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Evaluation of thyroid function monitoring in people treated with lithium: Advice based on real-world data

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Abstract

Introduction: Blood test monitoring is essential for the management of lithium treatment and National Institute for Health and Care Excellence guidance recommends 6-monthly serum testing of thyroid function. We examined conformity to these guidelines and the impact of monitoring outside these intervals.

Methods: We extracted serum lithium and thyroid hormone results at one centre between January 2009 and December 2020. We identified 266 patients who started lithium during this period with no history of thyroid abnormality within the previous 2 years and were at risk of developing thyroid abnormalities. We examined the interval between tests, time between onset of lithium testing and first thyroid-stimulating hormone (TSH) outside the laboratory reference range and assessed impact of testing outside recommended 6-monthly intervals.

Results: The most common testing frequency was 3 months (±1 month), accounting for 17.3% of test intervals. Kaplan-Meier analysis showed that most thyroid dysfunction manifests within 3 years (proportion with abnormal TSH at 3 years = 91.4%, 19.9% of total patients). In the first 3 months after commencing lithium therapy, eight patients developed subclinical hypothyroidism and had clinical follow-up data available. Of these, half spontaneously normalized without clinical intervention. In the remaining patients, thyroxine replacement was only initiated after multiple occasions of subclinical hypothyroidism (median = 2 years after initiating lithium, range: 6 months to 3 years).

Conclusion: The peak interval at 3 months suggests that thyroid function is frequently checked at the same time as serum lithium, indicating too frequent testing. Our data support the recommended 6-monthly testing interval and highlight poor adherence to it.

KEYWORDS
interval, lithium, monitoring, thyroid

1 | INTRODUCTION

Lithium is a common pharmacological intervention for the treatment of bipolar and mania or hypomania and is advocated by UK and international clinical practice guidelines.[1–4] Its use has been shown to decrease the risk of suicide attempts and halve mortality rates.[5]

Despite the efficacy of lithium, it is associated with a range of adverse effects including reduced glomerular filtration rate (GFR), hyperparathyroidism and thyroid dysfunction.[6] Thyroid abnormalities can include both hyper and hypothyroidism, with the latter being more common.[7,8] Certain risk factors have been shown to increase the likelihood of developing hypothyroidism, including females >60 years old, elevated serum lithium concentrations and duration of lithium exposure.[8] There are several proposed mechanisms for lithium-induced thyroid hormone abnormalities including reduced synthesis of thyroid hormones, altered iodine uptake, structural thyroglobulin alterations, reduced hepatic deiodination and decreased clearance of free thyroxine.[9] These aberrations are slightly mitigated by the fact that they may be reversible after discontinuation of the drug meaning life-long thyroxine replacement may not be required.[10]

In relation to these potentially adverse effects, blood test monitoring is an essential component of the management of lithium treatment. The UK National Institute for Health and Care Excellence (NICE) recommends 3-monthly monitoring of serum lithium levels for most patients and 6-monthly monitoring of thyroid function, estimated GFR and calcium to identify early end-organ abnormalities.[1] A recent study has demonstrated that adherence to the guidance on serum lithium levels is variable; in patients with serum lithium results within the therapeutic range only 25% of test requests for serum lithium levels occurred at 3-monthly intervals.[11] This is important as regular monitoring of serum lithium levels decreases psychiatric hospital admissions.[12] While there is clearly a case for ongoing monitoring, the evidence base underpinning these suggested testing frequencies is less clear, suggesting that it is based more on expert opinion than formal studies. Indeed, a recent study has additionally suggested that the NICE recommendation of 3-monthly lithium monitoring could be extended to 6-monthly intervals for patients who have 12 months of lithium results within the 0.40–0.79 mmol/L range, irrespective of age.[13]

The adherence to the recommended 6-monthly monitoring of thyroid function remains unknown. Biochemical monitoring of thyroid function is particularly important as the symptoms of hypothyroidism and bipolar disorder may overlap making it difficult to identify hypothyroidism based on clinical presentation.[6] Poor adherence to national guidance on testing intervals for biochemical monitoring is common and has been shown for a variety of similar situations where long-term monitoring is required, including assessment of glycaemic control in people with diabetes mellitus,[14] post-partum screening in women with gestational diabetes[15] and monitoring of thyroid function in people with hypothyroidism on thyroxine replacement therapy.[16] The COVID-19 pandemic has provided additional challenges for conditions which require regular blood test monitoring; this has been demonstrated for HbA1c where an estimated 1.41 million diabetes monitoring tests have been delayed or missed across the UK.[17]

In this study, we investigate the monitoring frequency of thyroid function testing in people on lithium treatment and explore its clinical impact.

2 | MATERIALS AND METHODS

2.1 | Data collection

The cohort included all patients (n = 582) who had serum lithium concentration measured between 1 January 2012 and 31 December 2018 at the University Hospitals of North Midlands NHS Trust (UHNM) Department of Clinical Biochemistry, as described previously.[11] All thyroid-stimulating hormone (TSH) and free T4 (fT4) tests requested from this patient cohort for the period 1 January 2009 to 31 December 2020 were then extracted from the Laboratory Information Management System (LIMS; 10,636 requests; Figure 1). Reference ranges were as follows: TSH before 1 November 2014 was 0.3–5 mIU/L, TSH after 1 November 2014 was 0.1–5 mIU/L, fT4 before 12 September 2018 was 8–19 pmol/L and fT4 after 12 September 2018 was 12–23 pmol/L. The study period for each patient began from the date of their first lithium test and continued until 31 December 2020. Patients were identified as developing subclinical hypothyroidism (TSH above reference range, fT4 within reference range), overt hypothyroidism (TSH above reference range, fT4 below reference range), subclinical hyperthyroidism (TSH below reference range, fT4 within reference range) or overt hyperthyroidism (TSH below reference range, fT4 above reference range) upon the first abnormal result.

In order to exclude those with a possible pre-existing thyroid disorder, individuals were removed from the data set if they had an abnormal TSH during the 2 years before the first lithium request (assumed start date of lithium treatment; Figure 1). Individuals were additionally removed if there were less than 2 years of run-in data before the first lithium request, as it could not be determined whether the patient had a pre-existing thyroid disorder. Results were compared to the reference range in place at the time of the request. Thyroid results were removed from the data set for patients before they commenced lithium therapy and after the first abnormal TSH result.

As this study is an audit of practice against guidelines provided by NICE, it did not require ethical committee approval. All data extracted from the LIMS and used in the statistical analysis were anonymized.

2.2 | Assessment of clinical outcomes

For patients with an abnormal TSH within the first 3 or 6 months of commencing lithium treatment, the clinical details accompanying thyroid hormone and antibody requests until they commenced

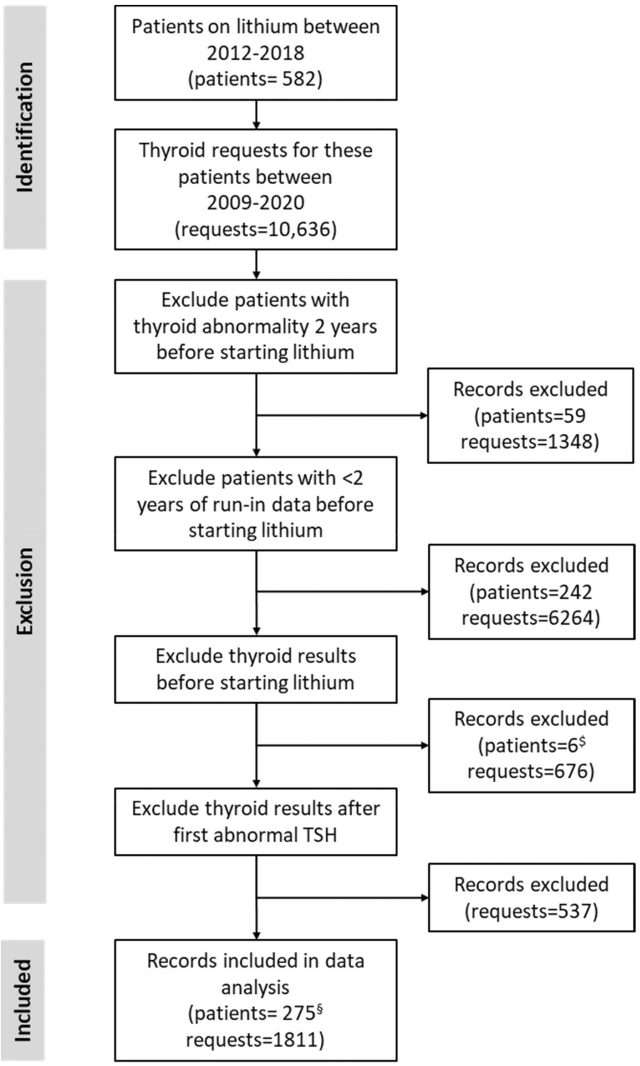

FIGURE 1 Study inclusion and exclusion criteria. *six patients were excluded as no thyroid results were available for the study period after the patient was initiated on lithium. †for Kaplan-Meier analysis a further nine patients were excluded (seven were lost to follow-up after the initial thyroid result and two had an abnormal TSH accompanying their first lithium)

thyroxine replacement or the end of the study period were obtained from the LIMS. The following information was documented: date of thyroid request, type of thyroid disorder indicated by results, thyroxine treatment and anti-thyroid antibody (thyroid peroxidase and TSH receptor antibody) results. Four patients were excluded from the clinical assessment: one was deceased 1 month after commencing lithium, and three had incomplete records. At UHNM, for all requests for thyroid function, the user is prompted to state whether the patient is on thyroxine. Clinical outcome data were charted in a timeline for each patient using Microsoft Excel 2010.

2.3 | Statistical analysis

Calculation of the interval (in weeks) between TSH requests for each patient was performed using Microsoft Excel 2010. The number of requests associated with each interval was then determined. For Kaplan-Meier analysis, patients were deemed at risk from the date of their first lithium request and were removed from the surviving fraction after either obtaining a TSH value outside the reference range or their last requested TSH. Kaplan-Meier curves and Mann-Whitney *U* tests were generated using Stata (version 14).

3 | RESULTS

3.1 | Patient demographics

The final data set contained 1811 requests from 275 patients (Figure 1). The average age for the cohort was 52.4 years and 57% were females (Table 1). During the study period, a total of 58 patients developed an abnormal TSH; 46 demonstrated subclinical hypothyroidism, six subclinical hyperthyroidism, three overt hypothyroidism and three overt hyperthyroidism. Of the patients who developed subclinical hypothyroidism, 32 (70%) were female and 6 (13%) progressed to overt hypothyroidism during the study period.

TABLE 1 Patient characteristics by thyroid disorder type

Disorder type	No. of patients (%)	Female (%)	Median age, years (range)	Median TSH requests per patient (range)	No. progressed to overt disorder (%)	Median time till abnormality, weeks (range)
Overall	275 (100%)	157 (57%)	52 (19–117)	5.0 (1–25)	–	–
No abnormality	217 (79%)	120 (55%)	52 (19–117)	6.0 (1–25)	–	–
Subclinical hypothyroidism	46 (17%)	32 (70%)	60 (21–92)	2.0 (1–21)	6 (13%)	43 (0–425)
Subclinical hyperthyroidism	6 (2%)	2 (33%)	41 (20–52)	3.5 (2–8)	1 (17%)	41 (17–173)
Overt hypothyroidism	3 (1%)	2 (66%)	47 (32–56)	3.0 (2–6)	–	105 (97–174)
Overt hyperthyroidism	3 (1%)	1 (33%)	45 (38–78)	2.0 (1–5)	–	75 (28–112)

Note: Disorder type refers to the initial abnormal result. Median time till abnormality indicates amount of time between first lithium request and either first abnormal TSH or last requested TSH.

3.2 | Lithium testing interval

The adequacy of thyroid monitoring for patients on lithium was determined by measuring the interval between TSH requests for each patient. The number of requests associated with each testing interval is shown in Figure 2. The modal testing interval was 13 weeks, and 265 requests (17.3% of the total) were made at intervals between 11 and 15 weeks. A secondary peak at an interval of approximately 26 weeks was also observed; the number of requests with an interval between 24 and 28 weeks was 147 (9.6% of the total). The data set includes 150 specimens (9.8% of the total) on 89 patients taken during the post-COVID-19 impact period (after 23 March 2020[17]). The median test request interval in this group was 21.5 weeks (interquartile range 12–36 weeks) compared with 17 weeks (interquartile range 9–32 weeks) in those collected during the pre-COVID-19 impact period ($p = 0.025$).

3.3 | Identification of patients who developed an abnormal TSH within the first 3 months of initiating lithium

To determine whether the testing interval led to early detection of thyroid disorder, the proportion of patients who developed an abnormal TSH within the first 13 weeks of initiating lithium therapy was examined in further detail. From the cohort, 266 patients remained at risk of developing a thyroid disorder at the time of their first lithium result (seven patients had no further follow-up following the initial request for lithium and TSH, and two had an abnormal TSH accompanying their first lithium).

The proportion of individuals who developed thyroid abnormality was 19.9% (53/266) after 153 weeks of lithium therapy (Figure 3). These represent 91.4% (53/58) of all patients who eventually developed an abnormality. The median follow-up period was 140 weeks between the first lithium request and either first abnormal TSH or last requested TSH. At 13 weeks (dark grey vertical line), corresponding to the most common monitoring interval, 10 people had developed an abnormal TSH. The annual incidence rate for thyroid abnormalities at the end of years 1, 2 and 3 was 12.8%, 6.4% and 8.2% respectively.

3.4 | Relation between clinical outcomes and earlier testing

It was next investigated whether early detection of thyroid abnormalities led to improved clinical outcomes. For this, the results and accompanying clinical details for thyroid hormone and antibody requests were reviewed. Of the 10 patients who developed an abnormal TSH within 3 months of starting lithium, one was deceased a month after their first lithium sample and a second had a 5-year hiatus from lithium requests. No clinical outcome data were evaluated for these patients. In the remaining eight patients, the first TSH abnormality was associated with subclinical hypothyroidism and there were no occasions of overt thyroid disorder by the end of the follow-up period (Figure 4). Patients 1–4 were started on thyroxine approximately 6, 18 months, 2 and 3 years after starting lithium respectively.

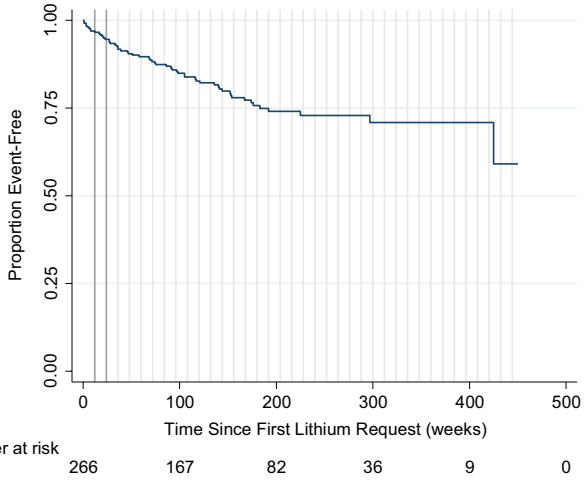

FIGURE 3 Kaplan-Meier analysis of thyroid disorder-free survival. Dark grey vertical lines at 13 and 26 weeks demonstrate where 10 and 6 patients, respectively, with an abnormal TSH were identified

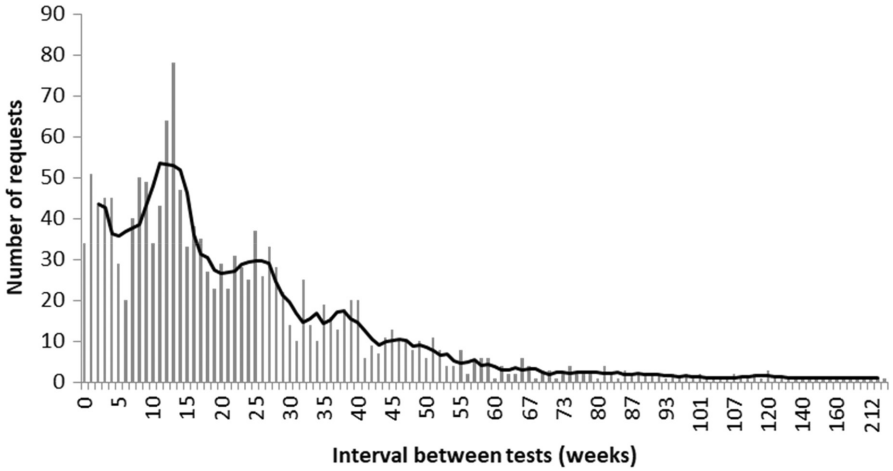

FIGURE 2 Interval between TSH requests for patients on lithium. The line shows centred moving average over a 5-week period

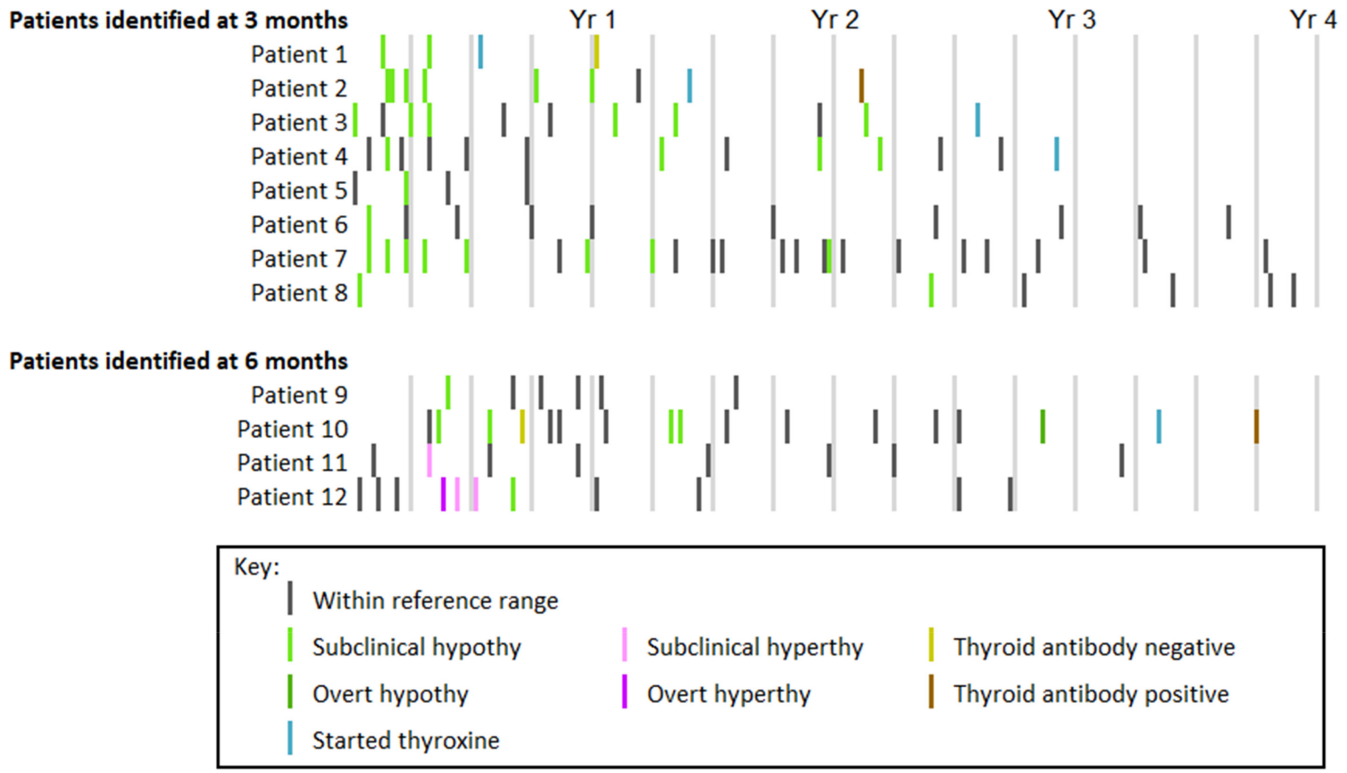

FIGURE 4 Timeline of thyroid disorder-related events in patients with an abnormal TSH at 3 and 6 months after starting lithium. Vertical grey lines represent 13-week intervals. The chart shows events occurring up to 4 years after initiating lithium therapy

In all these cases, there were multiple occasions of subclinical hypothyroidism before the initiation of thyroxine replacement therapy. The average peak pre-treatment TSH result was 9.2 mIU/L for patients who later received thyroxine and 7.0 mIU/L for those who did not (Table 2). Three out of the five patients who were treated with thyroxine had a maximum TSH value below 10 mIU/L. Patients 1 and 2 had antibody investigations performed, in both cases, thyroperoxidase (TPO) antibodies were requested after the initiation of thyroxine. Patient 1 was TPO negative and patient 2 was positive. In half of the patients (patients 5–8), the thyroid abnormality identified within the first 3 months normalized without intervention and for patients 5 and 6, the abnormality noted within the first 3 months of commencing lithium was the only abnormality identified during the study period. In all patients except patient 8, the abnormal result identified within 3 months of starting lithium was followed by a short interval before the next request.

A further six patients were identified as having an abnormal TSH between 3 and 6 months after starting lithium. Of these, two had incomplete records which did not provide sufficient information for follow-up. The remaining patients were equally divided between hypo and hyperthyroidism (Figure 4). The initial abnormality for patient 9 normalized without treatment, despite having a TSH of 53.5 mIU/L (fT4 = 9 pmol/L). For patient 10, the initial abnormal result was repeated after approximately 3 months and shortly after TPO and TSH receptor antibodies were both found to be negative. The patient's TSH value normalized but was followed by a second occasion of subclinical hypothyroidism 15 months later which again normalized. Eventually, the patient had an occasion of overt hypothyroidism and was started on thyroxine. After this, TPO antibody levels were re-checked and were found to be TPO positive.

Two patients developed hyperthyroidism within the first 6 months of lithium treatment. One had a single occasion of subclinical hyperthyroidism which spontaneously normalized; for this sample, TSH was 0.01 mIU/L and fT4 was 18 pmol/L. All subsequent results for this patient were normal and no antibody investigations were performed. The final patient had an initial occasion of overt hypothyroidism within the first 6 months. This was repeated three times over the following 15 weeks, with the third repeat demonstrating subclinical hypothyroidism. These normalized without treatment over the first 12 months and all subsequent results were within the reference range. No antibody investigations were performed.

4 | DISCUSSION

This study represents the first time that adherence to the NICE recommendation that thyroid function is monitored at 6-monthly intervals in people on lithium has been investigated.[1] We have demonstrated these tests are over-requested, which may lead to overdiagnosis of transient thyroid abnormalities which do not require treatment.

TABLE 2 Thyroid results accompanying patients who developed an abnormal TSH within 3 and 6 months after starting lithium

Patient number	Age	Gender	TSH range (mIU/L)	Antibody result	Weeks between Li initiation and antibody result	Weeks between Li initiation and thyroxine replacement	Weeks between initial abnormal TSH and thyroxine replacement
Patients identified within 3 months of commencing lithium							
1	69	M	5.75–7.03[a]	TPO negative	53	28	11
2	36	F	5.73–15.85[a]	TPO positive	110	73	65
3	65	F	1.81–7.96[a]	–	–	135	134
4	64	M	1.68–5.95[a]	–	–	152	144
5	36	F	2.10–7.10	–	–	–	–
6	41	F	1.53–5.85	–	–	–	–
7	27	M	0.54–8.87	–	–	–	–
8	68	M	0.16–6.21	–	–	–	–
Patients identified within 6 months of commencing lithium							
9	39	F	0.94–53.50	–	–	–	–
10	25	F	0.73–74.37[a]	TPO and TRAb negative TPO positive	37 195	174	155
11	36	M	0.01–3.37[b]	–	–	–	–
12	20	F	0.01–7.01[b]	–	–	–	–

Note: Age refers to the age at first lithium request.

Abbreviations: TPO, thyroperoxidase antibody; TRAb, TSH receptor antibody.

[a]Range only applies to results before patient started thyroxine replacement.

[b]Patients 11 and 12 developed hyperthyroidism.

4.1 | Interval for thyroid function testing

Treatment with lithium is known to increase the risk of thyroid abnormalities, with a particular risk of hypothyroidism.[7,8] For this reason, NICE recommends biochemical monitoring of thyroid function every 6 months for patients treated with lithium.[1] Previous work has demonstrated that therapeutic drug monitoring of serum lithium is not consistent with the 3-monthly guidance,[11] and we hypothesized that this would extend to biochemical monitoring of thyroid function.

In support of this, we found that <10% of thyroid requests were made at the recommended 6-monthly intervals. Instead, the most common requesting interval for thyroid function testing was 3 months, indicating that thyroid function tests are over-requested relative to guidance. This interval corresponds to the recommended serum lithium monitoring frequency, suggesting that lithium and thyroid function tests may be co-requested during routine serum lithium testing. Although the monitoring frequency for thyroid function tests for patients on lithium remains previously unknown, this has been investigated for hypothyroid patients on levothyroxine replacement.[16] Here, it has been shown that thyroid monitoring is not compliant with guidance and can be subject to both under and over-requesting depending on the nature of the thyroid results. This study implies that our findings are consistent with a wider issue of appropriately timed thyroid monitoring.

The COVID-19 pandemic has had a negative impact on conditions that require blood tests for monitoring and diagnosis. This has been recently demonstrated for diabetes mellitus, where an estimated 1.41 million diabetes mellitus monitoring tests have been delayed or missed across the UK.[17] The impact of the pandemic on monitoring of lithium complications has not previously been investigated and our study has demonstrated that the pandemic has increased the thyroid function testing interval in patients on lithium by approximately 1 month. Counter-intuitively, as thyroid function tests are over-requested in these patients, this delay may indicate closer adherence to the 6-monthly monitoring guidance. One of the potential implications of this finding is that therapeutic drug monitoring of serum lithium levels has also been affected by the pandemic, which may result in increased psychiatric hospital admissions.[12]

4.2 | Identification of patients with abnormal thyroid function within 3 months of commencing lithium

The fact that the peak monitoring interval for TSH was approximately 3 months, led us to investigate how many patients were identified as having an abnormal TSH earlier than if following the 6-monthly guidance. We hypothesized that more frequent monitoring may lead to early detection and treatment of thyroid disorders, particularly in patients pre-disposed to a thyroid disorder. To explore

this, we used Kaplan-Meier curves to visualize the rate of thyroid disorder development. We observed that >90% of patients who developed thyroid dysfunction did so within 3 years of commencing lithium. The rate of thyroid disorder development was similar to previous studies.[8,18] It has been recently suggested that the serum lithium testing interval could be extended to 6 months for patients on stable lithium therapy.[13] The apparent decrease in detection rates after the first 12 months of initiating lithium therapy could similarly imply that the testing interval for thyroid testing could increase for some patients, further work to establish this is on-going.

A small number of patients were identified who developed thyroid abnormalities within 3 months which would not have been detected until 6 months if the interval recommended by the guideline was being followed. These patients were characterized and the clinical outcomes were assessed to determine whether there was a benefit in early detection.

4.3 | Relation between clinical outcomes and test interval

Of the patients who were identified within 3 months of starting lithium, half were eventually started on thyroxine despite never developing overt hypothyroidism. In all cases, treatment was started after multiple occasions of subclinical hypothyroidism which occurred after the 6-month interval recommended in guidance.[1] One patient (patient 1) demonstrated a potential advantage of early detection; in this case, the patient was started on thyroxine 6 months after lithium initiation and following a second occasion of subclinical hypothyroidism. It is likely that thyroxine replacement would have been delayed if the initial abnormal thyroid result was not detected until 6 months post-lithium initiation.

For the other patients, there is little evidence to suggest that the early identification of abnormal TSH contributed to early treatment. In many cases, there was a short interval between the first abnormal result and subsequent TSH request suggesting that the initial abnormality was being confirmed. Despite this, there was evidence that, even when multiple subsequent results were abnormal, treatment was not initiated (patient seven) or only initiated after a prolonged time period of >1 year (patients 2 and 3). In total, half of the patients identified as developing an abnormal TSH within 6 months of starting lithium treatment spontaneously resolved without intervention. It may be argued that over-requesting of thyroid function tests causes over-diagnosis of thyroid dysfunction, and potentially initiates unnecessary replacement for transient abnormalities may spontaneously resolve. Overall, these data support the 6-monthly testing interval for thyroid disorders recommended by NICE.[1]

In keeping with other studies, we found that the most common thyroid abnormality in patients on lithium was subclinical hypothyroidism.[7,10] Multiple factors dictate whether subclinical hypothyroidism benefits from thyroxine replacement, including magnitude and duration of TSH abnormality, development of anti-thyroid antibodies and presence of symptoms.[19] In this data set, the level of TSH did not predict whether treatment was initiated, with levels as high as 53.5 mIU/L not receiving replacement.

4.4 | Strengths/Limitations

Anti-thyroid antibodies were only measured in a small number of patients despite the fact that these tests may particularly benefit female patients who are more likely to develop anti-TPO antibodies.[18] A limitation of this study is that it was not possible to determine whether the development of symptoms contributed to either thyroxine replacement or a shorter interval between thyroid hormone measurements. In addition, detailed analysis of clinical outcomes was only available for 12 patients. Nevertheless, we feel that the results of our analysis make a relevant contribution to the literature in this area.

5 | CONCLUSION

Our data suggest that thyroid function tests are typically requested too frequently in patients on lithium, potentially resulting in over-diagnosis of thyroid abnormalities. There was no evidence that early detection of abnormal thyroid results leads to earlier treatment and the initial thyroid dysfunction spontaneously resolves in half of the cases without intervention. More than 90% of patients who developed thyroid dysfunction did so within 3 years of commencing lithium. This work supports the 6-monthly testing interval recommended by NICE,[1] and highlights poor adherence to this important guideline.

CONFLICT OF INTEREST

All authors declare no conflict of interest exists.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from HD on reasonable request.

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REFERENCES

1. National Institute for Health and Care Excellence. Bipolar disorder: assessment and management (Clinical guideline number 185) 2014. https://www.nice.org.uk/guidance/cg185
2. Nederlof N, Kupka R, Braam A, Egberts A, Heerdink E. Evaluation of clarity of presentation and applicability of monitoring instructions for patients using lithium in clinical practice guidelines for treatment of bipolar disorder. *Bipolar Disord*. 2018;20:708-720.
3. Nikolova V, Pattanaseri K, Hidalgo-Mazzei D, Taylor D, Young A. Is lithium monitoring NICE? Lithium monitoring in a UK secondary care setting. *J Psychopharmacol*. 2018;32:408-415.
4. Nolen W, Licht R, Young A, et al. What is the optimal serum level for lithium in the maintenance treatment of bipolar disorder? A systematic review and recommendations from the ISBD/IGSLI task force on treatment with lithium. *Bipolar Disord*. 2019;21:394-409.

5. Toffol E, Hätönen T, Tanskanen A, et al. Lithium is associated with decrease in all-cause and suicide mortality in high-risk bipolar patients: a nationwide registry-based prospective cohort study. *J Affect Disord*. 2015;183:159-165.
6. Gitlin A. Lithium side effects and toxicity: prevalence and management strategies. *Int J Bipolar Disord*. 2016;4:27.
7. Kibirige D, Luzinda K, Ssekitoleko R. Spectrum of lithium induced thyroid abnormalities: a current perspective. *Thyroid Res*. 2013;6:3.
8. Shine B, McKnight R, Leaver L, Geddes J. Long-term effects of lithium on renal, thyroid, and parathyroid function: a retrospective analysis of laboratory data. *Lancet*. 2015;386(9992):461-468.
9. Czarnywojtek A, Zgorzalewicz-Stachowiak M, Czarnocka B, et al. Effect of lithium carbonate on the function of the thyroid gland: mechanism of action and clinical implications. *J Physiol Pharmacol*. 2020;71(2):191-199.
10. Lieber I, Ott M, Öhlund L, et al. Lithium-associated hypothyroidism and potential for reversibility after lithium discontinuation: findings from the LiSIE retrospective cohort study. *J Psychopharmacol*. 2020;34(3):293-303.
11. Parfitt C, Duff CJ, Scargill J, et al. Serum lithium test requesting across three UK regions: an evaluation of adherence to monitoring guidelines. *BMC Psychiatry*. 2021;21(1):32.
12. Holland D, Duff C, Farman S, et al. More frequent lithium testing in UK primary care associates with a lower hospital admission rate for bipolar disorder-what this can tell us about GP practice engagement with this group. *Int J Clin Pract*. 2019;73(4):e13277.
13. Heald A, Holland D, Stedman M, et al. Can we check serum lithium levels less often without compromising patient safety? *BJPsych Open*. 2021;8(1):e18.
14. Driskell O, Holland D, Hanna F, et al. Inappropriate requesting of glycated hemoglobin (Hb A1c) is widespread: assessment of prevalence, impact of national guidance, and practice-to-practice variability. *Clin Chem*. 2012;58(5):906-915.
15. Ward R, Fryer A, Hanna F, et al. Inadequate postpartum screening for type 2 diabetes in women with previous gestation diabetes mellitus: a retrospective audit of practice over 17 years. *Int J Clin Pract*. 2021;75(9):e14447.
16. Scargill J, Livingston M, Holland D, Duff C, Fryer A, Heald A. Monitoring thyroid function in patients on levothyroxine. Assessment of conformity to National Guidance and variability in practice. *Exp Clin Endocrinol Diabetes*. 2017;125(9):625-633.
17. Holland D, Heald AH, Stedman M, et al. Assessment of the effect of the COVID-19 pandemic on UK HbA1c testing: implications for diabetes management and diagnosis. *J Clin Pathol*. 2021;jclinpath-2021-207776.
18. Bocchetta A, Cocco F, Velluzzi F, Del Zompo M. Fifteen-year follow-up of thyroid function in lithium patients. *J Endocrinol Invest*. 2007;30(5):363-366.
19. National Institute for Health and Care Excellence. Thyroid disease: assessment and management. (Clinical guideline number 145). 2019. https://www.nice.org.uk/guidance/ng145

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