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FULL-LENGTH ORIGINAL RESEARCH

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# Newly diagnosed seizures assessed at two established first seizure clinics: Clinic characteristics, investigations, and findings over 11 years

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## Abstract

**Objective:** 'First seizure' clinics (FSCs) aim to achieve early expert assessment for individuals with possible new-onset epilepsy. These clinics also have substantial potential for research into epilepsy evolution, outcomes, and costs. However, a paucity of FSCs details has implications for interpretation and utilization of this research.

**Methods:** We reviewed investigation findings over 11 years (2000-2010) from two established independent FSCs at Austin Health (AH) and Royal Melbourne Hospital (RMH), Australia. These adult clinics are in major public hospitals and operate with similar levels of expertise. Organizational differences include screening and dedicated administration at AH. Included were N = 1555 patients diagnosed with new-onset unprovoked seizures/epilepsy (AH n = 901, RMH n = 654). Protocol-driven interviews and investigations had been recorded prospectively and were extracted from medical records for study.

**Results:** Median patient age was 37 (IQR 26-52, range 18-94) years (AH 34 vs RMH 42 years; $P < .001$). Eighty-six percent of patients attended FSC within three weeks postindex seizure (median AH 12 vs RMH 25 days; $P < .01$). By their first appointment, 42% had experienced ≥2 seizures. An EEG was obtained within three weeks postindex seizure in 73% of patients, demonstrating epileptiform discharges in 25% (AH 33% vs RMH 15%). Seventy-six percent of patients had an MRI within 6 weeks. Of those with imaging (n = 1500), 19% had potentially epileptogenic abnormalities (RMH 28% vs AH 12%; $P < .01$). At both sites, changes due to previous stroke/hemorrhage were the commonest lesions, followed by traumatic brain injury. ≥WHO level 1 brain tumors diagnosed at presentation comprised a very small proportion

These senior authors Patrick Kwan, Terence J. O'Brien, and Samuel F. Berkovic contributed equally.

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(<1%) at each clinic. At both sites, epilepsy type could be determined in 60% of patients; RMH had more focal and AH more generalized epilepsy diagnoses.
**Significance:** Differences between the clinics' administrative and screening practices may contribute to differences in investigation findings. Insight into these differences will facilitate interpretation and utilization, and planning of future research.

**KEYWORDS**
EEG, epilepsy, epileptogenic lesion, imaging, new-onset

## 1 | INTRODUCTION

'First seizure' or new seizure diagnosis clinics have been established with the intention of providing patients with a rapid specialist epileptological assessment in order to obtain an early diagnosis and facilitate management of new-onset seizures or epilepsy. These clinics aim to achieve short time periods between the index presentation and clinic consultation with an experienced epileptologist, usually with EEG and brain imaging obtained as soon as possible.[1-3]

Positioned at the entry-point of an individual's engagement with specialist epilepsy care, first seizure clinics (FSCs) also have substantial potential to facilitate efficient and comprehensive research programs. These programs may inform on epilepsy evolution, prognosis, costs, and outcomes.[4,5] However, the paucity of data addressing the design, demographics, findings, and other details of these clinics has been noted.[2] Without these details, research outcomes may be misinterpreted, with little insight into why study results differ between clinic sites.

Here, we studied the results from two well-established and independent Australian FSCs, produced over an 11-year period. These clinics are situated in major public hospitals in different areas of the same city. They both operate with similar levels of expertise using comparable protocols with a few points of administrative difference. We aimed to describe and compare the findings for patients who presented to these two clinics and obtained a new diagnosis of epilepsy or an unprovoked seizure. We examined elapsed times between index event and clinic presentation, assessments undertaken, investigation results, and patients' seizure history as experienced up to the point of FSC assessment. The contrasts between these two clinics will be instructive for interpretation and utilization of research in this area.

**Key Points**

- Data from patients seen in two established independent 'first seizure' clinics over 11 years were reviewed
- EEG showed epileptiform discharges in 25% of patients and imaging demonstrated potentially epileptogenic findings in 19%
- At both clinics, changes from previous stroke/hemorrhage were the commonest pathology, brain tumors (≥WHO Level 1) were < 1%
- The clinics differed in terms of EEG and imaging yield, possibly due to organizational differences between the sites
- An understanding of how local clinic characteristics shape research findings is essential for interpretation and application of research

## 2 | METHODS

### 2.1 | First seizure clinic sites

The two FSCs are predominantly adult clinics, located within public hospitals that service geographically different areas of the greater Melbourne area (Australia). The Royal Melbourne Hospital (RMH) is located on the edge of the central business district, and its surrounding areas incorporate inner city residential areas including several university campuses. The Austin Hospital (AH) is situated in suburban Melbourne, approximately 12 kilometers from the central business district, surrounded by residential areas.[6]

At both sites, referrals come from the community via general practitioners, the hospital emergency departments located at each site, or surrounding hospitals. Referrals from external medical consultants or from the hospital wards are rare.[6] At AH, the aim is to prioritize individuals who may otherwise find it difficult to obtain a diagnosis. Therefore, referred cases are initially screened by a clinician, and individuals with a clear underlying cause for seizures (such as known stroke or traumatic brain injury) or events that are clearly not epileptic (ie obvious substance-withdrawal seizures or syncope discernible via telephone assessment) are usually directed to other clinics. Clinic booking and other

administration are managed by a dedicated administrative staff member. At RMH, referred cases are booked directly via the hospital outpatient booking system with minimal or no screening.

## 2.2 | Routine first seizure clinic protocol

At each FSC, a detailed clinical history is taken from all patients, including a history of potential pre-index seizures, and a witness description of events when available. All patients have a routine EEG as soon as practical. At AH, protocol is that a sleep-deprived EEG is also obtained if the initial routine is uninformative, and a brain MRI is obtained for all patients except those with genetic generalized epilepsies. RMH protocol is that a sleep-deprived EEG is obtained if the initial routine is uninformative, and an MRI is obtained for all patients where possible. The MRI protocol at both sites is a dedicated epilepsy protocol, earlier MRIs were on a 1.5T scanner and later scans were 3T. MRI may be contraindicated due to implanted devices or the need for anesthesia (ie intellectual disability or dementia). In these cases, a CT scan is utilized. EEGs are assessed and reported by epileptologists and imaging is reported by neuroradiologists.

The clinical information and investigations are reviewed by epileptologists at the FSC, and a diagnosis is made of an unprovoked seizure/epilepsy,[7-10] acute symptomatic seizure, nonepileptic event (eg, syncopal convulsion, movement disorder, psychogenic disorder, etc), or unclassified event. In patients presenting with an unprovoked seizure—the epilepsy type (focal/generalized) and syndrome diagnosis are made where possible. Diagnoses are often made at first appointments but may also be made over two or three appointments, as there is often a time-lapse before investigations (particularly MRI) are undertaken and results become available. Once a diagnosis is made and anti-epileptic drug (AED) treatment established if required, the patient is discharged from the clinic to ongoing routine care by a neurologist and/or general practitioner.

## 2.3 | Study methods

### 2.3.1 | Inclusion/exclusion criteria

Included in this study are patients ≥18 years of age at presentation to the FSC, who received a new diagnosis of unprovoked seizure/s (as per Beghi et al[11]) or epilepsy at the clinics between the years 2000-2010. RMH cases incorporate many of the cases reported in Hakami et al,[12] which were rereviewed for this paper.

Excluded were patients with acute symptomatic seizures, nonepileptic events, unclassified events, and patients with a prior diagnosis of epilepsy or with AEDs prescribed for >3 months. Excepted from this were patients seen at the FSC who had a past history of epileptic seizures associated with a known brain lesion or abnormality which was completely resected (according to imaging reports) with postoperative seizure freedom for at least 12 months. The few tourists or individuals visiting from overseas were excluded, as they may have utilized services differently and may not have remained in situ long enough for investigations to be performed.

Each site was cross-checked for duplicate patients; we found only two who attended both clinics. For these patients, we used the information from the first visit that met the inclusion/exclusion criteria.

This study was approved by the human research ethics committee (HREC) at Melbourne Health (The Royal Melbourne Hospital) and Austin Health.

### 2.3.2 | Data collection and variable definitions

Study data were obtained via audit of the records of the AH and RMH FSCs.

*Patient assessment and investigation*

The 'index seizure' was defined as the seizure that prompted referral and attendance at the FSC as defined in the inclusion criteria. In a few cases where the index seizure was not clearly identified, the last seizure prior to presentation was used.[6] Index seizures were coded as convulsive, nonconvulsive, or unclassified.[6] Time from index seizure to first clinic attendance was calculated.

The proportion of patients who obtained EEGs and neuroimaging were noted, together with the days from index to investigation. Time from index seizure to EEG was noted for AH, whereas at RMH only the date of the EEG utilized for the study (see summary of EEG results below) was available. As a result, we did not make any direct comparisons between the two sites regarding time to EEG investigation. EEG and imaging reports up to 12 months after the first FSC consultation were reviewed and coded for this study by clinic neurologists. This time period was allowed as there was often a routine delay between the first consultation and these investigations. Any acute imaging findings that occurred after the index seizure were not included. Investigations before the index were also included if they were utilized in the clinic assessments and no other investigations were undertaken within this 12-month time frame.

EEG results (routine and sleep-deprived) were amalgamated and summarized by coding the highest level of abnormality in order of priority as 1) epileptiform; 2) slowing (focal/generalized); 3) normal.

Imaging findings were coded as demonstrating a possible epileptogenic abnormality (as per Hakami et al[12]), or

nonepileptogenic/nonspecific findings[12]. The type of potentially epileptogenic abnormality was noted. While collating imaging data we found that differentiating between stroke types (ischemic, hemorrhagic, hemorrhagic transformation) as well as other sources of brain bleeds (vascular malformation or aneurysm with hemorrhage) was difficult or impractical in some cases due either to the way they had been reported or (when we reviewed the scans) natural changes over the interval between the insult and the index seizure investigation. Therefore, these pathologies were counted as one group.

A positive history of possible seizure events occurring before the index seizure was noted.[1,6] As detailed in our previous study,[6] most prior seizures are unreported at the time they occur and only come to light during the detailed FSC clinical interview. We counted reported events if clinicians indicated in the notes that these events were possible seizures. Events that occurred <6 years of age were excluded from this count.[6] Seizures between the index and the first clinic visit were also noted. If no mention of potential seizures before the index or between index and clinic was made, these cases were coded as negative.

Then, total seizures/probable seizures before the first clinic visit were obtained by combining both of the above plus the index seizure. These were coded as per Firkin et al;[6] due to the issues mentioned above and the retrospective nature of these reports these frequencies are best estimates. Seizures that occurred within 24 hours or (when this information was not available) on the same calendar day were counted as one seizure. The count did not include myoclonic jerks, absences, or very brief seizures (thought likely to be absences or brief focal seizures) as these were difficult to quantify. Instead, the fact that these had been reported was noted separately.

Broad epilepsy type was determined for the study by FSC neurologists. This was done by review of the patient history given at the first clinic visit, together with investigation results compiled for the study. Patients were coded as having a focal or generalized epilepsy,[10] or unclassified epilepsy. This was intended as an overview for this study and does not reflect ability to determine the epilepsy type at first clinic visit.

We also noted nonattendance at the first scheduled FSC appointment; due to study time constraints, we were only able to obtain these data from the RMH clinic computer records. Only nonattendance without notice for the first appointment for each individual was considered for this study. Notified cancelations, changed appointments, and nonattendance for follow-up appointments were excluded.

#### 2.3.3 | Data analysis

Analyses used nonparametric measures as data were generally not normally distributed. These included summary statistics, Pearson chi-square test for categorical measures, and Mann-Whitney U tests for time and age variables. Results were considered statistically significant at the 5% level (two-sided).

## 3 | RESULTS

There were 1555 clinic attendees who met the inclusion criteria, 654 from RMH and 901 from AH. Median age at first attendance was 37 (IQR 25.9-52.2; range 18-94.3) years. The RMH cohort was older with a median age of 41.6 years vs 34.2 years at AH ($P < .001$). When stratified into four age groups, the differences are evident in the youngest and oldest groups (Table 1).

### 3.1 | Time from index seizure to clinic/investigations (Table 1)

Attendance at a FSC by 2 weeks was achieved in 53% of all patients and in 85.5% by three weeks. Time from index to clinic was shorter for those who attended AH, with the median time differing by almost two weeks between the clinics. Extensive delay (>6 months) between the index and clinic was <2% at both sites.

At RMH, nonattendance at a first scheduled clinic appointment without notice was found in 8% of patients in this study. Nonattendance ≥1 was associated with time between index and clinic of >6 months ($\chi^2[1, n = 606] = 46.5$, $P < .01$).

An EEG was obtained within 3 weeks *postindex seizure* in 73% of all patients. Ninety-six percent of patients had an EEG within the 12-month time frame. A brain MRI or CT had been obtained within 6 weeks after the *first clinic visit* in 76% of the total patients. By 1 year, 96.3% of patients had undergone neuroimaging. The proportion of patients with imaging at AH was slightly lower compared to RMH, concordant with AH protocol (see Methods). CT was the only imaging for 22% of patients in both cohorts.

### 3.2 | Investigation findings

Epileptiform discharges on EEG were found in one quarter of all patients, 33% at AH and 15% at RMH ($\chi^2$ [1]=58 $P < .001$) (Table 2). Imaging demonstrated potentially epileptogenic brain abnormalities in 28% of RMH patients and in 12% of AH patients ($\chi^2$ [1, n = 1500 with imaging] =54.8, $P < .01$). Pathological subtypes as reported are detailed in Table 2. In addition, 6 other patients in the RMH group had imaging signs of acute brain trauma and reports did not supply any other underlying nontrauma pathology. Witnesses and other evidence strongly suggested the trauma resulted from the convulsive index seizure—for example, the patient was seen to fall and hit their head during the index seizure.

**TABLE 1** Patient characteristics and time to investigation at first seizure clinic

| | RMH N = 654 | Austin N = 901 |
|---|---|---|
| Age at first clinic attendance[a] | 41.6 y | 34.2 y |
| *Median (IQR, range)* | (29-59, 18-94) | (25-49, 18-90) |
| Age at clinic—grouped n (%) | | |
| 18-30 years | 187 (28.6) | 362 (40.2) |
| 30.1-50 years | 239 (36.5) | 336 (37.3) |
| 50.1-65 years | 105 (16.1) | 118 (13.1) |
| >65 years | 123 (18.8) | 85 (9.4) |
| Sex[b] n (%) | Male 402 (62) | Male 505 (56) |
| Time index seizure to clinic[c] | 25 d | 12 d |
| *Median (IQR, range)* | (13-43 d, 0-1.4 y) | (8-21 d, 0-1.2 y) |
| >6 months between index and clinic n (%) | 12 (1.8) | 4 (0.4) |
| Nonattendance at 1st appointment[d] n (%) | None = 557 (85.2) | Not available |
| | ≥1 = 49 (7.5) | |
| | No info = 48 (7.3) | |
| Time index to 1st EEG | Not available | 1 d[e] |
| *Median (IQR, range)* | | (0-3 d, −180 to 373 d) |
| Time index to EEG used in study | 24 d[f] | Not available |
| *Median (IQR, range)* | (5-66 d, −284 to 424 d) | |
| EEG *before* index (<1 y) n (%) | 9 (1.4) | 7 (0.78) |
| EEG no dates available n (%) | 18 (2.8) | 3 (0.33) |
| No EEG in study time frame n (%) | 22 (3.4) | 2 (0.2) |
| EEG within 2 days *post*index n (%) | Not available | 661 (73) |
| Time clinic to imaging | 16 d[g] | 15 d[h] |
| *Median (IQR, range)* | (−16 to 44 d, −1.5 y to 11 mo) | (−7 to 36 d, −3.2 y to 10 mo) |
| Imaging type n (%) | | |
| None in study time frame | 4 (0.6) | 51 (5.7) |
| MRI | 502 (76.8) | 649 (72.0) |
| CT no MRI | 147 (22.5) | 200 (22.2) |
| Type no information | 1 (0.2) | 1 (0.1) |

[a]Mann-Whitney U test $P < .001$

[b]$\chi^2$ [1] 4.6, $P = .03$.

[c]Total N = 1555: median 16 days, IQR 9-31, range 0-516. Comparison RMH & AH: Mann-Whitney U test $P < .001$.

[d]Excludes cancelation or change of dates.

[e]N = 895. Includes x3 > 1 year postindex but < 1 year postclinic, x7 before index. Excludes x4 EEG missing dates, x2 no EEG. Due to a difference in data collection, this information was not available for RMH.

[f]N = 614. Includes x9 > 1 year postindex but < 1 year postclinic, x9 before index. Excludes x18 EEG missing dates, x22 no EEG. Not supplied for AH, see (e).

[g]N = 644. Excludes x6 imaging missing dates, x4 no imaging. Includes 25 (4%) with imaging before index.

[h]N = 837. Excludes x13 imaging missing dates, x51 no imaging. Includes 32 (4%) with imaging before index.

The higher proportion with potentially epileptogenic pathology seen at RMH compared to AH is evident over each of the four age-bands (18-30 years, $\chi^2(1) = 6.3$ $P = .012$; 30.1-50 years, $\chi^2(1) = 17.1$ $P < .01$; 50.1-65 years, $\chi^2(1) = 6.9$ $P < .01$; >65 years, $\chi^2(1) = 10.3$ $P < .01$).

## 3.3 | Seizure history

Index seizures were convulsive in approximately 85% of patients, nonconvulsive in 10% of patients, and unclassified in the remainder (RMH vs AH chi2[2, n = 1555] = 1.3 $P = .52$).

**TABLE 2** Investigation results

| | RMH N = 654 n (%) | Austin N = 901 n (%) |
|---|---|---|
| EEG summary results | | |
| Normal | 406 (62) | 363 (40.3) |
| Focal epileptiform | 62 (9.5) | 148 (16.4) |
| Generalized epileptiform | 35 (5.4) | 147 (16.3) |
| Generalized slowing | 42 (6.4) | 74 (8.2) |
| Focal slowing | 87 (13.3) | 167 (18.5) |
| Results not found/not done | 22 (3.4) | 2 (0.2) |
| Imaging findings[a] | | |
| No scan | 4 (0.6) | 51 (5.7) |
| Nonepileptogenic/Normal[b] | 470 (71.6) | 746 (82.8) |
| Potentially epileptogenic[c] | | |
| Gliosis/encephalomalacia/hemorrhage | | |
| Stroke/ hemorrhage[d] previous | 68 (10.4) | 30 (3.3) |
| Traumatic brain injury (TBI) previous | 25 (3.8) | 21 (2.3)[e] |
| Brain surgery previous | 10 (1.5)[f] | 4 (0.4)[g] |
| Other gliotic/encephalomalacia | 3 (0.5)[h] | 1 (0.1)[i] |
| Other pathologies | | |
| Cortical malformation/dysplasia | 16 (2.5) | 16 (1.8) |
| Vascular malformation[j] | 14 (2.1) | 2 (0.2) |
| Mesial temporal sclerosis | 7 (1.1)[k] | 4 (0.4)[l] |
| Tumor benign[m]/DNET | 12 (1.8) | 6 (0.7) |
| Tumor level 1-2 | 2 (0.3) | 2 (0.2) |
| Tumor level 3-4 | 2 (0.3) | 4 (0.4) |
| Brain metastasis | 0 | 3 (0.3) |
| Residual tumor after previous resection | 4 (0.6)[n] | 2 (0.2)[o] |
| Other epileptogenic | 9 (1.4) | 7 (0.8) |
| Dual pathologies | 2 (0.3)<br>TBI with craniotomy & AVM<br>Stroke & benign tumor | 2 (0.2)<br>Stroke & MTS unilateral<br>MTS unilateral & other |
| Acute brain trauma at presentation | 6 (0.9) | 0 |

[a]RMH: x502 (77%) MRI, x147 (23%) CT no MRI, x1 (0.2%) imaging type unknown, x4 (0.6%) no imaging; AH: x649 (72%) MRI, x200 (22%) CT no MRI, x1 (0.1%) imaging type unknown, 51 (6%) no imaging.

[b]Includes normal, nonepileptogenic (not potentially epileptogenic) (Hakami et al, 2013[12]) or nonspecific findings.

[c]Potentially epileptogenic (Hakami et al, 2013[12]).

[d]Includes stroke (ischemic, hemorrhagic, hemorrhagic transformation, type unknown), vascular malformation bleed, aneurysm bleed, subarachnoid hemorrhage.

[e]x1 with craniotomy.

[f]Fully resected (on imaging reports): benign tumor x5; AVM x4. Surgical procedure x1.

[g]Fully resected (on imaging reports): benign tumor x2, AVM x2.

[h]brain abscess with drainage x3.

[i]injury or ischemic stroke—unable to differentiate.

[j]no evidence of bleed on imaging report.

[k]All unilateral.

[l]Bilateral n = 2/4.

[m]i.e: ganglioglioma, oligodendroglioma, meningioma.

[n]Tumor benign x2, Tumor level 1-2 x2.

[o]Tumor benign x1, Metastases x1.

**TABLE 3** Seizure history[a]

| | RMH N = 654 n (%) | Austin N = 901 n (%) |
|---|---|---|
| Index seizure classification | | |
| Convulsive | 546 (83.5) | 770 (85.5) |
| Nonconvulsive | 68 (10.4) | 79 (8.8) |
| Unclassified | 40 (6.1) | 52 (5.8) |
| Possible prior epileptic seizure before clinic index seizure | | |
| Yes | 207 (31.7) | 378 (42) |
| No | 447 (68.3) | 523 (58) |
| Seizure between index & clinic ('in-between seizure') | | |
| None | 585 (89.5) | 826 (92) |
| One seizure | 35 (5.4) | 43 (4.7) |
| 2-5/few/several ± jerks/brief events[b] | 17 (2.6) | 19 (2) |
| >5/many/multiple ± jerks/brief events[b] | 3 (0.5) | 2 (0.2) |
| >1 seizure no further detail | 1 (0.2) | 2 (0.2) |
| Jerks/ brief events[b] only | 1 (0.2) | 5 (0.6) |
| Insufficient information | 12 (1.8) | 4 (0.4) |
| 'In-between' seizure & time to clinic[c] | | |
| Time from index seizure to clinic if no 'in-between' seizure/s. *Median (IQR, range)* | 22 d (11-39, 0-516) n = 585 | 12 d (I7-20, 0-430) n = 826 |
| Time from index seizure to clinic if positive for 'in-between' seizure/s. *Median (IQR, range)* | 48 d (33-92, 1-498) n = 57 | 17 d (10-34, 1-221) n = 71 |
| Seizure total any before clinic | | |
| Index only | 409 (62.5) | 493 (54.7) |
| Index + jerks/brief events[b] | 5 (0.76) | 33 (3.7) |
| 2-5/few/several ± jerks/brief events[b] | 165 (25.2) | 219 (24.2) |
| >5/many/multiple ± jerks/brief events[b] | 61 (9.4) | 129 (14.3) |
| >2 seizures no further detail | 11 (1.7) | 22 (2.4) |
| Jerks /brief events[b] only | 3 (0.5) | 5 (0.6) |
| Epilepsy type[d] | | |
| Focal | 347 (53.1) | 400 (44) |
| Generalized | 50 (7.7) | 141 (15.7) |
| Unclassified | 257 (39.3) | 360 (40) |

[a]Acute symptomatic seizure/s (as defined by Beghi et al, 2010[11]) excluded from study.

[b]Very brief often multiple, likely absences.

[c]RMH—Mann-Whitney U test, $P < .001$; AH—Mann-Whitney U test, $P < .001$.

[d]Assessed by clinician/fellows using seizure history, index information, EEGs, and imaging available up to 1 year post-1st FSC visit. Does not incorporate postindex seizure/s or information.

Approximately 20% of index seizures at each clinic arose out of sleep (Table 3).

A history of at least one event *before* the index seizure that the FSC clinician indicated may have been an epileptic seizure/s was found in 38% of all patients - 32% at RMH and 42% at AH ($\chi^2$ [1, n = 1555] = 17.1 $P < .001$).

A seizure/s *between* the index and the clinic appointment ('in-between' seizure) was experienced by 8% of patients (n = 128). RMH data demonstrates that a longer time between index and clinic was associated with 'in-between' seizure/s (Table 3). Patients who had at least one nonattendance for their first appointment had an increased likelihood of an 'in-between' seizure ($\chi^2$ [1, n = 595] = 21.36, $P < .001$).

By the time patients attended their first clinic appointment, 42% had experienced a total of ≥two likely seizures.

The proportion of patients where epilepsy type could be determined is detailed in Table 3. The proportion was the same across sites, RMH had more focal epilepsy and AH more generalized epilepsy diagnoses ($\chi^2$ [2, n = 1555] = 25.7], $P < .001$).

## 4 | DISCUSSION

In accordance with the clinics' primary aims, both FSCs had rapid review times, with 86% of all patients reviewed by an expert epileptologist within 3 weeks of their index seizure. Australian data from 2018 to 2019[13] demonstrate median wait-time from referral to first routine appointment at a public hospital neurological clinic ranged from 87 to 100 days. Although not directly analogous, these data suggest our two specialist FSCs provided a substantially quicker pathway. This is concordant with a Canadian 'single seizure' clinic, where mean waiting times for assessment by an epilepsy specialist were reduced by 70% compared to usual care (mean: 24 days vs 80 days).[2]

Of our two sites, AH demonstrated shorter times from the index seizure to clinic, possibly related to availability of dedicated administrative staff. Whether short waiting times result in improvement to other outcomes has yet to be determined. Not assessed in this study is the effect of total volume of patients seen, including those with nonepilepsy diagnoses.

Time periods of >6 months between the index seizure and clinic attendance were rare (<2%) at both sites and were related to failure to attend the first appointment. Seizures between the index and clinic were experienced by 8% of patients, similar to 9% in Breen et al,[14] and longer wait-times were associated with these in-between seizures. These circumstances likely increase seizure-related risks. Our assessment only included patients who eventually attended the clinic within the study time frame; those who fail to attend at all are potentially at greater risk.

Age distributions of clinic attendees demonstrate AH patients are generally younger compared to RMH. Clinic screening at the AH admission point (see Methods) may contribute, as patients with an obvious stroke or age-associated pathology may be transferred to other epilepsy clinics. Internal interests such as the epilepsy genetics research program at AH and the stroke program at RMH may also influence referrals.

EEGs demonstrated epileptiform abnormalities in one quarter of all individuals. These data are amalgamated from routine and sleep-deprived EEGs, possibly resulting in a higher yield than if all EEGs used routine protocol.[1,15,16] EEG yield was lower at RMH compared to AH for both generalized and focal epileptiform findings. Each site is close to the range of 17%-29% reported in other 'first seizure' cohorts.[14,17-19] Still to be determined is whether the lower yield at RMH is associated with their higher proportion of focal epilepsy,[20] frequency of sleep-deprived EEG or longer times to EEG,[1] in itself possibly related to lack of dedicated administrative resources.

Both clinics obtained MRIs for >70% of patients within 12 months. MRI is recommended[21] for identification of subtle epileptogenic lesions;[1,3,16,21-23] however, CT was the only imaging in 22% of patients at each site. While MRI is contraindicated in some patients, the frequency of CT-only suggests other issues may be problematic for long-running clinics. MRI may require an additional hospital visit, exacerbating loss to follow-up. Alternatively, patients with clear abnormalities on CT or a diagnosis of idiopathic/genetic generalized epilepsy may not have been offered an MRI.

A total of 19% of patients had potentially epileptogenic findings on neuroimaging; the largest group had acquired abnormalities. In both clinics, changes due to a previous stroke/hemorrhage were the most common etiology, followed by traumatic brain injury. In these tertiary referral hospitals, patients with previous brain surgery presented in small proportions (<2%). Mesial temporal sclerosis, which is relatively common among individuals with refractory epilepsy, comprised no more than 1% of either of these cohorts.

Potentially epileptogenic abnormalities were roughly double at RMH (28%) compared to AH (12%). The difference persists over four broad age-bands. Admission screening at AH may be associated with a lower proportion of CT identifiable abnormalities, but this is unlikely to account for the difference in developmental pathology numbers, particularly given the similar proportions with MRI. There may be sampling issues for relatively rare pathologies with small numbers, but an unknown difference in referral, administrative and reporting functions may also contribute.

Published literature demonstrates substantial variation in proportions with potentially epileptogenic abnormalities on brain imaging. A meta-analysis[3] of seven class II studies using predominantly CT for new-onset seizures found abnormal imaging in 1%-47% with an average yield of 10%. More recent new diagnosis clinics using MRI or MRI/CT report 20%-31%.[14,19,22] Study methodologies differ substantially in terms of ascertainment, sample characteristics (especially age distribution), and imaging modalities. This contributes to differences in reported imaging yield between studies.

In terms of specific pathologies–a Stockholm registry of population-based incident newly diagnosed epilepsy[24] demonstrated 10% with stroke, and two other population-based studies found 11%[25] and 15%[26] with clinical indicators of vascular disease. RMH figures are on par with these data, while initial screening at AH (see Methods) may account for lower stroke representation at that site. The Stockholm study[24] found 2.1% with traumatic brain injury which is roughly similar to our sites and 0.2% with cortical malformation which is less than in our study, possibly reflecting increased utilization of MRI imaging in our clinics (>70% vs 21%).

In both our independent clinics, ≥WHO level 1 brain tumors diagnosed at presentation comprised a very small proportion (<1%). These findings differ from the 4%-11% with primary/secondary/neoplastic tumors in population-based studies and other newly diagnosed cohorts,[1,24-27] probably reflecting tertiary hospital conditions where obvious malignant tumors presenting with seizures are revealed via CT in emergency departments and referred directly to neurosurgeons.

We have included 6 patients with acute brain trauma, likely as a consequence of a convulsive seizure. All 6 were from RMH, possibly an illustration of clinic screening differences. The prevalence of these injuries in new-onset cases has not been addressed in the literature and appears to be very low, but that may be because they are excluded from studies due to lack of clarity about underlying imaging findings. We also know little of their outcomes.

The preponderance of convulsive (vs nonconvulsive) index seizures is well established.[6,22,24,26-28] Both sites reported seizures before the index within the published range (23%-57%);[1,6,28,29] these are probably mostly nonconvulsive and therefore unrecognized.[6] The lower proportion at RMH may be related to patient characteristics or underlying pathology.

Based on clinical history, 42% of patients had experienced at least two possible seizures by the first clinic attendance. Broad epilepsy type was allocated to 60% in both cohorts using only seizure history and results of investigations included in this study. In reality, by the time investigation results were available this proportion may be higher due to additional seizures. Focal epilepsy was diagnosed more frequently at RMH, while generalized epilepsy diagnoses were common at AH. This likely reflects differences in age distributions and imaging results at each site.

This study has limitations due to its retrospective nature. However, these are large cohorts from long-running independent FSCs with rapid assessment and protocol-driven investigations. We did not assess time from referral to clinic attendance; our previous study[6] demonstrated this was relatively short and not a major source of attendance-time variation. However, given differences between the sites, this may benefit from further investigation. Potential further research includes examination of costs and benefits of additional or dedicated administrative resources in public hospital settings.

These two clinics operate with similar levels of clinical expertise, broadly similar protocols and within the same government-funded healthcare system. Despite these comparable features and some similar results, there were also some marked differences between sites in terms of time to clinic attendance, age profiles, EEG and MRI yield, and seizure history. The reasons have yet to be clarified. However, our data suggest that seemingly minor differences such as admission screening, dedicated administrative assistance, and local research and clinical interests may have a flow-on influence on clinic characteristics and outcomes. Further, although these are community-based referrals, our data suggest that FSC cohorts differ from true population-based cohorts. Our findings are a reminder that research data cannot be utilized or translated successfully without some thought of the inherent and underlying site differences that may have influenced the findings. First seizure or new-onset epilepsy clinics offer outstanding opportunities for research,[4,5] with the potential to incorporate systematic collection of high-quality data within the clinic workings. Further research into how local characteristics shape research findings will facilitate interpretation and utilization of these findings.

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## CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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