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A systematic review and meta-analysis of the prevalence of Parkinson's disease in lower to upper-middle-income countries

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Parkinson's disease (PD) is a common neurodegenerative disease that is a growing public health challenge. Estimates of the burden of PD have focused on data from high-income countries, with lower-income countries poorly described. We reviewed and examined the prevalence of PD reported by studies in low- to upper-middle-income countries. A systematic literature search was performed in the Medline/PubMed, Embase, LILACS, and Web of Science databases. Age group, sex, and geographic region were considered when analyzing the data. Of the 4327 assessed articles, 57 met the inclusion criteria for qualitative review, and 36 were included in the meta-analysis. Heterogeneity measures were high both as a whole and in each geographic region. Data analysis by geographic region showed that reported prevalence differed across regions, ranging from 49 per 100,000 (Sub-Saharan Africa) to 1081 per 100,000 (Latin America and the Caribbean). There was an increasing prevalence of PD with advancing age (per 100,000): 7 in 40–49 years, 158 in 50–59 years, 603 in 60–69 years, 1251 in 70–79 years, and 2181 in over the age of 80. The prevalence of PD in men and women was similar. There was a greater PD prevalence in populations with a higher 5-year GDP per capita and a higher life expectancy. Our findings suggest a higher prevalence of PD in lower and upper-middle-income countries than previously reported. Comparisons between regions are difficult, as the sociocultural differences and lack of methodological standardization hinder understanding key epidemiological data in varied populations.

Parkinson's disease (PD) is one of the most common neurodegenerative diseases. It is a chronic and progressive disorder that affects movements and is primarily caused by the degeneration of dopamine-producing neurons in the brain. PD affects people of all ages but is most commonly diagnosed in individuals over 60. The prevalence of PD varies worldwide, and while it is often considered a disease more common in higher-income countries, it is increasingly recognized as a significant health issue in lower-income countries[1].

Research on the prevalence of PD has predominantly focused on high-income countries, leaving a gap in our understanding of its impact on low- to upper-middle-income countries. Nonetheless, studying the prevalence and distribution of PD among lower-income countries is crucial to

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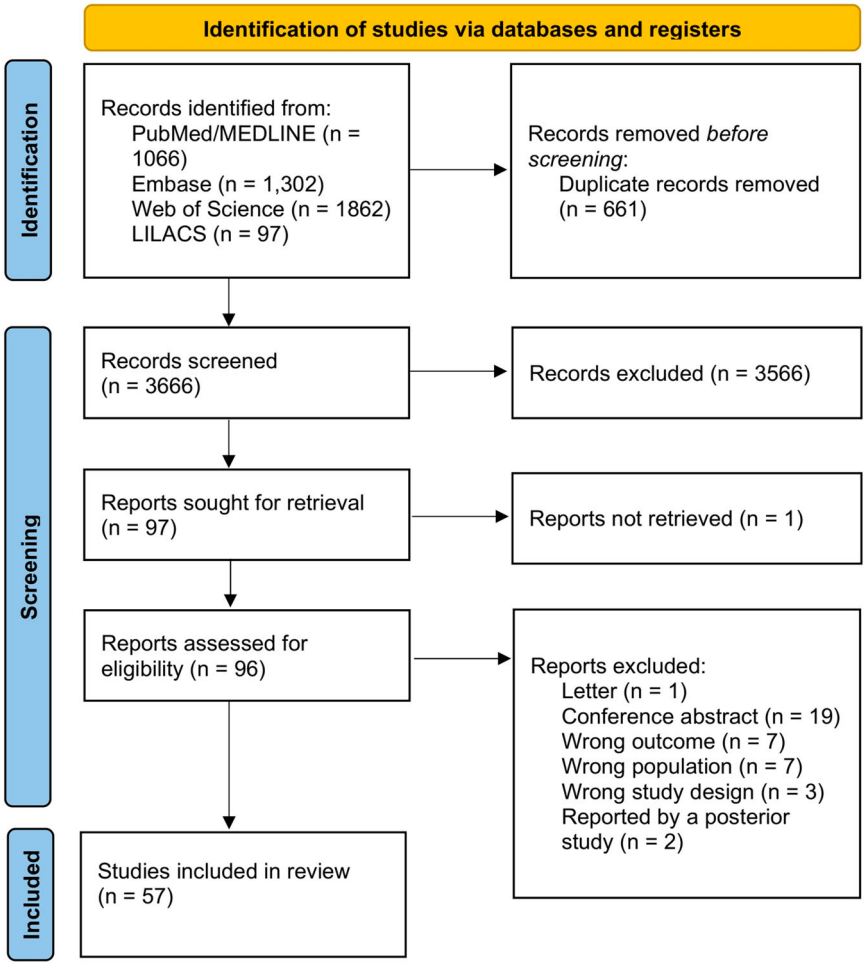

Fig. 1 | Flowchart of the selection process for eligible articles in the PubMed, Embase, and Cochrane databases.

acknowledge its burden and aid in planning healthcare services and public policies for these populations. It is anticipated that as lower-income nations develop and life expectancy rises, the majority of the PD burden will arise from these countries, posing challenges at local and global levels[2]. Additionally, investigating specific ethnic and environmental risk factors influencing PD prevalence in diverse settings can bring novel insights into understanding disease pathophysiology and epidemiology[3,4].

To better understand the prevalence and distribution of PD among lower-income and underrepresented countries, we conducted a systematic review of the literature to identify epidemiological studies that measured the prevalence of PD in populations or representative samples from least-developed to upper-middle-income countries according to the Organization for Economic Co-operation and Development (OECD) classification.

Results

General overview

A total of 4327 citations were identified in the initial search. After eliminating duplicates, the remaining 3666 unique articles underwent screening based on their titles and abstracts. Out of these, 96 articles met the predefined inclusion criteria. After thoroughly evaluating the complete articles, a total of 57 studies were deemed suitable for review. A complete overview of the selection process is presented in Fig. 1.

Of the 57 articles, we identified 63 studies (some articles reported data from studies in more than one country). There were 20 studies in Latin America & Caribbean (1 study investigated 7 different countries)[5–18], 18 in East Asia & Pacific[19–36], 10 in Sub-Saharan Africa[37–46], 7 in South Asia[47–53], 6 in Middle East & North Africa[54–59], and 2 in Europe & Central Asia[60,61]. The median sample size and number of PD cases were, respectively, 9411 (IQR 2526–34,874) and 31 (IQR 9–78). Studies varied greatly in the minimum age of inclusion and methodological aspects, but 50.8% of the cohorts evaluated patients at least 40 years of age. Most of the studies were door-to-door (85.7%), had a census or probabilistic sampling approach (65.1%), involved a final diagnosis by a neurologist or PD specialist (79.41%), and used standardized diagnostic criteria (54%). China (25.4%), India (9.5%), Egypt, and Mexico (each 6.3%) had the most studies (Supplemental Fig. 2). Among all studies, the average 5-year GDP per capita (USD) was 4486 ± 3708, highest in Europe & Central Asia and lowest in South Asia. The median life expectancy at birth was 71 (IQR 67–76), highest in Europe & Central Asia and lowest in Sub-Saharan Africa. Data for each region are detailed in Table 1 and Fig. 2. Of the 63 studies reviewed, only 36 met our pre-specified inclusion criteria for meta-analysis and reported data on the crude prevalence of PD. Among these, only 19 provided information on the mean age of the population, and 17 reported data on the adjusted prevalence of PD, of which 13 were adjusted for age, 2 for gender, and 2 for both gender and age. All detailed information on the data extracted in each study can be found in Supplemental Table 2.

Geographic region

PD prevalence was 516 per 100,000 inhabitants, significantly differing in all six geographic regions evaluated ($p < 0.01$; Fig. 3). Latin America & the Caribbean had the highest prevalence with 1081 per 100,000 inhabitants, followed by East Asia & Pacific (688 per 100,000), Europe & Central Asia (464 per 100,000), Middle East & North Asia (264 per 100,000), South Asia (94 per 100,000), and Sub-Saharan Africa (49 per 100,000). Heterogeneity measures were high both as a whole and in each geographic region. The Berg test was negative for publication bias ($p = 0.48$), but the Egger's test was positive ($p < 0.0001$). A sensitivity analysis, excluding one outlier

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Table 1 | General characteristics of the included studies according to global regions

	All Regions	Studies in the Meta-analysis	Latin America & Caribbean	East Asia & Pacific	Sub-Saharan Africa	South Asia	Middle East & North Africa	Europe & Central Asia
Study characteristics								
Number of studies	63[a]	36	20	18	10	7	6	2
Year of publication	2015 (2003–2020)	2013 (2004–2021)	2018 (2005–2022)	2016 (2003–2019)	2009 (1993–2016)	2016 (2002–2018)	2012 (1998–2013)	2018 (2016–2020)
Participants (n)	9411 (2526–34874)	6594 (1768–19,194)	1617 (1035–9694)	13,766 (6006–69,498)	19,542 (2647–51,470)	14,010 (7748–41,270)	11,833 (8066 –30,026)	18,039 (13,963–22,115)
PD cases (n)	31 (9–78)	24 (9–45)	27 (9–48)	88 (28–151)	7 (2–27)	9 (6–26)	34 (33–37)	69 (44–93)
Minimum age (yrs)	40 (15–60)	45 (18–64)	40 (32–65)	52 (37–60)	18 (0–45)	12 (2–25)	7 (0–40)	18 (18–18)
Study quality assessment (pts)	5.3 ± 1.7	6.0 ± 1.0	5.4 ± 1.6	5.4 ± 1.8	5.3 ± 2	4.6 ± 1.4	5.2 ± 2.5	6.5 ± 2.1
Study design, DTD	54 (85.7%)	36 (100%)	15 (75%)	17 (94.4%)	7 (70%)	7 (100%)	6 (100%)	2 (100%)
Census or probabilistic approach	41 (65.1%)	27 (75%)	8 (40%)	13 (72.2%)	8 (80%)	5 (71.4%)	5 (83.3%)	2 (100%)
Dx by a neurologist or PD specialist	50 (79.4%)	36 (100%)	17 (85%)	11 (61.1%)	7 (70%)	7 (100%)	6 (100%)	2 (100%)
Standardized diagnostic criteria	34 (54%)	24 (66.7%)	14 (70%)	10 (55.6%)	4 (40%)	7 (100%)	4 (66.7%)	2 (100%)
Area								
Urban	18 (28.6%)	10 (27.8%)	8 (40%)	7 (38.9%)	-	1 (14.3%)	2 (33.3%)	-
Rural	15 (23.8%)	10 (27.8%)	4 (20%)	1 (5.6%)	4 (40%)	5 (71.4%)	-	1 (50%)
Both or not specified	30 (45.5%)	15 (44.4%)	8 (40%)	10 (55.5%)	6 (60%)	1 (14.3%)	4 (66.7%)	1 (50%)
Country characteristics								
Most common country								
1°	China (25.4 %)	China (22.2%)	Mexico (20%)	China (88.8%)	Nigeria (30%)	India (85.7%)	Egypt (66.6%)	Turkey (100%)
2°	India (9.5%)	Egypt/India/Peru (8.3%)	Peru (15%)	Philippines (5.6%)	Tanzania (20%)	Pakistan (14.3%)	Libya (16.7%)	-
3°	Egypt/ Mexico (6·3%)	Mexico/Turkey (5·6%)	Colombia (15%)	Thailand (5.6%)	Other (10% each)	-	Tunisia (16·7%)	-
5-Year GDP Per Capita (USD)	3072 (1064–7941)	2473 (1,148–6776)	6636 (3612–9274)	6444 (1136–8870)	718 (546–1336)	1232 (690–1759)	2703 (2473–2703)	10,558 (9998–11,117)
Life Expectancy (yrs)	71 (67–76)	71 (70–74)	73 (71–75)	77 (72–78)	60 (56–65)	67 (63–70)	70 (70–70)	76 (76–76)

Life expectancy and 5 year GDP per capita were based on the year each study was published. Variables are expressed in percentage, mean and standard deviation or median and interquartile range.

DTD door-to-door, *GDP* gross domestic product; *Dx* diagnosis, *PD* Parkinson's disease.

[a]Of the 57 included, one was multicentric reporting data from 7 different countries.

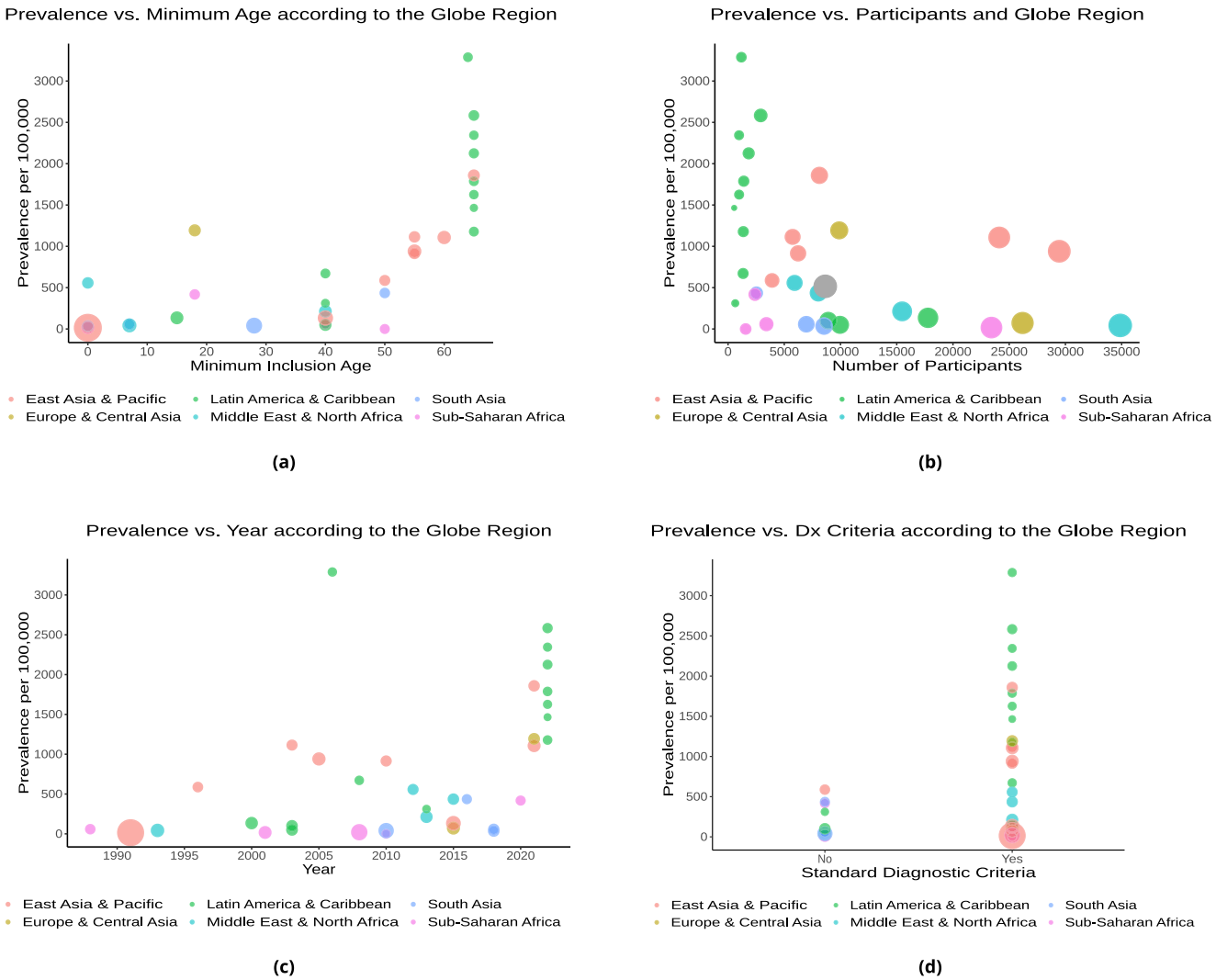

Fig. 2 | Global distribution of Parkinson's Disease (PD) prevalence. a PD prevalence categorized by the minimum age of participants included in the studies. **b** PD prevalence according to the number of participants in studies across different global regions. **c** Temporal distribution of PD prevalence based on the publication year of each study. **d** PD prevalence stratified by the use of diagnostic criteria to identify cases in the studies conducted globally.

study at a time, for up to 10 iterations, did not result in significant differences in overall heterogeneity and estimated measures (Supplemental Fig. 3). There was no significant difference to the crude PD prevalence estimates when performing analysis only with data from studies that reported the age-standardized prevalence (423 per 100,000 [95% CI 238–608]), as displayed in Supplemental Fig. 4.

Age and sex analysis

A meta-analysis of data from all regions revealed an increasing prevalence of PD with advancing age. The prevalence rates per 100,000 individuals were as follows: 7 for individuals aged 40–49 years, 158 for individuals aged 50 to 59 years, 603 for individuals aged 60–69 years, 1251 for individuals aged 70–79 years, and 2181 for individuals over the age of 80 (Table 2). The adjusted prevalence by sex was 423 per 100,000 inhabitants (Supplemental Fig. 4). East Asia & Pacific had the highest prevalence with 634 per 100,000, followed by South Asia (660 per 100,000), Middle East & North Africa (315 per 100,000), Europe & Central Asia (202 per 100,000), Latin America & Caribbean (97 per 100,000), and Sub-saharan Africa (53 per 100,000) with a high heterogeneity ($I^2 = 100\%$). No significant differences regarding PD prevalence among sexes were identified in the entire sample ($p = 0.72$) or specific geographic regions (Supplemental Table 3). Heterogeneity measures were high in all sex and age subgroups.

Sociodemographic indicators

PD prevalence increased as the 5-year GDP per capita increased. Meta-regression supported this significant and progressive increase, most pronounced between the third and fourth quartiles (USD 6776 and 11,677, respectively). Similarly, the prevalence of PD also significantly increased with life expectancy at birth, with a slight decrease observed in populations over 76 years of age (fourth quartile). These associations are graphically displayed in Fig. 4 and detailed in Table 3. Due to the limited number of studies reporting data for rural[10,25,34,48,54,55,57] or urban[25,34,54–56] housing areas, conducting a meta-analysis for these specific indicators was not feasible.

Methodological and data quality analysis

We analyzed whether prevalence data differed based on the study quality score or methodological variables (Table 3). For methodological variables, we performed a meta-analysis for minimum age, year of publication, number of participants, and standardized diagnostic criteria. High prevalence rates were found by meta-regression at the minimum age of 50 years or higher (1286 per 100,000), studies published after the year 2021 showed a higher prevalence (1901 per 100,000) than older studies published before 2004 (143 per 100,000). Studies with ≥19,194 participants found lower PD prevalence (301 and 148 per 100,000) than studies with ≤1174 participants (10,174 per 100,000). Also, studies that used standardized diagnostic criteria

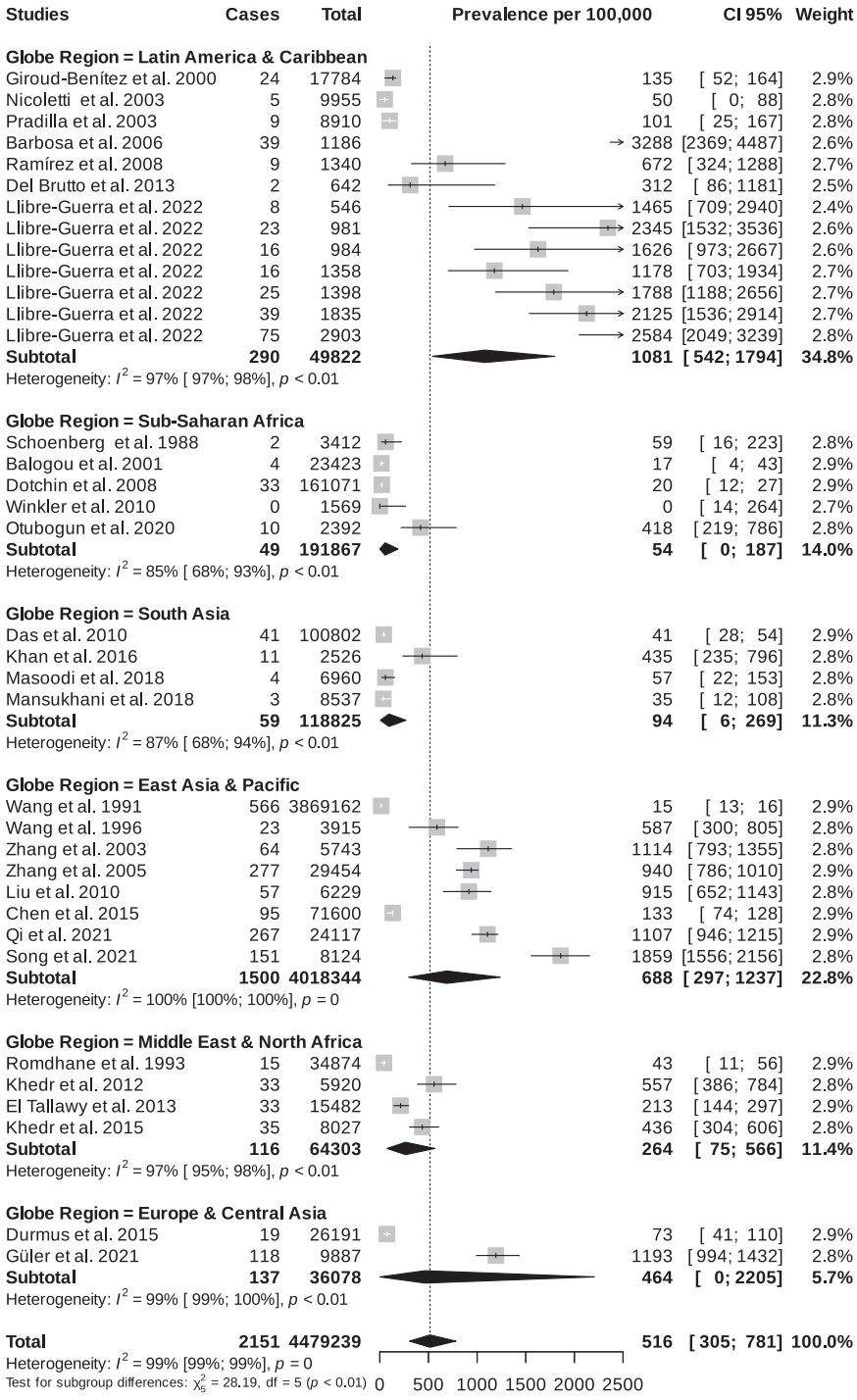

Fig. 3 | Prevalence rate according to the geographic region.

obtained a higher prevalence (809 per 100,000). No statistically significant difference was found by meta-regression in the high-quality studies (7 or 8 points) compared to the low-quality studies (5 or 6 points).

Discussion

This review aimed to provide an overview of PD prevalence in low- to upper-middle-income countries and how it varied according to geographic region, sex, and age. We identified that PD prevalence estimates varied greatly among geographical regions and factors such as countries' life expectancy at birth and GDP per capita were significantly associated with this prevalence. We observed no significant differences between the prevalence of PD among genders, although it significantly increased with age. Lastly, methodological factors of studies such as a lower minimum inclusion age, using standardized diagnostic criteria, and the number of participants also significantly affected PD prevalence, which probably contributes to the high heterogeneity identified in our analyses. We observed considerable imbalances in the distribution of studies by geographical region and ethnicity. While China was widely represented in the studies (25.4%), other ethnic groups were less studied, for example, populations from Europe & Central Asia (3.17%) and Middle East & North Africa (9.52%), which reveals a significant underrepresentation of certain populations in PD research as previously identified in other studies[3,62].

Age-adjusted prevalence estimates were similar to the crude prevalence estimates. However, this result must be interpreted with caution for some

reasons. First, the sample size for this sensitivity analysis is small, so there is a higher chance of bias. This is because some methodological and sample characteristics may be more common in this sample. For example, the minimum age for inclusion is higher than or equal to 40 years in 8 of the 13 studies that were chosen. Second, as this analysis was only performed with age-adjusted data, and was not adjusted by sex composition among samples due to a low number of studies that were adjusted by both factors, possible differences in demographic structure among studies are not accounted for. The abovementioned limitations are exemplified by the observation of a wide 95% confidence interval.

In the door-to-door studies conducted in low-to upper-middle-income countries, we observed a high crude prevalence of PD cases (516 per 100,000). This figure contrasts with the prevalence estimated by the Global Burden of Disease (GBD) in 2019 for countries with a low (65.71 per 100,000), lower-middle (82.16 per 100,000), and middle (112 per 100,000) socio-demographic index[1,63]. When examining different geographic areas, the prevalence identified in our meta-analysis exceeded the GBD´s estimated values for regions such as Latin America and the Caribbean (ranging from 87.4 to 100.8 per 100,000), East Asia (145.44 per 100,000), and Central Asia (83.07 per 100,000). Conversely, the GBD values for Sub-Saharan Africa (ranging from 55.94 to 71.79 per 100,000) and South Asia (72.7 per 100,000) closely aligned with the prevalence rates identified in our study[63].

Nonetheless, these data must be viewed cautiously, as differences observed in prevalence may be justified due to methodological differences between our study and the GBD, reflecting studies with different designs. Here, we included only the crude prevalence from door-to-door cohorts in the meta-analysis, in which there was also a diagnostic confirmation by a neurologist and minimum quality criteria. In contrast, the GBD also incorporates data from medical registry data, which has a higher risk of bias in the miscoding and misclassification of the disease and potential missed diagnosis due to the absence of screening procedures. Additionally, our study sought to obtain the crude prevalence of PD, which reflects the population structure and characteristics as they are, essential to estimate the extent of the need for health services. In contrast, the GBD results reflect the age-standardized rate of prevalence, a hypothetical value that can be helpful when comparing rates of health outcomes across samples. As our study evaluated PD prevalence using aggregated data, a calculation of an age-standardized prevalence was limited and not feasible, nonetheless, influences of age on PD prevalence are further studied in our age subgroup analyses. Our observed crude prevalence is also higher than the one identified by a study published in 2014 with a similar methodology that included all countries (315 per 100,000)[64]. Other factors may justify the observed difference in prevalence, such as the inclusion of newly published studies (especially those published after 2021, which identified a high prevalence of PD).

The results of a lower PD prevalence in sub-Saharan Africa and higher prevalence in Latin America for individuals aged ≥60 are consistent with the prevalence of other neurological diseases, such as Alzheimer's disease (AD). A meta-analysis on the prevalence of AD in low-income countries showed that there is a higher prevalence in Latin America (8.5%), and a distinctively lower prevalence in the four sub-Saharan African regions (2%–4%)[65]. Recognizing the wide variation in the number of elderly individuals and the speed of aging is crucial between and within regions. More developed regions tend to have higher percentages of their populations in older age brackets than developing regions. Projections suggest that by 2030, the proportion of individuals aged 60 and above will nearly double in less than 25 years in Asia, Latin America, and the Caribbean[66]. However, Sub-Saharan Africa presents a different scenario, with the proportion of individuals aged 60 and above increasing only slightly from 4.7% in 2005 to 5.5% in 2030, in contrast to other global regions[66]. This pattern suggests, in addition to the influence of methodological factors and available studies, a complex interaction between genetic, socioeconomic, and environmental factors in the epidemiology of these neurodegenerative conditions in different parts of the world.

Our data showed an increase in prevalence with increasing age, in keeping with previous studies that established aging as a risk factor for PD[67,68]. The prevalence rates in the age groups of 50 to 69 years old are similar to those found in studies conducted in Europe, North America, and

Table 2 | Prevalence of PD by age group (per 100,000)

Subgroup variables	Prevalence per 100,000 (95% CI)	I^2 (%) [95%-CI]	Cochran's Q
Sex			
Female	814 (480–1229)	99 (99–99)	0
Male	900 (538–1347)	99 (99–99)	<0.01
Age			
≥50 years	576 (81–1482)	98 (97–98)	<0.01
40–49 years	7 (0–48)	0 (0–90)	<0.01
50–59 years	158 (17–398)	85 (73–92)	<0.01
60–69 years	603 (126–1380)	98 (96–98)	<0.01
70–79 years	1251 (559–2154)	98 (97–98)	<0.01
≥80 years	2181 (662–4426)	98 (97–98)	<0.01

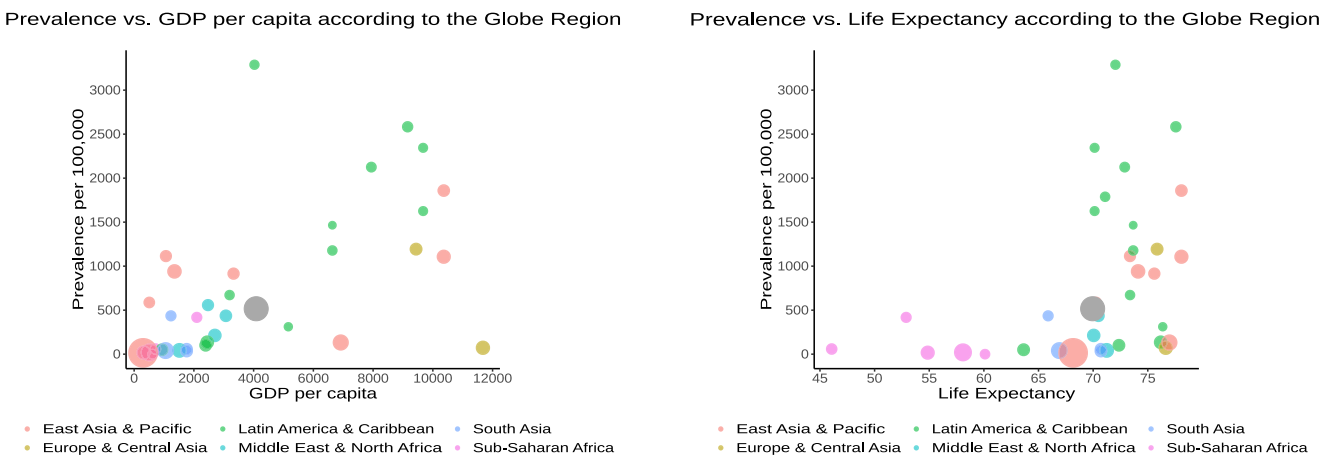

Fig. 4 | Prevalence of PD vs. a GDP per capita and (**b**) life expectancy according to globe region.*Differences observed in prevalence across regions herein presented are not directly comparable between regions due to a series of methodological caveats.

Table 3 | Influence of methodological and sociodemographic variables in PD prevalence

	Prevalence per 100,000 (95% CI)	Heterogeneity		Univariate Metaregression	
		I^2 (95% CI)	Cochran's Q	β coeficient	p-value
Sociodemographic variables					
Life Expectancy**					
First quartile (70 yrs)	64 (10–156)	92% (86–95)	<0.01	-	-
Second quartile (71 yrs)	614 (214–1207)	96% (94–97)	<0.01	0·0510	0.0133
Third quartile (74 yrs)	960 (404–1741)	99% (98–99)	<0.01	0.0708	0.0006
Fourth quartile (78 yrs)	724 (283–1359)	99% (99–99)	<0.01	0.0576	0.0050
5-Year GDP per Capita**					
First quartile (USD 1148)	107 (7–305)	97% (96–98)	<0.01	-	-
Second quartile (USD 2473)	230 (84–445)	98% (98–99)	<0.01	0.0150	0.4148
Third quartile (USD 6776)	876 (392–1538)	95% (91–97)	<0.01	0.0615	0.0015
Fourth quartile (USD 11677)	1214 (597–2039)	99% (99–99)	<0.01	0.0765	<0.0001
Methodological variables					
Minimum Inclusion Age**					
Lower than 50	160 (63–296)	98% (98–99)	<0.01	-	-
50 or Higher	1286 (868–1783)	93% (90–95)	<0.01	0.0729	<0.0001
Year of Publication*					
First quartile (≤2004)	143 (27–344)	98% (97–98)	<0.01	-	-
Second quartile (≤2013)	449 (117–980)	99% (99–99)	<0.01	0.0295	0.0975
Third quartile (≤2021)	430 (160–824)	99% (99–99)	<0.01	0.0274	0.1194
Fourth quartile (>2021)	1901 (1518–2326)	52% (0–79)	0.05	0.0996	<0.0001
Participants**					
First quartile (n = 1768)	1174 (538–2036)	93% (88–95)	<0.01	-	-
Second quartile (n = 6594)	820 (397–1388)	95% (93–97)	<0.01	−0.0193	0.3506
Third quartile (n = 19,194)	301 (75–674)	98% (98–99)	<0.01	−0.0554	0.0069
Fourth quartile (n = 3,869,162)	148 (21–387)	100% (99–100)	<0.01	−0.0721	0.0004
Standard Dx Criteria**					
No	116 (42–222)	89% (83–93)	<0.01	-	-
Yes	809 (480–1219)	100% (99–100)	0	0.0533	0.0006
Study Quality					
<7	521 (229–925)	99% (99–99)	<0.01	-	-
7 or 8	514 (237–892)	99% (99–99)	<0.01	−0.0003	0.9867

Dx diagnosis. 95% *CI* confidence interval at the 95% level.
* $p < 0.05$ ** $p < 0.01$ for the overall meta-analysis of subgroup variables.

Australia[64]. In contrast, when looking at the age groups above 70 years old, the reported prevalence tends to be higher in studies from higher-income countries (ranging from 1602 to 2953 per 100,000)[64]. This higher prevalence is likely driven by population growth and aging in these regions since life expectancy tends to be higher in those countries[69]. It could also be related to differences in healthcare-seeking behavior among the oldest old, which may be greater in more developed countries. A systematic review showed that having a higher socioeconomic index (better access to education, higher income, being unemployed and economically inactive at older ages, or having worked in formal sectors and enrolling in health plans) is related to the use of primary health care among older people in low- and upper-middle-income countries[70].

The prevalence of PD was higher in studies in countries with a higher 5-year GDP. It has been described that the prevalence of the disease increases as socioeconomic status improves, likely as a consequence of human activity, especially industrialization and intensive agriculture[71]. Moreover, a country's GDP per capita improves the life expectancy at birth by promoting economic development and growth[72], which leads to a rise in longevity and the burden of age-related neurodegenerative diseases.

Other aspects should be considered while interpreting lower PD prevalence associated with a lower economic index, such as lack of access to specialized care for movement disorders and lack of investment in carrying out studies with more robust methodologies. Furthermore, while aging garners increasing attention from policymakers and stakeholders in high-income countries, there is a lack of attention to age-related diseases in low- to upper-middle-income countries. As a result, epidemiological data on the burden of PD is limited. It is estimated that two-thirds of the population aged 60 and over will live in low- and middle-income countries by 2050[73]. In addition to dealing with growing aging, these regions will also need to address the escalating burden of chronic and neurodegenerative conditions, including PD, while facing limitations in terms of resources and infrastructure. Therefore, correctly understanding the current burden of PD and using this knowledge to predict future burden will be critical to mitigating the economic impact of aging and establishing sustainable healthcare systems for future generations.

Regarding differences between men and women, the prevalence of PD was similar in both sexes and each geographic region. Numerous studies have consistently shown a male-to-female ratio over 1.5:1 for PD cases,

particularly in Western countries[12,74–76]. However, a recent systematic review found a male/female ratio of 1.18, 95% CI, [1.03, 1.36], suggesting that the difference between genders is not so pronounced[77]. Studies conducted in Asian populations have reported a higher proportion of females affected by PD[78–81]. This difference has been attributed to women being more exposed to various risk factors, including pesticide use, head trauma, agricultural occupations, exposure to toxins, dietary deficiencies, and consumption of well water in this region[82]. The observed disparities in PD prevalence must consider the genetic heterogeneity and diverse environmental factors to which different populations are exposed. Notably, the number of studies conducted in Western and Asian populations in this meta-analysis was comparable, which may have influenced the observed prevalence rates concerning sex. Furthermore, it is crucial to consider the considerable heterogeneity in the minimum age of the individuals included in the studies, ranging from 18 to 45 years with a median age of 45. It is reasonable to expect that younger individuals may have a more significant contribution from genetic factors, with less influence from sex[83].

Regarding some specific methodological factors, it is important to note that, although diagnostic criteria have been available since the end of the 1980s[84–89], we found that only 54% of the studies in lower-income countries reported using some diagnostic criteria to identify PD cases. Additionally, we observed that approximately 20.6% of the published studies on this topic did not involve an evaluation by a neurologist or a movement disorders specialist and that only 65.1% used a census or probabilistic sampling approach. These and other findings illustrate that some estimates of PD prevalence in lower-income countries could be of lower quality and highlight the need for future studies to address these limitations.

Our analysis revealed significant variation in the prevalence of PD, reflecting high heterogeneity in our meta-analysis, even when considering each continental region separately. Despite the acknowledged significant differences within populations, the decision to group these diverse countries into a single category stems from their shared characteristic of being underrepresented in PD research. We aim to highlight and address the gap in PD epidemiology in these regions rather than obscure the heterogeneity that exists within them. The high variability in the minimum age inclusion criteria was an important factor that hindered group comparison. Many published studies using data from developed countries employ specific and higher cutoff points, such as 50 years, which align with the disease prevalence, which is more common among older individuals[90,91].

Several confounding factors may account for this heterogeneity. Firstly, we have to note that PD itself carries a heterogeneous burden in its clinical presentation, involving genetic and environmental factors, which can act as potential confounders when evaluating prevalence in regions with distinct characteristics. Secondly, intrinsic confounding factors of the samples may also influence the heterogeneity found, such as selection bias. Thirdly, the methodological differences among studies conducted within the same regions and across different regions are relevant confounding factors in our analysis.

Regarding the data quality scoring, our meta-analysis showed no statistically significant difference in the prevalence reported by high- and low-quality studies. However, when considering specific methodological and quality factors, some of them proved to have a substantial impact on the observed prevalence, such as the minimum age of the population and the number of participants included. Since the prevalence and incidence of PD are expected to increase with age[63], the lack of uniformity in the minimum age of the population included in the studies calls for a more careful look at the reported crude prevalence. Additionally, sufficient sample size is essential for precisely estimating prevalence, and random sampling is essential when a door-to-door survey is not possible. Using validated and standardized diagnostic criteria reduces the chance of misidentification of PD cases. A previous study demonstrated the impact of different configurations of diagnostic criteria, revealing a potential reduction of up to 65% in the identification of PD cases based on the chosen criterion[92].

Some limitations were relevant to this study. Heterogeneity in study methodology probably impacted the results found. Due to insufficient data, such as the provision of adequate raw data or by subgroups in some articles, limited our ability to make comparisons within subgroups of interest, such as the distinctions between rural and urban populations. Furthermore, Egger's test detected a potential publication bias, suggesting that certain conducted studies may not have been published, potentially introducing bias to our results. However, a sensitivity analysis, which excluded potential outliers, did not reveal significant differences even when excluding up to 10 outliers, which adds more robustness to our findings. Moreover, the clinical definition of PD itself is a great challenge and is accompanied by diagnostic errors when the diagnostic criteria are not standardized, increasing the risk of bias.

On the other hand, we need to consider several factors that have contributed to the importance of this study. We only included in our meta-analysis studies that met minimum quality criteria, ensuring that the prevalence obtained was representative of the population. Additionally, we investigated differences in geographic subgroups and the influence of sociodemographic factors and evaluated the effect of methodological factors on their results, thus providing valuable insights into PD prevalence and distribution within countries.

Conducting robust studies with standardized methodologies should be encouraged. Attention should be given to the clinical diagnosis, especially regarding the choice of a validated screening instrument, the utilization of recognized and recommended diagnostic criteria, and the selection of adequately trained professionals with experience in diagnosing movement disorders. These results will become increasingly important as world populations age, and correctly estimating the PD burden is necessary for planning and directing public policies to address PD management.

In conclusion, our results showed the differences in reported prevalence within low- to upper-middle-income countries, with populations often underrepresented and situated in diverse geographic areas with distinct cultural, environmental, and demographic factors. Our findings suggest an overall higher prevalence of PD in these populations than previously reported, exceeding the estimates provided by the GBD for countries with a low sociodemographic index. However, we highlighted that several social and economic factors may contribute to underestimating the real prevalence in poorer regions. For example, we found that PD prevalence was higher in countries with higher GDP and life expectancy and in studies that included older patients. Furthermore, our study highlighted various methodological challenges and emphasized the impact of methodological flaws and how the lack of standardization can affect the elucidation of fundamental epidemiological data such as prevalence, mainly when performed in populations with diverse characteristics.

Methods

Eligibility criteria, information sources, and search strategy

We conducted a systematic literature search to identify relevant articles on the epidemiology of PD in population-based studies conducted in low- to upper-middle-income countries. Our search included studies reporting the crude prevalence of PD, the total number of participants, and the number of diagnosed PD patients. We included studies with data on public or private health services with representative samples of the local population. Studies presenting data from specific groups (samples not representing the local community or population), such as veteran groups, elderly institutions, clinics, or patients admitted to teaching hospitals, were excluded from the review. Review articles or original studies that used data from previous studies were excluded. We considered articles available in English, Spanish, Portuguese, French, or Chinese languages. In cases where articles were unavailable or lacked the minimum required information in the abstract, the reviewers sought the full text (n = 01) from the corresponding authors. If there was no response, those articles were excluded from the analyses. When the entire article was unavailable, we included studies where the relevant information was presented in the abstract. Studies were included irrespective of their year of publication. Low- to middle-income countries were defined according to the OECD, with reporting of 2022 and 2023[93].

Two authors of this review (GMP and NMS) developed a comprehensive search strategy for four databases. Medline/PubMed, Embase, LILACS, and Web of Science databases were searched on February 2nd, 2023. This review followed all recommendations of the PRISMA methodology[94]. The search strategy included title/abstract analysis of articles. The complete search strategies with research terms used for each database are provided in Supplemental Table 1.

Selection and data collection process

Results were exported to Rayyan software (https://rayyan.ai/) to manage references and remove duplicates. Two reviewers (GMP and NMS) independently screened unique records. A third reviewer (DTS) evaluated and resolved the data divergences. After finalizing the selection of included articles, five reviewers (DTS, DCF, GAM, GMP, and NMS) were assigned to extract data from each report independently.

A structured data collection process was implemented using forms created for this review (Supplemental Fig. 1). The data extracted from each eligible study included the following characteristics: author and affiliation, country/city/province where the study was conducted, sample or population size, number of PD cases, crude and/or standardized prevalence or incidence (reported as cases per 100,000 persons), study design, mean age of participants, duration of the study, and the diagnostic criteria or protocol used to establish PD cases. If available, secondary prevalence measures such as sociodemographic data (sex, age) and living area (urban or rural) were also extracted. In cases where multiple studies were conducted in the same country, the data were summarized as a range of cases per region, while unique data were presented individually for each study measure.

Additional sociodemographic data from each study's country was obtained using data from the World Bank[69]. Countries were categorized geographically into different regions, including Latin America & Caribbean, Sub-Saharan Africa, South Asia, East Asia & Pacific, Middle East & North Africa, and Europe & Central Asia. For each study, representative estimates of the country's life GDP per capita were calculated by averaging the last five available measures preceding the year of the study's publication. This retrospective averaging approach aimed to provide a more accurate reflection of the social conditions of the country during the period in which the study was conducted. Life expectancy at birth was obtained from the last available measure next to the study's publication date.

Quality assessment

The quality of each included study was evaluated using a quality assessment instrument created from recommendations for evaluating prevalence studies[64]. This tool is based on eight criteria that measure the accuracy of the clinical assessment, the integrity of the statistical analysis, and the sample's representativeness for the target demographic. A score ranging from 0 to 8 was generated for each study, assigning 1 point for each positive or not applicable criterion.

Data analysis and synthesis

The primary outcome measure of this study was the crude prevalence of PD per 100,000 inhabitants, particularly within specific pre-specified age intervals. The calculation for the crude prevalence for each study was performed using the following Eq. (1):

$$Crude\ prevalence = \frac{PD\ cases}{total\ sample}\ x\ 100,000 \quad (1)$$

Geographical and methodological data from all included studies were described. To ensure a more reliable and representative estimate of prevalence, only those that met the following criteria were included in the meta-analysis: (1) utilized a door-to-door methodology, (2) involved evaluation by a neurologist or movement disorder specialist, and (3) attained a quality score of 5 or higher.

The criteria were selected to minimize bias in cross-study comparisons and ensure accurate case identification in diverse population settings. Door-to-door surveys conducted by a neurologist or movement disorders specialist enhance case identification accuracy, a method supported by previous systematic reviews[64]. This methodology includes individuals who may not seek medical care, particularly relevant in low to middle-income regions. Furthermore, selecting studies that meet a minimum quality threshold helps attribute observed outcomes to population variances rather than to study design and quality variations.

The "metaprop" package of the R Statistical Software 3.5.1 (R Core Team 2018) was used for a meta-analysis of proportions. The overall results were analyzed using the random effects model, which estimated both within-study and between-study variances[95]. The variance was stabilized using the Freeman-Tukey double arcsine transformation, which addresses issues with extreme prevalence rates or small sample sizes. The DerSimonian and Laird method was employed to estimate the between-study variability and calculate the overall effect size in the meta-analysis[96].

To quantify the heterogeneity between studies, the Cochran's Q test and Higgin's & Thompson's I2 statistic, along with their corresponding 95% confidence intervals, were utilized[97]. Publication bias was investigated using the Begg[98] and Egger's[99] tests. To identify the sources of heterogeneity in the meta-analysis, we conducted meta-regression analyses among all studies included in the meta-analysis using a mixed-effects model. This analysis considered both methodological factors, such as study quality, minimum included age, year of publication, and number of participants, as well as sociodemographic variables, including the geographical region of the country, life expectancy at birth, and GDP per capita. Lastly, we performed subgroup analyses to explore the influence of certain variables on PD prevalence and, for each, the Chi-square test was used to identify potential differences between subgroups. An additional sensitivity analysis was conducted, excluding outliers from the analysis, with a focus on removing studies exhibiting the highest standardized residuals. Also, we performed an analysis of prevalence data, adjusting for age to ensure a comprehensive understanding of the results. A second sensitivity analysis including only studies reporting an age-standardized prevalence was performed. This systematic review was registered on PROSPERO (n° CRD42023399992).

Data availability

All data generated or analyzed during this study are included in this published article (Supplemental Table 2).

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Author contributions

G.M.P. had the idea for the study, made the literature review, designed the study, interpreted data, constructed the database, wrote the report, and oversaw the revision of the report. D.T.S. did the statistical analysis, constructed the database, and revised the report. N.M.S. collected, analyzed data and revised the report. G.A.M. helped to collect data and revise the report. D.C.F. helped to collect data and revise the report. P.S.A. reviewed the report. B.L.S.L. reviewed the report. P.R.P.B. reviewed the report. A.J.N. reviewed the report. C.M. reviewed the report. I.F.M. reviewed the report. C.R.M.R. oversaw the study design and analysis and reviewed the report. A.F.S.S. had the idea for the study and oversaw the design, writing, and revision of the report.

Competing interests

The authors declare no competing interests.

Additional information

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