

## **RENAL OUTCOMES IN PEOPLE WITH BIPOLAR DISORDER TREATED WITH LITHIUM: A BRITISH RETROSPECTIVE COHORT STUDY**

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**PROBLEM:** Lithium is a key treatment option for bipolar disorder and depression. Lithium's pathological effects on the kidney remain an important influence on prescribing decisions, and monitoring of renal function is part of standard care. However, no large-scale study has ever been conducted to quantify the risk of renal failure through lithium use, adjusted for other potential risk factors.

**PURPOSE:** This study estimated a) the incidence of renal failure in patients with bipolar disorder according to age, gender, and use of lithium (long-term/short-term/never), and b) the relative hazard of renal failure, in patients with bipolar disorder according to use of lithium and adjusted for demographic and clinical risk factors for renal disease.

**DESIGN:** This retrospective cohort study used the General Practice Research Database to access records of 6360 adults aged over 18 with a diagnosis of bipolar disorder between 1 January 1990 and 31 December 2007. We conducted time-to-event analyses of renal outcomes using Cox proportionate hazards models with the control group comprising non lithium users, adjusting hazard ratios for age, gender, smoking and alcohol status, co-morbidities, and poly-pharmacy.

**FINDINGS:** Users of lithium had a two-fold increased risk of developing renal failure (age and sex adjusted HR 2.05 (95% CI 1.29- 3.27) and a two and a half fold increased risk of developing any form of chronic kidney disease (HR 2.41 (95% CI 1.96- 2.96). 2494 (39.21%) of the cohort were lithium users. The prevalence of known risk factors and co-prescribing associated with renal pathology were similarly distributed across lithium users and non users. Overall, 417 (6.6%) of cohort participants had chronic kidney disease and 77 (1.2%) had end stage renal failure. Lithium users had two-fold increase in all cause mortality (HR 2.19. 95% 1.93-2.49). Secondary analysis of dose adjusted exposure indicates an increased risk of renal failure as lithium exposure increases from 6 months to 5 years.

**CONCLUSION:** The absolute risk of developing renal failure remains small and should not discourage appropriate prescribing. The increased risk of renal failure among lithium users must be managed through regular, close monitoring, and appropriate management of associated risk factors such as cardiovascular disease. Further prospective studies are needed to fully quantify the risks.

**RELEVANCE:** Findings confirm the need to monitor the renal function of lithium users. This has important significance for lithium users, mental health practitioners and general practitioners who will need to consider the balance between long term mental health benefits and renal screening and monitoring.

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