Assessing the extent and determinants of socioeconomic inequalities in epilepsy in the UK: a systematic review and meta-analysis of evidence

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Summary

Background Socioeconomic inequalities in epilepsy incidence and its adverse outcomes are documented internationally, yet the extent of inequalities and factors influencing the association can differ between countries. A UK public health response to epilepsy, which prevents epilepsy without widening inequalities, is required. However, the data on UK epilepsy inequalities have not been synthesised in a review and the underlying determinants are unknown.

Methods In this systematic review and meta-analysis, we searched six bibliographic databases (MEDLINE, Embase, PsycINFO, CINAHL, Web of Science, and Scopus) and grey literature published between Jan 1, 1980, and Feb 21, 2024, to identify UK studies reporting epilepsy incidence or epilepsy-related adverse outcomes by socioeconomic factors (individual level or area level). We included longitudinal cohort studies, studies using routinely collected health-care data, cross-sectional studies, and matched cohort studies and excluded conference abstracts and studies not reporting empirical results in the review and meta-analysis. Multiple reviewers (KJB, EC, SER, WOP, and RHT) independently screened studies, KJB extracted data from included studies and a second reviewer (SM or EC) checked data extraction. We used Critical Appraisal Skills Programme checklists to assess quality. We used random-effects meta-analysis to pool incident rate ratios (IRRs) and synthesised results on adverse outcomes narratively. This study was registered on PROPSPERO (CRD42023394143).

Findings We identified 2471 unique studies from database searches. We included 26 studies, ten of which reported epilepsy incidence and 16 reported epilepsy-related adverse outcomes according to socioeconomic factors. Misclassification, participation, and interpretive biases were identified as study quality limitations. Meta-analyses showed an association between socioeconomic deprivation and epilepsy incidence, with greater risks of epilepsy incidence in groups of high-deprivation (IRR 1·34 [95% CI 1·16–1·56]; I^2=85%) and medium-deprivation (IRR 1·23 [95% CI 1·08–1·39]; I^2=63%) compared with low-deprivation groups. This association persisted in the studies that only included children (high *vs* low: IRR 1·36 [95% CI 1·19–1·57]; I^2=0%). Only two studies examined factors influencing epilepsy incidence. There is limited evidence regarding UK inequalities in adverse outcomes.

Interpretation Socioeconomic inequalities in epilepsy incidence are evident in the UK. To develop an evidence-based public health response to epilepsy, further research is needed to understand the populations affected, factors determining the association, and the extent of inequalities in adverse outcomes.

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Introduction

Epilepsy is a common disease, characterised by recurrent seizures and associated with significant morbidity and early mortality.[1] Internationally, the pooled incidence rate of epilepsy is 61 cases per 100 000 person-years.[2] The rate in the UK is 43 cases per 100 000 person-years, which results in nine in every 1000 people living with epilepsy.[3] Epilepsy occurs throughout the life course, with incidence varying by age. Epilepsy is both a primary brain disorder and one that occurs secondary to a wide range of local and systemic pathologies,[4] frequently co-occurring with intellectual disability.[5] Most epilepsy is controlled with anti-seizure medication (ASM); however, where this is not the case, frequent seizures can lead to recurrent hospital admissions, injuries, and death. Epilepsy can have a substantial physical, economic, and psychosocial burden on affected individuals and those who care for people with epilepsy.[1] In response to this burden, WHO member states, including the UK, adopted the Intersectoral Global Action Plan on epilepsy and other neurological disorders (IGAP) report in 2022, with strategic objectives including a public health response to epilepsy and epilepsy prevention.[6]

Evidence suggests that epilepsy incidence and prevalence are associated with socioeconomic factors, internationally and within the UK. Higher rates of

Research in context

Evidence before this study

The WHO Intersectoral Global Action Plan (IGAP) on epilepsy and other neurological disorders has focused the attention of its member states, including the UK, on the development of a public health response to epilepsy and epilepsy prevention. Understanding how epilepsy can be prevented, without widening existing inequalities, is a key factor when developing public health policy. Internationally, epilepsy incidence and adverse outcomes are associated with socioeconomic deprivation; however, the extent of the inequalities and the underlying factors will vary between countries and each country will require an IGAP approach tailored to its own population needs. We searched MEDLINE and PROSPERO for UK studies that reported socioeconomic inequalities in epilepsy and could directly inform a UK public health response, from inception to May 1, 2023, and included search terms "epilepsy" AND "socioeconomic" OR "deprivation" OR "inequalities", which indicated that there were no published or planned systematic reviews or meta-analyses on the topic to inform strategy development.

Added value of this study

To our knowledge, this systematic review and meta-analysis of UK socioeconomic inequalities in epilepsy is the first to appraise the evidence base on this topic. We identified ten studies (11 populations) reporting UK epilepsy incidence according to area or individual-level socioeconomic factors, and 16 studies reporting adverse outcomes. Meta-analyses of epilepsy incidence rates (IR) in seven populations showed an association between increasing deprivation and increasing epilepsy incidence, with the highest risk of epilepsy seen in the most deprived groups across the UK. The incidence of epilepsy in the medium-deprivation groups was 1·23 times that of the least deprived group. In the highest deprived groups, the incidence of epilepsy was 1·34 times the rate in the least deprived group. This association was also demonstrated in a subgroup meta-analysis of studies including only children, where previously there has been conflicting evidence. The only factor found to influence the association in this review was living in London versus the rest of the southeast of England, identified in a single study. There was limited evidence about socioeconomic inequalities in adverse outcomes, indicating the need for further research in this area.

Implications of all the available evidence

This systematic review and meta-analyses demonstrate that there are socioeconomic inequalities in UK epilepsy incidence, but the factors that influence this association are unknown. There is limited evidence regarding socioeconomic inequalities in adverse outcomes of epilepsy. There is also insufficient UK evidence to inform an evidence-based public health IGAP response and further research in this area is required. Future research exploring the association between socioeconomic deprivation and epilepsy incidence in the UK and other countries should consider the WHO's determinants of brain health and the roles of rural–urban environments, ethnicity, obesity, and multimorbidity.

epilepsy are observed in low-income to middle-income countries[1,2,7] and among individuals with lower socioeconomic positions within high-income countries.[3,8–14] These differences in epilepsy rates, according to socioeconomic factors at an individual level (eg, education, occupation, and socioeconomic status or position), area level (eg, Index of multiple deprivation [IMD] or Townsend score) or country level (eg, national income), represent socioeconomic health inequalities, defined as the "avoidable, unfair and systematic differences in health between different groups of people".[15]

There is limited understanding of the factors that underlie these socioeconomic inequalities, although it likely that the wider determinants of poor brain health have a role, including potentially modifiable behavioural factors (eg, physical inactivity, tobacco use, and harmful alcohol consumption), infectious diseases (eg, meningitis and encephalitis), non-communicable diseases (eg, diabetes, obesity, and hypertension), head-trauma, and environmental pollutant exposure.[6] Beyond these factors, epilepsy inequalities are likely multifactorial and related to complex intersections between genetic risk, coexisting intellectual disability, access to care (eg, inequalities, discrimination, and rural-urban divide), environmental exposures, individual behaviours, comorbid diseases, and the influences of wider social and commercial determinants of brain health.[16,17]

However, although the range of factors influencing this association is likely to be similar across countries, different factors might be responsible for higher proportions of disease burden or adverse outcomes between individual countries. The magnitude or extent of inequalities might also differ. To meet the IGAP objectives and reduce inequalities, countries, including the UK, will need to understand the extent of their own inequalities, the populations affected, and which potentially modifiable factors are influential. Studies in the UK have demonstrated the influence of socioeconomic inequalities in epilepsy incidence in adult and all-age populations.[3,13,18] However, there is conflicting evidence from studies that include children alone[13,19,20] and no studies in adults have stratified associations by age. Socioeconomic inequalities have been observed in adverse outcomes among people with epilepsy, with the most deprived UK populations having higher rates of comorbidities,[21,22] epilepsy-related mortality,[23,24] and epilepsy-associated emergency hospital admissions.[25]

To our knowledge, there are no systematic reviews or meta-analyses synthesising the UK evidence on socioeconomic inequalities and there is limited international evidence from which to draw relevant conclusions.[26–30] To enable the development of a UK public health response to epilepsy, in this review, we aimed to describe the extent of socioeconomic inequalities in UK epilepsy incidence; identify determinants underlying socioeconomic inequalities in UK epilepsy incidence; and describe the extent of socioeconomic inequalities in adverse outcomes including mortality, wellbeing, comorbidities, and emergency hospital care use in UK epilepsy populations.

Methods

Study selection criteria and search strategy

In this systematic review and meta-analysis, we searched six electronic databases MEDLINE (Ovid), Embase (Ovid), APA PsycINFO (Ovid), CINAHL, Web of Science, and Scopus using a combination of MEDLINE medical subject headings and appropriate keyword terms for articles published between Jan 1, 1980, and Feb 21, 2024, in the English language. We designed the search to identify all studies reporting UK epilepsy incidence according to socioeconomic factors and all studies reporting adverse outcomes in epilepsy populations according to socioeconomic factors. We included UK-wide studies and studies in England, Scotland, Wales, and Northern Ireland. The full search terms are included in the appendix (pp 1–3), all searches were performed by KJB. We performed grey literature searches of publications by epilepsy charities, key health-inequalities organisations, and professional organisations. We directly approached epilepsy charities to enquire whether they held unpublished inequalities data. Backwards and forwards citation searching of included studies was performed by KJB. All potentially relevant studies were dual screened against the review criteria (KJB, EC, SER, WOP, and RHT).

The study inclusion criteria were decided a priori and are presented according to the PICO framework. Populations: UK populations (all ages) for epilepsy incidence studies and UK populations with epilepsy (all ages) for adverse-outcome studies. Interventions: socioeconomic factors defined by individual measures of socioeconomic position (eg, occupation and education) or area-level measures (eg, IMD score); the methods used to define deprivation were not restricted to capture all available data. Comparators: different levels of socioeconomic factors. Outcomes included: epilepsy incidence and adverse outcomes in epilepsy populations (eg, epilepsy-related deaths, emergency health-care use, and quality of life), according to a measure of socioeconomic deprivation. Outcomes excluded: access to care and care provision according to a measure of socioeconomic deprivation.

We included longitudinal cohort studies, studies using routinely collected health-care data, cross-sectional studies, and a matched case–control cohort study in the review. We excluded conference abstracts due to limited data or insufficient information to assess quality and studies not reporting empirical results to avoid data duplication.

Identified references were managed in Endnote and duplicates removed. Screening was done using Rayyan.[31] Two authors independently screened all abstracts and full-text articles (KJB and EC or SER or WOP or RHT), and a senior third reviewer resolved discrepancies. The studies excluded at full-text screening are contained in the appendix (pp 4–8).

This systematic review and meta-analysis protocol was prospectively published on PROSPERO (CRD42023394143) and is reported according to PRISMA guidance.[32]

Data analysis

One author (KJB) extracted data from the full text of included studies. A standardised template was trialled and used to extract data (appendix p 8). A second reviewer

See Online for appendix

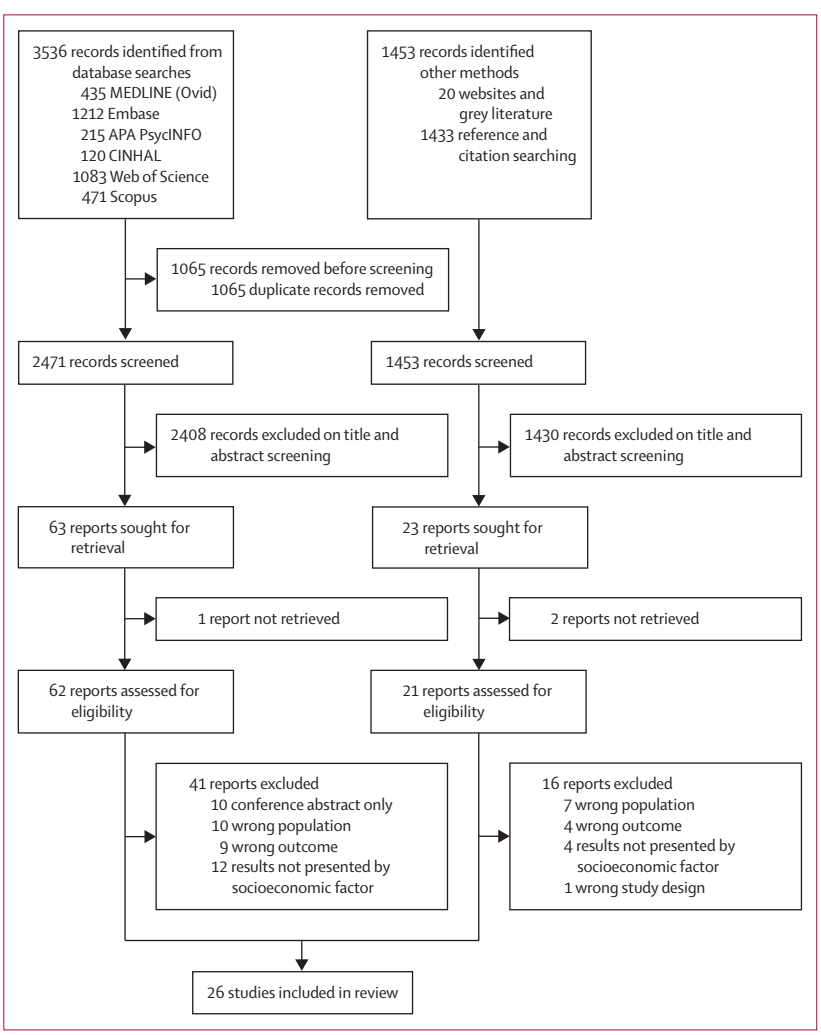

Figure 1: **Study selection**

(SM or EC) checked data extraction. The data extracted included: the year of publication, study aim, time period for data collection, study design, definition of epilepsy, socioeconomic factor measured, epilepsy population size, age and sex, type of population studied (eg, cohort or area level), details of comparator groups, epilepsy incidence, epilepsy adverse outcome rates; rates of underlying epilepsy determinants; statistical measures used to report socioeconomic inequalities; and adjustments made and details of any further analysis of factors underlying socioeconomic inequalities performed.

The appropriate Critical Appraisal Skills Programme checklist was completed for each study to assess validity, results, and applicability (KJB).[33] We used the quality assessment to aid the interpretation of study findings and no studies were excluded based on quality alone.

In a narrative synthesis, we explored study characteristics, populations included, definitions of deprivation and epilepsy used, outcome types, and the factors

	Countries included	Age	Epilepsy definition	Measure of socioeconomic status; levels (n)	Cohort size or person-years of follow-up; sex, n (%)	Number of people with epilepsy included; sex, n (%)	Study design	Study years
Epilepsy incidence								
Graham et al (2013)[37]	England (London)	All	≥2 unprovoked seizures—diagnosis was self-reported	Occupation; 2	3310 people with first stroke; 1673 (50·5%) male; 1637 (49·5%) female	213 incident cases; 110 (52·6%) male; 103 (48·4%) female	Prospective cohort study: South London Stroke Register	2003–17
Heaney et al (2002)[13]	England (London and southeast)	All	≥2 unprovoked seizures	Carstairs index; 5	369 283 person-years; sex breakdown not provided	190 incident cases; 96 (50·5%) male; 94 (49·5%) female	Prospective cohort study: 20 general practices in London and southeast England	1995–97
Hunter et al (2020)[20]	Scotland (Fife and Lothian)	0–59 months	Clinical diagnosis of epilepsy	Scottish IMD score; 5	Area population 45 244; 23 072 (51·0%) male; 22 172 (49·0%) female	59 incident cases; 36 (61·0%) male; 23 (39·0%) female	Prospective, population-based study: Neurodevelopment in Preschool Children of Fife and Lothian Epilepsy Study (NEUROPROFILES)	2013–15
Josephson et al (2017)[42]	UK	18–90 years	Epilepsy diagnostic code, or two codes for symptoms of epilepsy and ASM code	Townsend score (used as continuous variable)	THIN cohort 10 595 709; sex breakdown not provided	97 177 incident cases; 42 758 (44·0%) male; 54 419 (56·0%) female	Longitudinal cohort study: The Health Improvement Network (THIN) data	2007–15
Meeraus et al (2013)[38]	UK	0–7 years	Repeat ASM prescriptions, epilepsy diagnosis, or epilepsy symptoms	Townsend score; 5	329 823 with 1 045 629 person-years; 535 243 (51·2%) male; 510 386 (48·8%) female person-years	1214 incident cases; 678 (55·8%) male; 536 (44·2%) female	Birth cohort study: The Health Improvement Network (THIN) data	2001–08
Pickrell et al (2015)[18]	Wales	>18 years	Epilepsy diagnostic code and two ASM codes	Welsh IMD score; 10	1 178 558 with 8 100 232 person-years; 588 476 (49·9%) male; 590 082 (50·1%) female	2390 incident cases; sex breakdown not provided	Longitudinal cohort study: linked SAIL data	2004–10
Reading et al (2006)[36]	England (Norfolk)	29 days to 14 years	Clinical diagnosis of epilepsy	Townsend score; 4	Area population 77 952; sex breakdown not provided	155 incident cases; sex breakdown not provided	Cross-sectional study: children newly presenting with epilepsy	2001–04
Symonds et al (2021)[19]	Scotland	<3 years	≥2 unprovoked seizures	Scottish IMD score; 5	169 500 livebirths; sex breakdown not provided	405 incident cases; sex breakdown not provided	Prospective cohort study: children with seizures attending NHS clinics or attending for electroencephalogram	2014–17
Vessey et al (2002)[39]	England and Scotland	25–39 years	Referred to hospital with a diagnosis of epilepsy	Social class Registrar General's Classification; 6	17 032 women; 17 032 (100%) female	82 incident cases; 0 male; 82 (100%) female	Prospective cohort study: Oxford–Family Planning Association (Oxford–FPA) contraceptive study	1968–94
Wigglesworth et al (2023)[3] Gold cohort	UK (England, Scotland, Northern Ireland, and Wales)	All	Epilepsy diagnostic code and ASM code	IMD score; 10	21 049 510 person-years; 10 486 301 (49·8%) male; 10 563 208 (50·2%) female	9874 incident cases; 4884 (49·5%) male; 4990 (50·5%) female	Longitudinal cohort study: linked CPRD data (GOLD)	2013–18
Wigglesworth et al (2023)[3] Arum cohort	UK (England and Northern Ireland)	All	Epilepsy diagnostic code and ASM code	IMD score; 10	65 285 012 person-years; 32 785 477 (50·2%) male; 32 499 535 (49·8%) female	24 151 incident cases; 12 318 (51·0%) male; 11 833 (49·0%) female	Longitudinal cohort study: linked CPRD data (ARUM)	2013–18

(Table 1 continues on next page)

	Countries included	Age	Epilepsy definition	Measure of socioeconomic status; levels (n)	Cohort size or person-years of follow-up; sex, n (%)	Number of people with epilepsy included; sex, n (%)	Study design	Study years
(Continued from previous page)								
Adverse outcomes of epilepsy								
Allard et al (2017)[44]	England (Cornwall)	>18 years	Clinical diagnosis of epilepsy for ≥1 year and ≥1 accident and emergency department attendance	IMD score; 4	Hospital catchment 536 000; sex breakdown not provided	46; 29 (63·0%) male; 17 (37·0%) female	Cross-sectional study: interviews with people attending accident and emergency departments	2013–14
Baxendale et al (2011)[53]	England (London)	Not specified	Clinical diagnosis of epilepsy	IMD score; 5	Clinical database 292; 139 (47·6%) male; 153 (52·4%) female	292; 139 (47·6%) male; 153 (52·4%) female	Retrospective review of clinical surgical database	1990–unknown
Campbell et al (2013)[47]	Scotland	Not specified	Clinical diagnosis of epilepsy and taking ASM	Scottish IMD score; 5	Epilepsy and pregnancy register; >7000 pregnancies – exact number not stated	1457 pregnancies in women with epilepsy	Prospective registry study: The UK Epilepsy and Pregnancy Register	1996–2012
Carson et al (2015)[54]	Scotland	2–17 years	Children attending epilepsy clinics	Scottish IMD score; 5	Clinic population approached 97; sex breakdown not provided	87; 42 (48·3%) male; 45 (51·7%) female	Cross-sectional study of children with epilepsy	2011–12
Collings et al (1990)[51]	UK	16–74 years	Self-report of epilepsy and connected to an epilepsy support group, or attending hospital outpatients with epilepsy	Social Class Registrar General's Classification; 6	Total eligible population not stated	392; 189 (48·2%) male; 203 (51·8%) female	Cross-sectional study of adults with epilepsy	Not stated (pre-1990)
Hunter et al (2019)[40]	Scotland (Fife and Lothian)	1–59 months	Clinical diagnosis	Scottish IMD score; 5	Area population numbers not stated	46; 27 (58·7%) male; 19 (41·3%) female	Prospective, population-based study: Neurodevelopment in Preschool Children of Fife and Lothian Epilepsy Study (NEUROPROFILES)	2013–15
Josephson et al (2017)[41]	UK	>18 years	Epilepsy syndrome diagnostic code, or two codes for symptoms of epilepsy and ASM code	IMD rank; 32 844	CALIBER cohort 2 718 952; sex breakdown not provided	16 379; 7769 (47·4%) male; 8610 (52·6%) female	Longitudinal cohort study: linked dataset Clinical research using Linked Bespoke studies and Electronic health Records (CALIBER)	1997–2009
Josephson et al (2021)[43]	UK	>18 years	Epilepsy diagnostic code	IMD score; 10	CPRD cohort 10 916 166; sex breakdown not provided	23 606; sex breakdown not provided	Longitudinal cohort study: linked CPRD UK data	1990–2019
Lee-Lane et al (2021)[49]	Wales	>18 years	Epilepsy diagnostic code and two ASM codes	Welsh IMD score; 5	SAIL cohort 3 229 213; sex breakdown not provided	10 241; 5344 (52·2%) male; 4897 (47·8%) female	Longitudinal cohort study: linked SAIL Welsh data	2003–17
Macleod et al (2002)[45]	Scotland (Lothian)	>15 years	Clinical diagnosis of epilepsy in hospital clinical database	Carstairs score; 7	360 ICU admissions; 5227 deaths; sex breakdowns not provided	32 ICU admissions with epilepsy; male–female ratio 1·00:1·20; 69 deaths with epilepsy; male–female ratio 2·24:1·00	Cross-sectional study: hospital database	1995–99
Mbizvo et al (2022)[48]	Scotland	Not specified	Clinical diagnosis of epilepsy on medical record review	Scottish IMD score; 5	448 (case–control ratio 1:1); 228 (50·9%) male; 220 (49·1%) female	224 deaths in people with epilepsy; 114 (50·9%) male; 110 (49·1%) female	Case–control study: linked Scottish national datasets	2009–16
Mensah et al (2006)[22]	Wales (Cardiff)	>18 years	History of recurrent seizures, and prescription for ASM and no history of learning disability or dementia	Employment status; 2, and education status; 6	General practice population 233 882; sex breakdown not provided	515; 255 (49·5%) male; 260 (50·5%) female	Cross-sectional study: questionnaire	Not stated (pre-2006)
Mensah et al (2007)[50]	Wales (Cardiff)	>18 years	History of recurrent seizures and prescription for ASM and no history of learning disability or dementia	Employment status; 2 and education status; 6	General practice population 233 882; sex breakdown not provided	515; 255 (49·5%) male; 260 (50·5%) female	Cross-sectional study: questionnaire	Not stated (pre-2006)

(Table 1 continues on next page)

	Countries included	Age	Epilepsy definition	Measure of socioeconomic status; levels (n)	Cohort size or person-years of follow-up; sex, n (%)	Number of people with epilepsy included; sex, n (%)	Study design	Study years
(Continued from previous page)								
Morgan et al (2000)[46]	Wales (South Glamorgan)	Not specified	Inclusion in epilepsy clinic database or an inpatient admission coded for epileptic seizure or diagnosis on the learning disability hospital database or epilepsy on death certificate	Townsend score; 2	Area population 434 000; sex breakdown not provided	2809; sex breakdown not provided	Cross-sectional study: linked data from hospital admissions, outpatients, mortality data, epilepsy clinic, and social services community learning disability database	1991–97
Taylor et al (2011)[52]	UK	18–64 years	≥2 unprovoked seizures in the previous year	Composite measure of socioeconomic status; 2	Study population of 1881 people with epilepsy; sex breakdown not provided	617; 331 (53·6%) male; 286 (46·4%) female	Prospective cohort study: data from the Standard and New Antiepileptic Drugs (SANAD) trial	1999–2004
Weatherburn et al (2017)[21]	Scotland	>14 years	Epilepsy diagnostic codes and ASM code	Carstairsindex; 5	People in database 1 510 742; 743 982 (49·2%) male; 766 760 (50·8%) female	12 720 people with epilepsy; 6415 (50·4%) male; 6305 (49·6%) female	Cross-sectional study: Scottish multi-morbidity database	2007

ASM=anti-seizure medication. CPRD=Clinical Practice Research Datalink. IMD=index of multiple deprivation. NHS=National Health Service. SAIL=Secure Anonymised Information Linkage. THIN=The Health Improvement Network.

Table 1: **Characteristics of all included studies**

underlying the relationship between deprivation and outcomes.

We conducted a random-effects meta-analysis to calculate pooled incident rate ratios (IRR). We included studies that published the data required to calculate incidence rates, stratified by a measure of deprivation. If these data were not available, we wrote to study authors to request them. The data were extracted and, to allow analysis of data with differing numbers of levels, we decided a priori following consultation with a data synthesis expert to create three groups of low (least deprived 40%), medium (middle 20%), and high (most deprived 40%) deprivation. Where this was not possible, studies were included with caveats of potential limitations.

Meta-analyses compared epilepsy incidence rates in the medium and high-deprivation groups to the low-deprivation (baseline) group. We separately explored the effect of stratifying by population age. Statistical analysis was performed in R Studio (4.2.1) using meta[34] and metafor[35] packages. A random-effects model was used to pool effect sizes (Mantel–Haenszel) and allow for heterogeneity between studies. Knapp–Hartung adjustments calculated the pooled effect size 95% CIs and the Paule–Mandel estimator calculated between-study heterogeneity variance; I^2 values indicated low (25%), medium (50%), or high (75%) levels of heterogeneity. We performed sensitivity analyses by sequentially removing each study and observing the effect this had on the results (appendix p 9). To provide further detail about the association observed, a post-hoc meta-analysis was performed to include comparisons of epilepsy incidence rates per individual quintile.

The adverse outcome studies were synthesised narratively according to adverse outcome type. The adverse outcomes were grouped to include emergency health-care use, pregnancy, mortality, medical comorbidities, quality of life and wellbeing, epilepsy surgery, and behavioural and neurobehavioural. There were clinically significant differences between the populations and outcomes studied, which made conducting meta-analyses inappropriate.

Role of the funding source

The funders had no role in data collection, analysis, interpretation, report writing, or the decision to submit this report for publication.

Results

We identified 3536 records via database searches, 20 through grey literature searches, and 1433 from citation chaining. 83 papers, 62 identified from database searches and 21 identified from other methods, underwent full-text screening and 26 UK studies reporting relevant outcomes according to socioeconomic factors were included (figure 1): ten studies reported epilepsy incidence or risk and 16 studies reported adverse outcomes in people with epilepsy, published 1990–2023 (table 1).[3,13,18–22,36–54]

There were 15 prospective studies (cohorts, data-linkage, or registries),[3,13,18–20,37–43,47,49,52] ten cross-sectional studies,[21,22,36,44–46,50,51,53,54] and one case–control study.[48] Definitions of epilepsy and deprivation varied, with six studies using an individual-level measure of socioeconomic position[22,37,39,50–52] and the rest using area-level measures.

	Epilepsy incidence or hazard ratio (95% CI)	Results on inequality reported	Study results interpretation	Analysis of factors underlying socioeconomic inequalities performed
All age populations				
Heaney et al (2002)[13]	Incidence (1; least deprived group) 34·1 per 100 000 people per year (95% CI 23·4–49·7); (2) 36·8 per 100 000 people per year (25·4–53·3); (3) 54·3 per 100 000 people per year (39·9–74·1); (4) 52·8 per 100 000 people per year (38·1–73·2); (5; most deprived group) 87·7 per 100 000 people per year (67·1–114)	OR compared with least deprived group: unadjusted (1; least deprived) 1·00; (2) 1·07 (95% CI 0·67–1·69); (3) 1·50 (0·88–2·56); (4) 1·41 (1·02–1·94); (5) 2·35 (1·53–3·60); p<0·001; age and sex adjusted (1; least deprived) 1·00; (2) 1·05 (0·66–1·70); (3) 1·45 (0·84–2·51); (4) 1·38 (0·97–1·96); (5) 2·33 (1·46–3·72); p=0·001	Increasing levels of socioeconomic deprivation are associated with increasing epilepsy incidence	On further adjustment for London area the association weakened but the trend remained: OR in the most deprived group compared with the least 1·62 (0·91–2·88); p=0·12
Wigglesworth et al (2023)[3] Gold cohort	Incidence (1; least deprived group) 35·60 per 100 000 people per year (95% CI 32·88–38·48); (2) 42·60 per 100 000 people per year (39·64–45·72); (3) 50·73 per 100 000 people per year (47·43–54·20); (4) 38·56 per 100 000 people per year (35·65–41·63); (5) 40·05 per 100 000 people per year (37·35–42·89); (6) 54·01 per 100 000 people per year (51·03–57·11); (7) 48·18 per 100 000 people per year (45·61–50·86); (8) 47·28 per 100 000 people per year (44·21–50·50); (9) 47·61 per 100 000 people per year (45·07–50·26); (10; most deprived group) 58·35 per 100 000 people per year (55·32–61·50)	Pearson's correlation coefficient r=0·68	Increasing levels of socioeconomic deprivation are associated with increasing epilepsy incidence	No
Wigglesworth et al (2023)[3] Arum cohort	Incidence (1; least deprived group) 32·09 per 100 000 people per year (95% CI 30·59–33·65); (2) 33·83 per 100 000 people per year (32·34–35·37); (3) 32·74 per 100 000 people per year (31·31–34·22); (4) 33·71 per 100 000 people per year (32·24–35·22); (5) 39·39 per 100 000 people per year (37·78–41·05); (6) 38·17 per 100 000 people per year (36·67–39·70); (7) 38·11 per 100 000 people per year (36·75–39·51); (8) 38·04 per 100 000 people per year (36·67–39·46); (9) 36·51 per 100 000 people per year (35·19–37·87); (10; most deprived group) 45·09 per 100 000 people per year (43·51–46·71)	No calculation published	Increasing levels of socioeconomic deprivation are associated with increasing epilepsy incidence	No
Graham et al (2013)[37]	Proportion of stroke population developing epilepsy according to socioeconomic status; non-manual 8·1%; manual 6·8%; unknown 2·8%	p=0·224	The proportion of people who developed epilepsy did not differ according to socioeconomic status	Multivariate analysis performed: young age, specific stroke subtypes and specific stroke symptoms were independently associated with epilepsy
Adult populations				
Pickrell et al (2015)[18]	Incidence (1; least deprived group) 19·18 per 100 000 people per year; (2) 24·33 per 100 000 people per year; (3) 25·25 per 100 000 people per year; (4) 26·67 per 100 000 people per year; (5) 28·01 per 100 000 people per year; (6) 30·76 per 100 000 people per year; (7) 31·77 per 100 000 people per year; (8) 36·32 per 100 000 people per year; (9) 36·31 per 100 000 people per year; (10; least deprived group) 40·41 per 100 000 people per year; note 95% CI represented graphically	Adjusted IRR per Welsh IMD decile (most deprived is the reference group) 0·936 (0·923–0·950); p<0·001	Increasing levels of socioeconomic deprivation are associated with increasing epilepsy incidence	Results adjusted for age and sex
Vessey et al (2002)[39]	RR of epilepsy by Registrar General social class: (social class I and II high, including professional, managerial and technical occupations) RR 1·00 (social class III medium, including skilled occupations); RR 1·69 (1·00–2·96); (social class IV and V low, including part-skilled and unskilled occupations) RR 2·76 (1·33–5·57)	χ^2 value for trend 9·71; p=0·002	Increasing levels of socioeconomic deprivation are associated with increased epilepsy risk	No relationship between use of OCP and epilepsy demonstrated
Josephson et al (2017)[42]	HR of developing epilepsy per each incremental increase in value of the Townsend deprivation index	HR 1·11 (1·10–1·12); p<0·001	Increasing levels of socioeconomic deprivation are associated with increased epilepsy risk	Incident depression was associated with an increased risk of epilepsy, HR 2·54 (2·48–2·60); p<0·001; as were age at index date, female sex, and increasing Charlson comorbidity index (all p<0·001)

(Table 2 continues on next page)

	Epilepsy incidence or hazard ratio (95% CI)	Results on inequality reported	Study results interpretation	Analysis of factors underlying socioeconomic inequalities performed
(Continued from previous page)				
Child populations				
Hunter et al (2020)[20]	36 per 25 762 children in low socioeconomic status areas over 26 months (quintiles 1–3); 23 per 19 576 children in high socioeconomic status areas over 26 months (quintiles 4 and 5)*	RR in low socioeconomic status compared with high socioeconomic status 1·19 (95% CI 0·7–2·0); p=0·5	Epilepsy risk did not increase with increasing levels of socioeconomic deprivation	RR for all other ethnicities compared with people who were classified as White from the British Isles 1·89 (95% CI 1·1–3·4); p=0·03
Meeraus et al (2013)[38]	Incidence per 100 000 PYAR (1; least deprived group) 91·2 per 100 000 PYAR (95% CI 80·3–103·2); (2) 98·9 per 100 000 PYAR (85·9–113·3); (3) 140·9 per 100 000 PYAR (125·4–157·9); (4) 131·5 per 100 000 PYAR (116·0–148·5); (5; most deprived group) 131·0 per 100 000 PYAR (113·3–150·8)	Crude IRR (1) baseline; (2) 1·08 (p=0·388); (3) 1·54 (p<0·001); (4) 1·44 (p<0·001); (5; most deprived group) 1·44 (p<0·001); adjusted IRR on gender, age, and period (year) (1; least deprived group) baseline; (2) 1·08 (p=0·430); (3) 1·52 (p<0·001); (4) 1·41 (p<0·001); (5; most deprived group) 1·40 (p<0·001)	Epilepsy risk did not increase with increasing levels of socioeconomic deprivation in a linear relationship; the risk of epilepsy was increased in all groups when compared with the least deprived group	A linear trend was seen in reducing incidence between 2001 and 2008 (p<0·001)
Reading et al (2006)[36]	Incidence (1; least deprived group) 6·5 per 10 000 people per year (95% CI 4·8–9·0); (2) 8·0 per 10 000 people per year (5·9–10·6); (3) 4·1 per 10 000 people per year (2·6–6·1); (4; most deprived group) 7·9 per 10 000 people per year (5·8–10·5)	χ^2 value for trend 0·00005; p=0·98	Increasing levels of socioeconomic deprivation are not associated with increased epilepsy risk	No social gradient in the proportions of children who were investigated where epilepsy was a possible initial diagnosis (χ^2 for trend 0·064; p=0·80)
Symonds et al (2021)[19]	Incidence (1; least deprived group) 182 per 100 000 livebirths (95% CI 139–233); (2) 220 per 100 000 livebirths (173–277); (3) 220 per 100 000 livebirths (171–276); (4) 250 per 100 000 livebirths (202–309) (5; most deprived group) 301 per 100 000 livebirths (251–357)	χ^2 OR 1·7 (95% CI 1·3–2·2); p=0·001; χ^2 for trend p=0·01	Increasing levels of socioeconomic deprivation are associated with increased epilepsy risk	Results adjusted for age, presentation, seizure type, and aetiology: impact of stratifying according to known epilepsy aetiology (no association with deprivation) or unknown epilepsy aetiology (association with deprivation persists)

p values are presented as published. HR=hazard ratio. IMD=index of multiple deprivation. IRR=incidence rate ratio. OCP=oral contraceptive pill. OR=odds ratio. PYAR=person-years at risk. RR=relative risk.
*Published study data, we received the unpublished data by quintile from the study authors and this was used in the meta-analysis and the data per quintile are not published here due to small numbers.

Table 2: **Summary of study findings on the distribution of socioeconomic inequalities in epilepsy incidence**

The risk-of-bias assessment (appendix pp 12–17) identified misclassification, participation, and interpretive biases. Three studies risked misclassification of epilepsy and their results should be interpreted with caution, two defining epilepsy by self-report[37,51] and one study defining epilepsy as being referred to hospital for epilepsy.[39] A single study reported the numbers of and sociodemographic data for individuals declining to participate.[40] Three studies used postal outcome questionnaires, limiting participation to people with adequate literacy.[22,50,52] No study fully adjusted models for potential factors mediating or influencing the associations seen. One study risked interpretive bias by suggesting potential causal association.[42] One small study lacked precision around risk estimates.[20]

Ten studies[3,13,18–20,36–39,42] reported epilepsy incidence or risk according to socioeconomic factors and one study reported incidence[3] in two populations (table 2). Incident case numbers identified ranged from 59[20] to 24 151.[3] Three studies included both children and adults,[3,13,37] three included only adults,[18,39,42] and four included only children.[19,20,36,38] In seven populations, epilepsy incidence or risk was significantly associated with socioeconomic factors, with the highest incidence of epilepsy observed in the most deprived populations.[3,13,18,19,39,42] One study found the association between incidence and with socioeconomic factors differed when epilepsy aetiologies were known (no association) or unknown (association).[19]

Epilepsy incidence in the most deprived group ranged from 40 per 100 000 people per year in Welsh adults[18] to 301 per 100 000 people per year in Scottish children.[19] Socioeconomic deprivation was defined by area-level measures[3,13,18–20,36,38,42] and occupation-based measures.[37,39] Definitions of epilepsy included clinical diagnosis,[20,36,39] two or more unprovoked seizures,[13,19,37] and epilepsy clinical codes with or without ASM codes.[3,18,38,42]

Seven studies reported incidence rates[3,13,18–20,36,38] and six studies (seven populations) were included in the meta-analysis. One was excluded as the denominator was livebirths.[19] All studies included in the meta-analysis used area-level measures of deprivation (IMD, Welsh index of multiple deprivation, Scottish index of multiple deprivation, Carstairs index, or Townsend score).

Meta-analyses showed a significant association between higher levels of deprivation and increased epilepsy incidence (figure 2). The incidence of epilepsy in the medium deprivation groups was 1·23 (IRR 1·23 [95% CI 1·08–1·39]) times that of the least deprived group. In the highest deprived groups, the incidence of epilepsy was 1·34 (IRR 1·34 [1·16–1·56]) times the rate in the least deprived group. The overall I^2 values of 63% for medium deprivation groups versus low

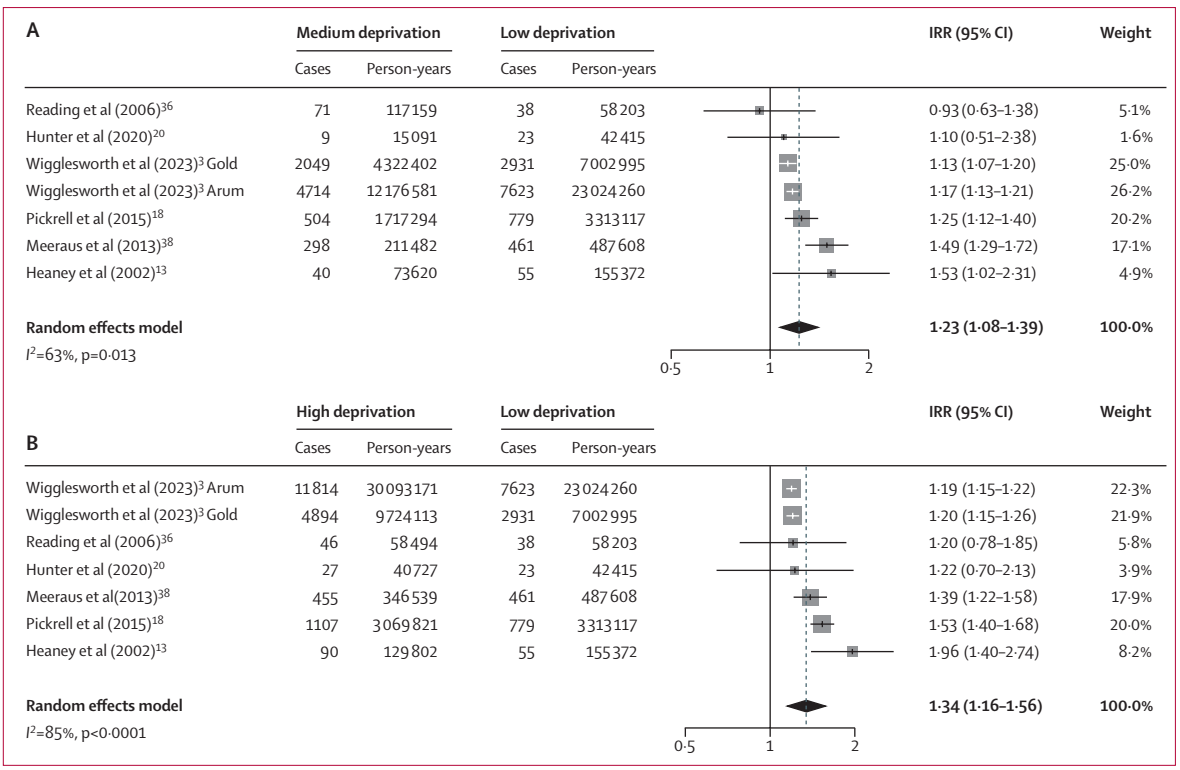

Figure 2: **Meta-analysis of epilepsy incidence rates according to levels of deprivation**
(A) Medium *vs* low deprivation groups. (B) High *vs* low deprivation groups. IRR=incidence rate ratio.

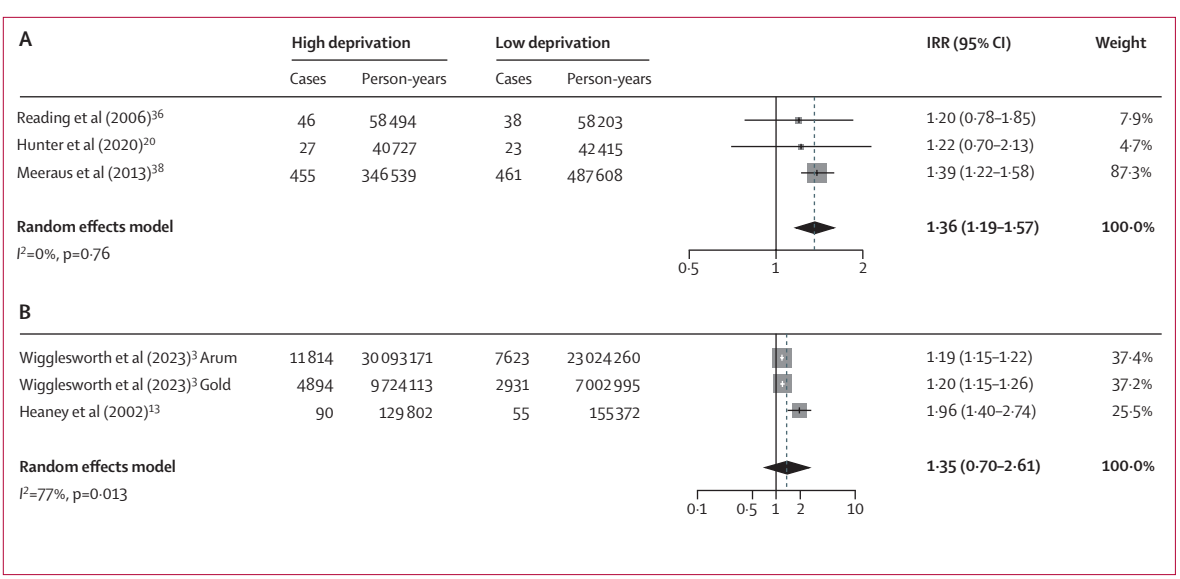

Figure 3: **Subgroup meta-analysis of high deprivation *vs* low deprivation by population age**
(A) High *vs* low deprivation groups in studies including only children. (B) High *vs* low deprivation groups in studies including children and adults. IRR=incidence rate ratio.

deprivation groups and 85% for high deprivation groups versus low deprivation groups show substantial heterogeneity between studies. Sensitivity analysis using the leave-one-out method did not identify any influential outliers (appendix p 9).

The same data were included in subgroup meta-analyses, examining associations stratified by age (figure 3). The IRR for epilepsy was 1·35 (95% CI 0·70–2·61) in the child and adult combined populations and 1·36 (1·19–1·57) in the studies including only

children. The adult-only subgroup contained a single study[11] and no further analysis was performed.

Six populations were analysed as quintiles of deprivation: low deprivation (least deprived 40%), medium deprivation (middle 20%), and high deprivation (most deprived 40%). The seventh study reported quartiles of deprivation.[36] In the sensitivity analysis removing this study had no significant effect on the pooled IRRs. A post-hoc meta-analysis comparing each individual quintile to the most deprived showed the same trend in association, with the highest pooled IRR seen when comparing the most deprived quintile to the least. (appendix pp 10–11).

Two studies reported potential factors influencing the association between socioeconomic deprivation and epilepsy incidence. One study reported that the association between deprivation and epilepsy was no longer significant when adjusted for living in London versus the rest of southeast England.[13] The second study found no significant associations in their cohort of children with epilepsy between Scottish index of multiple deprivation and any of the following factors: rates of referral for genetic testing or brain imaging, seizure type, age on presentation, drug-resistant epilepsy, or global developmental disability.[19]

One study presented epilepsy risk within a multivariate analysis model: the association between deprivation and epilepsy was robust when adjusting for incident depression, female sex, age at event, and increasing Charleston comorbidity index, all of which were associated with epilepsy risk in the model.[42] Other studies examined factors independently from deprivation in the same populations. Factors shown to have an association with incident epilepsy included higher BMI,[39] age when stroke occurred, stroke subtype or clinical features,[23] and non-White ethnicity.[20]

16 studies reported adverse outcomes in populations of people with epilepsy according to socioeconomic factors (table 3). Nine were cross-sectional in design.[21,22,44–46,50,51,53,54] Some studies reported multiple outcomes: three on emergency or unplanned health-care use,[44–46] one on pregnancy outcomes,[47] four on mortality,[41,45,46,48] five on comorbidity rates,[21,22,43,49,50] two on quality of life or wellbeing,[51,52] one on epilepsy surgery,[53] and two on childhood behavioural or neurobehavioural outcomes.[40,54] Exploring the association with socioeconomic factors was the main study aim in six studies.[45–47,51,53,54]

12 studies demonstrated socioeconomic inequalities, with the worst outcomes seen in the most deprived groups. Outcomes included rates of inpatient admissions with or without epilepsy;[46] all-cause mortality,[41,45,46] epilepsy-related mortality;[41,48] cardiovascular disease, depression, and anxiety;[21,22,43,50] poorer quality-of-life scores;[52] childhood behavioural problems;[54] generalised tonic-clonic seizures, multiple ASMs, and sodium valproate use in pregnancy.[47] One study showed a U-shaped association between deprivation and epilepsy intensive care admissions, not explained by hospital admission or death rates.[45]

Five studies did not demonstrate an association with deprivation, including emergency department attendance rates;[44] risk of major cardiovascular events;[49] overall wellbeing;[51] odds of neurobehavioral problems (except for autism spectrum disorder);[40] and age at epilepsy onset and surgical assessment, or duration of active epilepsy before surgery.[53]

Discussion

Our systematic review and meta-analysis demonstrate that medium and high levels of socioeconomic deprivation are associated with an increased risk of incident epilepsy compared with low levels of socioeconomic deprivation. This risk is most pronounced when comparing people living in high deprivation and those living in low deprivation, with an increased risk of incident epilepsy of around 34%. However, the risk is also increased by around 23% when comparing people living in medium deprivation with those living in low deprivation. These findings demonstrate clear evidence of the need for public health efforts in the UK to reduce socioeconomic inequalities in epilepsy. The factors influencing this association of socioeconomic deprivation with epilepsy incidence are unknown. No study reported incidence rates by socioeconomic factors for older adults alone. Notably, our findings show that socioeconomic inequalities in epilepsy incidence start in childhood, highlighting the fact that inequalities in epilepsy incidence, and the potentially preventable cases of epilepsy that they represent, should be considered across the life course.

This study is UK-specific, which limits its generalisability, yet highlights the need for country-specific studies on inequalities in epilepsy in other regions. In line with our findings, studies in Ireland (all ages), USA (all ages), and Sweden (children aged 2–17 years) found the same association in the incidence of epilepsy according to socioeconomic factors.[9,10,26,55] However, an Icelandic study reported that low socioeconomic status was a risk factor for epilepsy in adults but not children,[56] and a study of Swedish adults showed no association between socioeconomic status and epilepsy.[57]

One study of early-onset childhood epilepsy in the UK found the association with deprivation only persisted where the epilepsy aetiology was unknown,[19] which is similar to the results of an (all age) Irish study, demonstrating the association with structural and unknown aetiologies.[26] These inequalities could represent unknown determinants, such as polygenic risk or maternal exposures. Outside of UK specialist centres, in low-income countries, or in those without universal health-care provision, having an unknown aetiology might represent an inequality in access to investigations. Further understanding of how inequalities differ when

stratified by International League Against Epilepsy-defined aetiologies[4] might provide insight into identifying modifiable determinants in children, including vaccine-preventable infections or perinatal hypoxic brain injuries.

There is a scarcity of information on factors influencing the association between deprivation and epilepsy incidence. The only factor identified, in a single study, was living in London, compared with living in the rest of southeast England.[13] The London population had higher

	Adverse outcomes	Results on inequality reported with 95% CI	Study results interpretation	Analysis of factors underlying socioeconomic inequalities performed
Emergency (unplanned) health-care use				
Allard et al (2017)[44]	IRR for emergency department attendance	(1; least deprived group) 1·00; (2) 0·68 (0·21–2·12); (3) 1·50 (0·60–3·76); (4) 2·35 (0·98–5·67; most deprived group)	There was no association between increasing deprivation and increased risk of emergency department attendance	Factors predicting emergency department attendance: higher number of seizures in the previous year IRR 1·16 (95% CI 1·04–1·28) and anxiety IRR 1·91 (0·91–3·99)
Macleod et al (2002)[45]	Standardised rates of ICU admissions	U-shaped relationship between deprivation and rates of ICU admission with the highest rates being seen in deprivation categories 1 and 7 (P<0·05, χ^2)	The risk of ICU admissions was highest in the most deprived and the least deprived groups; there was no linear association between increasing deprivation and ICU admissions	No association between admission Glasgow Coma Score, or ambulance response time, and deprivation found
Morgan et al (2000)[46]	Pearson's r correlation between increasing deprivation and; the rate of all inpatient admissions; the rate of inpatient admissions with a primary diagnosis of epilepsy; and the rate of inpatient admissions with any diagnosis of epilepsy	r=0·62, p<0·001; r=0·39, p=0·007; r=0·43, p=0·002	There was an association between increasing deprivation and an increased rate of all inpatient admissions, admissions with a primary epilepsy diagnosis, and admissions with any epilepsy diagnosis; the association was strongest between increasing deprivation and all inpatient admissions	Results were standardised for underlying epilepsy prevalence per ward; population subset with epilepsy and no comorbidities: r=0·59, p<0·001; r=0·35, p=0·016; r=0·41, p=0·004
Pregnancy-related outcomes				
Campbell et al (2013)[47]	Proportion of women in quintile 1 *vs* quintile 5 compared using Fisher's exact test, Mann–Whitney U test, and Kruskal–Wallis; selected outcomes included only: generalised tonic-clonic seizure in pregnancy; polytherapy in pregnancy; sodium valproate in pregnancy; major congenital malformation rate; and all congenital malformation rate	Quintile 1 (least deprived) *vs* quintile 5 (most deprived); 13·0% *vs* 29·2%, p<0·0001; 13·5% *vs* 26·3%, p=0·0003; 19·5% *vs* 28·0%, p=0·05; 4·7% *vs* 4·4%, p=0·84; 7·3% *vs* 9·7%, p=0·37	There was an association between increasing deprivation and higher rates of generalised tonic-clonic seizure in pregnancy and poly-therapy in pregnancy; there was no association between deprivation and congenital malformation rates	Women in the least deprived quintile were on average 5·1 years older than those in the most deprived quintile, and more likely to have a higher intrinsic risk of major congenital malformations
Mortality-related outcomes				
Josephson et al (2017)[41]	Adjusted HR for all-cause mortality per 1 rank increase in IMD, deprivation increasing; adjusted HR for seizure-specific mortality per 1 rank increase in IMD	HR 1·01 (1·01–1·01), p<0·001; HR 1·01 (0·99–1·02), p=0·145	There was an association between increasing deprivation and increased risk of all-cause mortality; there was no association between increasing deprivation and risk of seizure-specific mortality	HR adjusted for serotonin reuptake inhibitor exposure, age, female sex, depression, and the Charleston comorbidity index; main exposure of interest for all-cause mortality was serotonin reuptake inhibitor exposure (HR 1·64; 95% CI 1·44–1·86), age and female sex were also significant p<0·001
Macleod et al (2002)[45]	Association between deprivation and rates of death	Individuals in most deprived group were 27·8 times more likely to die than those in the least deprived group (p<0·001, χ^2 for ranks)	There was an association between increasing deprivation and increased rates of death	No association between admission Glasgow Coma Score and deprivation found
Mbizvo et al (2022)[48]	Odds of an epilepsy-related death occurring, quintiles 1–5	Quintiles 1 and 2 least deprived as reference group; quintile 3 OR 1·8 (95% CI 1·0–3·2), p=0·06. Quintiles 4 and 5 OR 2·5 (95% CI 1·6–4·0), p=0·00	There was an association between increasing deprivation and increased odds of an epilepsy-related death	Multivariable model adjusted for recent emergency department attendance or hospital admission for seizures or epilepsy, congenital or genetic aetiology, and a higher burden of medical comorbidities: quintiles 1 and 2 (reference group); quintiles 4 and 5 OR 2·2 (95% CI 1·2–3·8), p=0·009
Morgan et al (2000)[46]	SMR for those classified as deprived compared with affluent	SMR: 1·66 (95% CI 1·27–2·05); results standardised for epilepsy prevalence	There was an association between increasing deprivation and increased mortality rates	Population with epilepsy and no comorbidities: SMR 1·80 (95% CI 1·27–2·32)

(Table 3 continues on next page)

	Adverse outcomes	Results on inequality reported with 95% CI	Study results interpretation	Analysis of factors underlying socioeconomic inequalities performed
(Continued from previous page)				
Medical comorbidities				
Josephson et al (2021)[43]	Propensity matched–adjusted Cox proportional HR for cardiovascular disease per 1 unit increase in IMD	HR 1·11 (95% CI 1·08–1·15), p<0·001; least deprived as reference group	There was an association between increasing deprivation and increased risk of cardiovascular disease	HR adjusted for baseline age, sex, epilepsy duration, hypertension, type 2 diabetes, and smoking status; primary study outcome: incidence of cardiovascular disease was higher following repeated exposure to enzyme-inducing anti-seizure medications
Lee-Lane et al (2021)[49]	Adjusted HR for major cardiovascular event per 1 quintile increase in WIMD	HR 0·97 (95% CI 0·94–1·00), p=0·87; most deprived as reference group	There was no association between decreasing deprivation and a decreased risk of a major cardiovascular event	No significant difference seen between those on enzyme-inducing anti-seizure medications and not; significant factors included age, male sex, smoking, hypertension, previous stroke, and co-prescription of anti-platelets, anticoagulants, and statins
Mensah et al (2006)[22]	Association between depression and employment status: no employment: 43·7% no depression and 89·5% depression; employed 56·3% no depression and 10·5% depression. Association between depression and education for no formal education: 36·9% no depression and 58·0% depression; O-Level (school exams at 16 years): 21·7% no depression and 24·0% depression; A-Level (School exams at 18 years): 6·1% no depression and 6·0% depression; Higher National Diploma (vocational qualification 16 years and older): 3·7% no depression and 0·0% depression; college or university: 19·2% no depression and 4·0% depression	OR 8·9 (95% CI 3·2–24·7), p<0·001; OR 2·1 (95% CI 1·3–3·5), p=0·018,	There was an association between depression and increased odds of unemployment; there was an association between depression and increased odds of lower levels of education	Depression was also associated with recent seizure activity, other chronic health problems, side effects of anti seizure medication, and previous depression
Mensah et al (2007)[50]	Association between anxiety and employment status for no employment: 41·7% no anxiety and 71·1% anxiety; employment 58·3% no anxiety and 28·9% anxiety; association between anxiety and education for no formal education: 36·3% no anxiety and 48·9% anxiety; O-Level (school exams at 16 years): 22·2% no anxiety and 21·7% anxiety; A-Level (school exams at 18 years): 5·5% no anxiety and 8·7% anxiety; Higher National Diploma (vocational qualification 16 years and older): 3·1% no anxiety and 4·3% anxiety; college or university: 19·8% no anxiety and 8·7% anxiety	OR 3·4 (95% CI 2·0–5·9), p<0·001; OR 1·7 (1·1–2·7), p=0·039,	There was an association between anxiety and increased odds of unemployment; there was an association between anxiety and increased odds of lower levels of education	Anxiety was also associated with female sex, seizure activity, other long-term health problems, medication side effects, and depression
Weatherburn et al (2017)[21]	Adjusted OR for (prevalent) depression in people with epilepsy; most deprived *vs* most affluent	Adjusted OR 1·51 (95% CI 1·27–1·79)	There was an association between increasing deprivation and increased odds of prevalent depression	Adjusted for age, sex, number of physical conditions; adjusted OR for depression for those with four or more physical comorbidities *vs* none: 5·82 (95% CI 4·90–6·91)
Quality of life and wellbeing				
Collings et al (1990)[51]	Pearson's r correlation between social class and overall wellbeing	r=–0·07, p>0·05	There was no association between social class and overall wellbeing	When adjusted for multiple other sociodemographic and epilepsy-related factors (r=0·08, p>0·05)
Taylor et al (2011)[52]	RR of good quality of life 4 years post-epilepsy diagnosis; socioeconomically advantaged, with good seizure control (reference group): 84% good quality of life. Advantaged with poor seizure control: 66% good quality of life; disadvantaged with good seizure control: 73% good quality of life; disadvantaged with poor seizure control: 49% good quality of life	RR 1·00 (reference group); RR 0·79 (95% CI 0·68–0·91); RR 0·87 (0·76–0·98); RR 0·58 (0·48–0·70)	There was an association between increasing deprivation and the reduced risk of good quality of life; seizure control had an impact on this association, with poor seizure control also reducing the risk of good quality of life	Factors associated with resilience (good quality of life while disadvantaged with poor seizure control) included absence of depression, fewer adverse treatment effects, and good quality of life at the point of epilepsy diagnosis
Epilepsy surgery				
Baxendale et al (2011)[53]	Correlations between IMD quintile and age at the time of assessment for epilepsy surgery; age at onset of epilepsy; duration of active epilepsy before the surgery; and comparing right hippocampal sclerosis and left hippocampal sclerosis groups	Lowest quintile compared with others: t=0·27, p>0·05; t=–0·02, p>0·05; t=–0·64, p>0·05; right hippocampal sclerosis (t=–0·10, p>0·05) and left hippocampal sclerosis (t=–0·11, p>0·05)	There was no association between deprivation and the age at the time of assessment for epilepsy surgery, age at onset of epilepsy, or duration of active epilepsy before surgery	Left hippocampal sclerosis group showed an association between IMD and deprivation, with lower scores neuropsychological function tests seen in the most deprived groups; in the right hippocampal sclerosis group, deprivation was not associated with the outcomes of the neuropsychological tests

(Table 3 continues on next page)

	Adverse outcomes	Results on inequality reported with 95% CI	Study results interpretation	Analysis of factors underlying socioeconomic inequalities performed
(Continued from previous page)				
Child-specific outcomes				
Carson et al (2015)[54]	Proportion with T score >63 indicating the presence of behavioural problems; high deprivation (quintiles 1–3); 54% (95% CI 39–67); low deprivation (quintiles 4–5); 30% (95% CI 18–44)	Univariable OR 2·74 (95% CI 1·14–6·63)	There was an association between increasing deprivation and increased presence of behavioural problems, as indicated by a T-score >63	Multivariable analysis for seizure frequency, seizure type, number of anti-seizure medications, presence of an MRI abnormality, known intellectual disability, and aetiology: OR 14·81 (95% CI 3·0–67·98)
Hunter et al (2019)[40]	Results by socioeconomic status only reported for autistic spectrum disorder risk with low socioeconomic status: 8 (47%) of 17 with autistic spectrum disorder; high socioeconomic status: 0 (0%) of 12 with autistic spectrum disorder	Difference in proportions 47·1%; univariable OR infinity; multivariable OR infinity	There was an association between increasing deprivation and increased risk of autistic spectrum disorder	Epilepsy-related variables are poorly associated with neurobehavioral disorders

p values are presented as published. HR=hazard ratio. ICU=intensive care unit. IMD=index of multiple deprivation. IRR=incidence rate ratio. OR=odds ratio. RR=relative risk. SMR=standardised mortality ratios. WIMD=Welsh index of multiple deprivation. SIMD=Scottish index of multiple deprivation.

Table 3: **Summary of study findings regarding the distribution of socioeconomic inequalities in epilepsy adverse outcomes**

levels of deprivation than the population in the rest of southeast England, although London is also distinctly different to other parts of the UK in terms of population age, ethnic diversity, pollution, and proximity of services. The role of rural–urban environments and their interplay with socioeconomic factors warrants further investigation.

There is limited evidence regarding the effect of socioeconomic inequalities on any single adverse outcome in the UK, although the narrative synthesis draws together the range of inequalities observed. Care is also required when interpreting results. Higher numbers of emergency attendances with epilepsy might indicate poorer epilepsy control but could also indicate an expressed need[58] in terms of how care is accessed.

The cross-sectional design of nine of the studies reporting on socioeconomic inequalities in epilepsy-related adverse outcome means that the findings cannot inform the sequence of events and direction of causality. The higher rates of adverse outcomes, including cardiovascular disease, anxiety, and depression, in the most deprived populations with epilepsy reflects wider UK health inequalities.[16] Epilepsy can be associated with these conditions, but it is not understood whether they are on the causal pathway (either direction) or are mediated by the same wider determinants of health. The intersection between deprivation and the other factors independently identified as being associated with epilepsy should be considered.

The strengths of this systematic review and meta-analysis include a broad search strategy, which aimed to capture the breadth of inequalities affecting people with epilepsy in the UK. We searched a wide range of databases, supplemented by reference and citation searching, and directly approached charities for resources. To minimise errors, we undertook independent screening by two different people and a second author checked data extraction for accuracy. We used a validated appraisal tool to assess study quality. Assuming the rate of change is the same across all deprivation categories, using the IRR in the meta-analysis was also a study strength as it remains comparable across time even if epilepsy incidence changes over time. Including the medium deprivation group in the meta-analyses strengthens the comparisons and considers all available data.

The limitations of this systematic review and meta-analysis include the exclusion of studies reporting on inequalities in access to care for epilepsy. The issue of inequalities in access to specialist care from neurologists has been previously highlighted by the Association of British Neurologists[59] and we wished to avoid replication of this work. However, it is important to acknowledge that access to care will have an effect on both epilepsy diagnosis rates and adverse outcomes. Furthermore, the included studies span a period more than 20 years and it is likely that improvements in access to specialist service provision have had an effect on diagnosis rates during this period. The heterogeneity of methods used to define both epilepsy and deprivation makes the direct comparisons of epilepsy rates between studies unwise. Epilepsy remains a clinical diagnosis, with no definitive test or biomarker. To preserve the integrity of epilepsy diagnosis, we excluded studies combining epilepsy and seizure diagnoses, as not all seizures indicate epilepsy. However, clinical definitions of epilepsy change over time and, following the 2014 changes to International League Against Epilepsy guidance,[60] some historical seizure cases would now be redefined as epilepsy and could potentially have contributed additional data to this review. We interpret the measures of heterogeneity in our meta-analysis (I^2=63% and I^2=85%) as reflecting the substantial heterogeneity between included studies, which included clinically different populations (by age and, hence, epilepsy aetiology) and changes to epilepsy diagnostic criteria and inequalities over the 21-year time period.

All studies included in the meta-analyses used area-level indicators of deprivation and we recognise that this

is inaccurate for some individuals (eg, those living in poverty in broadly affluent areas). Collapsing data into three deprivation groups for meta-analyses allowed the maximum number of studies to be included but introduced the potential for further misclassification bias and resulted in lost granularity. Using three deprivation groups might have resulted in some studies not being sensitive enough to reflect the true association between deprivation and the outcomes studied. As IMD scores differ in composition across the UK, they are not directly comparable. Being in the most deprived quintile is relative to the rest of the country studied but not equivocal between countries.

Additional evidence is required to develop an evidence-based UK public health response to the WHO IGAP report that prevents epilepsy and reduces socioeconomic inequalities in epilepsy.[6] Without further evidence-based solutions, there is a risk that epilepsy prevention strategies could widen existing inequalities. In the UK, large, linked, routinely collected datasets offer an opportunity to explore socioeconomic inequalities in epilepsy according to WHO preventable aetiologies, but case ascertainment methods must be clinically appropriate and validated. Stratifying large population datasets by age would provide further evidence regarding socioeconomic inequalities in children and new evidence about older adults. Linking to other national datasets (eg, census data) could give individual-level environmental data. Improving the understanding of the inequalities by age and epilepsy type will allow targeting of future research into identifying the burden of preventable epilepsy and its potentially modifiable underlying determinants throughout the life course. Future studies of the association between socioeconomic deprivation and epilepsy should consider the role of the wider social and commercial determinants of health, alongside the WHO brain health determinants. Such future studies should explore the complex intersections with genetic risk, individual behaviours, intellectual disability, rural–urban environments, ethnicity, obesity, and multimorbidity.

Contributors

KJB, SER, WOP, RHT, and AK were responsible for the study concept, methodology, and design. KJB, EC, WOP, SER, and RHT screened the abstracts and full texts for the review. KJB and SM performed data extraction and checking. KJB and AK performed the data analysis and produced the figures. This project was supervised by SER, AK, WOP, and RHT. KJB wrote the original manuscript and all authors contributed equally to the review and editing. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

RHT has received honoraria from Angelini/Arvelle, Bial, Biocodex, Eisai, Jazz/GW Pharma, LivaNova, NeuraxPharm, Sanofi, Takeda, UCB Pharma, UNEEG, and Zogenix; has received unrestricted research funding from Angelini/Arvelle; and his NHS Hospital Trust has entered into a joint working agreement with UCB Pharma. WOP has received honoraria from Angelini/Arvelle and UCB Pharma and unrestricted research funding from UCB Pharma. RFMC has received honoraria from UCB Pharma, Eisai, Jazz/GW Pharmaceuticals, Biocodex, and Zogenix and his institution has received educational grants from UCB and Jazz Pharmaceuticals. KJB, SER, AK, EC, and SM declare no competing interests.

Data sharing

The extracted data will be shared on request from the corresponding author via email, kathryn.bush@newcastle.ac.uk.

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