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LETTER

Methodological Considerations on the Reported Association Between Postoperative Chronic Back Pain Syndrome and Psychiatric, Brain, and Mortality Outcomes in a Korean Nationwide Cohort [Letter]

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Dear editor

We read with great interest the recent nationwide retrospective cohort study by Park et al,[1] which utilized the Korean National Health Insurance Service (NHIS) database to examine 603,272 patients undergoing lumbar spine surgery between 2009 and 2023. The authors report that "postoperative chronic back pain syndrome" (PCBPS) was associated with increased risks of psychiatric disorders (adjusted hazard ratio [aHR] 1.15), stroke (aHR 1.15), Parkinson's disease (aHR 1.40), dementia (aHR 1.07), and all-cause mortality (aHR 1.10), and conclude that a paradigm shift in postoperative care is required. The authors are to be commended for leveraging a nationally representative dataset of this scale in a clinically important and under-studied area. From the perspective of spinal surgery practice and observational methodology, however, we believe seven points merit further consideration to enhance the interpretability of the reported associations.

Protopathic Bias and the Parkinson's Disease Outcome

The reported association between PCBPS and Parkinson's disease (aHR 1.40) is, in our view, the finding most vulnerable to protopathic bias.[2] Axial postural abnormalities such as camptocormia and Pisa syndrome, together with chronic musculoskeletal and axial back pain, are well-characterized features that may precede the clinical diagnosis of Parkinson's disease by many years.[3] Patients in the prodromal phase may undergo lumbar spine surgery for what is subsequently recognized as a neurodegenerative axial disorder, and chronic postoperative back pain in this subgroup would therefore be a consequence rather than a cause of early Parkinson's disease. The authors did not perform a lag-time analysis excluding outcomes occurring within the first years of follow-up, nor did they present incidence rates stratified by time since surgery. Without these analyses, the direction of causality cannot be distinguished from reverse causation, and the magnitude of the observed aHR is precisely what a protopathic mechanism would be expected to produce.

Heterogeneity of the PCBPS Exposure Definition

The operational definition of PCBPS merges three clinically distinct entities into a single exposure group. Patients identified by the M96.1 diagnosis code (PCBPS-D), by ≥12 weeks of gabapentinoid prescription (PCBPS-G), and by reoperation (PCBPS-R) do not share a common pathophysiology. Reoperation on the lumbar spine is frequently performed for adjacent segment disease, recurrent disc herniation, hardware complications, or postoperative infection, none of which is equivalent to chronic pain. This heterogeneity is reflected in the authors' own data: the sub-definition aHRs for all-cause mortality ranged from 1.03 (PCBPS-G) to 1.42 (PCBPS-R), and the aHR for dementia was not significant in PCBPS-G at all. These substantial

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differences contradict the authors' claim that the findings are "consistent across all sub-definitions" and suggest that the three groups represent different populations with different outcome trajectories.

Gabapentinoids as a Competing Causal Pathway

The gabapentinoid-based sub-definition (PCBPS-G) raises a specific concern of pharmacological confounding. Gabapentinoids are listed in the American Geriatrics Society 2023 Beers Criteria as potentially inappropriate in older adults, with well-documented associations with sedation, dizziness, falls, fractures, and cognitive impairment.[4] Any apparent effect of PCBPS-G on dementia, fall-related stroke, or all-cause mortality is therefore open to an alternative explanation in which the drug itself, rather than chronic pain, mediates the outcome. The authors neither adjusted for gabapentinoid dose or duration beyond the 12-week threshold, nor considered an active-comparator design, and do not discuss this alternative pathway.

Differential Outcome Ascertainment

Patients meeting any PCBPS definition, by construction, interact more frequently with the healthcare system than those who do not: they attend more outpatient visits, receive more imaging, and undergo more neurological and psychiatric assessment. Each of these contacts represents an opportunity to code a diagnosis of anxiety, depression, stroke, Parkinson's disease, or dementia. In administrative datasets based on billing codes, such differential surveillance can inflate apparent incidence in the more intensively observed group in the absence of any true causal relationship. The authors did not report healthcare utilization as a covariate, did not compare diagnostic intensity between groups, and did not perform negative control outcome analyses to probe this bias.

Missing Key Covariates

Several covariates known to be among the strongest predictors of the outcomes studied were not included in the adjustment set. Preoperative psychiatric history is the single most powerful predictor of postoperative psychiatric outcomes after lumbar spine surgery and was not adjusted for. Preoperative and postoperative opioid use, which is itself independently associated with dementia, fall-related injury, and mortality, was likewise not addressed. Frailty and baseline functional status, preoperative cognitive function, and preoperative neurological examination findings are not available in claims data and were not proxied. The authors state that lifestyle variables were "acquired from health checkup cohort data" but do not specify the proportion of patients with complete lifestyle data, the missing-data mechanism, or the imputation or complete-case strategy applied.

Effect-Size Magnitudes and Residual Confounding

The magnitudes of the reported aHRs—1.07 for dementia, 1.09 for brain disorders overall, 1.10 for mortality, and 1.15 for stroke or psychiatric disorders—are precisely in the range where residual confounding dominates in non-randomized research. The VanderWeele–Ding E-value framework[5] would place the E-value for an aHR of 1.07 at approximately 1.34, meaning that an unmeasured confounder associated with both PCBPS and the outcome at modest risk-ratio strength would entirely explain the observed association. No such sensitivity analysis is reported. Absolute risk differences and numbers needed to harm are not presented, and statistical significance in a cohort of 603,272 cannot be equated with clinical importance.

Causal Inference, Multiple Testing, and Reporting Standards

The manuscript uses directly causal language ("PCBPS increased the risk") drawn from an observational administrative-database design and proposes a paradigm shift in postoperative care on the basis of these associations. The analysis involves three exposure definitions, seven outcomes, and stratified analyses by four lifestyle variables, yielding on the order of one hundred hypothesis tests; no multiplicity adjustment is described, and no primary endpoint is pre-specified. The manuscript does not report adherence to the STROBE statement for observational research,[6] nor to the RECORD extension for studies conducted using routinely collected health data,[7] which specifically addresses the validation of diagnosis codes, handling of missing data, and the management of immortal time bias[8] in claims-based designs—all of which are relevant here.

Suggestions for Re-Analysis

To permit a more confident interpretation of the current dataset and to strengthen future work in this area, we suggest the authors consider the following: (i) a lag-time analysis excluding outcome events occurring within 1–2 years of the index surgery, particularly for Parkinson's disease; (ii) separate reporting of the three PCBPS sub-definitions (PCBPS-D, PCBPS-G, and PCBPS-R) rather than a pooled "PCBPS-E" group, with formal tests of heterogeneity across definitions; (iii) adjustment for preoperative psychiatric history, preoperative and postoperative opioid exposure, and, where feasible, proxies for frailty; (iv) E-value sensitivity analyses for each reported aHR, reported alongside absolute risk differences; (v) negative-control outcome analyses to probe surveillance bias; and (vi) explicit RECORD-compliant reporting of diagnosis-code validation, missing-data handling, and the time-origin for the exposure definition.

In Summary

We do not dispute that chronic postoperative pain carries meaningful psychological and functional consequences; this is broadly accepted. We do suggest, however, that the specific claim—that PCBPS independently elevates the risk of Parkinson's disease, dementia, stroke, and all-cause mortality—exceeds what this design and these effect sizes can support, and that the conclusions would benefit from the analytical refinements noted above. We thank the authors for contributing a dataset of this scale to the field and look forward to further analyses that address these methodological considerations.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this Letter, the authors used Claude Opus 4.7 (Anthropic PBC, San Francisco, California, USA) to assist with language refinement and with the organization and formatting of reference information. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Data Sharing Statement

Data sharing is not applicable to this Letter, as no new datasets were generated or analyzed. All claims pertain to the published article by Park et al (J Pain Res. 2026;19:582506).[1.]

Author Contributions

K.Ş.: Conceptualization; Writing – original draft; Writing – review and editing. S.H.: Methodology; Writing – review and editing. M.T.P.: Investigation; Writing – review and editing. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this communication.

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