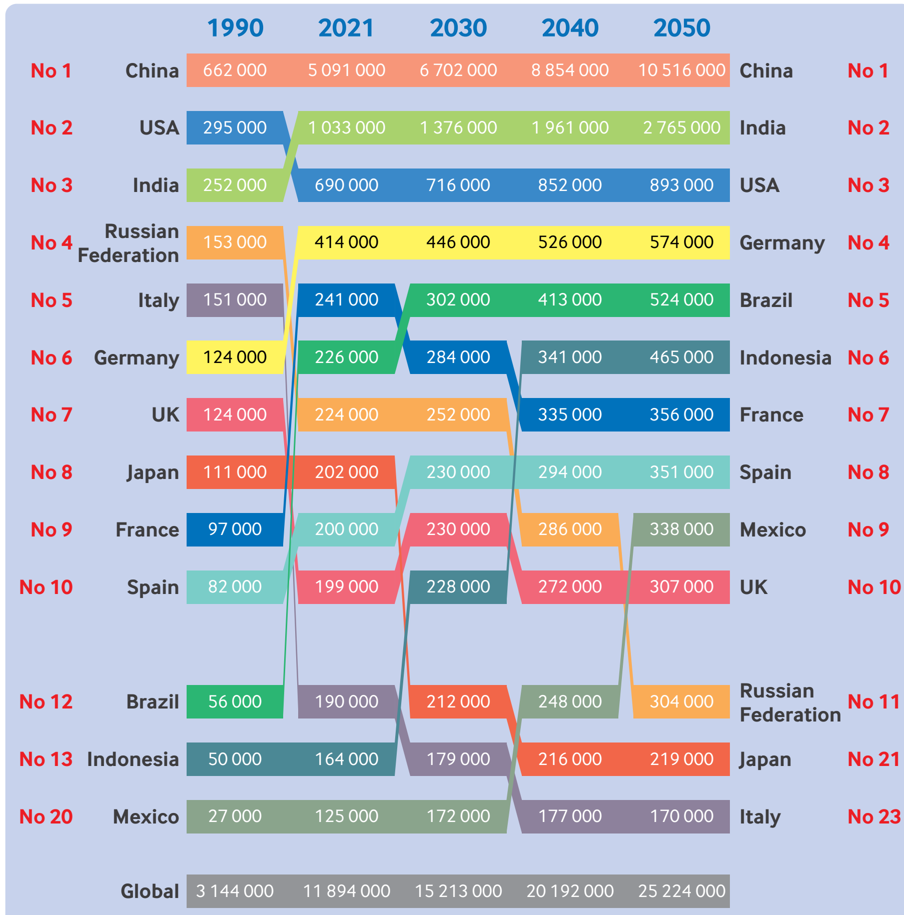


**Fig 7 | Estimated top 10 countries with highest number of Parkinson's disease (PD) cases in 1990, 2021, 2030, 2040, and 2050 globally. Corresponding boxes present number of PD cases in this country and their proportion among global PD patients, as well as global count**

expected to show an age dependent increase, and the gap in age standardised prevalence between men and women was projected to widen after 2021. Population ageing, population growth, and changes in prevalence would contribute 89%, 20%, and 3%, respectively, to the increase in the number of Parkinson's disease cases globally, with different patterns at the regional level and national level. The estimation of population attributable fractions highlights the important roles of physical activity and smoking in Parkinson's

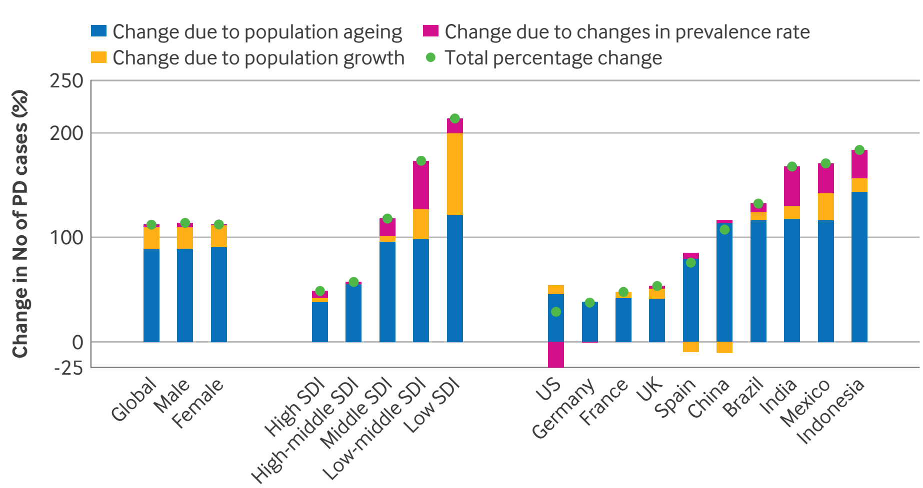


**Fig 8 | Decomposition of projected percentage change in number of people with Parkinson's disease (PD) between 2021 and 2050 globally and by sex, Socio-demographic Index (SDI) fifths, and top 10 countries**

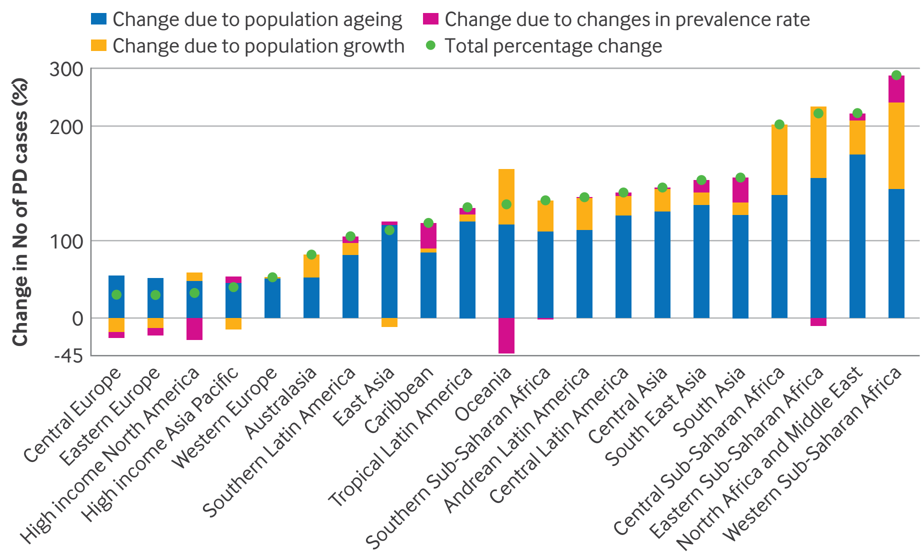


**Fig 9 | Decomposition of projected percentage change in number of people with Parkinson's disease (PD) between 2021 and 2050 by Global Burden of Disease regions**

disease prevalence. These predictions could serve as a foundation for decision making by governments and healthcare professionals, as well as for the rational allocation of resources.

### Comparison with previous studies

Our projection for the global number of Parkinson's disease cases in 2040 considerably surpasses the previous estimates by Dorsey and colleagues,[4] which relied on worldwide prevalence data from a meta-analysis conducted in 2014 and Global Burden of Disease 2015, along with population forecasts from the US Census Bureau. Not only did we forecast the global trends in the prevalence and number of cases of Parkinson's disease, but we also estimated the future prevalence and number of cases across 195 countries and territories, as well as 21 Global Burden of Disease regions, stratified by Socio-demographic Index, sex, and age group. At the national level, we anticipated the predicted future prevalence of Parkinson's disease in the US and France to be higher than previous forecasts by 12% and 7%, respectively.[5 6] Meanwhile, our forecasts for future number of Parkinson's disease patients in France, the US, and China were approximately 10%, 10%, and 40%, higher than previous estimates, respectively, although our prediction for Canada was 18% lower.[5-8] The significant disparities may stem from discrepancies in data sources, temporal intervals, forecasting frameworks, and methods. The prevalence data and population data for our forecasts came from Global Burden of Disease 2021 and 2017, respectively, which have been widely used in prevalence prediction.[13-19] Compared with Global Burden of Disease 2015 and other sources used in previous forecasting, Global Burden of Disease 2021 has been enhanced with additional data and refined analytical methods, owing to the contributions of a global network of collaborators.[34] Globally, the prevalence of Parkinson's disease in 2021 estimated by Global Burden of Disease 2021 (149 cases per 100 000) closely matched the results of a recent meta-analysis (151 cases per 100 000).[35] The prevalence of Parkinson's disease estimated by Global Burden of Disease 2021 in China and Italy aligns with findings from epidemiological studies.[36 37] In terms of prediction models, one previous study used a multi-state model that accounted for incidence and mortality to forecast the prevalence of Parkinson's disease. However, it overlooked important risk factors such as ageing and socioeconomic status.[6] Another projection assumed that the future prevalence of Parkinson's disease across all age groups would remain constant with that of past periods, disregarding the variation in age specific prevalence.[5] In contrast to previous forecasts, the prediction model in our study has been optimised through various approaches. We chose the Poisson regression model for projection because it is suitable for analysing events with low probabilities.[13-19] Then, we incorporated the key factors that contribute to changes in the prevalence of Parkinson's disease, as identified by large scale epidemiological studies and meta-analyses, into this model.[38] For trends not explained by the above covariates, we integrated them into forecasts by using the ARIMA method. Moreover, to account for the uncertainty of a single model in previous projections, we used a probabilistic bayesian model averaging approach to estimate the future prevalence of Parkinson's disease by using an ensemble of models.[31] The time frame for prediction was also extended to 2050. The validation showed the high accuracy of our predictions by comparing our forecasted prevalence of the period of 2011-21 with the Global Burden of Disease 2021 prevalence results. Considering that the data for our forecast primarily originate from Global Burden of Disease 2021, the incorporated predictors are systematic, and the prediction model is optimised, our projections for future prevalence and number of Parkinson's disease patients should be more comprehensive and accurate than previously reported estimates.

### Global trend of Parkinson's disease prevalence

Our projections indicate a global increase in the prevalence of Parkinson's disease across various regions, both sexes, and different age groups. The upward trend of Parkinson's disease prevalence will be driven by ongoing processes of industrialisation, urbanisation, population ageing, significant environmental changes, and other contributing factors. The decomposition analysis suggests that population ageing will be the leading contributor to the increasing number of Parkinson's disease cases from 2021 to 2050 globally and in all Socio-demographic Index regions. We estimated that the 76% rise in global all age prevalence of Parkinson's disease would be juxtaposed with a 55% rise in age standardised prevalence from 2021 to 2050. Moreover, we expected people aged 60-79 years to have the highest number of prevalent cases and those aged ≥80 years to have the highest prevalence in 2050 and the highest increase in number of Parkinson's disease cases. These projections are consistent with the notion that ageing is the predominant risk factor for Parkinson's disease. Global Burden of Disease 2017 estimated that the proportion of the world population aged over 65 years would increase from 9.3% in 2021 to 16.9% in 2050, and the world population of those aged ≥85 was projected to triple in the same time span.[27 28] The inevitable consequence of population ageing is the escalation in the prevalence of Parkinson's disease. Several major molecular hallmarks of brain ageing overlap with mechanisms implicated in neurodegeneration of Parkinson's disease.[39] Ageing is associated with the impairment of cellular pathways, which renders dopaminergic neurons vulnerable to environmental and genetic factors, thus promoting $\alpha$-synuclein pathology. Intervening in the drivers of ageing to achieve healthy ageing is likely to help to prevent Parkinson's disease.[39]

Changes in prevalence unrelated to demographics are the second most important contributor to the increase in the number of Parkinson's disease cases in countries with high, high-middle, and middle Socio-demographic Index after 2021. The prevalence of risk factors for Parkinson's disease, including but not limited to ageing, environmental agents, climate change, unhealthy lifestyle, metabolic diseases, and dietary factors, is on the rise in the course of industrialisation and urbanisation.[37 40] Many epidemiological investigations in recent decades have suggested that environmental factors contribute to the aetiology of Parkinson's disease. Associations between pesticide and onset of Parkinson's disease have been found, and some evidence indicates a dose-response relation.[41] Biological studies suggested that pesticides and solvents contaminating food and water further damage dopaminergic neurons.[42 43] Reducing the intake of harmful chemicals in food may significantly decrease the prevalence of Parkinson's disease.[44] Exposure to air pollution (PM 2.5, $O_3$, and $NO_2$) is associated with an increased risk of developing Parkinson's disease; moreover, almost all of the global population (99%) is exposed to air pollution.[45-48] The chain reaction of environmental pollution and global warming may affect the prevalence of Parkinson's disease. If we continue to emit greenhouse gases as we have done in the past decades, the world will warm even further and the prevalence of Parkinson's disease will be driven to a higher level, as it is positively correlated with climate warming.[49] For these environmental risk factors, particularly exposure to pesticides, a convergence of basic science and epidemiological evidence provides evidence for a causal role in Parkinson's disease; furthermore, these risk factors are mainly preventable. Therefore, interventions that decrease the prevalence of environmental risk factors should have significant potential for mitigating the increased trend of prevalence and burden of Parkinson's disease.

In addition to pollution, industrialisation and urbanisation have also resulted in changes in lifestyle and diet, including an increase in physical inactivity and higher consumption of processed foods and dairy products. Furthermore, dietary and lifestyle factors lead to a rise in the prevalence of metabolic diseases such as type 2 diabetes mellitus, which in turn increases the risk and rate of progression for Parkinson's disease. This highlights the significance of managing obesity and increasing physical activity to alleviate the burden associated with Parkinson's disease.[50] A meta-analysis and a recent cohort study showed a dose-response association between a high level of physical activity and reduced risk of Parkinson's disease.[51 52] We estimated that adherence to regular physical activity by all citizens would prevent nearly 5% of Parkinson's disease cases. The optimal type, intensity, and frequency of physical activity suitable for the prevention of Parkinson's disease still need to be investigated and customised to individuals. As well as physical activity, coffee, tea, and vitamin E can be considered as potential protective factors for Parkinson's disease.[53] These results highlight the public health initiatives aimed at promoting behaviour change, enhancing physical activity across the lifespan, and increasing intake of coffee and tea, for reducing the prevalence of Parkinson's disease. Not only should governments and policy makers focus on implementing public health policies to reduce the prevalence of risk factors contributing to Parkinson's disease, but individuals should also pay attention to the protective factors with high accessibility and favourable cost-benefit ratios.

Extensive epidemiological studies have shown that smoking is associated with a lower incidence of Parkinson's disease. As tobacco smoking remains one of the major global drivers of premature death and disability, substantial effort has been devoted to curbing the tobacco epidemic, which has led to a global decrease of 27.5% in tobacco smoking over the past three decades.[54 55] The declining prevalence of smoking may be associated with a rise in the prevalence of Parkinson's disease, which should be comprehensively considered for future projections. However, the detrimental effects of smoking on overall health far outweigh the potential benefits in terms of reducing the risk of developing Parkinson's disease. Therefore, persistently striving for a reduction in smoking rates remains imperative. We advocate against smoking as a preventive measure for Parkinson's disease.

Contrary to the trend of population ageing over the next three decades contributing more to the increase in the number of patients than in the previous three decades, we estimated that population growth would contribute much less to the global increase in Parkinson's disease cases from 2021 to 2050 compared with the period of 1990-2021, with a negative contribution in central Europe, high income Asia Pacific, eastern Europe, and East Asia. This trend is consistent with the decline in the rate of population growth projected by the United Nations in the future. As population ageing and growth were projected to be the main drivers of the increase in Parkinson's disease cases over the next three decades globally, the inevitable demographic shift will not only suggest a universal rise in Parkinson's disease prevalence but also underscore the urgent need to improve healthcare accessibility and conduct research on innovative prevention strategies, effective interventions, and disease modifying treatments for patients with Parkinson's disease. Governments will need to enhance healthcare infrastructure, fund research, and implement preventive measures effectively to manage the growing burden of Parkinson's disease. The importance of non-pharmacological and non-surgical interventions such as rehabilitation training, psychotherapy, and alternative therapies in improving patients' quality of life and delaying disease progression should be emphasised.[56-58] Furthermore, the focus should be not only on assisting individuals with Parkinson's disease but also on implementing measures to alleviate the increasing burden faced by care givers.[59 60]

### Projection by location and Socio-demographic Index

Although we estimated that most countries and regions will face a growing prevalence of Parkinson's disease in the foreseeable future to 2050, its spatial and temporal trends will vary considerably by geographical location and socioeconomic status, possibly reflecting secular changes in population structure, lifestyle, and toxic milieu related to industrialisation and urbanisation. The health level is expected to be higher in countries with a better socioeconomic status; however, the opposite holds true for Parkinson's disease. We estimated that from 1990 to 2050, the age standardised prevalence of Parkinson's disease would generally increase with Socio-demographic Index across the 21 Global Burden of Disease regions. A higher Socio-demographic Index indicates a greater level of social development, an increased degree of ageing, elevated life expectancy due to favourable medical conditions, and heightened exposure to risk factors resulting from industrialisation and urbanisation. These factors may partially explain the projected trend that countries with high-middle Socio-demographic Index will maintain the highest prevalence of Parkinson's disease in 2050, whereas low Socio-demographic Index countries will have the lowest prevalence and age standardised prevalence of Parkinson's disease. The middle Socio-demographic Index countries were projected to have the most substantial growth in both age specific prevalence and age standardised prevalence from 2021 to 2050. Decomposition analysis indicated that the change in prevalence would contribute more to the increase of Parkinson's disease cases in middle Socio-demographic Index countries than in countries with other Socio-demographic Index values, except for countries with high Socio-demographic Index. This trend can be attributed to effects of risk factors brought about by foreseeable rapid progress of population ageing, industrialisation, urbanisation, and socioeconomic level over the next three decades in middle Socio-demographic Index countries.[27 40] On the other hand, we projected that countries with high Socio-demographic Index will encounter the most limited future growth in both prevalence and prevalent numbers until 2050. This can be attributed, in part, to the severe population ageing, extensive industrialisation, and urbanisation already present in these countries, which will impede their potential for future change compared with countries with lower Socio-demographic Index.[61 62] The increase in number of Parkinson's disease cases is expected to be highest for countries with low Socio-demographic Index, primarily owing to a combination of latent population ageing and significant population growth. Furthermore, we note that low Socio-demographic Index countries also encounter challenges such as inadequate healthcare seeking rates, suboptimal diagnosis rates, and limited epidemiological research, potentially resulting in an underestimation of the prevalence of Parkinson's disease and treatment delays in these countries. In low Socio-demographic Index countries and regions, allocation of resources is inadequate and the actual disease burden of Parkinson's disease is increased.[1] Countries with inadequate healthcare provision are anticipated to face a formidable burden of Parkinson's disease in the future, necessitating strengthened resource allocation towards prevention, diagnosis, treatment, and research. As the Healthcare Access and Quality Index tends to be higher in countries with a higher Socio-demographic Index,[63] countries with well developed healthcare systems should provide support and assistance to those that do not.

Among the 21 Global Burden of Disease regions, we projected that East Asia would experience the highest increase in age standardised prevalence of Parkinson's disease after 2021, with the expectation of reaching the highest level in all age prevalence and age standardised prevalence by 2050. These trends not only indicate the significant impact of risk factors on the prevalence of Parkinson's disease in East Asia but also suggest the great potential for decreasing the prevalence by controlling modifiable risk factors. The largest increases in number of Parkinson's disease cases were projected in western Sub-Saharan Africa, primarily owing to the change in population ageing, along with the greatest contribution of population growth and changes in prevalence compared with other Global Burden of Disease regions. On the other hand, owing to negative population growth and a smaller contribution from population ageing, central and eastern Europe were estimated to have the smallest increase in numbers of Parkinson's disease cases. As these Global Burden of Disease regions are composed of countries with high or high-middle Socio-demographic Index, this trend is similar to the corresponding fifths.

### Projection by age and sex

Although we forecasted the prevalence of Parkinson's disease to increase with age, the middle aged group (40-59 years) and people aged 60-79 years were anticipated to experience comparable percentage increments in prevalence. Notably, the prevalence of Parkinson's disease in the 20-39 years age group showed a significantly greater increase in prevalence than other age groups, especially in regions with low or low-middle Socio-demographic Index. This trend will not only have significant negative effects on demographic dividend, which has already been decreased by ageing population structures, but also suggests the significant effect of risk factors other than ageing on the incidence of Parkinson's disease, especially for the middle aged population and younger. Industrial toxins or pesticides, which younger people are more likely to encounter than are older people, are significantly more associated with the development of Parkinson's disease than is residential pollution exposure.[64] As the effects of risk factors on Parkinson's disease may begin early and have a lag effect, implementing prevention and control measures no later than middle age, which may correspond to the prodromal phase of Parkinson's disease, is crucial.[65] By contrast, the older age group (≥60 years) is projected to maintain the highest prevalence of Parkinson's disease in 2050 and contribute the most to the surge in Parkinson's disease cases from 2021 to 2050, driven by an expected increase in life expectancy and population ageing. Hence, comprehensive approaches should be implemented to enhance healthcare services, support systems, and therapeutic interventions specifically tailored for these older populations.[66] Providing guidance for the evaluation and management of older patients with Parkinson's disease is also imperative, taking into account age related clinical outcomes.

We forecasted that the disparity in the age standardised prevalence of Parkinson's disease between men and women would widen, despite the global population having a tendency towards a balanced sex ratio. Sex differences in lifestyles, exposure rates to environmental risk factors, hormones, and the prevalence of metabolic diseases may contribute to the higher susceptibility of men to Parkinson's disease than women.[67-71] We estimated that high-middle and middle Socio-demographic Index regions would experience a greater increase in the male-to-female ratio of age standardised prevalence between 2021 and 2050, suggesting that men may bear a disproportionate occupational exposure to risk factors. Moreover, the prevalence of Parkinson's disease among women declines when the proportion of female smokers increases, with the strength of this correlation being comparable to the trend observed for lung cancer.[72] The upward trend in smoking rates among women since the early 20th century may have an important impact on the sex ratio of Parkinson's disease prevalence in the future. Sex imbalance in the prevalence of Parkinson's disease requires sex specific preventive strategy and interventions.

### Limitations of study

This study had several important limitations in modelling for projection. Firstly, the forecasting model did not directly incorporate risk factors other than Socio-demographic Index and demographic factors, primarily owing to unavailability of data and failure to meet the inclusion criteria of the Global Burden of Disease Study for risk factors.[73] Insufficient robust evidence supports a causal relation between these risk factors and Parkinson's disease, and the Global Burden of Disease Study has not provided data for forecasting the prevalence of risk factors, except for smoking. For trends not explained by Socio-demographic Index and demographic factors, we integrated them into forecasts by using the ARIMA method. Secondly, when calculating population attributable fractions, we included no more risk factors in analysis for paucity of prevalence data and corresponding prevalence ratio values, apart from smoking and physical inactivity. The results of population attributable fractions and potential impact fractions should be interpreted cautiously owing to the uncertainty about the lag effects of risk factors. Thirdly, as the prediction of future prevalence is based on prevalence trends in previous years, this forecast inherits the limitation of low availability and quality of data in some regions.[21] The statistics for these data sparse regions had to rely on predictive modelling using covariates. This can accentuate the influence of developed areas with more data, thereby affecting global and regional patterns. Fourthly, we could not accurately predict the prevalence of Parkinson's disease in various ethnic groups or that of genetic Parkinson's disease owing to a lack of data. Fifthly, the use of clinical criteria for diagnosing Parkinson's disease in Global Burden of Disease 2021 may result in a certain degree of deviation in the prevalence rate, which could be improved with advances in diagnostic biomarkers. Therefore, caution should be exercised when interpreting the projection for Parkinson's disease prevalence based on Global Burden of Disease 2021. Sixthly, we did not directly take into account the effect of incidence and mortality on prevalence in our prediction model. The Global Burden of Disease 2021 Collaborators not only identified inconsistencies between the incidence and prevalence of Parkinson's disease, as well as between mortality and prevalence of Parkinson's disease, but also indicated potential uncertainties and significant variation in both the incidence and mortality rates of Parkinson's disease, which may negatively affect the accuracy of predictions for Parkinson's disease prevalence.[1] Seventhly, spatial autocorrelation was not accounted for in our prediction. We attempted to incorporate spatial autocorrelation into our model by using a spatial weight matrix; however, it did not improve the predictive accuracy of the model (supplementary methods section 1.10). Finally, our projections only indirectly took into account the impact of covid-19 on the prevalence of Parkinson's disease, as the data source for our projection, Global Burden of Disease 2021, has estimated its effect on the prevalence of Parkinson's disease. Research is needed to understand the long term effects of potential infectious disease outbreaks on neurodegenerative disorders. Furthermore, advances in diagnosis, new drugs and therapies, and improved management may contribute to the change in Parkinson's disease prevalence. Therefore, projections need to be updated as important new factors that influence Parkinson's disease prevalence emerge.

## Conclusions

The global prevalence of Parkinson's disease was projected to continue its significant increase through 2050, with the upward trend being more pronounced in men, in East Asia, and in countries with middle Socio-demographic Index. Population ageing was estimated to be the leading contributor to the increasing number of Parkinson's disease cases from 2021 to 2050. The heterogeneity in the projected trends of Parkinson's disease prevalence across different age groups, sexes, and geographical locations necessitates tailored prevention strategies to tackle these structural inequalities and disparities. The projections can be used to plan control measures and call for urgent actions in meeting the increasing healthcare demands of patients with Parkinson's disease. Public health interventions, which may alter the prevalence of risk/protective factors, offer promising prospects for arresting the universal rise in prevalence of Parkinson's disease in the future. Given the inevitable population ageing, population growth, and disability experienced by individuals with Parkinson's disease owing to its chronic nature, an urgent need exists for future research to focus on the development of novel drugs, gene engineering techniques, and cell replacement therapies that are aimed at modifying the course of the disease and improving patients' quality of life.[74-77] Future iterations of forecasting for prevalence of Parkinson's disease will be improved by incorporating other risk/protective factors and gathering more data from currently under-represented regions.

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Data sharing: The data used in the study was sourced from public databases. The prevalence data from 1990 to 2021 was downloaded from the Global Health Data Exchange Global Burden of Disease Results Tool (https://vizhub.healthdata.org/gbd-results/); the data on forecasted population was downloaded from https://ghdx.healthdata.org/record/ihme-data/global-population-forecasts-2017-2100; the data used for calculating Socio-demographic Index were obtained from https://ghdx.healthdata.org/gbd-2019; and the prevalence of physical activity was acquired from WHO Global Health Observatory (https://www.who.int/data/global-health-estimates).

Code availability: Statistical code for the bayesian model averaging model used in this study is available at https://github.com/hechzh/Prevelance-2024-080952/tree/master. The README.txt file provides detailed information on the data sources and instructions for using the code. Additionally, to facilitate understanding and further verification, the document titled "The Main Results Corresponding to the Data File Output by the Code.doc" outlines the correspondence between the generated data files and the results presented in the paper.

Transparency: The lead authors (the manuscript's guarantors) affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities: We plan to disseminate these research findings

to patients and communities through both traditional and social media platforms and include a plain English summary of the manuscript in supplementary methods section 1.9. The findings will be presented at international conferences, academic forums, classrooms, and seminars to policy makers, scientists, healthcare professionals, students, and relevant researchers. Furthermore, we will invite patients with Parkinson's disease, their families, care givers, and other individuals involved in social welfare through outpatient recruitment and online channels to participate in the dissemination of our research. The invited individuals will be engaged in preparing understandable promotional materials (including a simple introduction, pictures, and multimedia content) and spreading information to the general public, policy makers, and scientists, as well as healthcare professionals through online and offline channels.

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**Web appendix:** Supplementary materials