# The impact of psychiatric comorbidity on Parkinson's disease outcomes: a systematic review and meta-analysis

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## Introduction

Parkinson's disease (PD) is a chronic neurodegenerative disorder, affecting more than 1% of adults 65 years and older[1]. Resulting from loss of dopaminergic neurons in the substantia nigra, PD is diagnosed based on motor symptoms, namely bradykinesia, rigidity and tremor[2].

Non-motor symptoms are extremely common and constitute a major burden for those with the disease and their carers[3]. Neuropsychiatric comorbidities form three clusters[4]:

1. Disorders of **affect** - depression and anxiety
2. Disorders of **perception and thinking** - hallucinations and psychotic experiences
3. Disorders of **motivation** - impulse control disorders and apathy

Whilst there is evidence to suggest that psychiatric conditions in PD detrimentally affect quality of life[5], their association with outcomes and overall disease prognosis has never been systematically evaluated.

? In individuals with PD, we aimed to **characterise the association between psychiatric comorbidities**: psychosis, depression, apathy, anxiety and impulse control behaviours (ICBs) **with prognosis and neurological outcomes**: cognitive impairment, death, disability, disease progression, falls or fractures and care home admission.

## Methods

Search run 13th November 2023 (MEDLINE, Embase, PsycINFO and AMED)

Key inclusion: **longitudinal observational studies** measuring **neurological outcomes** in people with PD, **with and without specific psychiatric comorbidities (exposures).**

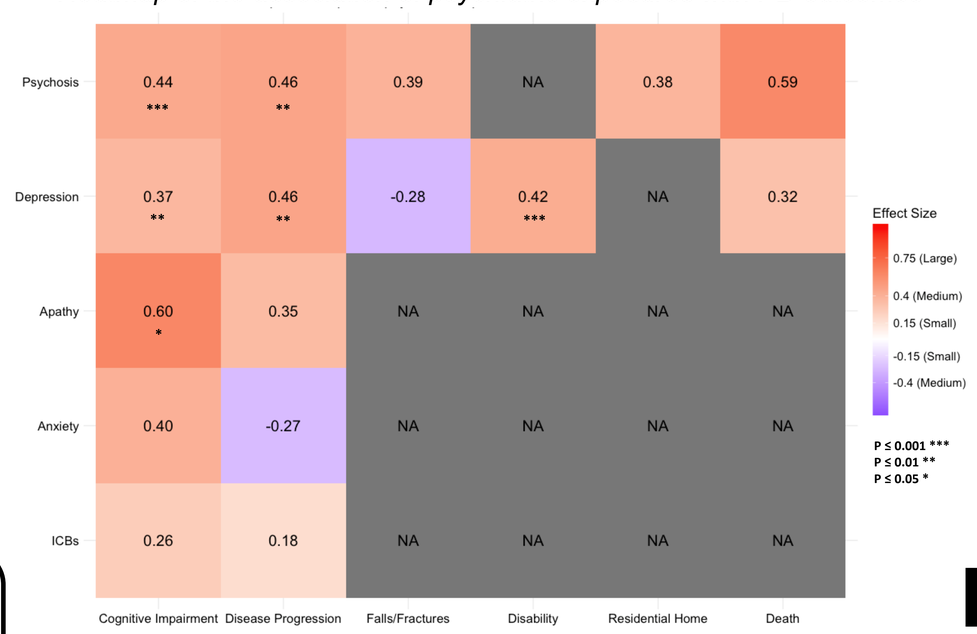
For each exposure-outcome pair, a **random-effects meta-analysis** was conducted based on **standardised mean difference**, preferentially using **adjusted effect sizes** when available.

**Study quality** was assessed using the **Newcastle–Ottawa Scale. Between-study heterogeneity** was assessed using the $I^2$ **statistic** and **publication bias** was assessed using **funnel plots**.

30,753 records identified → 26,389 titles + abstracts screened → 1,028 full texts assessed → 55 eligible studies (94 exposure-outcome pairs)

## Results

*Heatmap of the association of psychiatric exposures with PD outcomes*




*Characteristics of included subjects and studies*

| | |
|---|---|
| **N patients overall** | **165, 828** |
| **Country of study** | USA (14), Norway (6), Italy (5), Spain (5), UK (4), Korea (4), France, Germany, Japan, Israel, Singapore, multi-country <4 |
| **Study design** | |
| Case-control | 3 |
| Cohort | 52 |
| Prospective | 45 |
| Retrospective | 10 |
| Single-centre | 32 |
| Multi-centre | 23 |
| **Follow-up range (years)** | **1 - 11** |
| **Sex (n included = 164, 514)** | |
| Male (n, %) | 99, 182 (60.3%) |
| Female (n, %) | 65, 460 (39.7%) |
| **Age: mean (SD)** | **71.8 (11.4)** |

**Psychosis, depression, and apathy are significantly associated with greater cognitive impairment**

**Psychosis and depression are associated with faster disease progression**

**Depression is also associated with a significantly higher burden of disability**

## Conclusion & Future Directions

Psychiatric comorbidities in PD are common and should be considered markers of a poorer prognosis in patients.

These symptoms are a major burden for people living with PD, severely affecting quality of life and overall wellbeing.

Increased awareness amongst clinicians is crucial, as are more rigorous standards for symptom detection.

Further study is needed to evaluate the potential mechanisms underlying the associations between psychiatric comorbidity and neurological outcomes at an individual and epidemiological level, and whether effective treatments can affect disease outcome.

## References

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