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Age-stratified lithium therapeutic ranges for older adults with bipolar disorder – from awareness to an action plan

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ABSTRACT

Lithium is the first-line treatment for maintenance therapy in bipolar disorder. It is an effective mood stabilizer agent, and may have potential benefits in neuroprotection and reducing the risk of suicide. Toxicity has been a concern in recent decades, particularly in older adults (≥60 years). In 2019, the Older Adults Task Force within the International Society for Bipolar Disorder (ISBD) published recommendations for age-stratified lithium therapeutic ranges for therapy of Older Age Bipolar Disorder (OABD), namely 0.4 – 0.8 mmol/L for ages 60 to 79 and 0.4 – 0.7 mmol/L for ages 80 and above. Clinical laboratory practice surveys in Canada indicated that adoption and implementation of the proposed ranges has been limited to date. In this article, we describe the approach and

steps taken to evaluate and implement recommended lithium therapeutic ranges in Ontario and other provinces in Canada for laboratory quality improvement. Sources of variation in lithium reporting practices are discussed and shared here to highlight potential barriers to implementation. The overall goal of this article is to bring attention across the global laboratory community that lower lithium therapeutic target ranges in older patients are crucial for patient safety in OABD.

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Abbreviations

CV, coefficient of variation;

IQMH, Institute for Quality Management in Healthcare;

ISBD, International Society for Bipolar Disorders;

L-DOPA, levodopa;

OABD, old age bipolar disorder;

RCPAQAP, The Royal College of Pathologists of Australasia Quality Assurance Programs;

SD, standard deviation;

SE, standard error.

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INTRODUCTION

Older age bipolar disorder (OABD) is defined as bipolar disorder in individuals aged 60 and over, and it represents approximately 25% of all bipolar disorder (BD) worldwide [1]. This group includes individuals with both early and late onset BD. With the growing older population, the proportion of OABD is projected to be over 50% by 2030 [2]. Lithium carbonate remains the first-line treatment in the maintenance of OABD due to its effectiveness in both phases of the illness, including depression and mania/hypomania [3,4]. In addition to mood stabilization, it may also have additional benefits in reducing the risk of suicide [5,6] and have neuroprotective properties for the prevention of dementia [7]. Yet, lithium toxicity has been a concern in recent decades, especially in older adults where the laboratory community needs to highlight and thereby reverse the decline of prescribing practice [4,8].

In older adults, special considerations regarding the use of lithium include increased risk of toxicity associated with normal and pathological decreases in renal function, medical co-morbidities, and drug-drug interactions with commonly used medications such as diuretics, ACE inhibitors and nonsteroidal anti-inflammatories [9–11]. It has been reported that 33% of OABD patients are prescribed these common medications, which may increase the serum lithium level by up to 50% [8]. Moreover, lithium toxicity is often misdiagnosed and attributed to other common conditions in older adults, including gastrointestinal symptoms (diarrhea), urological disorder (polyuria), impaired cognition (dementia) and neurologic symptoms similar to parkinsonism (tremor and rigidity) [12]. If not recognized as toxicity secondary to lithium use, this can result in a “prescribing cascade” whereby inappropriate and unnecessary drugs are additionally prescribed for perceived new disorders [13]. For example, parkinsonism secondary to lithium therapy can result in unnecessary treatment with L-DOPA, while impaired cognition may be interpreted as dementia and managed inappropriately with cognitive enhancers [12].

To date, there is only one randomized controlled trial that specifically addressed pharmacological treatment using lithium carbonate in older adults with bipolar disorders - the GERI BD study (Acute Pharmacotherapy in Late-Life Mania) [14]. Recent clinical practice guidelines generally recommend a lithium target maintenance therapeutic range of 0.6 to 0.8 mmol/L, without considering the age of the patient, the

phase of their illness, or medical comorbidities [3]. There is also a lack of specific recommendations for OABD in international clinical practice guidelines [3,15].

Considering the lack of systematic evidence and direction from clinical practice guidelines for use of lithium in older adults, the International Society of Bipolar Disorder (ISBD) established an Older Age Task Force comprised of international experts with real-world knowledge and experience in OABD. The group has published a report as well as a Delphi consensus survey aimed to provide specific direction for lithium and its maintenance use in OABD [1,16]. In brief, the ISBD task force on OABD recommended that lithium remains the preferred choice for maintenance treatment of OABD [16]. Second line choices include: valproate, lamotrigine, quetiapine and olanzapine. It is recommended that serum lithium levels be monitored 5 to 7 days after a dose adjustment, three to six months thereafter, as clinically necessary and if co-medications were initiated or adjusted while receiving lithium therapy [16]. Monitoring of target serum lithium levels generally relies on trough levels as the efficacy of lithium are dose-dependent and correlates well with trough levels. Trough levels are typically collected just before the next dose. In clinical practice, lithium is mostly prescribed as lithium carbonate and may be administered in divided doses, so lithium trough levels are routinely measured 12 hours following the previous dose.

The ISBD task force on OABD also provided specific recommendation on reporting separate lithium level therapeutic ranges for older adults [16]. Serum lithium target therapeutic ranges were recommended for ages 60 to 79 in the range of 0.4 to 0.8 mmol/L, and for those 80 and over in the range of 0.4 to 0.7 mmol/L [16]. The most common therapeutic range reported by laboratories was in the range of 0.6 to 1.2 mmol/L and without specific age dependent stratification [16]. The lack of age stratification may pose risks in missing lithium toxicity in older adults. Providing narrower and lower therapeutic ranges in older patients would help to increase sensitivity to adverse side effects, particularly neurotoxicity.

Given the vulnerability to toxicity and the tendency for lithium to be underutilized in this population, requests were made to the clinical laboratory community to update and provide narrower and lower therapeutic ranges for lithium in older adults [4,17]. In this article, we share our approach aiming to determine the feasibility of implementing the ISBD OABD Task Force recommended standardized therapeutic ranges in Canada for laboratory quality improvement by: a) determining the association of serum lithium concentration with age via retrospective laboratory data review, b) evaluating method agreement between common lithium methods via reviewing proficiency testing survey reports, and c) determine the current practice of clinical laboratories in the reporting of lithium levels in Canada through two voluntary surveys of clinical laboratories conducted in 2017 and 2022. Sources of variation in lithium reporting practices are discussed and shared here to highlight potential barriers to implementation.

FEASIBILITY ASSESSMENT FOR ADOPTION OF STANDARDIZED THERAPEUTIC RANGES FOR SERUM LITHIUM

To evaluate the feasibility of adopting and implementing the ISBD OABD Task Force recommendation for standardized age-stratified therapeutic ranges for lithium, we retrospectively reviewed a Toronto hospital serum lithium data for association with age, and we reviewed results from two external quality assurance providers for lithium method performance agreement.

Serum lithium laboratory results from April 1, 2020 to March 31, 2022 (n = 504) were extracted from theSunnybrook Health Sciences Centre Laboratory Information System (Toronto, Ontario, Canada). Patients from emergency department, critical care and maternal care units were excluded, and the final analysis included clinically stable patients undergoing treatment with lithium. This retrospective study has been registered with the Sunnybrook Research Ethics Board as a quality improvement project.

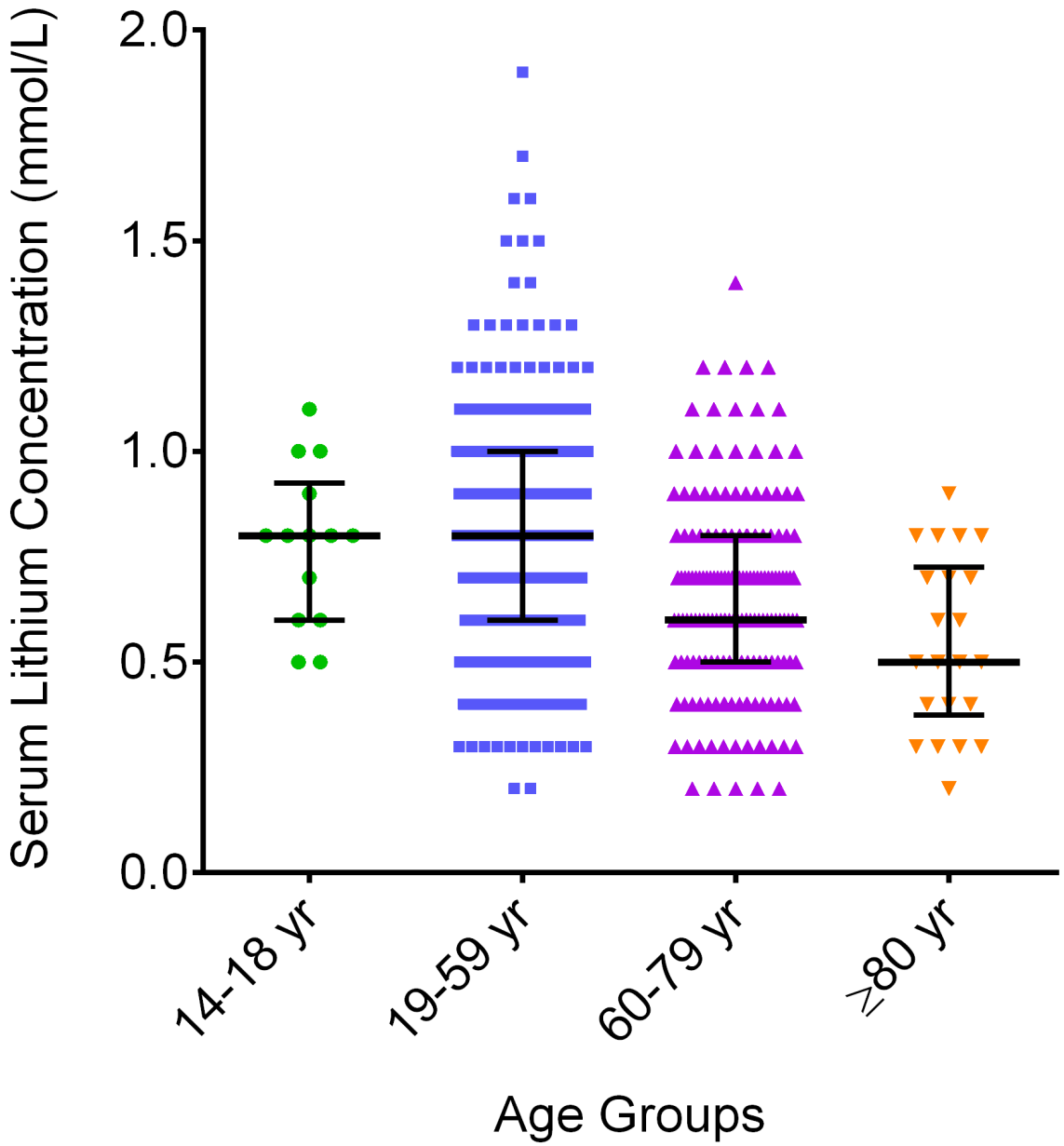
One-way ANOVA was used to compare mean serum lithium concentration between four age groups: ages 14 to 18, 19 to 59, 60 to 79, and ≥80 years old. Statistical analyses were performed by IBM SPSS Statistics V. 28.0.1.1 software. The analyses confirm that there is a significant difference in mean lithium concentration between the age groups of 19 to 59 years old and 60 to 79 years old (mean 0.80 *vs.* 0.65 mmol/L, $p < 0.001$), and between the age groups of 19 to 59 years old and ≥80 years old (mean 0.80 *vs.* 0.55 mmol/L, $p < 0.001$). Therefore, the serum lithium concentration in sera of older adults (60 to 79 years old and ≥80 years old) is significantly lower than in that of younger adults (19 to 59 years old). Figure 1 illustrates the distribution of serum lithium concentration for each age groups. This retrospective review of laboratory data provides supporting evidence that patients ≥60 years old should have a lower therapeutic target serum lithium level compared to younger adults. Prior to local implementation in other laboratory testing sites, similar results were observed from community laboratory data (i.e., Ontario and British Columbia) as well as in other provinces (data not shown).

To evaluate agreement between commonly used lithium methods for the use of standardized therapeutic target ranges, we reviewed proficiency testing survey reports between September 2020 to September 2022 from the Institute for Quality Management in Healthcare (IQMH) based in Toronto, Canada and The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) based in St Leonards, Australia. Both programs offer an ISO 17043:2010 accredited proficiency testing program to clinical laboratories.

The aggregate analytical performance is summarized in Table 1 and includes a total of seven surveys and 21 samples covering a range of lithium concentrations. The surveys included eight different instrument groups (Abbott Architect/Alinity c, Beckman Coulter AU, Beckman Coulter Unicel DxC, Ortho Vitros, Roche cobas c/Integra 400, Siemens Advia/Atellica, Siemens Dimension and Siemens Vista) from five major manufacturers, and reported data from 311 RCPAQAP and 86 IQMH clinical laboratory participants. All the methods are based on the colorimetric method principle. The all-methods' mean, standard deviation and coefficient of variation ranges were summarized for four categories of lithium ranges: a) <0.4 mmol/L, b) 0.4 - 0.8 mmol/L, c) 0.8 - 1.5 mmol/L, and d) >1.5 mmol/L, which represent major clinical decision limits.

The variation between lithium methods is minimal, with a range of all-methods' standard deviation of 0.04 - 0.06 mmol/L for concentrations ≤1.5 mmol/L, and <0.12 mmol/L for concentrations >1.5 mmol/L. A practice-oriented quality specification for lithium was proposed with a desirable imprecision of 5.2%, bias of 2.1% and total error allowable of 10.7% [18]. Overall, this indicates that there is acceptable and sufficient agreement between commonly used colorimetric lithium methods, and demonstrates feasibility to use narrow, age-stratified, and standardized therapeutic target ranges for serum lithium (i.e., 0.4 to 0.8 mmol/L for ages 60 to 79, and 0.4 to 0.7 mmol/L for ages ≥80).

Figure 1 **Serum lithium concentration distribution stratified by age groups**



Serum lithium concentrations (mmol/L) were plotted stratified by patient age groups (14 to 18 years, 19 to 59 years, 60 to 79 years, ≥80 years). The horizontal line and error bars represent the median and interquartile range for serum lithium concentration for each age group, respectively. This figure was generated by GraphPad Prism 5 software.

Table 1 Summary of analytical performance of colorimetric methods for serum lithium obtained from IQMH (Canada) and RCPAQAP (Australia) proficiency testing surveys between September 2020 to September 2022

Target Lithium Concentration (mmol/L)	Number of surveys	Number of survey samples included	Range of all-methods' mean# (mmol/L)	Range of all-methods' SD# (mmol/L)	Range of all-methods' CV# (%)
< 0.4	2	2	0.29 – 0.35	0.04 – 0.05	12.6 – 14.3
0.4 – 0.8	3	4	0.59 – 0.73	0.04 – 0.05	6.0 – 7.1
0.8 – 1.5	4	4	1.03 – 1.43	0.05 – 0.06	3.6 – 5.0
>1.5	7	11	1.71 – 2.70	0.05 – 0.12	3.1 – 4.5

 # All-methods mean, standard deviation (SD) and coefficient of variation (CV) presented are summarized from a total of 7 surveys and 21 samples from the Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) and Institute of Quality Management in Health Care (IQMH) proficiency testing surveys, and reported from 311 participating clinical laboratories in RCPAQAP and 86 IQMH Proficiency Testing Program. This data represents lithium measurements from eight instrument groups (Abbott Architect/Alinity c, Beckman Coulter AU, Beckman Coulter Unicel DxC, Ortho Vitros, Roche cobas c/Integra 400, Siemens Advia/Atellica, Siemens Dimension, and Siemens Vista) based on the colorimetric method principle.

SOURCES OF VARIATION IN LITHIUM THERAPEUTIC RANGES

Based on the proficiency testing survey results, we further explored whether there are other sources of variation in lithium therapeutic range such as method traceability, use of alternate method principles, and the use of outdated reference sources (e.g., manufacturer instructions for use (IFU), textbooks, publications, or clinical practice guidelines). There are currently 5 registered reference methods and 8 registered reference materials for lithium in serum or plasma in the Joint Committee for Traceability in Laboratory Medicine (JCTLM) Database [19]. Current routine commercially available lithium methods may be broadly categorized, from most common to least common as colorimetric, ion selective electrode, and atomic absorption spectrophotometry. Common colorimetric methods from 5 major manufacturers were further reviewed for traceability and were traceable to at least four different NIST standards (i.e., SRM956, SRM3129, SRM924, SRM 909). Review of recent 2022 proficiency testing survey reports from College of American Pathologists (CAP) based in the USA showed that although most methods are generally agreeable, there are some rarer methods, such as direct ion selective electrode, can have a bias of up to +0.3 mmol/L when compared to the all-methods' means. These biases may be present due to method specific differences and interferences, or the initial versions of a commercial assay released at a time when reference methods and/or materials are not available, or if the method's calibration traceability has not

been updated. Thus prior to adoption and implementation of the recommended standardized ISBD OABD therapeutic ranges, we continue to recommend a review of local, site-specific laboratory and clinical data.

Therapeutic ranges for lithium published from clinical practice guidelines, manufacturer IFUs, and textbooks were also reviewed. Reviews of recent clinical practice guidelines showed that target range varies, with the lower limit ranging from 0.4 to 0.6 mmol/L and upper limit ranging from 0.6 to 1.2 mmol/L [3,15]. Manufacturer IFUs of lithium assays from the five major vendors were reviewed, and the lithium therapeutic ranges and their reference source are summarized in Table 2. The main cited sources from these IFUs are based on the Tietz Textbook of Clinical Chemistry and Molecular Diagnostics [20,21], and the Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics [22,23]. The Tietz textbooks and Bakerman's interpretive laboratory reference account as the sources of the most used therapeutic ranges noted in the practice surveys [21–28]. Interestingly, newly commercially available analyzers, such as the Siemens Atellica or the Abbott Alinity, did not provide an update to their lithium IFU and continued to cite the original reference source published with their predecessors [29,30]. Additionally, some of the textbook editions did not reference the original source of their recommended ranges. For example, the latest edition of the Tietz Textbook provided an updated recommended range of 0.5 to 1.0 mmol/L for all age groups, however this modification did not provide a new reference source and continued to reference an older edition of the textbook [25,26].

Table 2 Common lithium methods therapeutic range referenced in manufacturers instructions for use

Source of therapeutic range from Manufacturer Instruction for Use (IFU) or Textbook	Therapeutic range for lithium level (mmol/L)	Reference cited
Abbott Architect [32]	1.0 – 1.2	Tietz Textbook 4th ed. [21]
Abbott Alinity [29]	1.0 – 1.2	Tietz Textbook 4th ed. [21]
Beckman AU [33]	1.0 – 1.2 (trough) 0.6 (minimum effective)	Tietz Fundamentals 6th ed. [23]
Beckman Synchron and DxC [34]	1.0 – 1.2 (trough) 0.6 (minimum effective)	Tietz Fundamentals 6th ed. [23]
Siemens Advia [35]	1.0 – 1.2	Tietz Textbook 2nd ed. [20]

Siemens Atellica [30]	1.0 – 1.2	Tietz Textbook 2nd ed. [20]
Siemens Dimension Vista [36]	0.6 – 1.2	Tietz Fundamentals 6th ed. [23]
Ortho Vitros [37]	0.6 – 1.2	Tietz Fundamentals 5th ed. [22]
Roche cobas [38]	0.6 – 1.2	Tietz Fundamentals 5th ed. [22]
Roche Direct ISE [39]	0.6 – 1.2	Tietz Clinical Guide 3rd ed. [28]
Tietz Textbook 6th ed. [26]	0.5 – 1.0	Tietz Textbook 5th ed. [25]
Bakerman's ABC's Interpretive Laboratory Data 5th ed. [24]	0.5 – 1.2 (acute mania) 0.5 – 1.0 (sustained prophylactic)	Practice Guideline 2002 Am J Psych [40]

For comparison, the ISBD task force on OABD has made specific recommendations on reporting for older adults with target therapeutic ranges for ages 60 to 79 in the range of 0.4 to 0.8 mmol/L, and for those 80 and over in the range of 0.4 to 0.7 mmol/L [17].

SURVEY OF LITHIUM REPORTING PRACTICE IN CANADA

Two surveys querying the Canadian clinical laboratories about their serum lithium reporting practices were conducted in 2017 and subsequently in 2022. Both surveys were conducted a few months prior to educational sessions on the safe and effective use of lithium in OABD presented at national and international clinical laboratory conferences (e.g., Canadian Society of Clinical Chemists Annual Scientific Meeting and International Association of Therapeutic Drug Monitoring and Clinical Toxicology Congress) [31].

The first survey was administered by IQMH with most laboratories representing the provinces of Ontario and Newfoundland. In May 2017, a 5-question voluntary survey about laboratory practices related to serum lithium collection instructions, reporting of therapeutic ranges and toxic levels were included with the IQMH DRUG proficiency testing survey and sent to clinical laboratories who subscribed to the program. Qualitative comments were received from a total of 85 laboratories that perform lithium testing, with a distribution of 77 (91%) hospital laboratories and 8 (9%) community laboratories. Of the 85 laboratories, 3 (4%) laboratories did not provide their lithium therapeutic ranges, 7 (8%) laboratories did not provide their lithium toxic alert concentration threshold, 2 (2%) laboratories provided pediatric (<18 years old) specific ranges, and 4 (5%) laboratories provided geriatric (≥65 years old) specific ranges. The surveyed lower therapeutic limit varied from 0.0 to 0.8 mmol/L, and the upper limit varied from 1.1 to 1.5 mmol/L, for all age groups (Figure 2). Like the Delphi survey results conducted by ISBD OABD Task Force, the majority (89%) of laboratories surveyed provided a single lithium therapeutic range for all age groups, and the most common range (62%) reported was 0.6 to 1.2 mmol/L [16]. For the surveyed

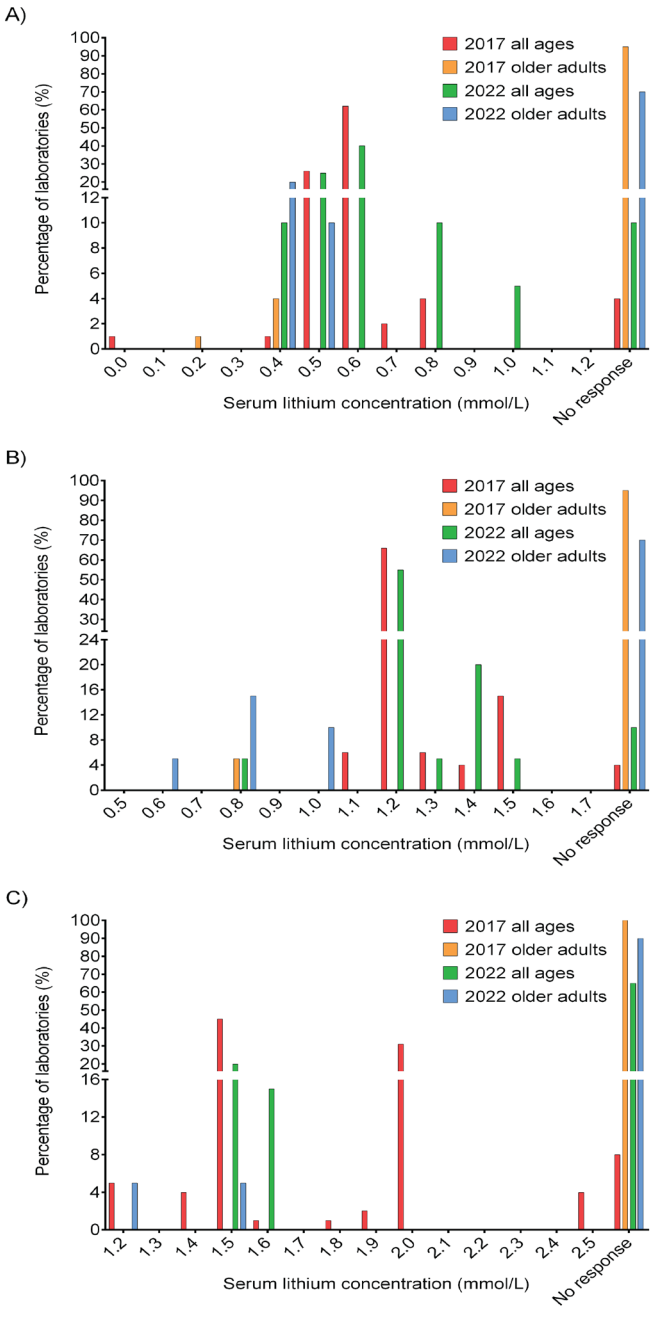
geriatric therapeutic ranges (≥65 years old), the lower limit of the therapeutic range varied from 0.2 to 0.4 mmol/L, and the upper limit was 0.8 mmol/L for all four sites. In terms of toxic alert levels, the upper threshold varied from 1.2 to 2.5 mmol/L and the most common toxic upper threshold is 1.5 mmol/L (45%) for all ages. No laboratory reported a separate toxic range for patients ≥65 years old. The therapeutic ranges for lithium are based on trough ranges. Forty-four of the 85 laboratories (53%) indicated they had collection instructions for measurement of lithium trough levels with 41 (91%) laboratories used the 12 hours post-dose instructions and 3 (9%) laboratories used the immediately prior to next dose instruction.

In May 2022, a second survey including 5 questions was circulated to members of the Canadian Society of Clinical Chemists (CSCC) via the CSCC electronic mailing list to determine whether the relevant clinical recommendations and educational efforts made an impact in raising awareness about the need for age-stratified therapeutic ranges for lithium in older adults. Qualitative responses were received from a total of 20 laboratories performing lithium testing from British Columbia, Manitoba, Ontario, and Quebec in Canada as well as Minnesota in the USA. Most of the responses (95%) were from hospital laboratories. Not every respondent answered all questions, but all responses received were included in the final survey report. Of the 20 laboratories who responded, 14 (66%) laboratories provided a single therapeutic range, and the most common therapeutic range used was 0.6 to 1.2 mmol/L (30%), followed by 0.4 to 1.4 mmol/L (10%), 0.5 to 1.2 mmol/L (10%), and 0.5 to 1.3 mmol/L (10%). Six (29%) laboratories provided a separate lithium therapeutic range for older adults, where the age limit varied between 60 to 65 years of age and over (Figure 2). Two of those six laboratories additionally provided a separate lithium therapeutic range for ages ≥80. For the geriatric population (age 60 and over) therapeutic lower limit varied from 0.4 to 0.6 mmol/L, and the upper limit varied from 0.6 to 1.0 mmol/L. The most common surveyed toxic alert limit was ≥1.5 mmol/L for all ages (35%). Toxic alert for older adults was reported by two laboratories with upper thresholds of 1.1 and 1.4 mmol/L. Eight (38%) laboratories provided collection instructions, and two (10%) laboratories provided interpretative comments regarding toxicity concentrations. The practice surveys in 2017 and 2022 suggest a slow but increasing adoption and implementation of age-specific therapeutic ranges for lithium (Figure 3).

DISCUSSION AND CONCLUSION

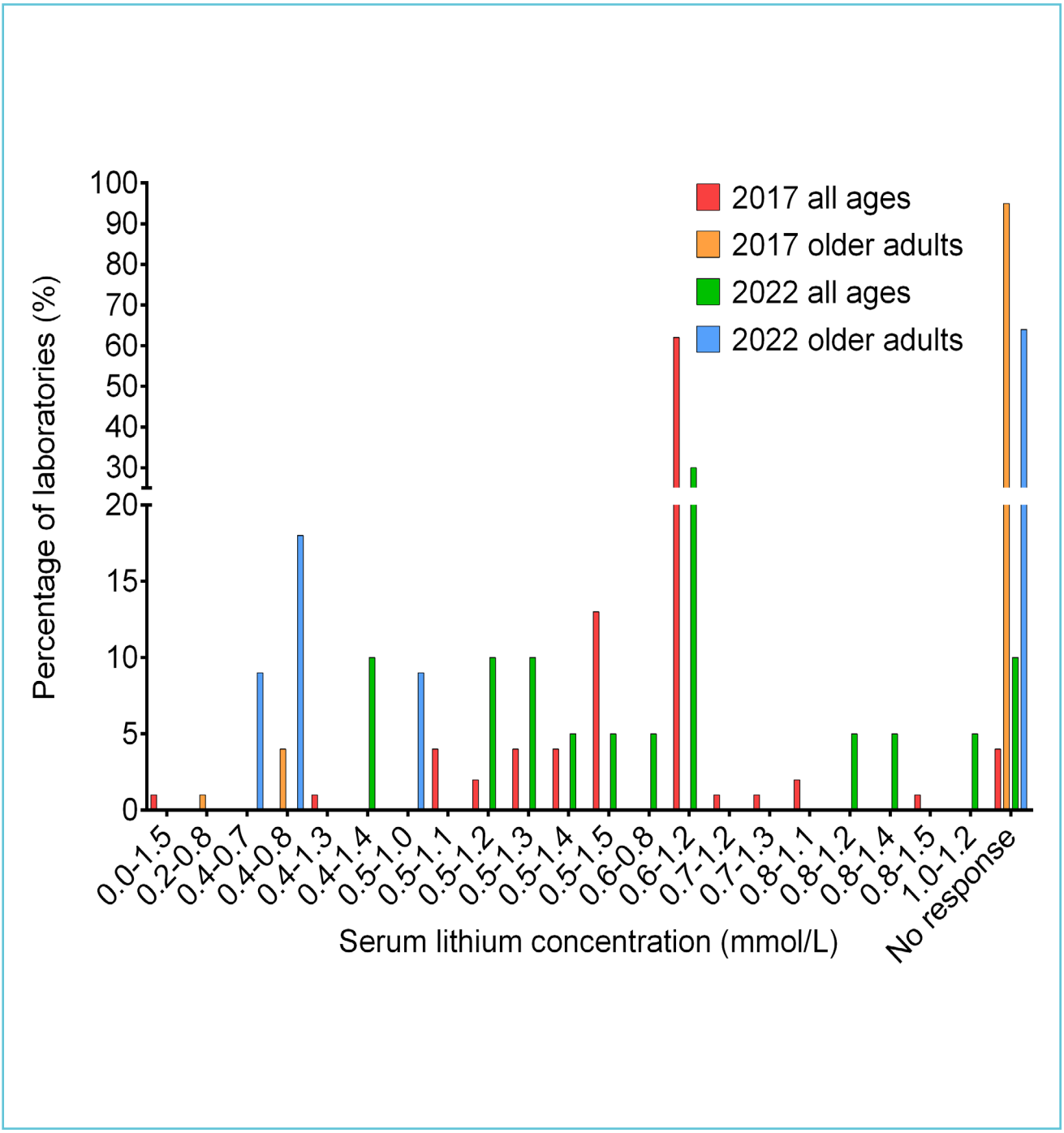
The Older Adults Task Force within the International Society for Bipolar Disorder (ISBD) has recommended age-stratified lithium therapeutic ranges for older adults with bipolar disorder (i.e., for ages 60 to 79 in the range of 0.4 to 0.8 mmol/L, and for ages ≥80 in the range of 0.4 to 0.7 mmol/L [17]). Here, we determine the feasibility of using standardized therapeutic ranges for lithium. Our analysis demonstrates that there is an association of lower serum lithium concentration with increased age, and there is generally good agreement between commonly used colorimetric lithium methods. Additional assessment of feasibility is required if using uncommon methods (i.e., ion selective electrode). Together, these data generally align the ISBD OABD Task Force recommendation with laboratory evidence. Interestingly, reporting practice surveys in Canada indicated that there is significant variability in the reporting of serum lithium therapeutic ranges with some laboratories reporting upper limit >1.2 mmol/L and up to 1.5 mmol/L. Review of potential sources of variation in therapeutic ranges shows that the upper therapeutic limit referenced from a variety of sources is generally not greater than 1.2

Figure 2 **Survey results for serum lithium reporting practices: variation in the (A) lower limit; (B) upper limit of therapeutic range; (C) toxic limit reported by laboratories**



Red denotes 2017 survey for all ages, orange denotes 2017 survey for older adults, green denotes 2022 survey for all ages, and blue denotes 2022 survey for older adults. For all age groups, majority of laboratories report a lower limit of 0.6 mmol/L and an upper limit of 1.2 mmol/L for therapeutic range, and ≥1.5 mmol/L for toxic limit. Considerable variability exists for both the therapeutic and toxic limits. The definition of older adult was variable and ranged between 60 to 65 years old. For older adults, majority of laboratories currently do not report age-stratified therapeutic ranges or toxic limits. This figure was generated by GraphPad Prism 5 software.

Figure 3 **Survey results for serum lithium reporting practices: variation in the therapeutic range reported by laboratories**



Red denotes 2017 survey for all ages, orange denotes 2017 survey for older adults, green denotes 2022 survey for all ages, and blue denotes 2022 survey for older adults. Majority of laboratories report a therapeutic range of 0.6 – 1.2 mmol/L for all ages, and a lack of age-stratified ranges defined for older adults. There is an increase in adoption of the ISBD recommended ranges for OABD from 2017 (orange) to 2022 (blue) in the therapeutic ranges of 0.4-0.7 and 0.4-0.8 mmol/L (i.e., for ages 60 to 79 in the range of 0.4 to 0.8 mmol/L, and for ≥80 years old in the range of 0.4 to 0.7 mmol/L [17].) This figure was generated by GraphPad Prism 5 software.

mmol/L, which suggests that reporting upper limits >1.2 mmol/L is an outdated practice. An upper therapeutic limit of >1.2 mmol/L can put older adults at a risk of lithium toxicity without being recognized by clinicians who may consider this level to be within the normal range. Although the Delphi survey did not make a specific recommendation on toxic alert concentrations, it has been suggested that 1.5 mmol/L is a practical, clinically-based toxicity alert for older adults. Together this highlights an important need for clinical laboratories to periodically review reference and therapeutic ranges and update obsolete ranges where clinically necessary. In addition, there is also a need to engage text book authors, editors, and manufacturers to review validity of their published lithium therapeutic ranges, and to include ISBD OABD recommendation through collaboration with national and international clinical chemistry and toxicology societies such as the Canadian Society of Clinical Chemists (CSCC), American Association for Clinical Chemistry (AACC), International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), and International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT).

In conclusion, the lack of age-stratified lithium therapeutic ranges may put older adults at risk of developing lithium toxicity as some potentially toxic results may be disregarded as "within the therapeutic range". Adoption and implementation of clinically appropriate, age-stratified therapeutic ranges for OABD have been slowly but steadily increasing in Canada. A small group of clinical laboratories in Ontario have championed the implementation of revised therapeutic lithium ranges for OABD and are now sharing their experience with interested laboratories in other provinces. Champion leaders have also been identified in provincial laboratory groups in British Columbia and Alberta to drive implementation across Canada where applicable. While we transform awareness of the ISBD OABD Task Force recommendations into action in Canada, we hope data presented in this article will help raise awareness and promote the safe and effective use of lithium in patients with OABD globally.

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Conflict disclosures

None to disclose.

Author contributions

A.F., P.Y. K.S, and L.F. devised the project, main conceptual ideas, and outline. L.F., P.Y., and J.S., planned and carried out the voluntary practice surveys. A.F., V.Y., D.K., H.V., J.S., L.F. carried out data analysis and prepare data table and figures. A.F., K.S., D.K., V.Y., P.Y., and L.F. wrote the manuscript. All authors provided critical feedback and contributed to the final manuscript.

Ethics

As confirmed by the Sunnybrook Health Sciences Centre Research Ethics Board (REB), the retrospective study on association of serum lithium concentration and patient age groups did not require REB approval as it was deemed to be a quality improvement project and not human subject research.

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