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REVIEW ARTICLE

Lithium monitoring patterns in the United Kingdom and Ireland: Can shared care agreements play a role in improving monitoring quality? A systematic review

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Background. The appropriate monitoring of patients on lithium therapy has been the subject of extensive research in the form of clinical audits and surveys culminating in the development of specific guidelines to help clinicians provide optimal care for patients on lithium. The concept of 'shared care' has also gained attention in the literature with various types of shared care interventions being introduced as potential ways of improving communication between primary and secondary care.

Objectives. This article aims to (1) review the literature evaluating lithium monitoring practices in the United Kingdom and Ireland in the last 25 years and (2) determine whether locally agreed shared care agreements have the potential to improve monitoring quality.

Methods. A literature search was conducted using the following databases: PubMed, Scopus, Web of Science, Academic Search Premier, CINAHL and PsychInfo. A total of 12 studies were selected for review including 11 audits/prospective chart reviews and one qualitative study using semi-structured interviews.

Conclusions. Overall, the quality of lithium monitoring seems to be improving throughout the years. However, none of the studies reviewed revealed complete adherence to monitoring guidelines. This may be due to a lack of effective communication between primary and secondary care. Several shared care interventions have been described in the literature but there is a paucity of studies concerned with the effects of local shared care arrangements designed for the specific purpose of lithium monitoring. Nonetheless, the extant data suggests that such agreements may help improve monitoring standards by allowing the responsibilities for managing the prescribing and monitoring of lithium to be more clearly defined and shared between primary and secondary care.

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Key words: Drug monitoring, lithium therapy, mental health, primary care, shared care.

Introduction and background

Unique benefits of lithium therapy

Although it was introduced over 60 years ago, lithium still has the strongest evidence base for effectiveness; it continues to be recommended as a first line treatment for bipolar disorder in guidelines such as the National Institute for Health and Care Excellence (NICE) and the Canadian Network for Mood and Anxiety Treatments guidelines (Yatham *et al.* 2013; NICE, 2014). A search of the literature yielded several studies confirming lithium's unique efficacy in the treatment and prevention of relapse in patients suffering from bipolar affective disorders (BPAD). For instance, a meta-analysis of five placebo-controlled lithium maintenance trials ($n = 770$) found that lithium reduces the risk of manic relapses by 38% and depressive relapse by 28% (Geddes *et al.* 2004). Furthermore, it has now been over 30 years that lithium salts are known to enhance the effects of anti-depressants in the treatment of refractory depression (de Montigny *et al.* 1981). Since then, several meta-analytic reviews as well as national and international guidelines have confirmed that augmentation with lithium is the best documented strategy for the treatment of unipolar depression in treatment-resistant patients (Bauer & Dopfmer, 1999; Bauer *et al.* 2010, 2013). Moreover, several studies have suggested an additional role for lithium as a prophylactic agent in the treatment of recurrent depressive disorder (Baastrup *et al.* 1970; Burgess *et al.* 2001; Cipriani *et al.* 2006; Bschor, 2014).

It is an accepted fact that the risk of suicide-related mortality is substantially higher (between 10–70 times

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greater, according to the literature; Muller-Oerlinghausen & Lewitzka, 2010) in psychiatric patients when compared with the general population; this is especially true of patients with affective disorders such as BPAD and major depressive disorder. Faced with this knowledge, researchers have been searching for a therapeutic agent which could also help decrease suicide in this particularly vulnerable patient group. Early epidemiological and observational studies were the first to suggest a potential link between long-term lithium therapy and suicide prevention (Barraclough, 1972; Kessing *et al.* 2005). In the first randomized control trial on the subject, Lauterbach *et al.* (2008) found that lithium therapy was associated with a significant decrease in the risk of completed suicide among patients with affective disorders who had recently attempted suicide. The results of several meta-analyses carried out in the last decade further support the view that lithium plays a role in reducing the rates of suicide and suicide attempts (Cipriani *et al.* 2005, 2013; Baldessarini *et al.* 2006). In a meta-analytic review of 31 studies comparing suicide rates in patients receiving lithium therapy *versus* those without lithium treatment, the overall risk of suicide attempts was found to be five times lower in patients who had been treated with lithium (Baldessarini *et al.* 2006). Further evidence emerged from two systematic reviews carried out by Cipriani *et al.* (2005, 2013). In both the initial review and the updated meta-analysis, lithium was found to be significantly more effective than placebo in reducing the number of suicides; it was also associated with a reduced risk of deliberate self-harm when compared with carbamazepine (Cipriani *et al.* 2013).

In conclusion, there is a strong body of evidence supporting the proposal that lithium has unique properties for reducing suicide risk. These effects, combined with lithium's proven efficacy in the treatment and prophylaxis of both bipolar and unipolar depression, contribute to maintaining lithium's status as a first line, evidence-based management option for patients suffering from affective disorders.

Lithium toxicity and the need for monitoring

Despite the clear beneficial effects of lithium described above, lithium therapy is complicated by its narrow therapeutic index and associated potential for toxicity and adverse effects. Thus, treatment with lithium necessitates serum levels to be checked regularly as well as frequent monitoring of patients' renal, thyroid and parathyroid function. A review of concurrent medication is also advised as there exists potential for interaction with certain drugs such as angiotensin converting enzyme inhibitors and non steroidal anti-inflammatory drugs (as these may potentiate renal impairment). Safe monitoring of lithium levels is crucial if one is to avoid the risks of toxicity. Clinical incidents relating to lithium toxicity have been reported in several studies carried out in both the United Kingdom and Ireland. For instance, the UK's National Patient Safety Agency (NPSA) reported that some patients taking lithium were harmed because their dosage had not been adjusted based on regular monitoring of their bloods (NPSA, 2009). The NPSA received a total of 567 incident reports relating to lithium between October 2003 and December 2008, two of which were 'severe harm' and 34 of 'moderate harm' (NPSA, 2009). Another study investigating lithium toxicity in the Cork region in Ireland identified 130 cases of toxicity over a 5-year period, of which 50% involved drug–drug interactions, suggesting a real need for improvements in the standards of lithium monitoring (Dennison *et al.* 2011).

In light of such incidents, several guidelines (e.g. NICE, 2014) have been issued to help clinicians achieve optimal standards for the safe monitoring of patients receiving lithium therapy. To determine whether the standards outlined in these guidelines are being met by the different prescribing agencies such as primary care trusts or specialist mental health services, it is essential to conduct regular audits as they allow performance to be assessed and areas requiring improvement to be identified.

Shared care protocol

Patients receiving lithium therapy are often under the care of both a specialist mental health clinician and a general practitioner. When this is the case, it is important that effective communication is achieved between both parties involved in the patient's care in order to provide optimal and safe monitoring of their treatment. Shared care models have been proposed as a way to achieve this. A working definition commonly used in the literature describes shared care as 'the joint participation of primary and specialty care practitioners in the planned delivery of care for patients with a chronic condition, informed by an enhanced information exchange, over and above routine discharge and referral notices (…)' (Hickman *et al.* 1994, cited in Smith *et al.* 2008: 213).

There exists several different interventions which fall under the general umbrella term of 'Shared Care,' with varying degrees of interaction between primary and secondary care (Foy *et al.* 2010). A shared care agreement or protocol for drug prescribing is a simple yet effective type of shared care intervention that specifically deals with the shared prescribing and monitoring of medicines between specialist services and primary care. The purpose of such an agreement is to allow the responsibilities for managing the prescribing of a medicine to be clearly outlined and shared between the specialist and a primary care prescriber. In the United Kingdom, due to its potential for toxicity, lithium is classified as an 'amber' class drug; as a result, regionally agreed shared care

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guidelines for the prescribing and monitoring of lithium were introduced in a number of National Health Service (NHS) primary care trusts. As part of these guidelines, a local Shared Care Agreement must be signed by both the mental health specialists and the GPs prior to transferring patients to be monitored in primary care. This practice is supported by NICE guidance, which states that 'lithium therapy should not be started *[in primary care]* for people who have never taken lithium before, except under shared care arrangements' (NICE, 2014: 18).

No such agreements appear to be in place in the Irish healthcare setting. It is worth mentioning, however, that the HSE issued a document in 2013 entitled *Advancing the Shared Care Approach between Primary Care and Specialist Mental Health Services* (HSE National Vision for Change Working Group, 2013) as part of an initiative to increase shared care between specialist mental health services and primary care. According to the most recent progress report entitled *A Vision for Change Nine Years On: A Coalition Analysis of Progress*, progress in the area of shared care has been slow at best; the authors state that 'although some plans have been made on the development of a "shared care" collaborative approach to mental health delivery in Ireland, national systems for shared care are not yet in place' (Mental Health Reform, 2015: 20).

Objective

The aims of this review are twofold: (1) to search the relevant literature evaluating the evolving patterns of lithium monitoring in the United Kingdom and Ireland in order to determine if they have been consistent with the accepted monitoring standards and (2) to assess the literature discussing existing examples of shared care agreements for patients on lithium therapy and to ascertain whether these were shown to improve the quality of monitoring.

Methods

A search strategy using several recognized electronic databases was employed to identify those articles most relevant to our two research objectives. As there are two research objectives, we ran two separate searches. Articles underwent a thorough selection process, which can be divided into five phases. Phase 1 consisted of the initial search strategy using selected keywords and *MeSH* terms. In phase 2, exclusion criteria were applied to narrow the search down. Phase 3 involved reading the titles and abstracts of the remaining articles and selecting those most relevant to the research questions. Finally, during phase 4 the remaining articles were read in their entirety to determine their ability to answer the research question and those that were deemed suitable progressed to stage 5 for inclusion in this review (See Fig. 1 for a simplified flow chart of this search process, based on the PRISMA guidelines (Moher *et al*. 2009). All phases of the search process were conducted by a single researcher.

Search number 1

Phase 1: Initial search strategy
A search strategy using PubMed, Scopus, and EBSCO databases (Academic Search Complete, CINAHL, PsycARTICLES and PsychInfo) was conducted to identify articles relevant to our first research objective. The literature search was conducted up to and including 9 April 2016. We employed the following search criteria:

i. One or more Lithium terms: 'Lithium/therapy' [MesSH] OR 'Lithium' [Mesh] OR 'lithium' [All fields]

AND

ii. One or more drug monitoring terms: 'Drug Monitoring' [Mesh] OR 'Drug monitoring/standards' [Mesh] OR 'Drug Monitoring/methods' [Mesh]

AND

iii. One or more terms relating to standards: 'standards' [Subheading] OR 'standards' [All Fields] OR 'reference standards' [MeSH]

The full search strategies used for each individual database can be found in Online Appendix 1.

Phase 2: Applying exclusion criteria
Studies were excluded from this review if they were not:

i. Available in full text
ii. Published in a peer reviewed journal
iii. In English
iv. Concerned with human adults >18 years of age
v. Carried out in the UK or Ireland.

Phase 3: The titles and/or abstracts of potentially relevant studies were screened.

Phase 4: Full-text copies of articles identified as potentially relevant were retrieved and individually assessed for inclusion in the review stage.

Phase 5: The selected articles were individually assessed with a recognized critical appraisal tool.

Search number 2

First, articles selected in the previous search, as well as their reference lists were screened to see if any of the studies discussed the concept of shared care agreements. A second search strategy was then constructed to find additional studies concerned with the subject of shared care arrangements developed for the purpose of monitoring lithium therapy. The same databases as in search 1 were used and articles went through the same five phases to be selected for inclusion in this review. Fig. 2 is a simplified flowchart illustrating this combined search process.

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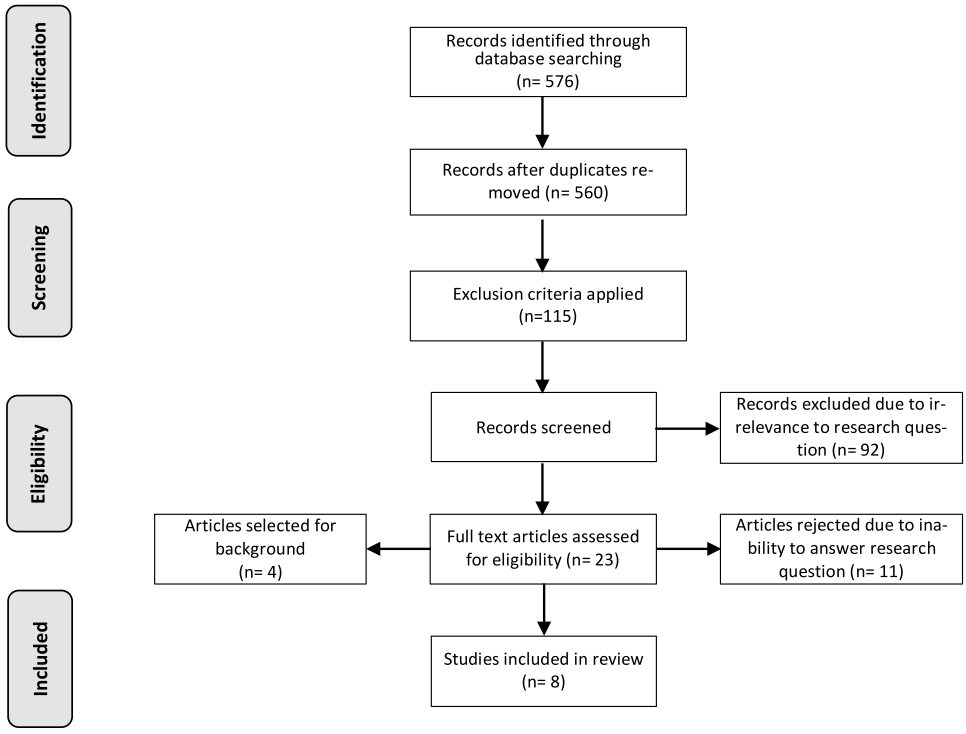

Fig. 1. Literature search and selection process for search number 1.

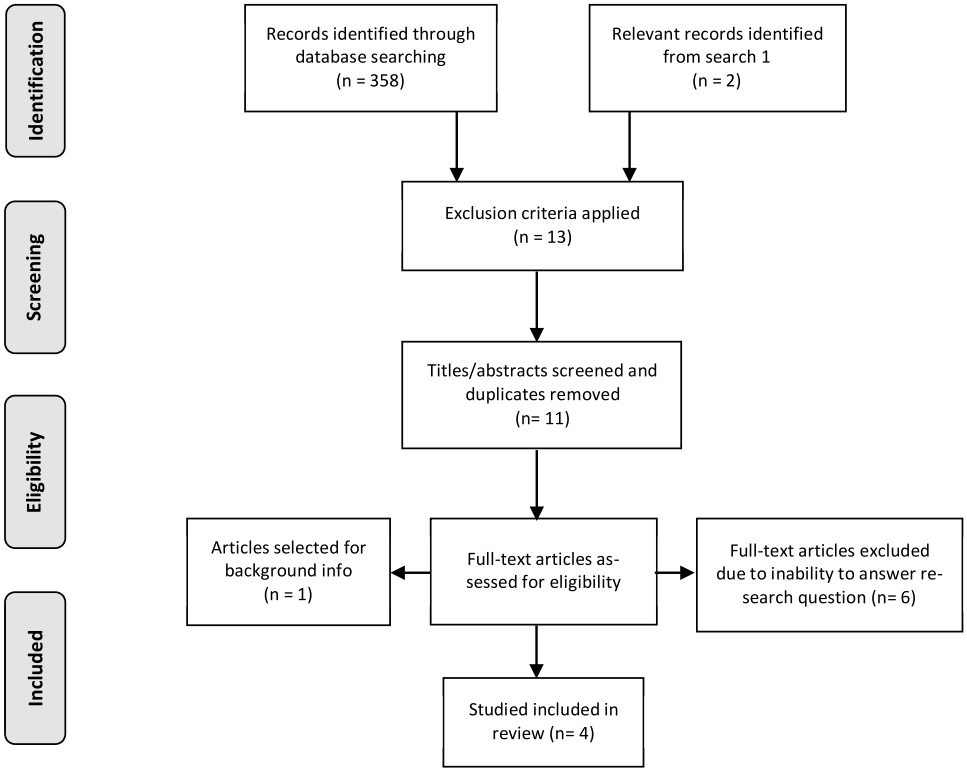

Fig. 2. Literature search and selection process for search number 2.

Results

Our first search identified 576 articles. After applying the exclusion criteria and rejecting studies that were unable to answer our research questions, a total of eight articles were selected for review. All studies consisted of audits intended to determine the quality of lithium monitoring in

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various settings across the United Kingdom and Ireland, spanning a time frame of 25 years. Two studies were designed as 'before/after' audits to determine the effect of an intervention conducted to improve monitoring standards (Eagles *et al.* 2000; Paton *et al.* 2013). Paton *et al.* (2013) conducted three audits (baseline, re-audit and supplementary audit) to assess the impact of a quality improvement program run by the Prescribing Observatory for Mental Health. An older study by Eagles *et al.* (2000) set out to determine whether the distribution of clinical practice guidelines improved monitoring quality. Interestingly, the literature search yielded only one study concerned with lithium monitoring in Ireland (Udumaga & Mannion, 2010). Table 1 summarizes the key findings of each individual study included in this review.

As for our second research question, only three studies (Eagles *et al.* 2000; Buckley & Sharrard, 2003; Glover & Lawley, 2005) specifically addressed whether the implementation of shared care protocol for patients on lithium therapy would improve monitoring quality. Two of these studies (Eagles *et al.* 2000; Glover & Lawley, 2005) had already been identified in the first search, while the third was identified by searching through reference lists (Kirkham *et al.* 2013). The second search strategy did not yield any additional studies with the potential to answer our research question. The key findings of these three studies in relation to the second research objective are summarized in Table 2.

In addition to this, our search strategies identified two studies discussing the level of communication between primary and secondary care in relation to the prescribing and monitoring of lithium treatment (Buckley & Sharrard, 2003; Crowe *et al.* 2010). The key findings of these studies are summarized in Table 3.

Assessment of the validity of included studies

The validity of each study included in this review was assessed by means of a verified critical appraisal tool. The 10 quantitative studies were analyzed by means of the evidence-based librarianship (EBL) critical appraisal checklist (Glynn, 2006), while the validity of the qualitative study was assessed by using the guidance offered in the *BMJ* article *Critically Appraising Qualitative Research* (Kuper *et al*. 2008). Validity of the 10 articles is illustrated in Table 4. All 10 studies demonstrated full overall validity (i.e. an EBL score $\geqslant 75\%$). A full table illustrating the calculation of these scores may be seen in Online Appendix 2. In general, the main limitations were related to methodology and study design; for instance, several studies failed to describe the guidelines used as the reference standard against which performance would be assessed, or how these guidelines were distributed to audit participants (Kehoe & Mander, 1992; Eagles *et al.* 2000; Udumaga & Mannion, 2010). The qualitative study (Crowe *et al.* 2010) met all criteria for validity, as can be seen in Online Appendix 3.

Discussion

Monitoring standards

This review, which spans 25 years of lithium monitoring shows an overall positive trend in the improvement of monitoring quality with older studies reporting more instances of substandard monitoring than audits conducted more recently. However, none of the studies included in this review reported complete adherence to monitoring guidelines. Studies which evaluated monitoring practices before and after the active distribution of guidelines did find a significant improvement in monitoring standards (Eagles *et al.* 2000; Paton *et al.* 2013). These results confirm the importance and need for regular auditing and active guideline distribution and implementation. There was a paucity of data regarding monitoring standards in Ireland. Our search yielded a single audit revealing disappointing results, with only 1/3 of patients meeting the standards in all monitoring parameters (Udumaga & Mannion, 2010). It is worth noting that the Irish Medication Safety Network (IMSN) had previously reported on this significant lack of available data in 2012; they noted that 'no national guidelines are in place for prescribing and monitoring lithium therapy in Ireland, and national statistics are not available for adherence with accepted monitoring standards' (IMSN, 2012: 3).

Some older studies sought to compare the performance of psychiatrists *versus* general practitioners to see whether patients receiving care from specialist psychiatric clinics received a better quality of monitoring than those cared for solely in primary care. Two studies found that patients monitored by GPs were less likely to meet ideal monitoring standards (Kehoe & Mander, 1992; Ryman, 1997), while a study by Eagles *et al.* (2000) found that monitoring was conducted more efficiently for patients seen as part of a joint care agreement between psychiatrists and GPs. Unfortunately, there was no recent studies conducted on the subject.

Poor communication between primary and secondary care

Poor communication between primary and secondary care was one of the main reasons advanced to explain failure to meet monitoring standards. Buckley & Sharrard (2003) conducted an audit investigating the level of communication between primary and secondary care in the monitoring of lithium therapy. They found the main problem to be that GPs and psychiatrists were not clear about who was responsible for the monitoring. They conducted a re-audit after the introduction of lithium

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Table 1. *Studies evaluating lithium monitoring patterns in the United Kingdom and Ireland*

Study	Objectives	Setting	*n*	Type of study/methods	Selection criteria	Key findings	Strengths/limitations	Guidelines
Butler & Taylor (2000)	To determine the monitoring patterns for serum lithium concentrations of a general adult psychiatry team	General adult psychiatry team, Greater London	55	Retrospective chart review: medical notes of study population requested; hand-searching of filed results, drug charts, correspondence and clinical notes, to find all serum lithium concentrations and corresponding lithium doses between January 1990 and December 1996	All patients receiving lithium therapy from current caseload of general adult psychiatry team	18% of outpatient measurements and 17% of inpatient measurements fell outside the recommended range of 0.4 mmol/l–1.0 mmol/l and 34% of dose changes appeared inappropriate Conclusion: standards of lithium monitoring fell below that recommended in BNF guidelines	*Strengths* Investigated dose changes as well as dose intervals to evaluate if reason for dose change was appropriate *Limitations* Small sample size Results may not be generalizable to the rest of population Only evaluated monitoring of lithium levels, not renal or thyroid function	BNF
Collins *et al*. (2010)	Benchmarking audit conducted as part of QIP to determine the quality of monitoring of patients prescribed lithium	United Kingdom	3373	Baseline audit as part of series of three benchmarking audits conducted by POMH-UK.	All NHS trusts in the United Kingdom providing mental health services were invited to participate	Lithium monitoring fell short of the standards recommended by NICE	*Strengths* First published, national-level audit of lithium prescribing and monitoring practice in the United Kingdom Large audit sample Findings generalizable to practice in other mental health trusts *Limitations* Potential bias in the selection of patient samples for audit by each participating trust	NICE and QOF
Eagles *et al*. (2000)	To evaluate the effectiveness of clinical practice guidelines in influencing the practice of lithium monitoring by primary care physicians and psychiatrists	Aberdeen, Scotland	422 in baseline audit 403 in re-audit	i. Baseline audit of general practice and psychiatric records prior to distribution of guidelines ii. Intervention (distribution of guidelines) iii. Re-audit	Patients maintained on lithium throughout 1995 and/or 1996 who lived within the catchment area of psychiatric services based in Aberdeen Only patients registered at some point with local psychiatric services were included	Two of the parameters within the guidelines showed statistically significant improvement Overall monitoring of patients on lithium continued to exhibit several inadequacies, even after the distribution of clinical practice guidelines to psychiatrists and general practitioners (>20% of patients did not have renal function tested at all during that year and appropriate action was not taken on nearly 20% of the occasions on which a high level was recorded	*Strengths* Before and after comparison of monitoring standards to determine effect of clinical practice guidelines *Limitations* No information regarding methods used to ensure implementation of the guidelines (i.e. development, dissemination and implementation strategies) Unclear if guidelines were actually read or used by the doctors concerned	Clinical practice guidelines based on review of the literature and discussion between the authors and relevant professional colleagues

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Glover & Lawley (2005)	To examine the standards of lithium monitoring in eastern Hull following the introduction of a local prescribing framework	Eastern Hull, UK	50	Audit of biochemistry records of patients currently prescribed lithium, identified from primary care computerized records	All patients on lithium therapy from practices within the Eastern Hull Primary Care Trust	Audit revealed poor levels of lithium monitoring, despite the introduction of a local prescribing framework	*Strengths* Measured the effect of introducing a local prescribing framework *Limitations* Small sample size Unable to access records from secondary care Incomplete response rate (only 18/19 eligible practices responded) No 'before' audit to determine monitoring standards prior to introduction of prescribing framework	Local prescribing framework (based on BNF)
Kehoe & Mander (1992)	To define current clinical practice of lithium prescribing and monitoring and to compare hospital-based practice with general practice	Psychiatric hospital day and OPD and general practices in Edinburgh and Midlothian district	458	Prospective study of doctors' practice: Patients were identified on the basis of an established lithium register and a copy of laboratory results sheet was collected to measure serum concentrations over a 1-year period	To be included in the study, patients had to Reside in Lothian psychiatric case register Taken lithium for >6 months Remain as outpatients during the year of study	Wide variation in frequency with which different practitioners carried out monitoring of lithium levels 85% of patients had lithium concentrations checked only once or twice a year and this tended to occur more often under the care of GPs *v.* in the hospital setting	*Strengths* Compared performance of psychiatrists to that of GPs Effort was made to determine reason for dose changes *Limitations* Only evaluated monitoring of lithium levels, not renal or thyroid function Performance was not compared with recommended guidelines Determining reason for dose change by asking practitioners may be subject to recall bias	Unclear
Paton *et al.* (2013)	To assess the impact of a quality improvement program on the quality of lithium monitoring in mental health trusts across the UK.	UK mental health trusts	3647 in re-audit and 5683 in supplementary audit	Re-audit and supplementary audit as part of a series of three benchmarking audits conducted by the POMH-UK	All UK mental health trusts were invited to participate	Improvements in biochemical monitoring of lithium treatment were achieved over time with participation in a QIP that included benchmarking of performance against clinical standards and customized change intervention Audits with personalized feedback are associated with improvements in practice Nonetheless, gaps remained between recommended standards and current practice	*Strengths* Large sample size, representative of UK population Re-audit and supplementary audit allowed for the effect of the quality improvement program to be measured	NICE

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Table 1. (*Continued*)

Study	Objectives	Setting	*n*	Type of study/methods	Selection criteria	Key findings	Strengths/limitations	Guidelines
Ryman (1997)	To determine the lithium monitoring practice of a general hospital and the general practices it serves and how their performance compared with BNF recommendations	Queen Elizabeth Hospital, Gateshead	270	Prospective audit of serum lithium levels The database of the biochemistry laboratory at Queen Elizabeth Hospital was used to identify all patients undergoing serum lithium estimations between 1994 and 1995	Patients for whom there was insufficient data or for whom the course of treatment was <3 months were excluded	Only 15.2% of all subjects met the ideal monitoring criteria in all parameters (frequency of lithium levels and renal and thyroid function tests) Subjects monitored by GPs were less likely to meet ideal monitoring standards (10.9% *v.* 17.4%).	*Strengths* Compared practitioners' performance against 'ideal' monitoring criteria which made results easier to interpret Compared GPs' and psychiatrists' performance *Limitations* Small sample size, may not be representative of UK population as a whole	BNF
Udumaga & Mannion (2010)	To evaluate the standards of lithium monitoring using the local prescribing guidelines in patients attending the lithium clinic of Galway University Hospitals (GUH)	Lithium Clinic, Galway University Hospital, Ireland	116	Retrospective chart review of all patients attending lithium clinic at GUH who met inclusion criteria	Adults aged 18 and above Maintained on lithium for 18 month period (July 2006 to December 2007) Registered with and attending the lithium clinic	Audit revealed poor monitoring standards for lithium-treated patients with just less than 1/3 of patients meeting all three standards for monitoring of lithium levels, renal and thyroid function	*Strengths* Only published audit of lithium monitoring standards conducted in Ireland *Limitations* Small sample size Conducted in dedicated lithium clinic which may not be representative of monitoring practice in the rest of Ireland Local prescribing guideline not described Proportion of patients monitored by lithium clinic only *v.* by GPs not made clear Unclear who was responsible for patients' monitoring	Local prescribing guideline

BNF, British National Formulary; QIP, quality improvement program; POMH-UK, Prescribing Observatory for Mental Health-UK; NICE, National Institute for Health and Care Excellence; QOF, quality outcomes framework; OPD, outpatients department; NHS, National Health Service.

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Table 2. *Studies investigating the effect of shared care agreements on monitoring quality*

Study	Objectives	Type of study/methods	Inclusion criteria	Key findings	Strengths	Limitations
Eagles *et al*. (2000)	To compare whether lithium monitoring quality of patients differed depending on whether they were seen only in primary care or in a general practitioner/psychiatrist shared care model	i. Baseline audit of general practice and psychiatric records prior to distribution of guidelines. 422 patients were included in baseline audit ii. Intervention (distribution of guidelines) iii. Re-audit. 403 patients were included in re-audit Adherence to guideline parameters were compared for patients seen in shared care arrangements and those seen in primary care only	Patients maintained on lithium throughout 1995 ($n = 422$) and/or 1996 ($n = 403$) who lived within the catchment area of psychiatric services based in Aberdeen Patients were included in the analyses only if both general practice and psychiatric records had been reviewed	At re-audit, monitoring was conducted more efficiently among patients seen in shared care arrangements	First study to investigate effect of a shared care arrangement on monitoring standards	The two groups compared were not matched: the 'shared care' group was twice as big as the 'primary care only' group
Glover & Lawley (2005)	To examine the standards of lithium monitoring in eastern Hull following the introduction of a local prescribing framework which emphasized the 'shared care' nature of prescribing	Audit of biochemistry records of patients currently prescribed lithium, identified from primary care computerized records ($n = 50$) after the introduction of a local prescribing framework This framework outlined the respective roles of the GP and consultant psychiatrist in relation to monitoring lithium therapy	All patients on lithium therapy from practices within the Eastern Hull Primary Care Trust	The audit revealed poor levels of lithium monitoring, despite the introduction of a local prescribing framework	One of the few attempts to measure the effect of introducing a local prescribing framework which emphasized the shared care nature of monitoring patients on lithium treatment	No 'before' audit to determine monitoring standards prior to introduction of the prescribing framework
Kirkham *et al*. (2013)	To evaluate the impact of implementing a lithium database and shared care policy on the quality of lithium monitoring in Norfolk	A retrospective audit of recorded blood results from the Norfolk lithium database was conducted on two separate occasions i. During the first year of database/local policy implementation (2005) ii. During most recent year since database implementation (2011/2012) Results were then compared to evaluate impact of the database/shared care policy on monitoring quality	Lithium monitoring tests (lithium levels, renal and thyroid function tests) of all patients registered on the database were included in the audit	The introduction of the Norfolk database contributed to significantly improve rates of lithium testing and monitoring and thus meet national targets	One of the few studies to clearly demonstrate the effect of the introduction of local policies, including a shared care agreement, on the quality of lithium monitoring	Lack of variation in Norfolk population limits the generalizability of the findings to rest of UK population Details of the shared care policy were not fully described

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Table 3. *Studies evaluating the level of communication between primary and secondary care in relation to lithium monitoring*

Study	Objective	Type of study/methods	Inclusion criteria	Key findings	Strengths	Limitations
Buckley & Sharrard (2003)	To measure the communication of responsibilities for lithium monitoring and the flow of information between primary and secondary care, before and after the introduction of clinical practice guidelines	Initial audit and re-audit after the introduction of guidelines i. Initial audit: consultant psychiatrists were sent a questionnaire asking them to identify all their patients on lithium and to indicate who was responsible for lithium monitoring. GPs were also sent a questionnaire, asking them if they were responsible for the monitoring and whether they received adequate information from the consultant psychiatrist ii. Guidelines were drawn up and sent to the participants iii. Re-audit	Questionnaires were sent to all learning disability consultant psychiatrists in the Bristol area and their identified GP counterparts	Initial audit revealed poor level of communication between primary and secondary care and confusion as to who was responsible for monitoring patients on lithium Improvement in communication of responsibility between primary and secondary care was demonstrated when guidelines were introduced	One of the only studies to quantify the level of communication between primary and secondary care specifically in relation to lithium monitoring	This study only included psychiatrists and GPs caring for patients with learning disabilities and therefore, the results may not be generalizable to the entire population of patients receiving lithium treatment
Crowe *et al*. (2010)	To explore the challenges facing GPs' adherence to shared care arrangements for specialist drugs	Qualitative study using semi-structured interviews Three stage sequential design i. Stage 1 aimed to seek the perspectives of a wide range of practice staff within three PCTs in one SHA which was chosen for its convenience in the North West of England ii. Stage 2 sought additional information and further explanation in a similar way from the pharmaceutical adviser/prescribing lead in each PCT iii. Stage 3: information was sought from stakeholders with a vested interest in the primary–secondary care interface	Participants were selected if they worked in the three chosen PCTs within one SHA in the North West of England	GP uncertainty and confusion surrounded the sharing of test results between primary and secondary care, and was felt to give rise to test duplication and omission. This was especially true for lithium monitoring	Study design allowed to gain a detailed understanding of the problems facing GPs when monitoring specialist drugs such as lithium The results of this study contribute to the growing evidence in favor of shared care arrangements between primary and secondary care as a way to improve communication and clarify the roles of each clinician involved in the monitoring of specialist drugs	Self-selection: primary–secondary interface might issue interested participants more than non-volunteers The study was undertaken within a single SHA in England which might limit the generalizability of findings

PCT, primary care trust; SHA, strategic health authority.

Table 4. *An illustration of section validity and overall validity scores of articles assessed by the evidence-based librarianship critical appraisal checklist*

Study	Article population validity score (%)	Data collection validity score (%)	Study design validity score (%)	Results validity score (%)	Overall validity score (%)
Butler & Taylor (2000)	100	50	100	100	92.8
Buckley & Sharrard (2003)	100	100	100	75	92.8
Collins *et al*. (2010)	100	50	100	100	92.8
Eagles *et al*. (2000)	100	50	75	100	85.7
Glover & Lawley (2005)	100	50	100	75	85.7
Kehoe & Mander (1992)	100	50	100	100	92.8
Kirkham *et al*. (2013)	100	50	75	100	85.7
Paton *et al*. (2013)	100	50	100	100	92.8
Ryman (1997)	100	50	100	100	92.8
Udumaga & Mannion (2010)	100	50	75	75	78.5

monitoring guidance sheets and found that communication was vastly improved as both parties were much clearer on their respective responsibilities. A limitation of this study was that it only included clinicians caring for patients with learning disabilities, and thus cannot be generalized to the entire population of patients receiving lithium therapy.

A more recent study by Crowe *et al.* (2010) sought to identify GPs and stakeholders' views on shared care arrangements for specialist drugs by means of semi-structured interviews. Participants identified the lack of a shared care protocol for lithium as one of the factors contributing to problems with monitoring, such as test duplication or worse, omission, due to confusion surrounding who was responsible for the monitoring tests. In light of this evidence, the idea of shared care management emerged as a potential way of increasing communication between GPs and psychiatrists, as well as clarifying their respective roles and responsibilities, ultimately leading to a better quality of lithium monitoring in both the primary and secondary care setting.

It should be kept in mind that the development of a shared care agreement is but a stepping stone in the move toward more seamless communication. Its implementation in practical terms depends on a multitude of factors including but not limited to technical, logistical and financial determinants. For instance, access to shared online laboratory data and clinical information is a basic requirement for successful communication at the primary/secondary interface. Moreover, the development of new guidelines and policies is a lengthy and costly process, which relies on an integrated organizational structure comprised of dedicated committees and regulatory bodies. While these essential structures are already in place in most Clinical Commissioning Groups in the UK's NHS, the situation is more difficult to assess in Ireland. The Irish mental health services underwent a major restructuring in 2006 as part of the health service executive's (HSE) *A Vision for Change* policy, yet from what we can gather from interim progress reports, this process seems far from being complete (Keogh, 2009; Mental Health Reform, 2015). As such, the introduction of a shared care agreement would represent a greater challenge than in the United Kingdom, where most healthcare services are already integrated within and funded by the NHS. Adherence to guidelines and the effective communication between primary and secondary care depends not only on the clinicians themselves but also on the healthcare management systems supporting them and their ability to provide adequate resources for sharing information.

Shared care agreements

The second objective of this review was to determine whether the introduction of local shared care agreements had the potential to improve the standards of lithium monitoring. Our literature search found a number of studies addressing various interventions (e.g. telepsychiatry, joint consultations or videoconferencing) falling under the general umbrella term of 'shared care' and their effects on a variety of mental health outcomes such as patient factors (e.g. severity of mental illness or symptom improvement) or health economics factors (e.g. health services use and cost) (Foy *et al.* 2010). However, we struggled to find studies investigating existing shared care agreements designed specifically for the purpose of lithium monitoring and the effects such agreements might have on monitoring standards.

In addition to assessing lithium monitoring standards before and after the distribution of clinical guidelines, the study by Eagles *et al.* (2000) also sought to determine if monitoring standards were higher for patients seen under a general practitioner/psychiatrist shared care arrangement *versus* those seen solely in primary care. They found that patients who were in shared care arrangements received better monitoring across the majority of

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parameters examined when compared with patients seen solely by general practitioners. A potential limitation of this study lies in the fact that this comparison was not originally designed to be the focus of the study, and as a result subjects in the two groups compared were not matched; indeed, the 'shared care' group was twice as big as the 'primary care only' group.

Glover & Lawley (2005) also addressed the effect of introducing a local shared care framework on the quality of lithium monitoring. The results of this audit revealed poor levels of lithium monitoring despite the introduction of a local prescribing framework. However, as their methodology did not include a 'before' component to the study, it is not possible to determine whether the shared care framework might have improved standards that were initially worse. A more recent study conducted by Kirkham *et al.* (2013) in Norfolk set out to determine the impact of implementing a lithium database and shared care policy on the quality of lithium monitoring. They found that the development of a lithium database and the move toward shared care contributed to the improvement of monitoring quality by aiding communication between primary and secondary care. Unfortunately, this study also contained some limitations; the lack of variation in the Norfolk population may limit the generalizability of the findings to the rest of UK population. In addition, details of the shared care policy used were not fully described.

Strengths and limitations of this review

Our study consists of a thorough review of the literature on a topic for which there is a paucity of available data. Several databases were used to find articles relevant to the research objective. However, all phases of the search process were conducted by a single researcher. For this reason, there remains a potential for bias and misinterpretation of the literature assessed in this review. In addition, validity of this review was not assessed by an independent reviewer.

Perhaps a more detailed search of the gray literature could benefit this review if it were to uncover additional information or examples on the use of informal shared care agreements that might exist between individual GPs or GP practices and secondary care.

Finally, to compare an investigation of lithium monitoring practices in the setting of two different countries with two different models of healthcare organization is not optimal. What applies to the UK's NHS might not translate to the situation in the Irish health services limiting our ability to draw comparisons or extrapolate findings from the UK studies into the Irish setting; further research is needed to investigate the feasibility of shared care arrangements for lithium monitoring in Ireland.

Conclusion

The literature reviewed suggests that overall, the quality of monitoring lithium therapy has been improving in the United Kingdom in the last 25 years; regular auditing and active implementation of monitoring guidelines have played an important role in improving these standards. However, monitoring habits are still failing to fully meet all the parameters outlined in the guidelines. This may in part be due to a lack of effective communication between primary and secondary care (Buckley & Sharrard, 2003; Crowe *et al.* 2010).

Several shared care interventions have been described in the literature but there is a paucity of studies concerned with the effects of local shared care arrangements designed specifically for the purpose of lithium monitoring. A total of three studies attempting to evaluate the impact of shared care agreements on lithium monitoring in the United Kingdom were identified (Eagles *et al.* 2000; Glover & Lawley, 2005; Kirkham *et al.* 2013). Two of them showed that such agreements have the potential to improve standards by allowing the responsibilities for managing the prescribing of lithium to be clearly defined and shared between primary and secondary care (Eagles *et al.* 2000; Kirkham *et al.* 2013). While the limited amount of evidence precludes us from drawing any robust conclusions concerning the role of shared care agreements in the improvement of monitoring standards, this review does provide new insights into the important issue of drug monitoring and communication at the primary/secondary care interface. Finally, the marked lack of Irish data prevents us from evaluating the evolution of monitoring quality in Ireland or the impact of any strategy aimed at its improvement.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the

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relevant national and institutional committee on human experimentation with the Helsinki Declaration of 1975, as revised in 2008.

Supplementary material

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