Medical and surgical treatment of epilepsy in older adults

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RESEARCH ARTICLE

Medical and surgical treatment of epilepsy in older adults: A national survey

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Abstract

Objective: There are no clinical guidelines dedicated to the treatment of epilepsy in older adults. We investigated physician opinion and practice regarding the treatment of people with epilepsy aged 65 years or older. We also sought to study how our opinion and practice varied between geriatricians, general neurologists, and epilepsy neurologists (i.e., epileptologists).

Methods: We initially piloted our survey to measure test–retest reliability. Once finalized, we disseminated the survey via two rounds of facsimiles, and then conventional mail, to eligible individuals listed in a national directory of Canadian physicians. We used descriptive statistics such as stacked bar charts and tables to illustrate our findings.

Results: One hundred forty-four physicians (104 general neurologists, 25 geriatricians, and 15 epileptologists) answered our survey in its entirety (overall response rate of 13.2%). Levetiracetam and lamotrigine were the preferred antiseizure medications (ASMs) to treat older adults with epilepsy. Two thirds of epileptologists and almost half of general neurologists would consider prescribing lacosamide in >50% of people aged >65 years; only one geriatrician was of the same opinion. More than 40% of general neurologists and geriatricians erroneously believed that none of the ASMs mentioned in our survey was previously studied in randomized controlled trials specific to the treatment of epilepsy in older adults. Epileptologists were more likely as compared to general neurologists and geriatricians to recommend epilepsy surgery (e.g., 66.6% vs. 22.9%–37.5% among older adults).

Significance: Therapeutic decisions for older adults with epilepsy are heterogeneous between physician groups and sometimes misalign with available clinical evidence. Our surveyed physicians differed in their approach to ASM choice as well as perception of surgery in older adults with epilepsy. These findings likely reflect the lack of clinical guidelines dedicated to this population and the deficient implementation of best practices.

KEYWORDS

antiepileptic medication, antiseizure medication, elderly, epilepsy surgery

1 | INTRODUCTION

Epilepsy is the third most common neurological disorder affecting older adults (generally defined as aged at least 65 years).[1] The incidence and prevalence of epilepsy in adults increases dramatically with age, peaking at age 80 years. The annual incidence at 80 years surpasses 500 cases per 100 000 individuals, nearly double that among younger adults.[2] Older adults with epilepsy also have a two to three times higher risk of mortality as compared to the general population, and are more vulnerable to the potential consequences of seizures, such as fractures and cognitive decline.[3,4] As the global population ages, older adults with epilepsy will become an increasingly prevalent population. Both the optimal medical treatment and the role for epilepsy surgery in older adults remain uncertain.[5–7]

Comorbidities, polypharmacy, and frailty are factors that complicate the appropriate treatment of epilepsy in older individuals. Age-related physiological changes can alter antiseizure medication (ASM) pharmacokinetics and pharmacodynamics.[8–10] Older adults often have a decreased ratio of muscle to body fat, and a reduced ability of albumin to bind protein-bound ASMs, which increase the volume of distribution and their free fraction.[11,12] Renal and hepatic diseases are common in this age group and may require ASM dosage adjustments, and impaired cognition or swallowing difficulties may necessitate a different route or frequency of administration.[5,13] The high prevalence of comorbidities and frailty in older adults make them more vulnerable to the adverse effects of ASMs such as osteoporosis, and often lead to polypharmacy, which increases the risk of drug–drug interactions.[14] Although these general treatment considerations are acknowledged, guidelines focused on the medical and surgical treatment of epilepsy in older adults are lacking.[5]

The primary objective of our study was to survey Canadian geriatricians and neurologists (those with and without specialty training in epilepsy) to evaluate their opinions and approaches to the treatment of epilepsy in older (>65 years) as compared to younger adults with epilepsy. Our hypothesis was that the findings from this study would identify knowledge gaps and emphasize the need to improve knowledge dissemination about the treatment of older adults with epilepsy.

2 | MATERIALS AND METHODS

We carried out a cross-sectional survey of Canadian neurologists and geriatricians. We followed the CROSS guidelines for conducting and reporting survey research (the complete CROSS checklist can be found in Appendix S1).[15]

Key points

- Geriatricians, general neurologists, and epileptologists differ in their approaches to the treatment of older adults with epilepsy.
- Close to 40% of physicians surveyed erroneously believed that none of the antiseizure medications in our survey had been subjected to randomized controlled trials in older adults.
- Geriatricians and general neurologists were less likely to refer an older adult for epilepsy surgery as compared to epileptologists.
- Our results point to the need for clear, well-disseminated clinical guidelines for the treatment of epilepsy in older adults.

2.1 | Questionnaire

To inform the design of our survey and its questionnaire, we conducted a pragmatic literature review to identify surveys about people with epilepsy, with ASM as its central subject, and physicians as respondents. We searched the electronic databases PubMed and Google Scholar on February 17, 2019 using the following keywords: epilepsy, antiepileptic medication, survey, seizures, older adults, and elderly. Dissertations, theses, and books were not included. We identified four relevant surveys, but an additional two articles were also identified through hand searching.[16–21] We extracted the survey design, question categories, broadcast method, and limits of each survey. The initial drafts of our survey questionnaire and dissemination plan were based on these already published surveys. After this initial step, we consulted three specialists in the diagnosis and management of epilepsy (N.J., C.B.J., and M.R.K.) to confirm, complete, modify, and reduce the number of items in our survey. Our goal was to create a survey that could be completed in <10 min. We divided our survey questionnaire into four blocks: (1) items on individual characteristics of the participants: city they currently practice in, speciality of clinical practice, last year of residency, and number of patients aged 65 years and older with epilepsy seen per month; (2) items on pharmacological treatments of epilepsy; (3) items on general knowledge of epilepsy and its treatment; and (4) questionnaire items on surgical treatments of epilepsy.

The final questionnaire included 19 closed questionnaire items that were initially drafted in English. The questionnaire was translated into French by fluently bilingual members of the research team, back-translated to English, and the different versions were compared to ensure that the meaning of the questions was similar in

the two languages. The questionnaires were imported into SurveyMonkey (www.surveymonkey.com), an online tool commonly used in web-based surveys. To evaluate the clinical decision-making of our participants, our questionnaire used rankings (e.g., rank these four priorities when treating epilepsy in older adults), rating scales (e.g., would consider prescribing in [fewer than 25] [25–49] [50–74] [75 or more] % of older adults), and multiple-choice questions (e.g., most common reason to switch ASMs in older adults). The final survey questionnaire in both languages can be found in Figures S1 and S2.

2.2 | Pretesting

We completed a pilot study by sending the survey to 18 physicians (10 English-speaking and eight French-speaking) practicing at the University of Montreal Hospital Centre or the McGill University Health Centre. Pilot participants were emailed the survey in their first language. We asked these physicians for their feedback regarding the relevance, clarity, and flow of questions. We used this feedback to modify or eliminate ambiguous questions. To examine the test–retest reliability of the survey, the pilot participants completed the survey a second time 2 weeks after the first completion. The survey was revised based on the feedback received from the pilot testing.

2.3 | Study population, sampling techniques, and questionnaire administration

We surveyed two groups of physicians: neurologists and geriatricians. Among neurologists, we distinguished between those with versus without subspecialty training in epilepsy (i.e., epileptologists and the remainder whom we refer to as general neurologists). The survey asked participants to self-report whether they had completed a 2-year postresidency training in geriatric medicine or a 5-year residency in neurology (the standards recognized by the Royal College of Physicians and Surgeons of Canada). A neurologist who self-reported additional training for at least 1 year of postresidency training in epilepsy was considered an epilepsy specialist.

We used a convenience sampling method by contacting all individuals listed as a neurologist or a geriatrician in Scott's Medical Directory. This database, the largest in Canada (including information on >89 000 physicians), collects the contact information of general practitioners and medical specialists in Canada by contacting relevant institutions and organizations (jurisdictional medical registrars, medical schools, the Royal College of Physicians and Surgeons of Canada, the College of Family Physicians of Canada). We used two methods (facsimile and conventional mail) to broadcast the survey. We sent a first facsimile to a total of 1090 geriatricians and neurologists on March 9, 2020. We sent a second facsimile on September 14, 2020. Our protocol had planned for a delay of 2 weeks between these facsimiles, but this was delayed due to the COVID-19 pandemic. These facsimiles included the typed link to the survey questionnaire on the SurveyMonkey website. SurveyMonkey allowed for participants to complete the survey on a personal computer, tablet, or cellphone. On November 20, 2020, 8 weeks after the final facsimile, we used conventional mail through Canada Post to send a printed copy of the survey questionnaire (printed from the SurveyMonkey website) to those who did not respond to the faxed link to the online questionnaire, along with a preaddressed and stamped envelope. We received the last completed questionnaire on January 18, 2021. In total, the recruitment spanned 36 weeks, with three inquiries (Figure S3).

A member of the research team manually entered the responses from the surveys received by conventional mail. To minimize transcription errors, a second member independently duplicated each transcription and compared it to the first one. All survey responses were directly downloaded from SurveyMonkey as a data file. SurveyMonkey was set to block any attempt to complete the survey a second time from the same IP address. SurveyMonkey also ensured that all questionnaire items were answered before allowing the participant to submit their completed survey. In the event that a survey sent by facsimile was not completely received, we removed the whole questionnaire from our dataset.

To ensure participant confidentiality and anonymity, Scott's Medical Directory assigned a unique identification number to each physician. Those same identification numbers were used to identify questionnaire responses.

Participants were entered into a raffle for one of two Amazon.ca gift cards (CAD$250 each, approximately USD$210) to encourage participation.

2.4 | Statistical analysis

During the pilot study, the test–retest reliability of questionnaire items was assessed by estimating a Fleiss kappa coefficient (95% confidence interval [CI]) for categorical items and an intraclass correlation coefficient (95% CI) for ordinal scale items. We qualitatively assessed as ranging from poor to almost perfect/excellent reliability based upon prior recommendations.[22,23]

We used stacked bar charts to present the differences in treatment choices between the specialties for both adults

younger and older than 65 years (Figures 1–4). Descriptive statistics, such as percentages and sample sizes, were added to the stacked bar charts to help visualize any differences. The remaining survey results are presented in Tables S1 and S2 or Figures S4–S8.

3 | RESULTS

The intrarater agreement among our pilot participants indicated almost perfect/excellent test–retest reliability, with Fleiss kappa and intraclass correlation coefficients ranging from .90 (95% CI = .85–.93) to 1.0 (95% CI = .97–1.00).

Of the 1090 physicians invited from across Canada, 144 responded to our survey in its entirety (response rate of 13.2%). Full details on the individual characteristics of the respondents' medical training and clinical practice are presented in Table S1. An additional 17 questionnaires were excluded from our study, as only portions of the questionnaire were received by fax. The sample of participants who answered the entire survey was composed of 104 (72.2%) general neurologists, 25 (17.4%) geriatricians, and 15 (10.4%) epileptologists. The distribution of specialists in the survey (105 neurologists, 25 geriatricians, and 15 epileptologists) was fairly representative of the Canadian distribution of those specialties according to the 2019 Canadian Medical Association report (1080 neurologists, 304 geriatricians).[24] Respondents were from >20 cities in Canada. One hundred eight (75.0%) respondents completed their medical training after the year 2000. One hundred twenty-two (84.8%) respondents treated between one and 19 older adults with epilepsy per month (Table S1), whereas eight participants treated zero patients with epilepsy per month (Table S1).

The respondents' perception of the influence of age on the treatment of epilepsy is presented in Table S2. The majority of physicians (93.1%) responded that they prescribe ASMs differently in older as compared to younger adults. Seventy-five respondents (55.6%) stated that, in their experience, achieving seizure freedom in older adults with epilepsy was similarly or more difficult than in younger adults with epilepsy. Figure 1 ranks the parameters likely to differ in the treatment of older adults compared to younger adults. The most likely parameter to differ was the choice of ASM (according to 55 [44.0%] respondents), whereas the least likely parameter to differ was the frequency of clinical follow-up appointments (according to 65 [52.0%] respondents).

We rank the main reasons selected by respondents for switching ASMs in older adults in Figure S4. Ninety-nine (68.7%) respondents answered that intolerable side effects are the most common reason for switching ASMs in older adults.

Figure 2 shows the ratings of ASMs based on their appropriateness in older versus younger adults among our three groups of specialists. Levetiracetam and lamotrigine were the preferred ASMs for older adults. Twelve (80%) epileptologists, 77 (74%) general neurologists, and 15 (60%) geriatricians would consider prescribing levetiracetam in >75% of people with focal onset epilepsy. Eleven (73.3%) epileptologists, 55 (52.9%) general neurologists, and 10 (40%) geriatricians would consider prescribing lamotrigine in >75% of people with focal onset epilepsy. Ten (66.6%) epileptologists and 50 (48.1%) general neurologists would consider prescribing lacosamide in most (>50%) people older than 65 years. Only one (4.0%) geriatrician would consider lacosamide in most people older than 65 years. More than 75.0% of geriatricians were unfamiliar with this ASM. Epileptologists who responded to our survey were less inclined than general neurologists or geriatricians to prescribe pregabalin. Six (24.0%) geriatricians would prescribe pregabalin in >75% of older people

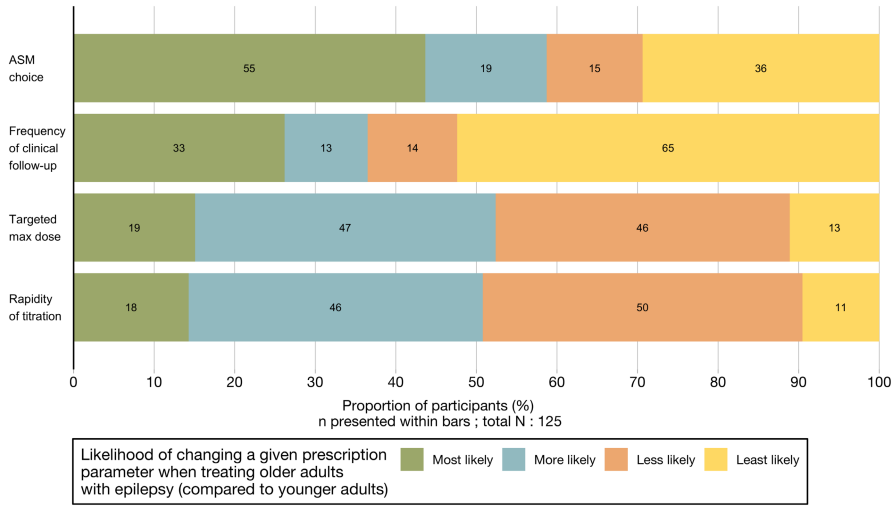

FIGURE 1 Likelihood of changing a given prescription parameter when treating older adults with epilepsy (compared to younger adults). The *y*-axis lists four parameters that may be adjusted for in the treatment of older adults with epilepsy. The *x*-axis represents the proportion of participants who supported a given parameter. The colors represent how likely the participants were to adjust each parameter (from most to least likely). ASM, antiseizure medication.

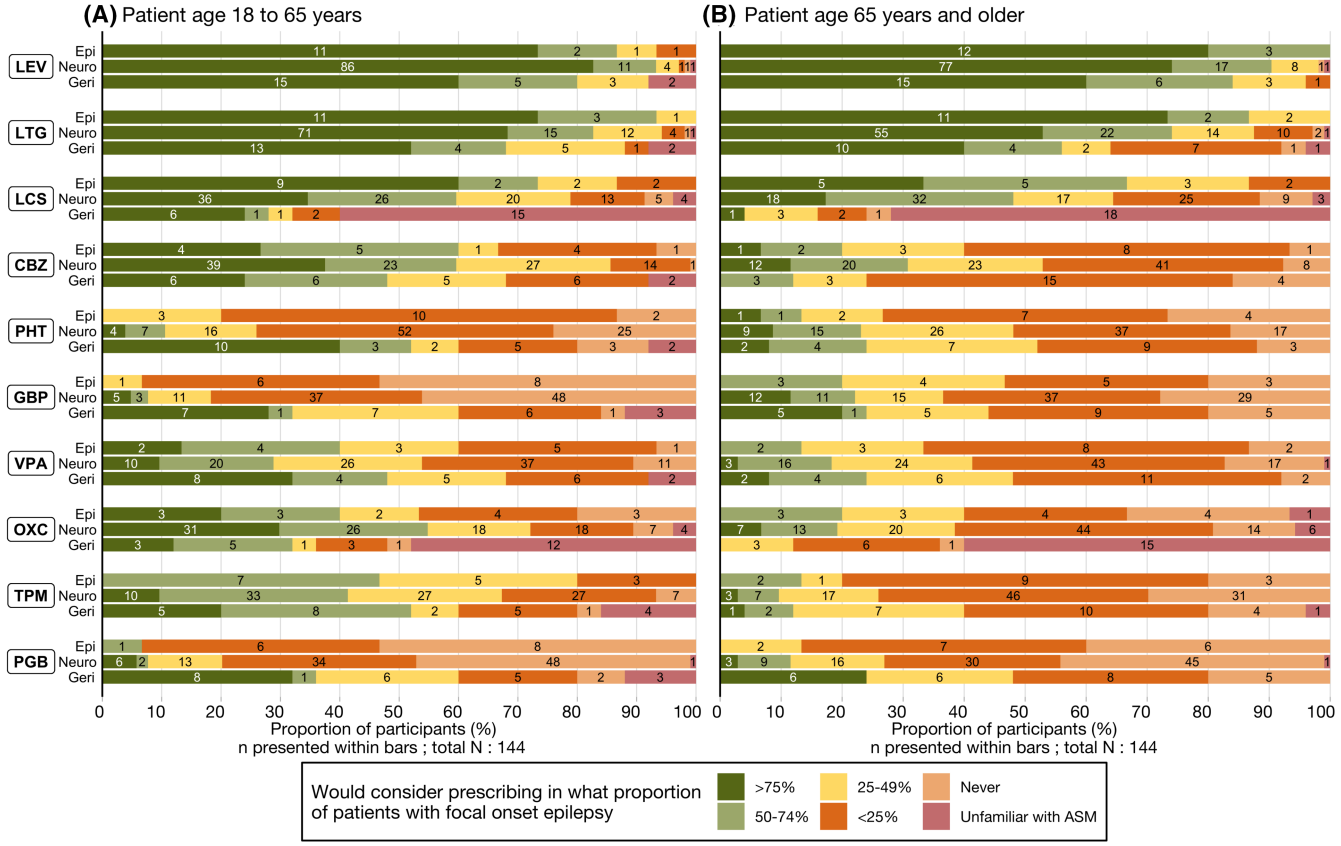

FIGURE 2 Ratings of antiseizure medications (ASMs) based on their appropriateness in older versus younger adults. The *y*-axis lists the 10 ASMs studied, stratified by the three specialist groups. The *x*-axis represents the proportion of participants. The colors represent the proportion of patients for whom the participants would consider prescribing each ASM (from >75% to <25% and unfamiliar with the ASM). (A) Results for younger adults (age = 18–65 years). (B) Results for older adults (age ≥65 years). CBZ, carbamazepine; EPI, epileptologists; GBP, gabapentin; Geri, geriatricians; LCS, lacosamide; LEV, levetiracetam; LTG, lamotrigine; Neuro, general neurologists; OXC, oxcarbazepine; PGB, pregabalin; PHT, phenytoin; TPM, topiramate; VPA, valproic acid.

as compared to no epileptologists, and only three (2.8%) general neurologists.

Figure S5 shows the ranking by respondents of different priorities when prescribing an ASM to an older adult with new focal onset (i.e., partial) epilepsy. The two highest ranked priorities were controlling seizures (34.0%) and the cost of the ASM (33.3%).

In Figure S6, we present the four most commonly prescribed ASMs according to the respondents. Ninety-two (66.7%) physicians believed that levetiracetam is the most commonly prescribed ASM in older adults. Phenytoin came in second place with 22 (15.3%) physicians. Only topiramate was never chosen as the most commonly prescribed ASM in older adults.

Figure 3 presents the ASMs believed to have previously been subjected to randomized controlled trials (RCTs) in older adults with epilepsy. Fifty-six (38.8%) surveyed physicians believed that none of the 10 ASMs described in our survey had previously been studied in RCTs specific to the treatment of epilepsy in older adults. This was least likely to be the case among epileptologists (26.7%), as compared to general neurologists (44.2%) and geriatricians (41.7%).

The opinions of our respondents on the appropriateness of a referral for epilepsy surgery are presented in Figure S7. One hundred nineteen respondents (82.6%) would at least consider referring an older adult for surgery if they see an epileptogenic lesion on neuroimaging, whereas only 39 respondents (27.1%) would do the same in the absence of such a lesion on neuroimaging. Forty-seven respondents (32.6%) would consider referring an older adult with a minor neurocognitive disorder that is "without functional impairment." The number of respondents with an affirmative response dropped from 47 (32.6%) to 14 (9.6%) when the cognitive deficit was moderate to severe (resulting in at least some functional impairment). Two respondents stated that an older adult should never be referred for epilepsy surgery. The number of disabling seizures providers felt were necessary for an older adult to be a candidate for epilepsy surgery is presented in Figure S8. Twenty-five respondents (18.5%) would only consider an older adult for epilepsy surgery if

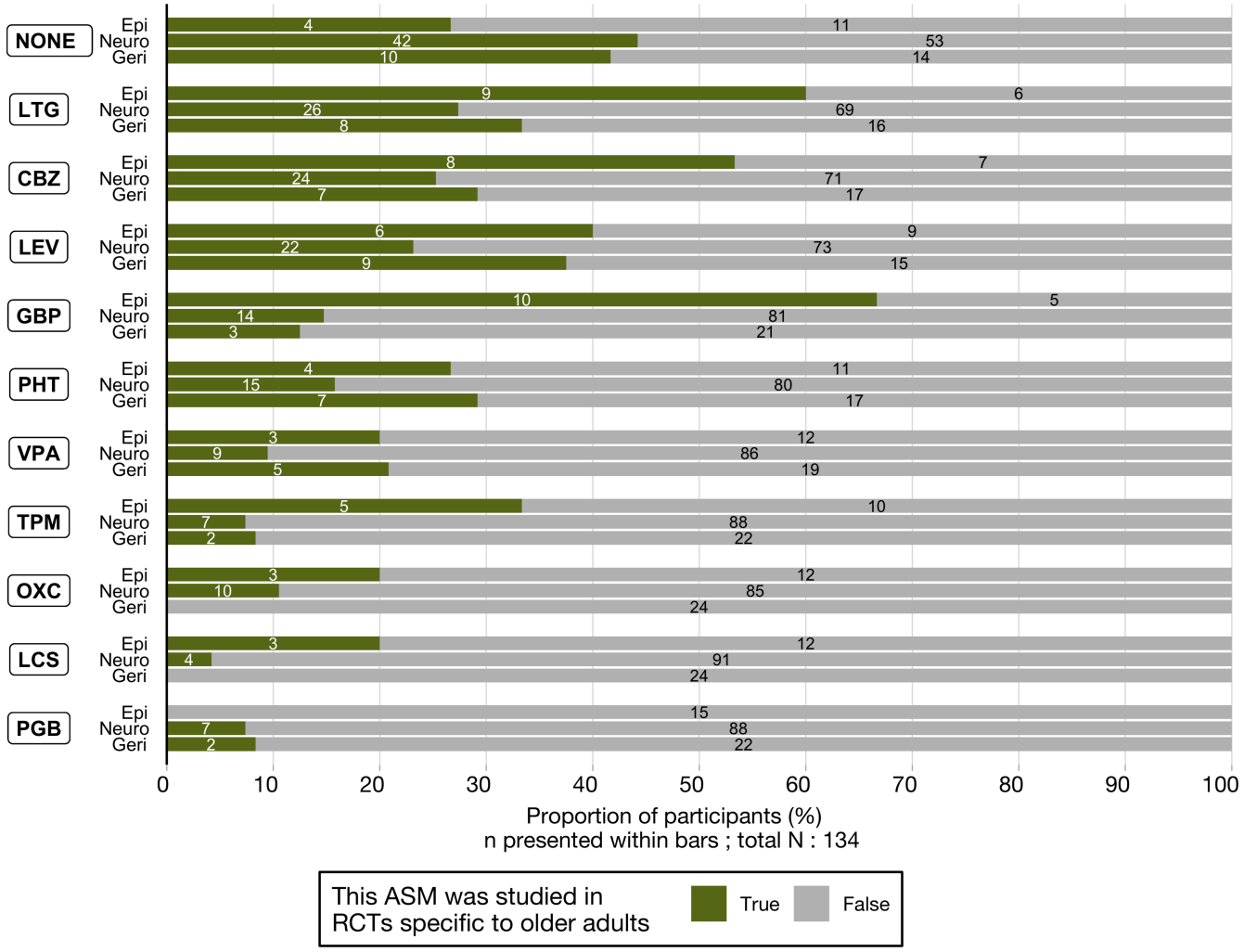

FIGURE 3 Physicians' belief of antiseizure medication (ASM) to have previously been subjected to randomized controlled trials (RCTs) in older adults with epilepsy. The *y*-axis lists the 10 ASMs studied, as well as no ASM, stratified by the three specialist groups. The *x*-axis represents the proportion of participants responding true or false. CBZ, carbamazepine; EPI, epileptologists; GBP, gabapentin; Geri, geriatricians; LCS, lacosamide; LEV, levetiracetam; LTG, lamotrigine; Neuro, general neurologists; OXC, oxcarbazepine; PGB, pregabalin; PHT, phenytoin; TPM, topiramate; VPA, valproic acid.

the person were experiencing seizures monthly or more frequently.

Figure 4 compares the proportion of the three groups of surveyed physicians considering referring for epilepsy surgery based on age, frailty, and epilepsy type. All three groups of physicians were more open to proposing surgery to younger individuals. Epileptologists were generally more open to recommend surgery as compared to general neurologists and geriatricians (e.g., 10 epileptologists [66.7%] were extremely likely to propose surgery in people aged 60–69 years with bilateral tonic–clonic seizures as compared to 22 general neurologists [22.9%] and nine geriatricians [37.5%]). General neurologists were the least open throughout. The proportion of physicians that recommended surgery fell drastically among all groups of physicians when the person was considered frail, with only one epileptologist (6.7%), one general neurologist (1.0%), and three geriatricians (12.5%) extremely likely to propose surgery to frail individuals aged 60–69 years.

4 | DISCUSSION

Our study surveyed physicians on the medical and surgical treatment of epilepsy in adults older and younger than 65 years. Our hypothesis was that the findings from this study would identify knowledge gaps and emphasize the need to improve knowledge dissemination about the treatment of older adults with epilepsy. One hundred forty-four geriatricians, general neurologists, and epileptologists across Canada completed our survey in its entirety. Prior surveys in epilepsy focused on pediatric or younger adult populations.[16–21]

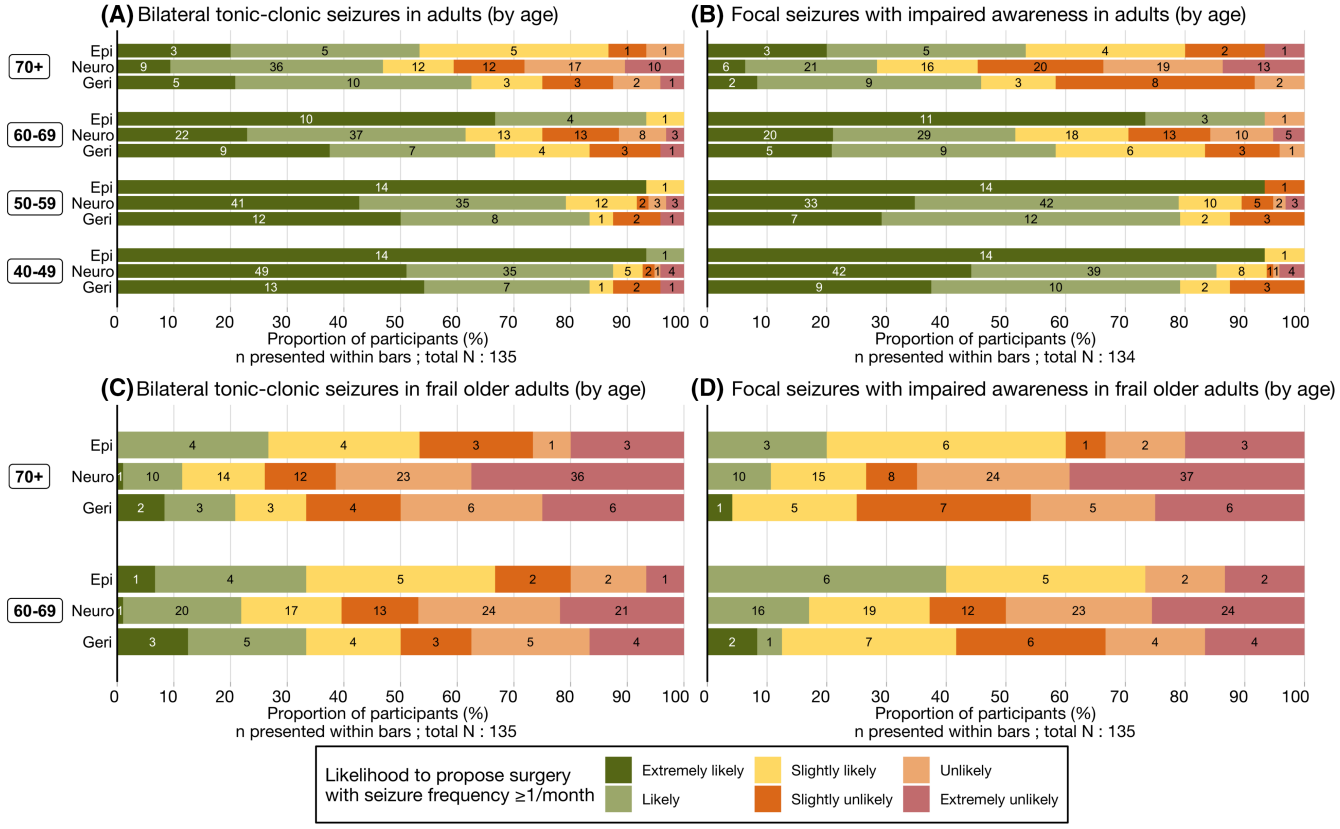

FIGURE 4 Likelihood of proposing surgery with seizure frequency ≥1/month. The *y*-axis lists age groups (in years), stratified by the three specialist groups. The *x*-axis represents the proportion of participants. The colors represent how likely the participants are to propose epilepsy surgery (from extremely likely to extremely unlikely). (A) Results for patients with bilateral tonic–clonic seizures. (B) Results for patients with focal seizures with impaired awareness. (C) Results for frail older adults with bilateral tonic–clonic seizures. (D) Results for frail older adults with focal seizures with impaired awareness. EPI, epileptologists; Geri, geriatricians; Neuro, general neurologists.

The physicians surveyed in our study agreed that older adults should be treated differently than younger adults. Many lines of reasoning suggest that older adults with epilepsy require a different treatment approach as compared to younger individuals. Comorbidities, polypharmacy, and frailty as well as age-related physiological changes are factors requiring special consideration during treatment selection for older adults with epilepsy.[8–14] The physicians surveyed in our study endorse this treatment principle, with the vast majority stating that they prescribe ASMs differently in older as compared to younger individuals and that intolerable side effects are the most common reason for switching ASMs in older adults.

The three groups of physicians surveyed partially disagreed regarding which medical treatment should be preferred in older adults. Whereas epileptologists and general neurologists were very comfortable prescribing lacosamide, three quarters of geriatricians were unfamiliar with this medication. This represents a considerable knowledge gap with an ASM whose utility in older adults is confirmed by an RCT.[25] Geriatricians were much more comfortable prescribing pregabalin, potentially due to other indications for these drugs (neuropathic pain, anxiety) that are commonly seen in older adults.

There is discordance between our results, published studies, and recommendations on the medical treatment of older adults. Despite a recent systematic review that identified 18 RCTs of ASMs in older adults,[5] our study showed that close to 40% of the surveyed physicians believed that none of the 10 ASMs mentioned in our survey had been previously subjected to RCTs. Despite evidence supporting the use of gabapentin in older adults and this being one of the only two medications recommended by 2013 International League Against Epilepsy practice standards for older adults with epilepsy,[26,27] gabapentin was less favored by the surveyed physicians, especially by epileptologists. Their opinion might be influenced by the poor efficacy and limited evidence of this ASM in younger adults.[26] More than half of our respondents (55%) perceived that achieving seizure freedom in older adults was as or more difficult than in younger adults despite evidence that it is generally easier.[28] These results were striking and show a clear gap in knowledge dissemination from research to clinical practice.

There is also discordance between the answers of our respondents and the literature on the surgical treatment of epilepsy. There was a reluctance of geriatricians and general neurologist to refer older adults for surgery in our study, despite evidence showing that surgery in carefully selected older adults compares favorably to surgery in younger age groups.[29,30] All surveyed physicians refrained from referring frail individuals for surgery, although there is a lack of clinical studies addressing this important clinical question. This represents a need for future research. The proportion of respondents who would refer an older person with epilepsy if there was an epileptogenic lesion on neuroimaging (83%) was much higher compared to if there was no lesion (27%). These findings are relevant given that published guidelines stipulate that "normal" neuroimaging should not deter a referral for an epilepsy surgery evaluation.[31]

Our study has several strengths. We developed our survey based on a literature review of similar surveys, followed by a pilot study that demonstrated almost perfect/excellent test–retest reliability. We followed the 2021 CROSS standards for conducting and reporting high-quality survey research. The distribution of specialists among our respondents was fairly representative of the Canadian distribution of those specialties.

The findings from our study should be interpreted while considering the following limitations. Our sample size was limited. It is difficult to assess whether the knowledge and opinions of our survey respondents are generalizable to the entire population of neurologists and geriatricians in Canada. Our results are potentially biased toward the opinions of the type of physicians who may be more likely to respond to research surveys, including those practicing in academic centers. Our sample also was slightly skewed toward physicians early in their careers (75.0% of respondents completed their training after the year 2000). This could be explained by two of three survey administration attempts being through an online survey. For the sake of brevity, respondents were unable to provide explanations to the reasoning behind each of their answers, which limits the interpretation of the results. Considering that we used a convenience sampling method and participation was on a voluntary basis, nonresponse error is difficult to approximate. The precise results of our study cannot be directly extrapolated to the entire Canadian population of general neurologists, epileptologists, and geriatricians. Finally, we removed from our dataset 17 surveys received by fax that were not completely answered. We assumed that those surveys with missing data were not "completely at random" (e.g., those with missing data were those responding via mail; those responding electronically could not submit their survey with missing data), and therefore we could not replace these missing data using multiple imputation. It is important to note that the majority of the answers actually provided for those with incomplete surveys were about the individual characteristics of the participants (city they currently practice in, speciality of clinical practice, last year of residency, and number of patients aged 65 years and older with epilepsy seen per month).

In conclusion, our study showed that among our survey respondents, the decision-making landscape around the treatment of epilepsy in older adults is heterogeneous and sometimes misaligned with the available clinical evidence. These findings highlight the need for ongoing physician education. Older adults are treated differently than younger adults, they are treated differently by physicians of different medical specialties, and most striking, they are treated differently than what would be expected from the available evidence in some instances. Considering the high prevalence and burden of epilepsy in older people, we hope that the results of our study will motivate the development and dissemination of clear and specific evidence-based guidelines on the treatment of epilepsy in older adults. There is a pressing need to translate current research knowledge to clinical practice, which would likely help to minimize deficient implementation of best practices.

AUTHOR CONTRIBUTIONS

Mark R. Keezer was the initiator of the idea and primary investigator of the research. Nafisa Husein developed the questionnaire and collected, cleaned, and analyzed the data. Timothé Langlois-Thérien helped with the analysis and the redaction of the manuscript. Bastien Rioux helped with the analysis and formatting of the figures. Nathalie Jetté and Colin B. Josephson contributed to the manuscript revision.

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CONFLICT OF INTEREST STATEMENT

M.R.K. reports unrestricted educational grants from UCB and Eisai, research grants for investigator-initiated studies from UCB and Eisai as well as from government entities (Canadian Institutes of Health Research, Fonds de Recherche Québec–Santé), academic institutions (Centre Hospitalier de l'Université de Montréal), and foundations (TD Bank, TSC Alliance, Savoy

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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