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ORIGINAL RESEARCH

Provider Perspectives on the Current Use of Lithium Medications and Lithium Monitoring Practices for Psychiatric Conditions

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Purpose: Despite lithium being a gold standard treatment for bipolar disorder, the percentage of patients with bipolar disorder who are prescribed lithium medication has declined in many parts of the world over the past two decades. The use of lithium is limited by its narrow therapeutic window and adverse side effects, which necessitates frequent serum lithium monitoring; hence, there is a critical need for improved ways to monitor lithium levels in psychiatric patients. We have recently shown that saliva lithium levels are highly correlated with those in blood, thereby presenting an alternative to venipuncture. Saliva sampling could open the door for at-home collections – potential that has been exemplified throughout the COVID-19 pandemic – thereby allowing samples to be collected remotely and delivered to a specific site for testing. In addition, prototype point-of-care devices have been developed by others for serum lithium monitoring, suggesting potential for a saliva lithium monitoring device. Our objective was to query the perspectives of American psychiatrists on lithium treatment practices and obstacles, the potential for at-home saliva collection and point-of-care devices, for lithium monitoring, as an alternative to pathology-based blood testing.

Methods: Data was collected through an online, anonymous survey, distributed to American psychiatric societies.

Results: Sixty-five respondents from 21 American states completed the survey. The majority of respondents were female, over 65 years of age, and/or had practiced for 30 years or more. The most frequent obstacles encountered with regard to lithium monitoring were adverse drug effects, and the need for monitoring. Overall, respondents believed saliva lithium monitoring and point-of-care devices would be useful, however raised concerns regarding validity and time-delay.

Conclusion: Point-of-care devices and saliva lithium monitoring are promising alternatives to blood testing that would be welcomed by psychiatric societies, however, require extensive development and validation before implementation into a clinical setting.

Keywords: lithium, saliva, drug monitoring, point-of-care, survey

Introduction

Lithium medication is commonly used for the treatment of bipolar disorder, other mood disorders, and suicidality.[1–3] However, the narrow therapeutic window of lithium prophylaxis, and the risk of adverse side effects, necessitates frequent serum lithium level monitoring.[4–6] This can be uncomfortable and inconvenient for the patient and is dependent on patient compliance and ability to regularly attend a pathology clinic. In India, almost 30% of surveyed psychiatrists perceived low adherence to serum-level monitoring as an obstacle for the prescription of lithium, whereas the majority of surveyed psychiatrists in Spain indicated adverse side effects as the main reason to avoid lithium treatment.[7,8]

Recently, we showed that the monitoring of therapeutic lithium levels in saliva may be a viable alternative to blood tests. Specifically, we showed that saliva lithium levels are correlated with those in blood, and this association could be improved by accounting for daily lithium dose, a diagnosis of type 2 diabetes, and smoking status.[6] Our findings are consistent with previous studies dating back 30 years that have demonstrated significant correlations between serum lithium and salivary lithium.[9–12] However, many of these past studies suffered from inconsistencies in saliva collection

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and storage procedures, variations in saliva processing methods and differences in the lithium detection method,[13] which resulted in weaker saliva-serum associations reported in other studies.[14–17]

Saliva collection and analysis has many advantages over blood, as it is simple and cost-effective, can be done at home or in the community without the need for trained laboratory personnel, and does not require venipuncture. It is hypothesized that saliva lithium monitoring could therefore circumvent many of the obstacles faced with serum lithium monitoring, increasing the ease of collection and patient compliance.

The advantages of saliva collection and analysis present us with two hypothetical avenues of lithium monitoring: at-home patient self-collection of samples and/or the development of a point-of-care lithium monitoring device. Protocols for at-home saliva collection have increased dramatically since the Covid-19 pandemic with several papers reporting on the feasibility of saliva home collection for monitoring Covid-19 positivity and avoiding in-patient visits.[18–21] Point-of-care devices have been investigated and developed by others for lithium monitoring using finger-prick or serum blood samples,[22–24] suggesting feasibility for saliva lithium monitoring. Despite these scientific advances in lithium treatment, the percentage of patients with bipolar disorder who are prescribed lithium medication has declined in many parts of the world over the past two decades;[8] in the United States, the percentage of clinic appointments which included lithium prescriptions dropped from 30.4% (1997–2000) to 17.6% (2013–2016).[25]

For saliva lithium monitoring to be pursued as a clinical and viable alternative to blood lithium monitoring, it is necessary to determine whether it would be considered and adopted by current psychiatrists and psychiatric mental health nurses. In this study, we surveyed psychiatrists and psychiatric mental health nurses in the United States to determine their perspectives on lithium treatment, point-of-care devices, and the potential use of at-home saliva collection for lithium monitoring.

Materials and Methods

Study Design

The survey used in this study was developed and distributed by researchers from The University of California, Irvine (UCI). The use of an anonymous survey for data collection, which did not collect any Protected Health Information, or any other information which may be used to identify respondents, categorized this study as exempt from UCI Institutional Review Board (IRB) review (UCI IRB policy #12; "exempt self-determination"). Furthermore, the survey was distributed, and data collection, through a public URL link provided to American psychiatric societies for advertisement in associated research newsletters and listservs. As no direct contact was made between researchers and respondents, no informed consent was sought for or required (UCI IRB policy #12). This research study followed the guidelines outlined in the Declaration of Helsinki.

The anonymous, online survey was developed based on the structure and content of currently available nation-wide survey studies on lithium prescription, conducted in India and Spain.[7,8] Input was also sought from co-author colleagues, including two practicing psychiatrists. Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at The University of California, Irvine.[26,27] REDCap is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

Questionnaire

The purpose of the anonymous survey was to investigate the perspectives of American psychiatrists and psychiatric mental health nurses on lithium treatment, point-of-care devices, and the potential use of at-home saliva collection for lithium monitoring. The survey contained 24 multiple-choice, likert-scale and single-response questions, and a final text box where participants may freely input any concerns or comments regarding the study or field. Questions regarding sample characteristics (total questions: 7) covered participant demographic data (age, gender, US state), place, type and years of work, and pay/insurance model. These were followed with questions regarding the participant's experience in prescribing lithium and current lithium-treated cohort, including whether they used the

Lithiumeter visual guide for lithium decision-making (total questions: 6), and their perspectives on the incorporation of point-of-care devices and at-home saliva collection for lithium monitoring (total questions: 11) (Figure S1). A question pertaining to the use of the *Lithiumeter* guide was included due to its developed purpose as a visual guide to combat clinical misconceptions surrounding lithium use, which may influence the prescription of lithium medications.[28] Request emails were distributed to a total of 82 American psychiatric societies (Table S1), and participant responses were obtained, between October 2021 and February 2022. Data were analyzed using descriptive statistics, which were obtained directly from REDCap, or exported into Excel. All sample and percentage values reported in this paper refer to the number and percentage of psychiatrist and psychiatric mental health nurse respondents who indicated the associated response, except where clearly defined otherwise.

Results

Respondent Characteristics

A total of 65 responses were obtained from 21 US states. The majority of respondents were psychiatrists (96.9%), female (53.8%), over 65 (38.5%), and/or had practiced for 30 years or more (46.2%) (Table 1). We queried respondents on how many of their patients lived more than 1 hour commute away, as these patients would likely benefit from at home saliva

Table 1 Respondent Characteristics

Characteristic		n (%)
US state	California	10 (15.4)
	Connecticut	3 (4.6)
	District of Columbia	3 (4.6)
	Georgia	1 (1.5)
	Hawaii	2 (3.1)
	Illinois	2 (3.1)
	Iowa	1 (1.5)
	Kentucky	1 (1.5)
	Maryland	9 (13.8)
	Michigan	2 (3.1)
	Missouri	1 (1.5)
	New York	5 (7.7)
	North Carolina	3 (4.6)
	North Dakota	1 (1.5)
	Ohio	3 (4.6)
	Pennsylvania	2 (3.1)
	Tennessee	1 (1.6)
	Texas	4 (6.2)
	Virginia	5 (7.7)
	Washington	1 (1.5)
	Wisconsin	5 (7.7)
Age bracket [years]	25–34	10 (15.4)
	35–44	11 (16.9)
	45–54	8 (12.3)
	55–65	11 (16.9)
	Over 65	25 (38.5)
Gender	Male	30 (46.2)
	Female	35 (53.8)
	Non-binary	0 (0.0)
Profession	Psychiatrist	63 (96.9)
	Psychiatric-mental health nurse	2 (3.1)

(*Continued*)

Table 1 (Continued).

Characteristic		n (%)
Institute type	Private practice	21 (32.3)
	General hospital	12 (18.5)
	Psychiatric hospital	10 (15.4)
	University medical center	17 (26.2)
	Community agency	15 (23.1)
	Court and/or prison	2 (3.1)
	Emergency room	4 (6.2)
	Other[a]	6 (9.2)
Years of work	Less than 5	9 (13.8)
	5–9	8 (12.3)
	10–14	4 (6.2)
	15–19	6 (9.2)
	20–24	4 (6.2)
	25–29	4 (6.2)
	30 or more	30 (46.2)
Reimbursement/pay model	Private insurance	28 (43.8)
	Public insurance	27 (42.2)
	Health Maintenance Organization (HMO)	18 (28.1)
	Preferred Provider Organization (PPO)	19 (29.7)
	Government/Community program	37 (57.8)
	Cash pay	21 (32.8)
Conditions respondent prescribes lithium for	Bipolar Disorder	63 (100.0)
	Schizophrenia	7 (11.1)
	Schizoaffective Disorder	40 (63.5)
	Autism	3, 5.0
	Depression	37 (58.7)
	Anxiety	0 (0.0)
	Suicidal or self-injurious behavior	37 (58.7)
	Other[b]	4 (6.3)
Age brackets respondent prescribes lithium for	10 and under	2 (3.2)
	11–20	24 (38.0)
	21–30	55 (87.3)
	31–40	59 (93.7)
	41–50	53 (84.1)
	51–60	49 (77.8)
	Over 60	34 (54.0)
Patients living 1 hour or more commute from clinic [% of respondent's patients] (median, range)		20, 0–80
Patients on lithium [n of respondent's patients] (median, range)		5, 0–100

Notes: [a]Other institutes were: 5x military/veterans-based, 1x student health center. [b]Other conditions were: 2x agitation, 2x intermittent explosive disorder.

collection, or self-administered point-of-care devices. Unfortunately, responses were received as either percentages or absolute numbers. Considering only responses that included a clear percentage (69.2%), respondents reported a median 20% of their patients lived more than 1 hour commute away (range = 0–80%).

Lithium-Prescribed Patient Characteristics

At the time of survey completion, respondents reported having a median of 5 patients currently on lithium medication (range 0–100). Sixty-three (96.9%) respondents prescribed lithium to patients; of these, all prescribed it for treatment of bipolar disorder (n = 63; 100%), followed by schizoaffective disorder (n = 40; 63.5%), depression (n = 37; 58.7%), and suicidal or self-injurious behavior (n = 37; 58.7%) (Table 1). Of the respondents who prescribed lithium, two (3.2%) prescribed lithium to patients 10 years of age and under, 24 (38.0%) prescribed lithium to patients ages 11–20, and the majority prescribed to patients aged between 21 and 50 (n = 53–59, 84.2–93.7%), followed by age 51 and above (n = 34–49, 54.0–77.8%) (Table 1).

Protocol for Prescribing Lithium

The determination of an appropriate maintenance level lithium dose was decided by the ongoing remission of symptoms for 50 respondents (76.9%), and the measurement of blood lithium levels being within range for 53 respondents (81.5%). Four respondents outlined additional means of determining an appropriate maintenance level lithium dose, such as patient history of wellbeing at a previous blood lithium level, remission at the lowest blood lithium level, the presence of dyscoordination as a sign of toxicity, and tolerability (Table 2). The majority of respondents (n = 46; 70.8%) were not familiar with the *Lithiumeter* visual guide for determining lithium levels;[15,28] of the remaining respondents, 11 (16.9%) did not use the *Lithiumeter* guide, and 8

Table 2 Protocol and Obstacles for Lithium Monitoring

Query	n (%)	
Means of determining an appropriate maintenance level lithium dose		
Ongoing remission of symptoms	50 (76.9)	
Blood lithium level within range	53 (81.5)	
Other[a]	5 (7.7)	
Reference to the *Lithiumeter* clinical guidelines when prescribing lithium		
Yes	8 (12.3)	
No	11 (16.9)	
I do not know what that is	46 (70.8)	
Desired frequency for monitoring lithium levels in maintenance phase		
	Current outpatient	**New, stabilized patient**
Multiple times a month	1 (1.5)	8 (12.3)
Every month	2 (3.1)	26 (40.0)
Every 3 months	18 (27.7)	16 (24.6)
Every 6 months	28 (43.1)	6 (9.2)
Every year	6 (9.2)	0 (0.0)
Based on feasibility	7 (10.8)	8 (12.3)
Respondent does not treat these patients	3 (4.6)	1 (1.5)
Obstacles encountered with regards to lithium monitoring		
Adverse drug effects	40 (61.5)	
Difficulty in dosing	5 (7.7)	
Lack of experience or training	1 (1.5)	
Patient's clinical comorbidities	25 (38.5)	
Patient medication non-compliance	20 (30.8)	
Patient's low adherence to monitoring of drug levels and serum chemistry	22 (33.8)	
Slow action of lithium	3 (4.6)	
Patient symptoms better addressed by another medication	9 (13.8)	
Need for monitoring	34 (52.3)	
Other[b]	6 (9.2)	

Notes: [a]Other responses were: tolerability; remission at lowest blood level for patient; clinical signs and symptoms; history of wellbeing at a previous blood level; dyscoordination as a sign of toxicity. [b]Other responses were: stigma or patient reluctance (x4), age (x1), and not ideal for military population (x1).

(12.3%) did. The majority of respondents preferred to monitor maintenance lithium levels every 6 months in outpatients (n = 28; 43.1%), and every month in new, stabilized patients (n = 26; 40.0%). For the majority of respondents, obstacles to lithium prescription included adverse drug effects (n = 40; 61.5%), and the need to monitor levels (n = 34; 52.3%) (Table 2).

Perspectives on Point-of-Care Devices

The majority of respondents (46.2%) believed that a point-of-care device would be very useful, whereas only two respondents (3.1%) believed that the device would not be useful (Table 3). Most respondents indicated that a point-of-care device would be useful when modifying a lithium dose (87.3%), followed by "monitoring for medication adherence" (79.4%) and "in patients who do not tolerate venipuncture" (76.2%) (Table 3). Respondents who selected "other" as an option (7.9%), provided instances such as "just being able to get a lab done", when patients are not adherent with lab requests, any time a patient is not hospitalized, and during a pregnancy (Table 3).

Table 3 Respondent Perspectives on Point-of-Care Devices and Saliva Lithium Monitoring

Query	n (%)
Would a point-of-care device be useful?	
Not useful	2 (3.1)
Somewhat useful	13 (20.0)
Quite useful	18 (27.7)
Very useful	30 (46.2)
Undecided	2 (3.1)
When do you think a point-of-care device be useful?	
When changing the dose	55 (87.3)
Monitoring for medication adherence	50 (79.4)
Monitoring side effects	36 (57.1)
In patients who do not tolerate venipuncture	48 (76.2)
Other[a]	5 (7.9)
Would you find it useful if lithium levels could be effectively monitored in saliva instead of blood?	
Yes	64 (98.5)
No	1 (1.5)
If saliva samples could be collected at home and dropped off or mailed in for lithium monitoring, would you find this useful for your patients and hence your clinical decision making?	
Not at all	3 (4.6)
Somewhat useful	21 (32.3)
Quite useful	13 (20.0)
Very useful	27 (41.5)
Undecided	1 (1.5)
When do you think at-home saliva collection would be useful?	
Changing the dose	46 (75.4)
Monitoring for medication adherence	40 (65.6)
Monitoring side effects	36 (59.0)
In patients who do not tolerate venipuncture	51 (83.6)
For patients with long commutes or to avoid coming into the clinic	49 (80.3)
Other[b]	5 (8.2)

(*Continued*)

Table 3 (Continued).

Query	n (%)
Would you be willing to provide patients with at-home saliva collection kits to drop off or mail in samples for lithium analysis?	
Yes	61 (93.8)
No	4 (6.2)
How compliant do you think patients would be with at-home saliva collection?	
Not at all	0 (0.0)
Somewhat compliant	23 (35.4)
Quite compliant	27 (41.5)
Very compliant	11 (16.9)
Undecided	4 (6.2)

Notes: [a]Other responses were: patient not adherent with lab requests; just being able to get a lab done; any time a patient is not hospitalized; during pregnancy. [b]Other responses were: when patients are making changes that could change their levels; just being able to get a lab done; for reliable patients; during pregnancy.

The preferred means of billing for a point-of-care test was as an office visit (Table S2). For respondents who indicated that they would use a cash payment model (Table 1) and bill a point-of-care test as an office visit (Table S2), the majority indicated that they would charge $25 or less per test (n = 7; 46.7%), with all relevant respondents indicating a value that was $50 or less per test (Table S2).

Monitoring of Lithium in Saliva

Sixty-four respondents (98.5%) stated that they would find it useful if lithium levels could effectively be monitored in saliva instead of blood. When asked whether they would find it useful if patients could collect saliva samples at home and mail in or drop off the samples for lithium monitoring, the majority (41.5%) responded on a likert-like scale that they would find it "very useful". The majority (83.6%) of respondents reported that saliva lithium monitoring would be useful in patients who do not tolerate venipuncture, followed by patients who have a long or inconvenient commute and when changing the dose (80.3%) (Table 3). Finally, 93.8% of respondents indicated that they would be willing to provide patients with at-home saliva collection kits to take home, and 93.8% indicated that they believed their patients would be at least somewhat compliant with at-home saliva collection (Table 3).

Respondent Comments and/or Concerns

Respondents were provided the opportunity to express any additional comments or concerns. Two respondents commented that they treated high-functioning patient populations who would benefit from saliva lithium monitoring or a point-of-care device, however one respondent noted that blood draws would still be necessary for the measurement of other markers such as thyroid-stimulating hormone, blood urea nitrogen, and creatinine. Other respondents raised concerns regarding the time-lag between at-home saliva collection, and reception by a laboratory, however noted that a time delay currently exists with serum lithium monitoring as well. Two respondents stated that they would prefer to obtain and monitor saliva lithium levels in an office, rather than via at-home collection, whereas another stated that patients with good adherence would benefit from at home monitoring if it was properly structured. Overall, respondents' main concern regarded the validity, including time sensitivity, of saliva collection and lithium monitoring, followed by the cost (see Table S3 for all feedback).

Discussion

In this study, we found that overall, psychiatrists in the United States were open to the potential use of saliva, and point-of-care devices, for lithium monitoring. The majority of respondents indicated that the need for monitoring, and the

potential for adverse side effects, were obstacles they had encountered regarding the prescription of lithium, mirroring reports from India and Spain.[7,8] Interestingly, the need for monitoring, and the potential for side effects, were not perceived as barriers by psychiatrists in Saskatchewan, Canada, suggesting nation-specific perspectives on lithium monitoring.[29] Our survey results suggest that saliva lithium monitoring would be most useful for the monitoring of new, stabilized lithium-users, as the majority of respondents indicated that they would prefer to monitor lithium levels in these patients every month. For outpatients, the majority of respondents indicated that they would prefer to monitor lithium levels every 6 months. These findings can be compared to that of a previous worldwide survey study, which found that the majority of psychiatrists preferred to monitor maintenance lithium levels 1–3 times per year, followed by 4 or more times per year.[30] Despite these findings, which are in line with the International Society for Bipolar Disorders guidelines for maintenance level lithium monitoring,[5] it is likely that patients are not attending the recommended number of pathology visits. While we did not query patient attendance of scheduled appointments, 33.8% of respondents reported that a "patient's low adherence to monitoring of drug levels and serum chemistry" was an obstacle for lithium monitoring. Similarly, a study conducted in Sao Paulo, Brazil, found that none of their 36 study participants attended the recommended minimum of two blood tests per year,[31] and a large retrospective study in the Netherlands found that only 46% of patients were monitored every 6 months.[32]

Notably, our survey respondents reported a median 20% of total patients who lived an hour or more commute away, and 10.9% and 12.5% of survey respondents indicated that they preferred to monitor lithium levels "based on feasibility" in current outpatients, and new, stabilized inpatients, respectively. Therefore, it is possible that despite psychiatrists preferring patients to attend the recommended 2–4 serum lithium monitoring appointments per year, many patients may find it difficult to attend these in-office or pathology-based appointments, either due to a long commute, or other factors not queried, such as personal circumstances or symptom presentation.[33] Indeed, the majority of our survey respondents indicated that at-home saliva collection would be useful for patients who either do not tolerate venipuncture (83.6%) or have long commutes (80.3%). In addition, the current COVID-19 pandemic presents a third scenario where at-home collection of samples would be advantageous: current recommendations suggest that patients monitor symptoms at-home during lockdown or restriction periods, and attend a consultation when possible to measure lithium levels.[34] The measurement of lithium levels, and other blood markers, may therefore be a limiting factor in the otherwise telehealth treatment of patients, and in some cases may be the sole reason why a patient would need to attend a clinic. Furthermore, the *Lithiumeter* clinical guidelines recommend adjusting the maintenance lithium dose depending on the presentation of symptoms (mania, depression, or maintenance);[28] at-home sample collection would allow clinicians to monitor lithium levels at the time of symptom presentation, rather than when circumstances permit the patient to attend a pathology clinic. At-home collection would also allow patients to collect samples closer to the 12-hour post-dose time-point that is currently used to determine serum lithium levels for dose adjustment; a requirement that one respondent noted their patients rarely get right. Of note, for the sake of survey simplicity, we queried psychiatrists on the percentage of total patients with a long commute, rather than the percentage of lithium-prescribed patients; however, with additional research, saliva monitoring of therapeutic drugs may be expanded beyond that of lithium and thus the findings of this study, with regard to saliva monitoring, may be applicable to remote patients who are and are not currently on lithium medication.

While most respondents (93.8%) would be willing to provide patients with an at-home saliva collection kit to drop-off or mail-in samples for analysis, a number of respondents expressed concerns regarding the at-home collection model. One limitation to the implementation of saliva lithium monitoring, as noted by one respondent, is the concurrent need for a blood draw to measure other biological markers, such thyroid-stimulating hormone, blood urea nitrogen, and creatinine. Previous studies by Nederlof et al found that prescribers of lithium reported that markers of renal function, thyroid function, and electrolytes are most often measured 2–3 times per year in patients on maintenance lithium treatment,[30] however creatine and thyroid-stimulating hormone are often measured fewer times than guidelines recommend.[32] In line with the drawback of no at-home testing for other markers, two respondents in our study indicated a preference for in-office or point-of-care lithium monitoring, over at-home collection and mail-in of saliva samples. Overall, respondents' main concern was the validity of saliva lithium monitoring, and potential time delay associated with both saliva and serum lithium monitoring. Through another study in progress, which utilizes at-home collection and mail-in of saliva

samples from participants with bipolar disorder, we have observed a sample return rate of approximately 85% and have confirmed that saliva lithium levels are not affected by up to 4 days at room temperature, as may occur with the mail-in of samples (unpublished; data not shown). Anecdotally, and in line with the respondents' concern, the greatest obstacle faced in this in-progress study has been the timeliness of saliva collection and mail-in – a factor which may vary if saliva collection were for clinical, rather than research, purposes.

Regarding the validity of saliva lithium monitoring, we have previously shown that saliva lithium levels are highly correlated with serum lithium levels, which is consistent with other, older studies and methodologies,[9,35–38] and that this correlation may be improved through consideration and incorporation of daily lithium dose, smoking status, and diabetes status.[6] Further research into potentially confounding factors in the prediction of serum lithium levels from saliva would improve the validity of saliva lithium monitoring. In our earlier publication, we also found that the relationship between saliva and serum lithium levels was less variable for participants under 55 years of age.[6] The majority of psychiatrist and psychiatric mental-health nurse respondents in the current study (84.2–93.7%) reported prescribing lithium to patients between 21 and 50 years of age, which suggests that their patient population would be appropriate for saliva lithium monitoring from this perspective. Moreover, 93.8% of respondents indicated that a point-of-care device would be at least somewhat useful in monitoring lithium levels and, while most agreed with all uses presented (when: changing the dose; monitoring for medication adherence; monitoring side effects, and in patients who do not tolerate venipuncture), other instances included: just being able to get a lab done; any time a patient is not hospitalized; and during pregnancy. The use of an in-office point-of-care device, at a respondent-suggested cost of $50 or less to the patient, would reduce perceived issues with time-delay, either from time of appointment to sample collection, or sample collection to analysis, as well as the need for patients to attend a pathology service. While this may not reduce the need for patients to travel to a hospital or clinic, as at-home collection would do, it would likely reduce the duration of a clinical appointment – by replacing a pathology appointment with an in-office test- and, if saliva-based, the need for venipuncture or a fingerprick. Patient attendance at scheduled clinic appointments may alternatively be improved through more in depth patient education regarding the need to monitor lithium levels.[39] For example, in the UK, increased education on the side effects of lithium, the risk factors for toxicity, and the signs and symptoms of toxicity, coincided with an increase in the frequency of maintenance serum lithium level testing.[40] In our study, two respondents commented on the stigma regarding lithium treatment, both in the public and health-care community. Patient education may also be limited by low psychiatrist education on lithium prophylaxis: while only one respondent in our study indicated "lack of experience or training" as a barrier to prescribing lithium, we acknowledge that this is a subjective measure. In addition, 70.8% of respondents were not familiar with the *Lithiumeter* visual guide for determining optimal plasma lithium levels.[28] While familiarity of the *Lithiumeter* visual guide is not itself an indication of psychiatrist education or awareness, the guide was developed to combat misconceptions surrounding lithium use, and so this lack of familiarity may suggest that clinical practices do not see the need and/or have not made attempts to improve clinician awareness. We acknowledge that our findings are limited by a moderate sample size, and that the perspectives of psychiatrists in the U.S., where lithium is underutilized, may not be generalized globally.[41] We also acknowledge that, while our survey was distributed to 82 American psychiatric societies and responses were received from 21 states, our response rate was overall low (on average less than 1 response per society) and predominated by older psychiatrists; therefore, our findings may not be representative of all American prescribers of lithium.

Conclusion

Overall, our study suggests that the implementation of both saliva lithium monitoring, and at-home sample collection, may be too novel and preliminary for current clinical practice; however, the incorporation of a point-of-care lithium monitoring device, particularly for saliva, into offices may reduce the need for pathology appointments, and increase medication adherence. Following the development and analysis of this study, we, in collaboration with others, have begun research into at-home collection and mail-in of saliva samples, the diurnal characteristics of saliva lithium levels, and the development of a saliva-based lithium point-of-care device.

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Disclosure

The authors report no conflicts of interest in this work.

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