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Author/s:

Marquina, C;Foster, E;Chen, Z;Vaughan, DN;Abbott, DF;Tailby, C;Jackson, GD;Kwan, P;Ademi, Z

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ORIGINAL ARTICLE

Work productivity, quality of life, and care needs: An unfolding epilepsy burden revealed in the Australian Epilepsy Project pilot study

Clara Marquina¹  | Emma Foster²  | Zhibin Chen^{2,3}  | David N. Vaughan^{4,5,6}  |
David F. Abbott^{4,6}  | Chris Tailby^{4,6,7}  | Graeme D. Jackson^{4,5,6}  |
Patrick Kwan^{2,3}  | Zanfina Ademi^{1,2}  | for the Australian Epilepsy Project

¹Health Economics and Policy Evaluation Research (HEPER) Group, Centre for Medicine Use and Safety, Monash University, Melbourne, Victoria, Australia

²School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia

³Department of Neuroscience, Central Clinical School, Monash University, Melbourne, Victoria, Australia

⁴Florey Institute of Neuroscience and Mental Health, Heidelberg, Victoria, Australia

⁵Department of Neurology, Austin Health, Melbourne, Victoria, Australia

⁶Florey Department of Neuroscience and Mental Health, University of Melbourne, Melbourne, Victoria, Australia

⁷Department of Neuropsychology, Austin Health, Melbourne, Victoria, Australia

Correspondence

Zanfina Ademi, Centre for Medicine Use and Safety, Faculty of Pharmacy, Monash University, Melbourne, Vic., Australia.
Email: zanfina.ademi@monash.edu

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Abstract

Objective: Epilepsy is a common and serious neurological disorder. This cross-sectional analysis addresses the burden of epilepsy at different stages of the disease.

Methods: This pilot study is embedded within the Australian Epilepsy Project (AEP), aiming to provide epilepsy support through a national network of dedicated sites. For this analysis, adults aged 18–65 years with first unprovoked seizure (FUS), newly diagnosed epilepsy (NDE), or drug-resistant epilepsy (DRE) were recruited between February–August 2022. Baseline clinicodemographic data were collected from the participants who completed questionnaires to assess their quality of life (QOLIE-31, EQ-5D-5L), work productivity (Work Productivity and Activity Impairment [WPAI]), and care needs. Univariate analysis and multivariate regression was performed.

Results: 172 participants formed the study cohort (median age 34, interquartile range [IQR]: 26–45), comprising FUS ($n=44$), NDE ($n=53$), and DRE ($n=75$). Mean QOLIE-31 score was 56 (standard deviation [SD] ± 18) and median EQ-5D-5L score was 0.77 (IQR: 0.56–0.92). QOLIE-31 but not EQ-5D-5L scores were significantly lower in the DRE group compared to FUS and NDE groups ($p < 0.001$). Overall, 64.5% of participants participated in paid work, with fewer DRE (52.0%) compared with FUS (76.7%) and NDE (72.5%) ($p < 0.001$). Compared to those not in paid employment, those in paid employment had significantly higher quality of life scores ($p < 0.001$). Almost 5.8% of participants required formal care (median 20 h/week, IQR: 12–55) and 17.7% required informal care (median 16 h/week, IQR: 7–101).

Significance: Epilepsy is associated with a large burden in terms of quality of life, productivity and care needs.

Clara Marquina and Emma Foster shared first-authorship.

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Plain Language Summary: This is a pilot study from the Australian Epilepsy Project (AEP). It reports health economic data for adults of working age who live with epilepsy. It found that people with focal drug-resistant epilepsy had lower quality of life scores and were less likely to participate in paid employment compared to people with new diagnosis epilepsy. This study provides important local data regarding the burden of epilepsy and will help researchers in the future to measure the impact of the AEP on important personal and societal health economic outcomes.

KEYWORDS

Australian Epilepsy Project, epilepsy, HRQoL, productivity

1 | INTRODUCTION

Worldwide, approximately 46 million people live with epilepsy.^{1,2} Its impact on individuals is profound, accounting for 182.6 per 100 000 disability-adjusted life years globally, which translates to a substantial societal burden.² A recent Australian analysis reported that epilepsy-related productivity losses approximated US \$22.1 billion in lost gross domestic product, outstripping the health economic burden per person of diabetes, hypertension, and smoking-related illness.³ Previous research has already identified clear gaps in high-income countries' healthcare systems that contribute to this burden. These include substantial delays to receiving epilepsy diagnoses and commencing effective treatments, and low and declining referrals for epilepsy surgery which is a highly effective intervention for eligible candidates.⁴⁻¹² Bridging these diagnostic and therapeutic gaps remains a significant challenge even in countries like Australia with universal healthcare. But it clearly is in all of society's interest to improve on the current clinical paradigm. A radical shift is needed. This goes well beyond what can be achieved through changing an individual clinician's practice or updating institutional policy. An overhaul in the way epilepsy diagnostic and therapeutic care is delivered is a mammoth task, but is likely the only effective way to dismantle existing barriers.

The Australian Epilepsy Project (AEP) is an ambitious initiative that aims to accelerate the diagnosis of epilepsy, improve the detection and prognosis of surgically curable disease, and overall result in fewer seizures, fewer deaths, and better quality of life for people living with epilepsy.¹⁶ Currently, neurologists across Australia may refer adults with a first unprovoked seizure, a new diagnosis of epilepsy, or pharmacoresistant epilepsy to a network of dedicated AEP sites for state-of-the-art neuroimaging, neurocognitive testing, and genetic analysis. Three AEP sites across two Australian states are active, with plans for further sites to come online in the next few years. AEP

Key points

- Epilepsy may substantially impact quality of life (QOL) and work productivity, and cause people to require varying levels of care.
- Our cross-sectional study demonstrates that the health economic burden of epilepsy varies at different stages of the disorder.
- People with focal drug-resistant epilepsy (DRE) had significantly lower QOL scores compared to people with new diagnosis epilepsy.
- People with focal DRE were also significantly less likely to participate in paid employment compared to people with new diagnosis epilepsy.
- Almost one in five people in the study cohort required informal care (median 16 h/week), provided through friends and family.

returns a summary report to referring clinicians to support timely, evidence-based diagnostic and therapeutic decision-making, for example, comment on the presence of epileptogenic lesions based on advanced neuroimaging results, detect early disturbance in cognitive profile or mood, and use genetic data for prediction of risk-profiles.

Robust, local, epilepsy-related health economic data are needed to justify investment in novel healthcare strategies, such as AEP, and to provide a crucial, evidence-based foundation against which the cost-effectiveness of new care models versus usual care may be measured. From an Australian point of view, current health economic analyses are based on data extrapolated from international cohorts or small, local studies with

limited generalizability^{13–15} and are inadequate for comprehensively understanding the burden of epilepsy in Australia.

We report cross-sectional baseline quality of life, productivity, and care requirement data of English-speaking participants of working age referred by neurologists from a state-wide population to the AEP.

2 | METHODS

2.1 | Australian Epilepsy Project pilot study aims, design, and eligibility criteria

The prospective, single site AEP pilot study commenced February 2020, with the overarching aim of ensuring the recruitment process and outcomes captured were feasible for the nationwide AEP roll-out. AEP was widely advertised through local and national epilepsy and neurology symposiums, conferences, and societal correspondence. Neurologists based in Victoria (the second most populous state in Australia) were invited to refer people aged 18–65 years with first unprovoked seizure (FUS), newly diagnosed epilepsy (NDE), or focal drug-resistant epilepsy (DRE) to AEP's main hub located at The Florey's clinical-research facilities on the Austin Hospital campus in Melbourne, Australia. The determination of seizure onset as focal/generalized/unknown was a clinical assessment based on all available data, primarily the clinical history and seizure semiology. Participants in the FUS group did not meet ILAE criteria for new-onset epilepsy, and specifically, did not have EEG or MRI findings sufficient to make a new diagnosis in the setting of a single seizure only. Exclusion criteria were <18 or >65 years of age, a developmental or epileptic encephalopathy, inability to comprehend or complete simple English-language questionnaires, or a condition that would preclude cerebral magnetic resonance imaging (MRI). Referrals were made through an online platform. AEP research coordinators screened and consented eligible participants, and collected baseline clinicodemographic data. Participants underwent neuropsychology interviews via telehealth,¹⁶ traveled to the AEP Florey hub to undergo neuroimaging, and completed online self-report questionnaires regarding quality of life, productivity, and their formal and informal care needs. This paper reports the results of these self-report questionnaires, detailed below.

2.1.1 | Quality of life

Quality of life was captured using both generic and disease-specific internationally validated health-related

quality of life self-report instruments, the EuroQol 5 dimensions, 5 levels (EQ-5D-5L) questionnaire and Quality of Life In Epilepsy (QOLIE-31) inventory, respectively.^{17,18} EQ-5D-5L comprises five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with five scoring levels. Scores range from 0–1, with higher values indicating better quality of life. This generic scale allows comparisons across different diseases, and is recommended by several health technology assessment agencies across the globe.¹⁹ QOLIE-31 contains 31 items divided across seven subscales that capture psychological, health, and social factors. Scores range from 0 to 100, with higher scores indicating better quality of life.¹

2.1.2 | Productivity

The Work Productivity and Activity Impairment (WPAI) questionnaire is a validated, generic self-report instrument that captures whether an individual is involved in paid work, their hours worked, and hours of work missed due to a particular health issue (for the AEP pilot study, the health issues were seizures or epilepsy), as well as hours missed for reasons other than that particular health issue, over the prior week.²⁰ WPAI also includes a visual analogue scale from 0 to 10, to indicate the overall impact of a particular health-related issue (seizures or epilepsy) on all activities, with higher scores indicating greater impact.

2.1.3 | Care needs

Formal and informal care needs and hours used per week were captured through two custom-built questionnaires. The former questionnaire also captured healthcare utilization (e.g., accessing general practitioners, undertaking medical tests, attending the emergency department) since enrolment in the AEP pilot study. Both these custom-built questionnaires are available in the Appendices S1 and S2.

2.2 | Statistical analysis

Data distribution was assessed using Shapiro–Wilk tests. Continuous variables were described using mean $\pm$ standard deviation (SD) or medians and interquartile ranges (IQR), and categorical variables were described using count and percentages (n and %). Differences between the groups were tested using one-way analysis of variance for normally distributed data, Kruskal–Wallis for skewed data and χ^2 -test for categorical data. If the difference between groups was found significant, pairwise comparison with Bonferroni

Adjustment were run to confirm the difference between each pair. To evaluate the independent associations between diagnostic categories and the main outcomes, multivariate linear regression was performed for continuous outcome variables and logistic regression analysis was performed for categorial outcome variables. The statistically significant differences were inferred when the p -value was <0.05 . All confidence intervals were computed at the 95% level. All analyses were performed with R software (version 4.1.3).

2.3 | Standard protocol approvals, registrations, and participant consent

This pilot study was reviewed and approved by the Human Research Ethics Committee (HREC) of Austin Health under the application number HREC/68362/Austin-2022. Written informed consent was obtained from all people participating in the pilot study.

2.4 | REDCap

Pilot study data were collected and managed using the REDCap (Research Electronic Data Capture) electronic data capture tool hosted at The University of Melbourne. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources.^{21,22}

3 | RESULTS

3.1 | Participant characteristics

Of the 229 people enrolled in the AEP pilot study, 174 completed self-report health economic questionnaires. Data from two participants were ultimately excluded from the final analysis owing to missing clinicodemographic data. The final pilot study cohort ($n=172$) comprised 52.3% females ($n=90$), median age 34 years (IQR: 26–45). Distribution across diagnostic categories were FUS 25.6% ($n=44$), NDE 30.8% ($n=53$), and DRE 43.6% ($n=75$). More females than males were enrolled in the DRE group (64.0% F vs. 36.0% M), whereas less females were enrolled in the FUS group (36.4% F vs. 63.6% M), otherwise age and sex distribution was non-significant across diagnostic groups. Data on seizure onset were available for three-quarters ($n=126$) of participants: focal onset (69.8%, $n=88$), generalized onset (4.0%, $n=5$), and unknown onset (26.2%, $n=33$). More females than males had focal seizures (80.3% F vs. 58.3% M, $p<0.001$), and all DRE participants had focal seizures (100%, as selected for by the pilot study inclusion/exclusion criteria), compared to NDE (61.8%) and FUS (28.6%). These baseline characteristics are displayed in Table 1.

3.2 | Quality of life

QOLIE-31 and EQ-5D-5L questionnaires were completed by all participants, and 165 (95.9%) also completed the EQ-5D-5L visual analogue scale (VAS). QOLIE-31 mean score was 55.9 (SD $\pm$ 18.2), and EQ-5D-5L median score was 0.77 (IQR: 0.56–0.92). Diagnostic group was significantly

Variable	FUS ($n=44$)	NDE ($n=53$)	DRE ($n=75$)	p -Value
Demographics ($n=172$)				
Sex, n (%)				
Male	28 (63.6)	27 (50.9)	36.0% (27)	0.009*
Female	16 (36.4)	26 (49.1)	64.0% (48)	
Age (years), median (IQR)	35 (29–49)	34 (24–47)	32 (25–41)	0.2
Type of seizure ($n=126$)				
Focal, n (%)	10 (28.6)	21 (61.7)	57 (100)	<0.001*
Generalized, n (%)	3 (8.6)	2 (5.8)	0 (0)	
Unknown, n (%)	22 (62.8)	11 (32.5)	0 (0)	

TABLE 1 Participants stratified by patient category.

Abbreviations: DRE, drug-resistant epilepsy; EQ-5D-5L, EuroQol 5 dimensions 5 levels quality of life questionnaire; FUS, first unprovoked seizure; IQR, interquartile range; NEP, new diagnosis of epilepsy; QOLIE-31, quality of life in epilepsy questionnaire; SD, standard deviation.
* p -values <0.05 are statistically significant.

associated with QOLIE-31 scores ($p < 0.05$), with the DRE group scoring lower (50.6 ± 19.0) than FUS (60.9 ± 16.6) and NDE (59.2 ± 16.2) groups ($p < 0.05$ after adjusting for multiple comparisons). Self-report participation versus non-participation in paid work in the prior week was associated with significantly higher scores for QOLIE-31 (59.6 ± 16.6 paid work vs. 49.4 ± 19.3 non-participation in paid work, $p < 0.001$), EQ-5D-5L (0.81 [IQR: 0.65–1.00] paid work vs. 0.66 [IQR: 0.46–0.86] non-participation in paid work $p < 0.001$), and EQ-5D VAS ($p = 0.001$). The need for formal or informal care each week was also significantly associated with lower QOLIE-31 scores compared to those that did not indicate care requirements (57.2 ± 36.1 vs. 36.1 ± 16.9 for not requiring vs. requiring formal care, $p = 0.003$; 58.5 ± 17.4 vs. 45.1 ± 17.3 for not requiring vs. requiring informal care, $p < 0.001$). Sex, age, and seizure onset type were not significantly associated with

either QOLIE-31 or EQ-5D-5L scores. Table 2 and Figure 1 displays the QOLIE-31 and EQ-5D-5L scores.

3.3 | Productivity

Productivity data were available for 98.8% ($n = 170$) participants. The majority participated in paid work (64.5%), with a median 30 h worked in the prior week (IQR: 15–38). The hours missed from work due to epilepsy-related issues ranged from 0 to 40 h, but the majority of participants did not miss any time from paid work in the prior week (median 0, IQR: 0–0). There were no significant differences by sex in the proportion of participants engaged in paid work or in the hours worked or missed from work in the prior week (Table 3). The proportion of paid work

TABLE 2 Quality of life scores for all the reporting instruments, stratified by participant characteristics.

	QOLIE-31 ($n = 173$)	<i>p</i> -Value	EQ-5D-5L scores ($n = 173$)	<i>p</i> -Value	EQ-5D VAS ($n = 165$)	<i>p</i> -Value
Overall score						
By age group						
Less than 30 years	56.7 ± 16.8	0.12	0.78 (0.58–0.94)	0.78	74 (53–85)	0.43
30–40 years	51.0 ± 19.0		0.67 (0.53–0.87)		71 (50–82)	
40–50 years	58.8 ± 18.0		0.77 (0.58–0.92)		72 (50–80)	
50–60 years	59.5 ± 19.2		0.81 (0.57–1.00)		74 (55–90)	
60–65 years	49.4 ± 19.7		0.80 (0.80–0.91)		70 (50–79)	
By sex						
Males	57.5 ± 16.7	0.44	0.793 (0.66–0.92)	0.44	74 (55–80)	0.94
Females	54.5 ± 19.3		0.732 (0.55–0.92)		72 (50–84)	
By patient category						
FUS	60.9 ± 16.6	0.002*	0.762 (0.56–0.92)	0.24	73 (60–80)	0.48
NDE	59.2 ± 16.2		0.812 (0.60–1.0)		74 (55–87)	
DRE	50.6 ± 19.0		0.744 (0.56–0.91)		71 (50–83)	
By type of seizure						
Focal	53.8 ± 18.8	0.29	0.754 (0.54–0.92)	0.84	75 (50–85)	0.39
Generalized	57.8 ± 14.5		0.805 (0.74–0.86)		60 (51–72)	
Unknown	59.5 ± 16.1		0.754 (0.55–0.92)		69 (50–78)	
By working status						
Participate in paid work	59.6 ± 16.6	<0.001*	0.81 (0.65–1.00)	<0.001*	75 (60–85)	0.0013*
Not participate in paid work	49.4 ± 19.3		0.66 (0.46–0.86)		66 (40–78)	
By care requirements						
Formal care required	36.1 ± 16.9	0.003*	0.53 (0.47–0.64)	0.08	63 (40–79)	0.3
No formal care required	57.2 ± 17.6		0.78 (0.57–0.92)		73 (50–83)	
Informal care required	45.3 ± 17.3	<0.001*	0.54 (0.46–0.65)	0.12	62 (39–75)	0.27
No informal care required	58.5 ± 17.4		0.80 (0.58–0.93)		72 (51–85)	

Note: QOLIE-31 are presented as mean and standard deviation, and EQ-5D-5L scores and EQ-5D VAS are presented as median and interquartile range.

Abbreviations: DRE, drug-resistant epilepsy; EQ-5D-5L, EuroQol 5 dimensions 5 levels quality of life questionnaire; FUS, first unprovoked seizure; NDE, new diagnosis of epilepsy; QOLIE-31, quality of life in epilepsy questionnaire.

**p*-values < 0.05 are statistically significant.

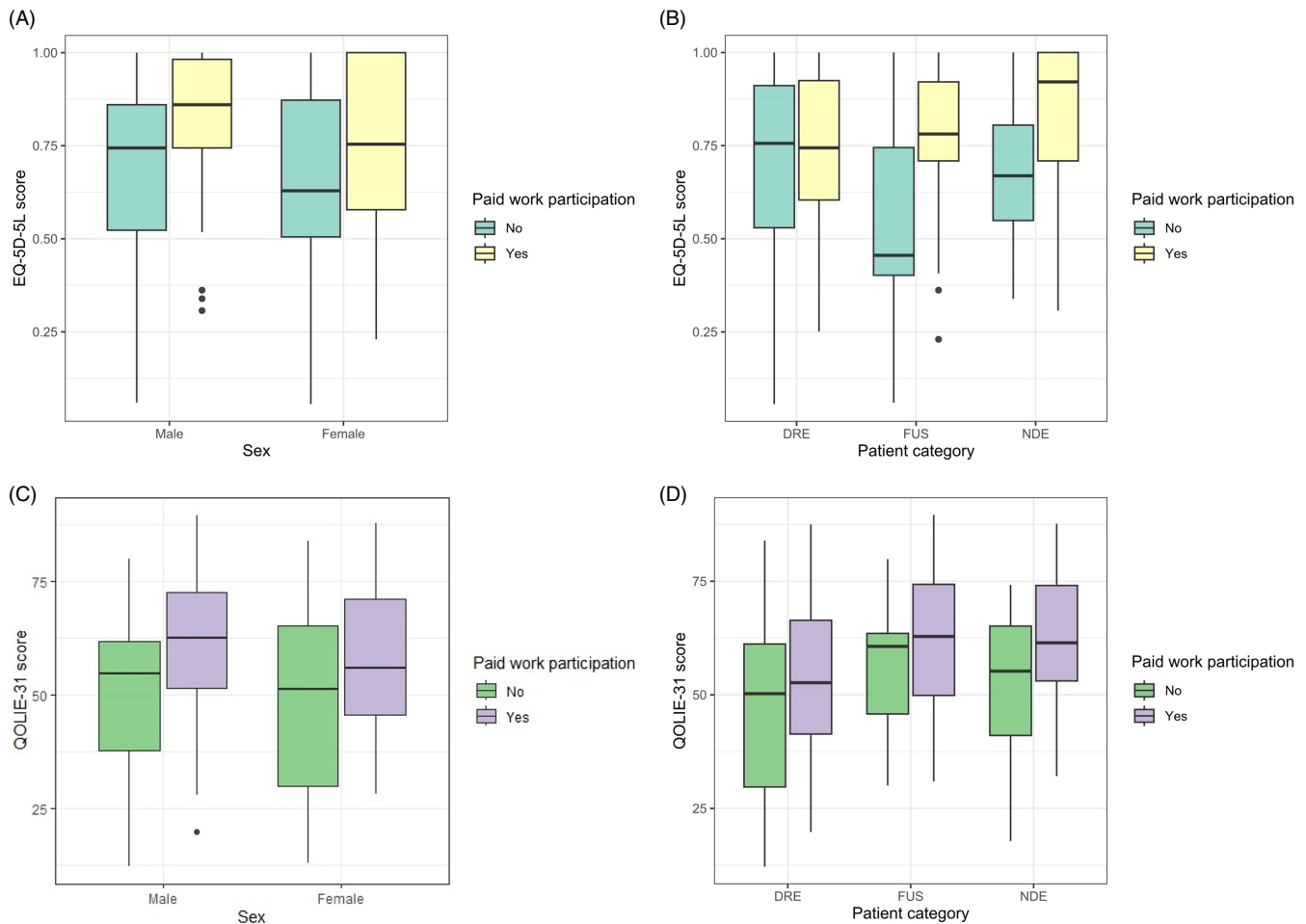


FIGURE 1 Quality of life scores measured with the EQ-5D-5L or QOLIE-31 instruments, and stratified by sex (A, C) and by patient category (B, D). DRE, drug-resistant epilepsy; FUS, first unprovoked seizure; NDE, newly diagnosed epilepsy.

TABLE 3 Productivity scores by sex and patient category.

Productivity (<i>n</i> = 169)	Overall	By sex			By patient category			
		Males	Females	<i>p</i> -Value	FUS	NDE	DRE	<i>p</i> -Value
Participated in paid work								
Yes (% , <i>n</i>)	64.5% (109)	66.7% (54)	62.5% (55)		76.7% (33)	72.5% (37)	52.0% (39)	0.009*
No (% , <i>n</i>)	35.5% (60)	33.3% (27)	37.5% (33)	0.16	23.3% (10)	27.5% (14)	48.0% (36)	
Hours worked in the last week	30 (15–38)	31 (15–38)	29 (16–36)	0.11	31 (15–41)	30 (12–38)	24 (17–35)	0.50

Abbreviations: DRE, drug-resistant epilepsy; FUS, first unprovoked seizure; NDE, new diagnosis of epilepsy.

*p-values <0.05 are statistically significant.

participation was different among the diagnostic categories ($p < 0.001$). A significantly smaller proportion of participants with DRE participated in paid work compared to FUS and NDE (DRE 52.0% vs. FUS 76.7% and NDE 72.5%, $p < 0.05$ after adjustment for multiple comparison). Logistic regression analysis showed that participants in the DRE group had lower odds of participating in paid work, even after adjustment for age and sex (odds

ratio [OR]=0.30, 95% confidence interval [CI]: 0.12–0.70) (Table 4). However, among all the participants that took part in paid work, there were no differences by diagnostic category in the hours worked or the hours missed from work in the prior week (Table 3). Participants with focal or generalized seizures reported similar participation in paid work (44.3% and 40.6%, respectively, data not shown) compared to participants with unknown seizure

onset type (18.5%, $p < 0.05$, data not shown). For those that reported participation in paid work, there were no significant differences based on seizure type in term of hours worked or hours missed.

3.4 | Formal and informal care requirements

Formal and informal care requirements data were available for 98.3% ($n = 169$) participants. Only 5.9% ($n = 10$) reported needing formal care in the prior week, and of these, only seven participants supplied the number of hours of care required (median 20h, IQR: 12–55). There were no significant differences in formal care requirements based on sex. Females required a median of 20h per week (IQR: 14–30) and males a median of 45h per week (IQR: 27–62). When

participants were stratified by diagnostic group, there were more DRE participants requiring formal care (12.0%) compared to NDE (2.0%) or FUS (0%), $p = 0.009$ (Table 5).

In contrast, 30 (17.7%) participants reported needing informal care in the prior week, with 23 reporting the number of hours required (median 16h, IQR: 7–101). There were no significant differences by sex in the proportion of participants requiring informal care or in the number of informal care hours required (Table 4).

4 | DISCUSSION

This prospective health economic study, embedded within the AEP pilot study, provides a comprehensive cross-sectional analysis of quality of life, productivity, and care requirements for people with first unprovoked seizures, new diagnosis epilepsy, and focal DRE. This large, granular dataset may be useful for approximating the burden of epilepsy in other high-income countries, particularly those with universal healthcare, and will serve as an evidence base to calculate the cost-effectiveness of AEP in future analyses. As the AEP network expands, further data will be reported in the coming years.

This pilot study revealed that people living with DRE had significantly lower health-related quality of life, as measured by QOLIE-31, but not when measured by EQ-5D-5L, compared to people with first unprovoked seizures or new diagnosis epilepsy. Our findings are consistent with that of a large, retrospective study of 509 people living with epilepsy that determined EQ-5D-5L and QOLIE-31 results were correlated (i.e., when one instrument indicates an improvement in quality of life,

TABLE 4 Regression models examining the association between participation in paid work and demographic and clinical parameters.

Variable	OR	95% CI
Sex		
Male (reference)	1.00	
Female	1.09	0.55–2.16
Age	0.98	0.95–1.01
Epilepsy category		
FUS (reference)	1.00	
NDE	0.76	0.28–1.94
DRE	0.30	0.12–0.70

Abbreviations: CI, confidence interval; DRE, drug-resistant epilepsy; FUS, first unprovoked seizure; NDE, new diagnosis of epilepsy; OR, odds ratio.

TABLE 5 Care requirements by sex and diagnostic category.

Care requirements	Overall	By sex			By diagnostic category			
		Males	Females	<i>p</i> -Value	FUS	NDE	DRE	<i>p</i> -Value
Required formal care (<i>n</i> = 170)								
Yes (% , <i>n</i>)	5.9% (10)	3.7% (3)	7.9% (7)	0.07	0% (0)	2.0% (1)	12.0% (9)	0.009*
No (% , <i>n</i>)	94.1% (160)	96.3% (79)	92.1% (81)		100% (44)	98.0% (50)	88.0% (66)	
Hours of formal care in the last week (<i>n</i> = 10)	20 (12–55)	20 (14–30)	45 (27–62)	0.9	NA	NA	20 (12–55)	NA
Required informal care (<i>n</i> = 169)								
Yes (% , <i>n</i>)	17.7% (30)	11.0% (9)	24.1% (21)	0.08	25.7% (4)	13.7% (7)	74.3% (19)	0.04*
No (% , <i>n</i>)	82.3% (139)	89.0% (73)	75.9% (66)		74.3% (40)	86.3% (44)	25.7% (55)	
Hours of informal care in the last week (<i>n</i> = 23)	16 (7–101)	70 (30–140)	10 (5–45)	0.9	7 (4–25)	7 (3–23)	96 (12–138)	0.08

Abbreviations: DRE, drug-resistant epilepsy; FUS, first unprovoked seizure; NDE, new diagnosis of epilepsy.

*p-values < 0.05 are statistically significant.

the other does as well), but that QOLIE-31 had better responsiveness (was more sensitive to clinical change) compared to EQ-5D-5L.²³ This underscores the importance of ensuring epilepsy-specific measures of quality of life are included in health economic analyses to sensitively and comprehensively capture the burden of disease.²⁴ It follows that the differences in QOLIE-31 scores between the diagnostic groups may reflect the accumulated burden of epilepsy over time, but it is also possible that QOLIE-31 fails to capture critical domains that substantially affect quality of life of people with single seizures or in the very early stages of their epilepsy. This is because QOLIE-31, and other epilepsy-specific health-related quality of life instruments, have not been designed nor validated for use in first unprovoked seizure populations.²⁵

Comparing EQ-5D-5L utilities from our study with published utilities for other common neurological conditions provides an indication of the burden of disease as it pertains to the domains of mobility, self-care, usual activities, pain, and mood. Our pilot study reports a mean EQ-5D-5L score of 55.9, with DRE participants scoring significantly less (mean 50.6) compared to NDE (mean 59.2) and FUS (mean 60.9) participants. As with epilepsy, migraine is a chronic neurological disorder characterized by episodic attacks. Alarming, a study reported EQ-5D-5L utilities of 0.66 and 0.00 for mild and severe migraine, respectively, with the latter corresponding to a quality of life equivalent to “being dead”.²⁶ Another study reported EQ-5D-5L utilities of 0.79 and 0.72 for mild and moderate dementia, respectively, and identified that anxiety was the variable most strongly associated with the overall EQ-5D-5L score.²⁷ A study reported EQ-5D-5L-VAS to be 64.2 (lowest possible score = 0, highest possible score = 100) at 24-months following an acute ischemic stroke; this dropped to 55.3 for people who developed poststroke epilepsy.²⁸ Further, researchers from this study identified that seizure frequency, depression, and functional impairment were independent determinants of quality of life for people living with poststroke epilepsy, consistent with the findings of other epilepsy quality of life studies.^{29–32} Finally, a systematic review of studies administering EQ-5D for different neurological conditions in eight Central and East European countries found that from a total 13005 people, those with multiple sclerosis, epilepsy, and essential tremor reported higher quality of life compared to people with Parkinson's disease, stroke, Duchenne Muscular Dystrophy, dystonia, neuropathic pain, and carpal tunnel syndrome.³³ However, there were significant limitations for this systematic review that were clearly noted by the authors. These included rare or scarce data for all conditions (e.g., epilepsy QOL data were extracted from a single study) apart from multiple sclerosis that had QOL data extracted from 14 studies; small sample

sizes in one-third of included studies; and the use of different value sets to estimate EQ-5D index scores. The inclusion of generic ‘common denominator’ instruments such as EQ-5D in health economics studies such as this one may assist healthcare policy decision-makers in triaging conditions to determine funding priorities. However, it is likely that certain generic instruments will better capture the impact of some diseases compared to others, and may provide false reassurance regarding the impact of a particular disease. It is, therefore, clearly desirable that when assessing burden of disease and efficacy of healthcare interventions, QOL scores from both disease-specific as well as generic instruments are considered, as is done in this AEP pilot study.

As with quality of life, participation in the paid workforce also differed significantly for people with focal DRE compared to people with first unprovoked seizures or new diagnosis epilepsy. For comparison, 64.6% of the Australian general population aged 18–65 years were participating in the paid workforce at the time of the pilot study.³⁴ This is lower than the participation rates for the FUS group (76.7%) and NDE group (72.5%), but may be driven by the fact the median age for pilot study participants was 34 years. The workforce participation rate for 34-year-olds in the Australian general population at the time of the pilot study was 84.3%,³⁴ suggesting single seizure and epilepsy defining events may still impact workforce participation. The significantly lower workforce participation for the focal DRE group compared to the FUS and NDE groups may relate to reduced educational attainment, sick days due to seizures and seizure-related problems, and time off work to attend medical appointments. A recent Australian survey of 265 people living with epilepsy that had voluntarily enrolled on the Australian Epilepsy Research Register noted <50% were in paid employment and 46% were receiving financial support from the national welfare program.³⁵ The lower employment rate compared to the AEP pilot study may be due to the higher proportion of survey respondents that were retirees (13%), home makers (8%), and those actively seeking employment (9%), but was perhaps less likely due to epilepsy severity, as 45% of respondents to the survey reported having been seizure free for the past 12-months. Internationally, studies have reported variable effect of epilepsy on paid employment. A cross-sectional multicenter analysis from Spain found that employment rates for 872 adults living with epilepsy were similar to that of the general population.³⁶ In contrast, a prospective study from Brazil found that compared to heart disease, epilepsy was associated with significantly higher unemployment rates ($p < 0.0001$), job layoffs ($p = 0.001$), and being considered unfit to work ($p < 0.0001$).³⁷ Several international studies have examined variables associated

with employment in people living with epilepsy. A survey of 262 people living with epilepsy, recruited from four US epilepsy centers, identified that younger age, Caucasian race, higher socioeconomic status, and fewer medical comorbidities were associated with higher levels of employment.³⁸ A cross-sectional study of 146 people recruited from a Malaysian epilepsy clinic identified that higher education level, well-controlled epilepsy, and good mental health was associated with higher employability.³⁹ Finally, a large registry-based cross-sectional Swedish study of 126 000 people living with epilepsy and >350 000 matched controls reinforced the association between educational attainment and employment, and this interaction was significantly amplified ($p < 0.001$) for people living with epilepsy.⁴⁰ All these studies suggest that epilepsy itself is not necessarily a barrier to achieving a productive working life, but other socioeconomic variables are also important. This premise is supported in the AEP pilot study that demonstrated people living with DRE who were in paid employment held similar work hours to people in the FUS and NDE groups. Seizure control, adequate treatment of mood disorders, and supporting accessible education are key factors for improving quality of life and employment prospects, and further underscores the need for holistic management.

Care requirements is an often-overlooked burden of disease, and it is important that researchers consider not just formal care but also informal care provided by friends and family when assessing the extent that a condition may impact our community. The aforementioned recent Australian survey highlighted the importance of social support in facilitating good quality of life.³⁵ Family, particularly partners (46%) and parents (24%) provided the majority of support, and respondents who were able to rely on a partner for emotional support reported the highest quality of life. Although this aspect of patient care may traditionally fall outside the remit of healthcare providers, clinicians nevertheless have an important role to advocate for and support caregivers, and provide mutually beneficial opportunities for them to engage in professional societies and research. Likewise, the often-overlooked contribution of caregivers to our economy is immense, and should be a fundamental consideration in health economic analyses.

4.1 | Limitations

This pilot study was open to referrals from neurologists only. As such, the pilot study cohort was drawn primarily from hospital-based comprehensive epilepsy programs and the private practices of neurologists with a special interest in epilepsy. This provided a well-characterized pilot study cohort with low diagnostic uncertainty. However,

this excluded people who had their epilepsy managed by non-neurologist specialists, for example, general practitioners or gerontologists, as well as those who were unable to access specialized epilepsy services due to geographical, financial, and cultural/language barriers. Due to the focus on working age people in the AEP, this pilot study did not include the perspective of children, adolescents, or older adults (age > 65 years) with epilepsy. Further, due to the pilot study design which collected health economic data via internationally validated English-language questionnaires, outcomes were unable to be captured for people unable to comprehend English, or with reduced capacity to complete questionnaires. These limitations mean the results may not be representative of all people living with epilepsy in the general population. Finally, covariates such as socioeconomic background, level of educational attainment, and comorbidities may have also influenced outcomes, but these data were not included in the analysis.

In conclusion, the health economic data from this pilot study sets a very clear evidence base regarding the burden of epilepsy, and incentivizes changes that may improve delivery of epilepsy healthcare, such as those proposed in the AEP. Earlier, more efficient workup through the AEP may reduce the need for future medical consultations, reduce the time to effective antiseizure medication prescription, and reduce time to epilepsy surgery. This will assist people in gaining more independence and improve their quality of life more quickly than usual care, benefiting not just individuals and their families, but our whole community. This pilot study also identifies several important future directions for research. This includes exploration of the factors that are associated with quality of life in people with single seizures or in the very early stages of epilepsy, and considering designing and validating an instrument to capture quality of life in these groups. This will facilitate measuring the efficacy of future interventions designed to support people during these difficult periods. We recommend that future randomized trials that seek to improve seizure freedom or optimize mood disorders, should also consider employment status of participants, and the combined role of these factors on quality of life. Future aspirational interventions may include long-term, concerted efforts to support people living with epilepsy to fulfill their academic potential, and assess the association with future work productivity. And finally, future in-depth qualitative analyses of the informal care provided by friends and family members may provide the evidence base needed to effectively advocate for more funding, resources, and respite care.

AUTHOR CONTRIBUTIONS

CM analyzed data and contributed to data interpretation and to writing of the first draft. EF contributed to data interpretation and to writing of the first draft. PK and ZA

contributed to the study design, data interpretation and editing of the manuscript. All coauthors contributed to data interpretation and editing of the manuscript. The full list of AEP investigators is presented in Appendix S3.

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CONFLICT OF INTEREST STATEMENT

CM does not have any conflicts of interest to disclose. EF/her institution has received research support from Brain Foundation (Australia); LivaNova (USA); Lundbeck (Australia); Monash Partners STAR Clinician Fellowship; Sylvia and Charles Viertel Charitable Foundation; and The Royal Australian College of Physicians Fellows Research Establishment Fellowship. ZC is supported by the National Health and Medical Research Council of Australia Early Career Fellowship (GNT1156444) and has received grants from the Monash University. His institution has received research funding from UCB Pharma, outside the submitted work. DV does not have any conflicts of interest to disclose. D.F.A. acknowledges fellowship funding from the Australian National Imaging Facility. CT does not have any conflicts of interest to disclose. G.J.D. has received support from The Australian Epilepsy Project, which received funding from the Australian Government under the Medical Research Future Fund. PK does not have any conflicts of interest to disclose. ZA has received support from The Australian Epilepsy Project, which received funding from the Australian Government under the Medical Research Future Fund.

DATA AVAILABILITY STATEMENT

Upon formal request and ethics approval, de-identified data may be shared with authorized researchers on request.

ETHICS STATEMENT

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.

ORCID

Clara Marquina  <https://orcid.org/0000-0003-2582-0374>
 Emma Foster  <https://orcid.org/0000-0001-8958-3844>
 Zhibin Chen  <https://orcid.org/0000-0002-1888-6917>
 David N. Vaughan  <https://orcid.org/0000-0002-6225-7739>
 David F. Abbott  <https://orcid.org/0000-0002-7259-8238>
 Graeme D. Jackson  <https://orcid.org/0000-0002-7917-5326>
 Patrick Kwan  <https://orcid.org/0000-0001-7310-276X>
 Zanfina Ademi  <https://orcid.org/0000-0002-0625-3522>

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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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