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Highlights

- We quantified constipation's relationship with epilepsy & anti-seizure medication
- Irritable bowel syndrome was five times more frequent in people with epilepsy (PWE)
- Functional constipation was reported in over a third of PWE
- Constipation was the 2nd most common co-morbid condition in children with epilepsy
- Constipation was reported as a common side effect of Anti-Seizure Medication in PWE

Review

Poo Matters! A scoping review of impact of constipation on epilepsy

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ABSTRACT

Background: Epilepsy is a common neurological disorder which frequently presents with co-morbid physical health conditions, including constipation. However, the nature of the relationship between the two conditions has not been well defined.

Aim: To quantify constipation's relationship with epilepsy and anti-seizure medication (ASM).

Method: A scoping review registered on PROSPERO (CRD42022320079) with suitable search terms was conducted and reported in accordance with PRISMA guidance. CINAHL, Embase, PsycInfo and MEDLINE electronic databases were searched by an information specialist. The Joanna Briggs Institute (JBI) critical appraisal tools alongside the Oxford Centre for Evidence Based Medicine (OCEBM) levels of evidence were used to assist in assessing relevance, quality, and results of the included publications.

Results: Nine articles selected for inclusion in the review. The prevalence of irritable bowel syndrome (including constipation) was reported to be up to five times more frequent in people with epilepsy (PWE). Functional constipation was reported in 36% of PWE. Constipation was found to be the second most common co-morbid condition in children with epilepsy. Two studies found constipation to precede seizures. Constipation was reported as a common side effect of ASMs in PWE. Two studies rated OCEBM level 2 the remaining level 3.

Conclusion: Our findings suggest a higher prevalence of constipation in PWE. Co-occurring multimorbidity and resulting polypharmacy adds further complexity to the process of establishing etiology of constipation in PWE. Potential contributory etiological factors for constipation such as neurodevelopmental and genetic disorders, ASM side effects and the epilepsy itself require better understanding and research.

Keywords

seizures; intestinal movement; irritable bowel syndrome; functional gastrointestinal disorder

1. Introduction

1.1. Epilepsy

Epilepsy is a chronic neurological disorder, caused by excessive or abnormal neuronal discharges in the brain (1) that predisposes to recurrent seizures (2). It is a common neurological condition, affecting approximately 600,000 people in the United Kingdom (UK) (3). Epilepsy has a multifactorial aetiology,

ranging from single gene mutations to a complex interplay between genetic and environmental factors (4), and overall heritability estimates of 32% have been reported in the literature (5). The consequences of an epilepsy diagnosis reach far beyond physical health implications alone, and can result in loss of education, employment, and independence (6), thus contributing to poorer socioeconomic outcomes (7).

1.2. Physical health concerns in people with epilepsy (PwE)

When data is pooled form large population evaluations an estimated 27-84% of PWE have at least one comorbid physical health condition and 5.9 – 64% experience psychiatric comorbidity (8). The range of data is secondary to variance in case ascertainment and limitations in methodologies but highlights the challenges in accurately understanding the health needs of PWE. These complex health profiles often require comprehensive care and access to robust preventative health interventions. However, epilepsy-related inequities, including access to appropriate care and socioeconomic determinants, contribute to poorer health outcomes in PWE (9, 10, 11) and play a part in the premature all-cause mortality seen in PWE (12).

Physical health conditions such as cerebrovascular disease, migraines, gastrointestinal disorders, and Alzheimer's disease are estimated to have a two-to-five-fold higher prevalence in PwE compared to the general population (13). A potential causal association has also been found between epilepsy and hypertension (14). All these conditions require treatment which adds to the overall medication burden. The prescribing of 5 or more medications to a person is referred to as polypharmacy (15) and is known to contribute to adverse outcomes (16)

1.3. Constipation

Constipation is characterised by infrequent bowel movements or incomplete bowel evacuation, frequently co-occurring with other symptoms such as straining and abdominal pain (17). Constipation can occur in isolation or as part of irritable bowel syndrome (IBS), a Functional gastrointestinal disorder (FGID)

which, in the absence of organic or structural abnormalities, causes pain and altered bowel habits (18). One in seven adults and one in three children in the UK are thought to be affected by constipation at any one time, and 182 people are admitted to hospital for constipation every day (19). Constipation can be a debilitating condition, with significant adverse effects on quality of life (20).

1.4. Constipation and anti-seizure medication (ASM)

ASM is the mainstay of epilepsy treatment (21), and aims to achieve seizure freedom or, if this is not possible, to reduce seizure frequency (22). ASM monotherapy is recommended (23). For patients with a new diagnosis of epilepsy, the literature reports rates of seizure freedom at one year following initiation of treatment to be 63.7%, with 86.8% achieving this by taking a single ASM. However, for those who do not become seizure free on the first ASM, the prospect of seizure freedom becomes less likely (24).

Adverse effects from ASM have been well described in the literature, and gastrointestinal disturbances, including constipation, have been highlighted amongst the more commonly reported concerns (22, 25, 26). Those receiving ASM polytherapy are particularly at risk of unwanted side effects (27).

1.5. Psychiatric disorders, psychotropics and epilepsy

Furthermore, psychiatric disorders are more common in PwE than in the general population; lifetime prevalence of major depressive disorder and anxiety disorder have been reported to be 17.4% (95% CI 10.0-24.9) and 22.8% (95% CI 14.8-30.9) respectively, compared to 10.7% (95% CI 10.2-11.2) and 11.2% (95% CI 10.8-11.7) respectively in the general population (28). Psychiatric multi-morbidity is common (29) and many people will receive between-class polypharmacy (30).

Adverse effects to psychotropic medication are multiple and have been well described in the literature (31, 32, 33, 34). Whilst side effect profiles differ between the individual medications, constipation has been commonly described in the literature with estimated rates of over 50% for patient's prescribed antipsychotic medication (35) and between 11 and 12.5% of those taking antidepressants (36).

Research interest into the close and reciprocal relationship between brain and gut has grown in recent years (37). Brain-gut inflammatory pathway has been implicated in the development of epilepsy, constipation and other FGIDs (38).

This review seeks to enumerate the relationship between constipation and epilepsy, including the prevalence of constipation in PwE, the relationship between constipation and seizures and the impact of ASMs and other commonly prescribed medication in PwE.

2. Methods

This review was carried out using pre-defined search criteria (PROSPERO registration number CRD42022320079) and reported in accordance with the PRISMA guidance for scoping reviews. It focused on peer-reviewed publications from index-linked journals. Grey literature searches were not conducted, nor searches for published opinion pieces.

2.1. Search strategy

The search strategy was created collaboratively by the research team and the information specialist, utilising Embase (Ovid), CINAHL (EBSCO) , MEDLINE (Ovid) and PsycInfo (ProQuest). The search strategy included all identified keywords and index terms, combined with Boolean operators and adapted for each database. Only papers published in English and on human subjects were included. In order to capture all relevant literature, no restrictions to the publication

period were applied. A complete list of search terms is provided in Appendix 1, and the search strategy is outlined in appendix 2. The ancestry method was also performed for eligible articles.

2.2. Article selection

After the initial search, duplicates were removed using Endnote. Titles were then screened and those irrelevant to the review topic manually removed by the research coordinator. The remaining articles were screened more closely and the inclusion criteria strictly applied. Opinion pieces, those where full text was not available and those which were not relevant to the research question were eliminated.

The research lead (senior author) was consulted for any studies where there was ambiguity around suitability. The ancestry method was used to identify any additional articles meeting eligibility criteria. Any disagreement was resolved through discussion, until consensus was reached.

The JBI critical appraisal tools (39) were used to assist in assessing relevance, quality, and results of the included publications, alongside the Oxford Centre for Evidence Based Medicine levels of evidence (40), which provided a grading system based on the quality of the data in each study (Level 1 being highest level of evidence). A flowchart of the selection of studies for inclusion can be found in Appendix 3.

3. Results

The search generated a total of 9,256 titles. After duplicates were removed using Endnote, 7,126 articles were listed. Titles were then screened, and 27 articles were sought for retrieval. One publication (a book chapter) could not be found by the research coordinator or the information specialist and was therefore excluded. The remaining 26 articles were screened more closely, and the inclusion criteria strictly applied. This resulted in the inclusion of eight eligible

articles identified. The research lead was consulted for any studies where there was ambiguity around suitability and this resulted in the inclusion of a further article, resulting in the identification of a total of nine eligible research articles. The ancestry method failed to identify any additional articles meeting eligibility criteria. Table 1 provides study details, study origin, year of publication, study population, study objectives, study numbers, methodology, key findings, study limitations and OCEBM level for all nine studies. Five themes emerged from these nine studies and have been discussed as such.

3.1. Theme 1 - Constipation in adults with epilepsy

A population-based cohort study conducted in Taiwan reported that patients with IBS have a 1.37-fold increased risk of developing epilepsy in their lifetime compared to healthy controls (41). However, the retrospective design of the study opened up to concerns around diagnostic validity, as authors were unable to establish which (if any) classifications systems had been used to diagnose epilepsy and IBS in the study cohort. Camara-Lemarroy (42) reported similar results in their cross-sectional study of a Mexican population. They reported IBS to be 5 times more frequent in PwE than in age- and sex-matched healthy controls. Avorio et al (43) reported functional constipation to be present in 35.8% of 113 PwE compared with 15% of healthy controls. Moreover, FGID was present in 62.5% of PwE compared to 39.8% of controls. When constipation and IBS was considered together, the prevalence amongst PwE was as high as 43.3% (compared to 21.2% in controls).

3.2. Theme 2- Constipation in children with epilepsy

A 2016 nationwide Norwegian registry study found close to 80% children with epilepsy (CwE) to have more than one comorbidity, with the most frequent being gastrointestinal (GI) disorders such as gastroesophageal reflux disorder and constipation (19.1% compared to 5.4% in the general population) (44). A Turkish study screening for FGID in CwE found 33.3% to have at least one FGID (compared to 19.1% in controls), and constipation was the second most common condition, however the sample size was small and rarer forms of FGID may not have been represented (45).

3.3. Theme 3- Constipation as a trigger factor for epilepsy

A 2013 cross-sectional study of 405 PwE in an Indian population found 9% of participants to report constipation as a trigger factor in their last seizure (46), but the lack of longer term follow up could be considered a weakness of this study. An Italian study using stool charts and seizure diaries to explore possible links reported that out of a total of 216 documented seizures, 67.6% occurred during a period of altered bowel movements and 45.4% of those during an episode of constipation (43). The same study reported a weak negative correlation between the number of days with normal bowel movement and the number of seizures reported in a month.

3.4. Theme 4 -Antiseizure medication and constipation

A 2010 study (47) exploring the GI adverse effects of long-term use of ASMs in male patients with intractable post-traumatic epilepsy found carbamazepine (as monotherapy or as part of combination therapy) to have the highest rate of GI side effects of the commonly prescribed ASMs, with constipation being the third most common side effect (27.3%). The authors highlighted untreated constipation as a point of concern in this population, as it may affect drug absorption, lead to reduced efficacy or non-compliance with ASMs, further contributing to poor seizure control. Kamel et al (48) corroborated these concerns in their 2010 retrospective analysis of 80 patients commenced on pregabalin, which reported that constipation led to withdrawal of medication in 6.3% of cases, although severity of constipation was dose dependent. However, Avorio et al (43) in their 2021 study did not find a correlation between higher prevalence of constipation and intake of ASM. With regards to CwE, a study of 101 children with cerebral palsy and epilepsy found an association between the use of Gamma-aminobutyric acid (GABA) based ASMs and constipation (49).

3.5. Theme 5 - Seizure localization and constipation

Avorio et al (43) sought to explore correlations between FGID and lobar localization of onset of seizure (frontal, temporal, parietal, or occipital). They found the highest FGID prevalence to be 26.9% higher in people with Temporal lobe epilepsy (TLE) compared to other focal onset epilepsies.

4. Discussion

The findings of this review from literature across the world indicated there is evidence to support the hypothesis of a higher prevalence of constipation (and other FGIDs) in PwE compared to the general population. Specific patient groups may be especially at risk. Prevalence of epilepsy in autistic people and people with intellectual disability is higher than in the general population (50, 51), and the research points to a higher prevalence of constipation in both these groups (52). Seizures of focal origin arising in the temporal lobe are often preceded by an aura or ictal autonomic symptoms can include epigastric symptoms (including GI upset). Such symptoms in the context of epilepsy may mask true abdominal symptoms and delay diagnosis of gastrointestinal disorders (53). The adverse effects of medication add further to the complexity of establishing etiology

The relationship between gut and brain may play an important role in our understanding of the higher prevalence numbers described above. Improving our understanding of the association between epilepsy and the microbiota gut-brain axis could open the door to new treatments, especially for those with refractory epilepsies (54), and offer further non-invasive treatment options in cases where vagal nerve stimulation or epilepsy surgery might otherwise be considered (55).

Despite the introduction of new ASM in recent years, the number of people experiencing treatment resistant epilepsy remains static at around 30%, and represents a major challenge to clinicians (56) Treatment resistance is thought to be caused by a number of contributing factors rather than being attributed to one single mechanism (57), and may justify the use of “rational polytherapy” with different medication addressing different mechanisms of resistance (58).

This does however add to polypharmacy, which alongside multimorbidity is commonplace in PwE (59). Prescribers should optimize communication with clinicians from other specialties to provide holistic treatment and reduce side effect burden from the overall medication load. Specific consideration should be taken to anticholinergic burden, which has been reported to be higher in PwE than the general population (60) and is linked to constipation (61).

4.1. Limitations

This review has several limitations. Multiple databases were used in the search process, which we believe is replicable, and given the paucity of evidence on the subject we believe all relevant papers have been captured. However, we did not include opinion pieces or grey literature in the review in an effort to reduce publication bias, and this could be viewed as a limitation. The articles included in this review varied in overall design. The majority received level 3 evidence grading based on limitations in study design, small sample sizes and there are between-study differences in defining the study population and diagnoses of interest (epilepsy and constipation), which may limit the usefulness and preciseness of their results. Whilst the lower level of evidence of heterogeneity of the included articles can be considered a limitation of this review, the application of a quality assessment process to each individual article is a strength as it highlights areas of potential weakness and bias. Further larger scale studies are needed to clarify the relationship and explore direct links between epilepsy and constipation.

4.2. Implications for clinical care

It is important to educate patients about constipation as a potential side effect prior to commencing ASMs with such adverse effects. Furthermore, clinicians need to explore emergence of constipation following commencement of ASM, as this may contribute to remediable morbidity and/or ASM non-compliance. The medical needs of PWE are complex and benefit from a holistic approach during clinical reviews.

4.3. Implications for research

Further research involving large study populations is required in order to establish whether constipation is a widespread precipitant for seizure activity. If such a causal link is clearly established, this would emphasise a need for prioritisation of constipation treatment in PWE. As discussed, there is increasing interest in the gut-brain axis and may represent a novel target for future epilepsy treatments. Those who could likely benefit from such research would be patients with other neurological problems, including intellectual disability. So, this cohort of patients are likely to be of particular interest in any planned ongoing or longitudinal studies.

5. Conclusion

Bowel health needs to be considered actively in terms of epilepsy management. There is currently no mention of constipation or changing bowel habits in the NICE guidance for adult epilepsy (62). Our findings suggest that constipation is substantially more prevalent in this patient group and should thus be considered with respect to initial assessment, and ongoing epilepsy monitoring, particularly following the commencement or change of dose of ASM's.

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.

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Author Contributions

All authors satisfy the ICMJE guidance by substantially contributing to the design, analysis and interpretation of the work, drafting of the manuscript, final approval of the manuscript and all agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work is appropriately investigated and resolved.

Data statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Competing Interest

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Appendix 1

Seizure	Constipation
Seizures	Bowel obstruction
Epilepsy	Intestinal obstruction
Fits	Ileus
Epileptic encephalopathy	Gastrointestinal
	Bowel movement

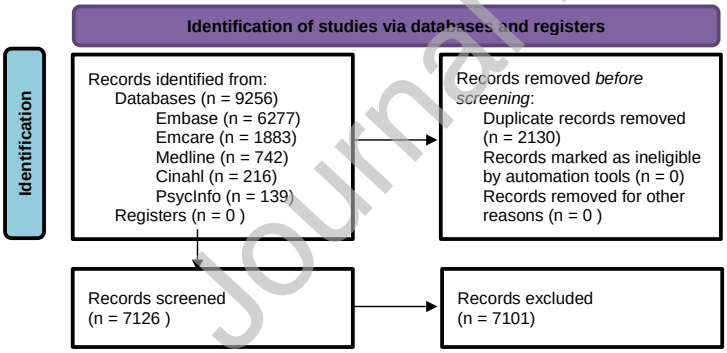
	Intestinal movement
	Intestinal hypomotility
	Bowel hypomotility
	Intestinal irregularity
	Bowel irregularity
	Faecal impaction
	Irritable bowel syndrome

Appendix 2: Search strategy
Embase <1974 to 2022 March 16>

1. "seizure*".ab,ti. 199393
2. "epilep*".ab,ti. 210731
3. exp seizure/ 161296
4. exp epilepsy/ 254661
5. "convuls*".ab,ti. 37160
6. "epileptic encephalopathy".ab,ti. 3793
7. 1 or 2 or 3 or 4 or 5 or 6 415678
8. "constipat*".ab,ti. 48364
9. (bowel adj1 (obstruction or movement or hypomotility or irregularity)).ab,ti. 20704
10. (intestinal adj1 (obstruction or movement or hypomotility or irregularity)).ab,ti. 13881

11. exp constipation/ 101456
12. "Gastrointestinal disorder*".ab,ti. 14372
13. "Faecal impact*".ab,ti. 232
14. "Fecal impact*".ab,ti. 686
15. Ileus.ab,ti. 17677
16. 16 "Irritable bowel syndrome".ab,ti. 23173
17. exp feces impaction/ 1856
18. exp ileus/ 14855
19. 19 exp irritable colon/ 29063
20. exp intestine obstruction/ 82988

Appendix 3: Prisma flow chart of identified studies



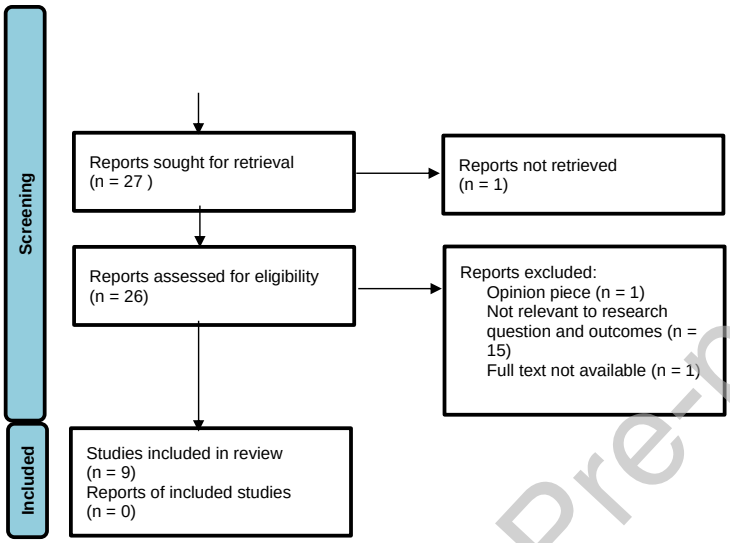


Table 1: Characteristics of publications included in the review

Authors	Title	Study origin	Year of publication	Study design	Population	Objective	Participant Numbers	Methodology	Key findings	Limitations	Level of evidence (OCEBM)
Aaberg et al (44)	Comorbidity and childhood epilepsy: A	Norway	2016	Registry study (observational)	Norwegian Children with epilepsy (CWE) born in Norway	To describe frequency of medical, neurological,	Total study population: 1125 161 Nb who met study inclusion criteria for	Data from period 2008-2013 extracted from Norwegian patient registry (NPR) CWE	Most frequent medical condition on CWE and controls was gastrointestinal (GI) disorders Constipation and GOERD most	Lack of validity data for epilepsy and other recorded diagnoses Risk of underestimation	Level 2

	nationwide registry study				between 1996-2013	developmental, and psychiatric co-morbidity before and after diagnosis of childhood epilepsy	diagnosis of epilepsy: 6625	compared to age and sex matched controls in general population	common GI disorder (19.1% in CWE compared to 5.4% in children in general population	of some diagnoses inherent to registry studies Lack of data from NPR prior to 2008 Missed data from CWE diagnosed exclusively in practice	
Avorio et al (43)	Functional GI disorders in patients with epilepsy: reciprocal influence on seizure occurrence	Italy	2021	Case control	Adults with diagnosis of epilepsy in Italy	1. Define prevalence of FGID in PWE 2. Define possible relationship between FGID and epilepsy characteristics 3. Define possible relationship between seizure occurrence and bowel movements	Total study population: 120 Controls: 113	120 consecutive PWE enrolled through outpatient clinic Validated questionnaire Rome III criteria to evaluate GI symptoms Evaluation of seizure trends paired to bowel habits assessed using Bristol stool chart and seizure count integrated diary	Higher prevalence of FGID in PWE (62.5%) than in healthy subjects (HS) (39.8%), $p < 0.001$ Constipation the most frequently observed disorder (43.3 in PWE vs. 21.2% in HS, $p < 0.001$). No association between constipation and ASM in PWE FGID was significantly associated with TLE as compared with other lobar localization ($p = 0.03$).	Not able to exclude influence of ASM on FGID	Level 3

Balamurugan et al (46)	Perceived trigger factors of seizures in PWE	India	2013	Cross-sectional study	Children and adults with epilepsy in North India	Identify triggering factors for seizures in PWE from a North Indian population	Total study population: 405	Recruitment through outpatient clinic Trigger assessment tool (TAAT) utilised to collect data on relevant to triggering factors	Constipation reported as triggering factor in las seizure for 9% (n = 36) of study population Trigger factors reported consistently in recent and past seizure episodes: 1. missing medication (40.98%) 2. emotional stress (31.35%) 3. sleep deprivation (19.75%) 4. fatigue (15.30%) 5. missing meals (9.13%) 6. fever (6.41%) 7. smoking (6.41%)	Self-reported information open to bias Longer term monitoring not conducted Diagnosis of epilepsy based on clinical diagnosis alone	Level 3
Chen et al (41)	IBS increases the risk of epilepsy	Taiwan	2015	Retrospective cohort study	People with IBS >20 years of age, compared to HS in the Taiwanese population	Examine the association between IBS and subsequent development of epilepsy	IBS cohort (n= 32,122) non-IBS cohort (n = 63,295)	Data collected from the National Health Insurance Research Database (NHIRD) People on insurance database, age 20 years or older with newly diagnosed IBS from 2000-	IBS patients had greater cumulative incidence of epilepsy than the cohort without IBS IBS cohort had a higher risk of epilepsy after adjusting for age, sex, and epilepsy-associated risk factors IBS increases the risk of developing subsequent epilepsy	Concerns of validity of IBS and epilepsy diagnoses in some cases Patients with IBS more likely to seek medical care compared to patients without IBS, therefore more likely to receive diagnosis of epilepsy during follow up	Level 2

								2011 included Criteria for IBS followed ICD-9-CM and Rome criteria			
Ferreira et al (49)	Constipation, anti-epileptic drugs, and gingivitis in children and adolescents with cerebral palsy	Brazil	2019	Cross-sectional study	Brazilian children and adolescents, aged 4-18, diagnosed with spastic cerebral palsy	Explore possible association between constipation, gingivitis and the use of ASM in children and adolescents with Cerebral Palsy (CP).	Total study population: 101	Recruitment from physical rehabilitation and treatment centre Data regarding daily food and fluid intake collected from caregivers Rome III criteria to assess for constipation Functional toilet transfer item utilised to classify participants according to assistance required for transfer Gingival index evaluation using periodontal probe	Pointed to an association between intestinal constipation and GABA ASM used by children and adolescents with spastic CP	Possible selection bias	Level 3
Jahromi	GI	Iran	2010	Cross-	Iranian war	Explore	Total study	Recruitment	Carbamazepine	Dichotomised	Level 3

et al (47)	adverse effects of antiepileptic drugs in intractable epileptic patients			sectional study	veterans with post-traumatic intractable epilepsy secondary to cranial injury from Iraq-Iran war (1980-1988)	the GI side effects of long-term ASM therapy in a group of patients with intractable post-traumatic epilepsy Recognise GI complications of ASM individually or in combination	population: 100	through outpatient clinic Side effect checklist used	showed highest GI adverse effects Constipation was the third most common side effects (27.3%) following heart burn, nausea, regardless of whether patient was taking mono- or combination ASM Constipation can affect drug absorption in people with epilepsy and increase the probability of seizures	side effect complaints as present or not present Enrolled only men with post-traumatic intractable epilepsy	
Kamel et al (48)	Severe and disabling constipation: an adverse effect of pregabalin	Australia	2010	Retrospective analysis	Adults with partial – onset epilepsy attending tertiary epilepsy clinic	To explore a potential association between Pregabalin and constipation	Total study population: 80	Recruitment through outpatient clinic Audit of clinical notes to assess tolerance to medication Naranjo Adverse Drug Reaction Probability Scale utilised	Constipation was the most frequent adverse effect that required Pregabalin to be withdrawn (6.3%, n = 5) Severity of symptoms was dose dependent Onset of symptoms occurred at starting dose of 150mg/od in divided doses in four patients	Small sample size Possible selection and reporting bias	Level 3

Aydemir et al (45)	Screening for functional gastrointestinal disorders in children with epilepsy	Turkey	2020	Cross-sectional study	Turkish children with epilepsy, aged 4-8 years	Examine frequency of FGID amongst CWE Explore any association between FGID and epilepsy characteristics	Total study population: 78 Age and sex-matched control group	CWE enrolled from Gastroenterology and neurology clinic Rome IV criteria to assess for FGID	FGID found in 33.3% of CWE, compared to 19.1% of age and sex-matched HS Most common FGID in CWE was IBS (14.1%) compared to 6.4% in HS, followed by constipation (7.7%) compared to 6.4% in HS	Small sample size complicating diagnosis of rarer forms of FGID Enrolment process not clear	Level 3
Camara-Lemarroy et al (42)	Prevalence and impact of irritable bowel syndrome in people with epilepsy	2016	Mexico	Cross-sectional observational study	Adults with epilepsy in Mexico	To determine the prevalence and impact of irritable bowel syndrome (IBS) in patients with epilepsy.	Total study population: 65 Age and sex-matched healthy controls as comparator: 64	Consecutive patients enrolled from outpatient clinic Epilepsy diagnosis defined according to International League Against Epilepsy (ILAE) guidelines IBS and FD diagnoses based on Rome III criteria IBS Quality of life (QOL) tool to evaluate	IBS more frequent in PWE compared to HS IBS does not appear to affect health-related QOL, but is associated with a greater burden of affective symptoms and insomnia	Small sample size Did not evaluate for possible GI effects of ASM	Level 3

								Becks depressive inventory (BDI) to assess depression Beck's anxiety inventory for anxiety Quality of life epilepsy inventory (QOLIE-10) Pittsburgh sleep index (PSQI) and Insomnia severity index utilised to assess subjective quality of sleep			