

**Frame 1.** Summary of studies

	Study Design	Sample	Instruments for diagnosing depressive symptoms/ depression	Main findings
Ma et al., 2022 [33]	Prospective and cohort	423 with early PD (before age 40), 64 with prodromal PD, 196 healthy	Geriatric Depression Scale (GDS)	High predictive value of REM sleep disorders, together with depression, for the development of PD
Roos et al., 2022 [35]	Prospective and cohort	775 elderly individuals	The Center for Epidemiologic Studies Depression Scale e Hospital Anxiety and Depression Scale	The combination of prodromal symptoms (two or more) seems to be an important finding for identifying Prodromal Parkinson's disease, surpassing any isolated symptom. Depression follows the same logic, it must be accompanied by other findings to raise diagnostic suspicion. 11% of individuals had at least two known risk factors for PD; promoting worse motor outcomes.
Schrag et al., 2015 [31]	Case-control study	8,166 individuals with PD and 46,755 without PD	Report in medical record of diagnosis of depression	5 years before PD diagnosis, the incidence of tremor, imbalance, depression, anxiety, fatigue, urinary symptoms, hypotension, dizziness, erectile dysfunction and constipation was higher among individuals who would develop PD (n=4,769) compared to controls.

<p>Kazmi et al., 2022 [36]</p>	<p>Cross-sectional study</p>	<p>36 individuals with late-onset depression and 30 controls</p>	<p>DSM IV and Hospital Anxiety and Depression Scale (HADS) criteria</p>	<p>10 years before PD diagnosis, the incidence of tremor and constipation was higher among individuals who would develop PD (n=1,680) compared to controls</p> <p>24% of patients with late-onset depression, compared to 4% of controls, showed changes in the dopamine transport test in the basal ganglia ( <sup>123</sup>I-ioflupane SPECT)</p>
<p>Gaenslen et al., 2014 [32]</p>	<p>Case-control study</p>	<p>698 individuals</p>	<p>ICD 10 or DSM IV criteria</p>	<p>Individuals with depression showed greater visuospatial impairment, anxiety, painful muscle tension; when compared to individuals with sleep disorders and hyposmia. Individuals with two or three of the selected prodromal symptoms were at greater risk of developing motor symptoms when compared to individuals with only one of the selected symptoms.</p>

<p>Gustafsson et al., 2015 [37]</p>	<p>Prospective and cohort study (follow-up with between 1987 and 2012)</p>	<p>140,688 individuals with depression and 421,943 controls</p>	<p>ICD 9 and ICD 10 criteria</p>	<p>Hospitalization was an independent risk factor for individuals with depression to develop PD (OR=1.4); depression in members of the same family was not a risk factor</p>
<p>Bohlken et al., 2021 [34]</p>	<p>Case-control study</p>	<p>17,702 individuals with PD and 17,702 controls</p>	<p>Report in medical record of diagnosis of depression</p>	<p>Depression, dizziness, insomnia and constipation were, in descending order, the most prevalent prodromal symptoms among individuals who developed PD. However, these symptoms were also highly prevalent among controls.  Memory impairment, increased tremor and difficulty walking were, among the symptoms researched, those with the greatest impact (relative risk) for the development of PD</p>
<p>Liu et al., 2018 [39]</p>	<p>Cross-sectional study</p>	<p>98 individuals with PD, 210 first-degree relatives, 250 controls</p>	<p>Beck Depression Inventory</p>	<p>Siblings of patients with PD are more likely to develop depression (OR=2.438), REM sleep disorder (OR=4.120) and anxiety (OR=3.434) compared to the general population</p>

Walter et al., 2014 [42]	Prospective cohort (follow-up for 10 years)	46 individuals with major depressive disorder	Beck Depression Inventory e Hamilton Depression Rating Scale	Idiopathic hyposmia, asymmetric motor slowing and hyperechogenicity of the substantia nigra combined with at least two of the four: family history, non-smoking, constipation and non-consumption of coffee; these were predictive factors for patients with MDD to develop PD
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**Source:** The authors

**Notes:** **PD** (Parkinson's disease), **DSM** (APA Diagnostic and Statistical Manual of Mental Disorders, IV Edition), **ICD** (International Classification of Diseases, 9th and 10th Editions), **MDD** (Major depressive disorder)