Lithium Use, but Not Valproate Use, Is Associated With a Higher Risk of Chronic Kidney Disease in Older Adults With Mental Illness

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ABSTRACT

Objective: Lithium is an essential mood disorder treatment; however, it remains unclear whether lithium increases chronic kidney disease (CKD) risk. There are few data on this in the elderly, even though older adults may be particularly susceptible to CKD. We wished to determine whether lithium is associated with increased CKD risk relative to valproate in older adults.

Methods: This nested case-control study analyzed province-wide administrative health data from mental health service users aged ≥ 66 years in Ontario, Canada, from 2003 to 2014. Five-year incident CKD risk was compared in lithium users, valproate users, and patients who used neither medication. *ICD-10* was used to assign CKD diagnosis. We used conditional logistic regression to control for hypertension, diabetes mellitus, acute kidney injury, medications associated with lithium toxicity, and other potential confounders.

Results: 21,741 cases and 86,930 age- and sex-matched controls were identified, including 529 lithium users and 498 valproate users. After controlling for confounders, we found that lithium use was associated with increased risk of incident CKD (adjusted odds ratio [OR] = 1.76 [95% CI, 1.41–2.19]), while valproate use was not (adjusted OR = 1.03 [95% CI, 0.81–1.29]).

Conclusions: Lithium is independently associated with an almost 2-fold increase in CKD risk in this community sample of older mental health service users. In the absence of clear information about certain contributing factors, such as inadequate monitoring and acute and chronic lithium level elevations, causes for this increase will need to be determined in future research.

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Lithium remains the gold-standard treatment for bipolar disorder[1] and is useful in treatment-resistant depression. While recent studies report that lithium users may have an up to 2 to 8 times elevated risk of end-stage renal disease and chronic kidney disease (CKD),[2–5] these findings remain controversial. When factors such as pharmacotherapy and medical comorbidity (eg, hypertension) were controlled, the effects of lithium exposure on CKD were minimal.[6–8] Almost all of this research has been in patients younger than 65 years or in mixed-aged samples in which CKD is relatively uncommon.[8] The limited amount of data in the elderly is a particular concern,[9–12] since up to 40% of older bipolar patients respond preferentially to lithium[13] and more than 50% of patients with bipolar disorder and unipolar depression will be older than 60 years by 2030.[14] The possibility of lithium toxicity and subsequent CKD may theoretically be more common in older adults due to low premorbid renal function,[15] medical comorbidities (eg, hypertension), and a higher likelihood of drug interactions.[16] Despite this, the prevalence of CKD in older lithium users and nonusers appears relatively similar (42%–50%[9,10] vs 37%[17]). Also, most cross-sectional[10,12] and longitudinal studies[11,18] in geriatric lithium users have failed to demonstrate an association between lithium levels or lithium use duration and CKD. One recent mixed-aged community-based longitudinal study by Kessing et al[6] included a large subsample of geriatric patients: they found that lithium was not associated with end stage renal disease but with an increased risk for milder CKD. However, aside from that, longitudinal studies have used relatively small samples (usually n < 100) in academic settings, where lithium levels < 0.8 mmol/L (or even < 0.5 mmol/L) were used and lithium/renal monitoring occurred every 3 months.

There is an urgent need for large-scale, longitudinal, real-world data examining late-life lithium use and the potential for CKD. This research could comprehensively account for medical comorbidity, mental illness, medication use, and other important covariates while investigating the CKD risk (or lack thereof) in older lithium users. We used population-based administrative data to create a large longitudinal cohort of older adults with mental illness. We hypothesized that lithium use would not be independently associated with increased risk of CKD. We also examined whether increased lithium duration would be associated with a higher risk of CKD relative to other older adults with mental illness, including a group of valproate users.

METHODS

Data Sources

Data from multiple linked health care databases from Ontario, Canada, were used. Ontario subsidizes health coverage for outpatient prescription drugs to all people older than 65 years and physician services to all Ontarians. Medication use information was obtained from

Clinical Points

- Previous research has not determined whether older lithium users are at increased risk of chronic kidney disease (CKD).
- In our large population-based study, lithium use was independently associated with an almost 2-fold increase in CKD risk.
- Lithium is a highly effective medication but should be used cautiously, with adequate monitoring of lithium levels and renal function, in patients for whom benefits outweigh potential risks.

the Ontario Drug Benefit database (ODB), which records all outpatient prescription drugs covered by ODB that are dispensed to all residents aged ≥ 65. The Ontario Health Insurance Plan (OHIP) database records data from all outpatient and inpatient physician billing claims, including whether the physician was a psychiatrist, and *International Classification of Diseases* billing diagnostic codes given during physician appointments (including mental health diagnoses). The Canadian Institute for Health Information Discharge Abstract Database contains data on all acute inpatient hospitalizations, and the National Ambulatory Care Reporting System records information from all emergency department visits, including *ICD-10*/*ICD-9* diagnoses. The Ontario Mental Health Reporting System is a centralized database with extensive clinical information on inpatients admitted to psychiatric units in Ontario. The Ontario Registered Persons Database includes all Ontario residents' age, sex, and date of death. These data were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences (ICES). The data set from this study is held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the data set publicly available, access can be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS. The full data set creation plan is available from the authors upon request. Ethics approval for this study was obtained from Sunnybrook Health Sciences Centre's Research Ethics Board.

Study Design, Setting, and Cohort

This was a nested case-control study. We used information from a base cohort of all patients aged ≥ 66 who had a mental health visit. A mental health visit was defined as a visit to either (1) a psychiatrist or (2) another physician who used a billing code to signify that the visit was primarily to address mental health care needs (eg, family doctor who used the code "primary mental health care"). The cohort entry date was the first date between April 1, 2003, and March 31, 2008, when a patient both had a mental health visit and was aged ≥ 66 years. Exclusion criteria included diagnosis of CKD in the 5 years prior to cohort entry (to ensure identification of incident CKD cases), death prior to cohort entry, invalid health care cards, and patient age > 105 years. Individuals with dementia and epilepsy diagnoses were also excluded since lithium and valproate are sometimes used in the treatment of epilepsy and behavioral symptoms of dementia, which may have associations with CKD.[19] Individuals were followed from cohort entry until the earliest date when 1 of the following cohort exit criteria were met: censoring events (death, epilepsy diagnosis, dementia diagnosis, or cholinesterase inhibitor prescription), first occurrence of CKD (defined in Cases section), or the end of follow-up, March 31, 2014. To be selected as either a case or control, individuals were required to be in the cohort for at least 5 years to allow for comprehensive characterization of drug exposure prior to the outcome.

Cases

Cases were defined as individuals who had a first occurrence of CKD at least 5 years after cohort entry. The date of CKD diagnosis was taken as the index date. CKD was defined by the presence of chronic dialysis (≥ 2 dialyses within > 90 days, with dialyses occurring within 150 days of each other[11]), renal transplantation, or any of the following *ICD-10* "chronic kidney disease" codes: N18 (chronic kidney disease), I12 (hypertensive chronic kidney disease), I13 (hypertensive heart and chronic kidney disease), N08 (glomerular disorders in diseases classified elsewhere), N16.5 (renal tubulo-interstitial disorders in transplant rejection), E10.2 (type 1 diabetes mellitus with renal complications), E11.2 (type 2 diabetes mellitus with renal complications), E13.2 (other specified diabetes mellitus with renal complications), E14.2 (type 2 diabetes mellitus with incipient diabetic nephropathy), Z94.0 (transplanted kidney), T86.100 (kidney transplant rejection), T86.101 (kidney transplant failure), and T86.102 (kidney transplant infection), N19 (unspecified kidney failure) during hospitalizations or emergency visits. These CKD codes have been used in other renal studies: they have been demonstrated to have a specificity of > 94% for estimated glomerular filtration rate (eGFR) levels < 45 mL/min (laboratory-defined CKD)[20] and are well validated.[21,22]

Controls

Each case was matched to up to 4 controls for age (± 1 year), sex, and date of cohort entry (± 30 days). Controls were sampled in such a way that they would have the same index date as the cases (CKD diagnosis date). Controls were free of CKD as of the index date (they could, however, be identified as a case at a later date).

Exposures

For our primary exposures, we looked for any lithium or valproate prescriptions filled in the 5 years preceding index date in each cases and controls. From there, we created 4 mutually exclusive groups based on exposure history: lithium-only exposure (at least 1filled lithium prescription, but no valproate prescriptions), valproate-only exposure (at least 1 filled valproate exposure, but no lithium prescriptions), lithium and valproate exposure (at least 1

filled prescription of each lithium and valproate), and neither lithium nor valproate exposure (reference category).

For our secondary exposures, we quantified lithium duration and valproate duration as the total number of days these medications had been supplied to a patient by any Ontario pharmacy in the 5 years prior to index date.

We included valproate as a comparator exposure because (1) outpatient physician billing codes are not as reliable for mental health diagnoses[23] and (2) lithium and valproate are both usually prescribed for serious mood disorders, which may theoretically have up to twice the rates of CKD compared to the rest of our mental illness base cohort.[24] It is increasingly thought that severity of mental illness may be independently associated with elevated medical comorbidity risk.[25] Therefore we chose valproate as a comparator to capture the potential effect of difficult-to-treat mood disorder on CKD (if any): it is often prescribed in bipolar disorder, but not directly associated with CKD.

Covariates

To control for potential confounding, we examined several covariates known to be associated with CKD.[9] These included medications used in the 5 years prior to the index date: loop diuretics,[16] diuretics (eg, hydrochlorothiazide),[9] potassium-sparing diuretics,[26] angiotensin converting enzyme inhibitors,[16] angiotensin II receptor blockers,[26] nonsteroidal anti-inflammatory drugs/cyclooxygenase-2 inhibitors,[26] statins,[27] and antipsychotics.[9,28] Medical conditions in the 5 years preceding the index date were also assessed: diabetes mellitus, hypertension, and ischemic heart disease.[9,26] Acute kidney injury (AKI) and nephrogenic diabetes insipidus (NDI) were ascertained using methods previously described.[9]

Additional Descriptors

We also described other clinical variables: antidepressant, lamotrigine, carbamazepine, and benzodiazepine use.

Data Analysis

Demographic and clinical variables were measured in CKD cases and non-CKD controls at the index date.

Using conditional logistic regression to control for covariates, we assessed whether patients who had exposure to lithium only, valproate only, or a combination of lithium/valproate had increased risk of CKD compared to no lithium/no valproate exposure (reference group). This allowed us to generate unadjusted and adjusted odds ratios (aORs) and 95% confidence intervals (95% CIs). To examine whether increased lithium duration was associated with CKD risk, we then repeated the conditional logistic regression and substratified lithium- and valproate-only users by duration of exposure (using total days supplied in the 5 years prior to index): < 1 year, 1–2 years, 2–3 years, 3–4 years, and > 4 years. We formulated our hypotheses prior to the creation of the base cohort using administrative data and before performing any analyses. All analyses were performed using SAS statistical software (SAS version 9.4, SAS Institute, Cary, NC).

Table 1. Characteristics of Chronic Kidney Disease (CKD) Cases and Age- and Sex-Matched Non-CKD Controls at Index Date[a]

Characteristic	CKD Cases (n = 21,741)	Non-CKD Controls (n = 86,930)
Age at index date		
70–74 y	5,029 (23.1)	20,157 (23.2)
75–84 y	11,759 (54.1)	47,063 (54.1)
85+ y	4,953 (22.8)	19,710 (22.7)
Female gender	11,956 (55.0)	47,808 (55.0)
Long-term care resident	451 (2.1)	1,009 (1.2)
Medical comorbidity		
Diabetes mellitus	10,796 (49.7)	24,606 (28.3)
Hypertension	20,122 (92.6)	68,714 (79.0)
Ischemic heart disease	8,217 (37.8)	17,446 (20.1)
Acute kidney injury	896 (4.1)	447 (0.5)
Nephrogenic diabetes insipidus	372 (1.7)	851 (1.0)
Lithium and valproate use		
Use of lithium and valproate in the 5 years prior to index date		
Lithium only	134 (0.6)	395 (0.5)
Valproate only	115 (0.5)	383 (0.4)
Both lithium and valproate	30 (0.1)	61 (0.1)
Lithium duration, days supplied, mean ± SD[b]	803.4 ± 913.7	699.8 ± 880.5
Valproate duration, days supplied, mean ± SD[c]	574.4 ± 847.6	517.3 ± 801.5
Medication use in the 5 years prior to index date		
Angiotensin-converting enzyme inhibitors	12,984 (59.7)	35,969 (41.4)
Angiotensin receptor blockers	9,069 (41.7)	22,853 (26.3)
Nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 inhibitors	13,406 (61.7)	48,896 (56.2)
Hydrocholorothiazide	10,762 (49.5)	30,952 (35.6)
Loop diuretics	8,318 (38.3)	13,805 (15.9)
Potassium-sparing diuretics	3,674 (16.9)	6,583 (7.6)
Statins	15,375 (70.7)	48,464 (55.8)
Typical antipsychotics	1,755 (8.1)	4,665 (5.4)
Atypical antipsychotics	1,210 (5.6)	3,736 (4.3)
Antidepressants	9,587 (44.1)	32,982 (37.9)
Lamotrigine	38 (0.2)	110 (0.1)
Carbamazepine	302 (1.4)	1,067 (1.2)
Benzodiazepines or zopiclone	9,956 (45.8)	35,612 (41.0)

[a]Values expressed as n (%) unless otherwise noted.
[b]Cases, n = 164; controls, n = 456.
[c]Cases, n = 145; controls, n = 444.

RESULTS

A total of 420,141 Ontario patients were aged ≥ 66–105 years and had a mental health visit during the study period, meeting our cohort's inclusion and exclusion criteria.

We identified 21,741 CKD cases and 86,930 non-CKD controls (matched on age, sex, and date of entry ± 30 days), including 529 lithium-only users, 498 valproate-only users, and 91 patients with both lithium and valproate exposure. Clinical and demographic characteristics at the index date are described in Table 1.

After controlling for covariates, lithium-only use was associated with increased risk of incident CKD relative to nonuse (aOR = 1.76 [1.41–2.19]), while valproate-only use was not (aOR = 1.03 [0.81–1.29]). Patients with both lithium and valproate exposure also had increased risk (aOR 1.95 [1.19–3.18]) compared to the reference group (nonusers of lithium and valproate) (Table 2).

Table 2. Risk of Incident Chronic Kidney Disease (CKD) in Lithium Only, Valproate Only, and Lithium and Valproate, Relative to Nonusers

Parameter	Incident CKD Unadjusted[a] OR (95% CI)	Incident CKD Adjusted[b] OR (95% CI)
Lithium only	1.37 (1.12–1.67)	1.76 (1.41–2.19)
Valproate only	1.21 (0.98–1.49)	1.03 (0.81–1.29)
Lithium and valproate[c]	1.98 (1.28–3.06)	1.95 (1.19–3.18)
Neither lithium nor valproate (reference)	1.00	1.00

[a]Adjusted for age and sex (via matching), but not adjusted for any other covariates.
[b]Adjusted for diabetes mellitus, hypertension, ischemic heart disease, nephrogenic diabetes insipidus, acute kidney injury, loop diuretics, hydrochlorothiazide, nonsteroidal anti-inflammatory drugs/cyclooxygenase-2 inhibitors, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, atypical antipsychotics, and statin use. The cases and controls were matched for age and sex.
[c]Any lithium and valproate use during the 5 years prior to index date.
Abbreviation: OR = odds ratio.

Increased duration of lithium was associated with a higher risk of CKD: Patients with 3–4 years or > 4 years of lithium exposure had significantly elevated CKD risk (aORs = 2.28 [1.25–4.13] and 2.22 [1.67–2.95], respectively), while patients with less than 3 years of use did not have an increase in risk relative to the reference group. Regardless of duration of valproate use, there was no association with CKD risk (Table 3).

DISCUSSION

We found that lithium exposure is associated with an almost 2-fold increased risk of CKD in older adults with mental illness. This association was stronger after controlling for several confounding variables from the literature,[26] perhaps because prescribers tended to avoid using lithium when other CKD risk factors were present.[29] There was an effect of lithium duration, with patients with more than 3 years of lithium exposure having an especially high risk of CKD (OR > 2.2). In contrast, there was no association between valproate exposure and CKD, suggesting that the risk of CKD conveyed by lithium is unrelated to the inherent risk of CKD in mood disorder patients (risk driven by aspects of mood disorder biology such as inflammation, oxidative stress, and endothelial dysfunction). Taken together, these findings strongly suggest that lithium is independently associated with an increased risk of CKD, particularly with long-term use.

This study adds to the literature on the potential risks of CKD by examining older lithium users. Recent large studies in younger adult and mixed-aged samples have found a similar association between lithium and CKD,[2–6,30] with one of these mixed-aged studies by Kessing et al[6] having a substantial number of patients aged > 60 years (n = 2,059 and 2,029 received lithium and antiepileptics, respectively). However, in that article and similar ones, the effects of lithium on CKD were usually nonsignificant when controlling for covariates and using appropriate mood disorder or psychotropic medication comparator groups.[6–8,31] Similarly, the limited geriatric literature has not found an association between long-term lithium use and CKD,[10–12,18] particularly when baseline renal function was normal.[15] These small geriatric studies were largely performed in the context of optimal management in academic settings where, generally, lithium levels < 0.8 mmol/L were used and lithium/renal monitoring occurred regularly every 3 months. It is possible that in those studies a lithium-related CKD risk was not observed because lithium was prescribed safely, which may not have been the case in our population-based sample.

We conclude that with usual clinical prescribing practices, older lithium users are at an elevated risk of CKD. Unlike younger lithium users, older adults commonly have premorbid renal function decline (> 40% have an eGFR < 60 mL/min/1.73 m^2),[10] putting them at a higher risk for further lithium-associated renal declines[15] and the type of more moderate-severe CKD quite likely captured in our study. Lithium level elevations have been associated with AKI and NDI,[26] which are correlated with increased CKD risk.[9] Although we controlled for AKI and NDI, it is possible that chronic or acute lithium level elevations contributed to the increased risk of CKD. Older adults are also more likely to encounter drug-drug interactions, making lithium level elevations more common.[16] It is also likely that lithium prescribing practices in community settings may promote lithium toxicity: Many Ontario laboratories report lithium levels between 0.6–1.2 mmol/L (if not higher) as therapeutic, when lithium levels > 0.8 mmol/L may actually be nephrotoxic in older adults.[26] Community lithium prescribing patterns may be similar in many other parts of the world, especially since there are not yet international geriatric lithium guidelines.[32] Finally, lithium monitoring practices are often suboptimal in real-world settings, with < 30% of patients receiving adequate monitoring.[33]

Strengths and Limitations

This study had several strengths. It made use of large-scale, province-wide data on older adults with mental illness. This is important since there have been few previous geriatric studies of lithium use and CKD, with the exception of 1 notable study[6]; previous investigations of late-life lithium users have usually been much smaller (< 100 patients)[11,18]; and studies have not usually used reference groups with mental illness.[30] Our study used multiple years' worth of data, allowing for a more confident assessment of potential causality than most previous efforts,[8] particularly in late-life lithium research.[26] Recent studies have not necessarily controlled for the effects of mental illness diagnosis, pharmacotherapy,[9] and medical comorbidity.[5,30] We attempted to be as comprehensive as possible in our inclusion of covariates to control for potential confounding.[26] Finally, we also used a valproate comparator group, which helped us assess whether the increased risk of CKD in lithium users was independent of effects related to having a mood disorder.

In terms of limitations, we lacked laboratory markers of renal function (eg, eGFR or creatinine levels at baseline

Table 3. Conditional Logistic Regression: Risk of Incident Chronic Kidney Disease (CKD) in Lithium Only, Valproate Only, and Lithium and Valproate, Relative to Nonusers, Examining the Effect of Lithium Duration

	CKD Cases (n = 21,741)[a]	Controls (n = 86,930)[a]	Incident CKD Unadjusted[b] OR (95% CI)	Incident CKD Adjusted[c] OR (95% CI)	Wald χ^2	*P* Value
1. Duration of lithium only (n = 529)						
< 1 y	19 (0.1)	70 (0.1)	1.10 (0.66–1.82)	1.11 (0.63–1.95)	0.13	.72
1–2 y	7 (0.0)	32 (0.0)	0.89 (0.39–2.01)	1.25 (0.52–3.01)	0.24	.63
2–3 y	7 (0.0)	38 (0.0)	0.74 (0.33–1.67)	0.73 (0.31–1.75)	0.50	.48
3–4 y	18 (0.1)	49 (0.1)	1.49 (0.87–2.55)	2.28 (1.25–4.13)	7.30	.007
> 4 y	83 (0.4)	206 (0.2)	1.62 (1.26–2.10)	2.22 (1.67–2.95)	30.23	< .0001
2. Duration of valproate only (n = 498)						
< 1 y	38 (0.2)	139 (0.2)	1.10 (0.77–1.57)	0.85 (0.58–1.27)	0.61	.44
1–2 y	> 5 (0.0)[d]	> 30 (0.0)[d]	1.16 (0.57–2.33)	0.89 (0.42–1.87)	0.10	.76
2–3 y	≤ 5 (0.0)[d]	> 20 (0.0)[d]	< 0.5 (0.09–1.55)	0.31 (0.07–1.37)	2.41	.12
3–4 y	15 (0.1)	39 (0.0)	1.54 (0.85–2.79)	1.06 (0.55–2.04	0.03	.87
> 4 y	50 (0.2)	148 (0.2)	1.36 (0.98–1.87)	1.37 (0.96–1.96)	3.01	.083
3. Previous use of both lithium and valproate (n = 91)	30 (0.1)	61 (0.1)	1.98 (1.28–3.06)	1.95 (1.19–3.18)	7.03	.008
4. No lithium, no valproate (reference, n = 107,553)	21,462 (98.7)	86,091 (99.0)	1.00	1.00		

[a]Values expressed as n (%).
[b]Adjusted for age and sex (via matching), but not adjusted for any other covariates.
[c]Adjusted for diabetes mellitus, hypertension, ischemic heart disease, nephrogenic diabetes insipidus, acute kidney injury, loop diuretics, hydrochlorothiazide, nonsteroidal anti-inflammatory drugs/cyclooxygenase-2 inhibitors, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, atypical antipsychotics, and statin use.
[d]Exact values have not been provided to protect patient confidentiality of the < 6 patients in one of the cells (valproate users with 2–3 years of valproate exposure who were CKD cases).
Abbreviation: OR = odds ratio.

and follow-up) or serum lithium levels (eg, to detect acute and chronic lithium toxicity); however, our outcome measures have been validated in previous studies and are highly specific for CKD (> 94%). We could not control for surveillance bias: clinicians may be more observant of renal dysfunction and systematically monitor renal function in patients treated with lithium compared to valproate and other lithium nonusers. The follow-up period was 5 years, which meets the literature's standard of > 3 years' follow-up to assess incident CKD risk,[34] but may not have captured the 15–20 years it can sometimes take to develop CKD. Also, with our current data and study design, we cannot be sure whether CKD and death were competing events—that is, whether the difference in CKD incidence between lithium users and nonusers was related to excess mortality among nonusers. However, we controlled for medical comorbidities that are commonly associated with increased mortality risk. Although we captured almost all of the major covariates previously identified in lithium/CKD research,[26] we did not have access to data regarding smoking[5] or obesity. We also did not have access to reliable bipolar disorder diagnosis, which can be independently associated with CKD,[6] although we used a sample of mental health service users and a valproate comparator exposure group and controlled for many of the cardiovascular risk factors that may explain increased CKD risk in bipolar disorder.

Future Directions

Future studies should examine the potential reasons underlying increased CKD risk in older lithium users. Since sufficiently powered, long-term randomized controlled trials are extremely challenging to conduct in older adults with bipolar disorder and other late-life lithium users,[11] continued efforts using administrative health data will be helpful. Studies could identify whether chronic and acute exposure to certain lithium levels is associated with a higher risk of CKD (eg, > 0.8 mmol/L or > 1.0 mmol/L[35]). Studies could examine CKD using laboratory measurements of renal function (eGFR) and could specifically examine the important outcome of end-stage renal disease. Further research could also clarify the role of drug interactions, premorbid reduced renal function, and poor lithium/renal monitoring in late-life lithium-associated CKD.

CONCLUSIONS

Lithium is independently associated with an almost 2-fold increase in CKD risk in this community sample of older adults with mental illness. Without clear information about certain contributor factors, such as poor lithium monitoring and acute and chronic lithium level elevations, causes for this increased risk should be determined in future research. In the meantime, clinicians should carefully consider other alternatives in patients with particularly low preexisting renal function (eg, eGFR < 45 mL/min/1.73 m^2) and ensure adequate monitoring of lithium levels and renal function when lithium is used. Given lithium's superior effectiveness[1] in many older mood disorder patients[13] and the 1.5–2 times increased CKD risk also observed with other psychotropics (eg, antipsychotics[9,28]), use of lithium can continue, with caution, in patients for whom the benefits outweigh the risks.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Geriatric Psychiatry section. Please contact Jordan F. Karp, MD, at jkarp@psychiatrist.com, or Gary W. Small, MD, at gsmall@psychiatrist.com.