Bone health in adults with epilepsy and intellectual disability

Epilepsy is more prevalent in individuals with intellectual disability (ID) compared to the general population, and this prevalence increases with increasing severity of ID. Epilepsy affects approximately 22% of people with ID, while 25% of people with epilepsy (PWE) have an ID.\[1\] Anti-seizure drug (ASD) side-effects like ataxia, sedation, and seizures, especially convulsive ones, can increase the risk of falls and subsequent fractures particularly in those with reduced bone mineral density (BMD).

Attention, however, has focused mainly on ASDs and their role in abnormal bone metabolism. The relationship between abnormalities of bone health and epilepsy in recent years. PWE who are housebound or institutionalised, avoid sunlight for cultural reasons, or have poor nutrition are at increased risk of vitamin D deficiency. This can predispose to osteopenia/osteoporosis and proximal myopathy leading to weakness and increased fall liability. Associated conditions such as cerebral palsy with inability to weight bear, reduced physical activity, or visual impairment can be contributory factors.\[1\] Anti-seizure drug (ASD) side-effects like ataxia, sedation, and seizures, especially convulsive ones, can increase the risk of falls and subsequent fractures particularly in those with reduced bone mineral density (BMD).

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BONE HEALTH AND EPILEPSY

There has been growing interest in the association between abnormalities of bone health and epilepsy in recent years. PWE who are housebound or institutionalised, avoid sunlight for cultural reasons, or have poor nutrition are at increased risk of vitamin D deficiency. This can predispose to osteopenia/osteoporosis and proximal myopathy leading to weakness and increased fall liability. Associated conditions such as cerebral palsy with inability to weight bear, reduced physical activity, or visual impairment can be contributory factors.\[1\]

Risk factors identified for osteoporosis include use of ASDs (particularly older ones), immobility, and history of falls and fractures. It has been recommended that screening for risk factors associated with lower BMD in adults with ID should take place.\[4\] Epilepsy and ASD medication have been found to be strong predictors for fractures.\[7\]

Both low BMD and vitamin D deficiency are established independent risk factors for fracture, although 80% of individual variability in BMD is explained by heredity, lifestyle factors including sex and ethnicity.\[1\] Anti-seizure drug (ASD) side-effects like ataxia, sedation, and seizures, especially convulsive ones, can increase the risk of falls and subsequent fractures particularly in those with reduced bone mineral density (BMD).

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Vitamin D deficiency, defined as a serum vitamin D level <50 nmol/L, has been found in nearly twice as many people with ID in the community, compared to controls. Winter season, dark skin pigmentation, impaired mobility, and obesity were independently associated with reduced BMD.\[2\]

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Non-ambulatory status was significantly associated with low BMD. Because of co-existing comorbidities such as cerebral palsy, other movement disorders, psychiatric disorders, and obesity, PWE and ID may not be able to weight bear or may be exposed to less sunlight. The management of some of these comorbidities may also contribute to poor bone health outcomes such as proton pump inhibitors, psychotropics, diuretics, diabetes medication, and ASDs. Box 1 provides a list of key factors influencing bone health in PWE and ID.

IMPLICATIONS FOR PRIMARY CARE

A community survey of individuals with ID and their carers revealed significant shortcomings in their knowledge of the relationship between ID, epilepsy, ASDs, and vitamin D deficiency.\[8\] Non-ambulatory status was significantly associated with low BMD. Because of co-existing comorbidities such as cerebral palsy, other movement disorders, psychiatric disorders, and obesity, PWE and ID may not be able to weight bear or may be exposed to less sunlight. The management of some of these comorbidities may also contribute to poor bone health outcomes such as proton pump inhibitors, psychotropics, diuretics, diabetes medication, and ASDs. Box 1 provides a list of key factors influencing bone health in PWE and ID.

The authors undertook a community study of PWE and ID attending a specific epilepsy clinic (n=104 participants).\[6\] Is it possible to provide a reference for this study? Normal serum vitamin D levels were accepted at >80 nmol/L given the complex multiple comorbidities of this patient group. This target is considered to provide ‘optimal’ health.\[9\] Of the study population, 77 (74.2%) were vitamin D insufficient (30.0%) or deficient (44.2%). Of the 76 (73.1%) who had a DEXA scan, 25 (32.9%) were osteoporotic, 30 (39.5%) osteopaenic, and only 21 (27.7%) had a normal BMD. There was a significant difference [P=0.05] in DEXA hip T-scores between ambulant and non-ambulant patients. A raised alkaline phosphatase level significantly predicted lower vitamin D levels. An approximate dose of vitamin D 1200 IU replacement was sufficient to correct vitamin D insufficiency, or 2000 IU for deficiency.

The study showed that the rate of vitamin D deficiency/insufficiency and osteoporosis/osteopenia was very high.\[10\] Non-ambulatory status was significantly associated with low BMD. Because of co-existing comorbidities such as cerebral palsy, other movement disorders, psychiatric disorders, and obesity, PWE and ID may not be able to weight bear or may be exposed to less sunlight. The management of some of these comorbidities may also contribute to poor bone health outcomes such as proton pump inhibitors, psychotropics, diuretics, diabetes medication, and ASDs. Box 1 provides a list of key factors influencing bone health in PWE and ID.
QOF influenced integration or coordination of care, holistic care, self-care, or patient experience.11

With advanced age, bones are more prone to fracture. Thus, the ageing ID population with epilepsy has further risk concerns. Other apprehensions include that popular osteoporosis screening tools such as Q-Fracture and FRAX have not been validated in the ID population.12 Small-scale studies have shown that these tools regularly show a ‘false negative’ for people with ID thus putting this population at further risk of iatrogenic harm.12

An audit in primary care practices in the south-west of the UK looked into the quality of health checks in people with ID prescribed ASDs and antipsychotics to see if relevant blood monitoring was being done.13 The result showed poor person-centred annual health checks. The authors highlighted the potential of patient- or carer-held records and how they could be linked to annual health checks to improve quality. Bone health screening elements could be included within this framework. A simple baseline screen consisting of bone profile, magnesium, and vitamin D levels, and a baseline DEXA scan, would identify the majority of people with ID vitamin D levels, and a baseline DEXA scan, consisting of bone profile, magnesium, and vitamin D, parathyroid hormone, and 24-hour urinary calcium excretion.

### Box 1. Major factors influencing bone health in people with epilepsy and intellectual disability

<table>
<thead>
<tr>
<th>Factor</th>
<th>Examples and points of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>Age, sex, skin tone, and weight</td>
</tr>
<tr>
<td>Neurodevelopmental issues</td>
<td>Level of intellectual disability, presence of cerebral palsy, and ambulatory status</td>
</tr>
<tr>
<td>Existing treatment of bone</td>
<td>Calcium supplementation, vitamin D replacement, or bisphosphonate therapy</td>
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<tr>
<td>conditions</td>
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<tr>
<td>Biochemical markers</td>
<td>Serum calcium, phosphate, alkaline phosphatase, magnesium, vitamin D, parathyroid hormone, and 24-hour urinary calcium excretion</td>
</tr>
<tr>
<td>Bone mineral density</td>
<td>DEXA hip T-score</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Correction of vitamin D and insufficiency/deficiency</td>
</tr>
<tr>
<td>Anti-seizure drugs</td>
<td>Older anti-seizure drugs such as first-generation drugs like phenytoin and phenobarbitone are considered less bone friendly</td>
</tr>
<tr>
<td>Psychotropic medication</td>
<td>Antipsychotics, antidepressants, and multiple psychotropics</td>
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<tr>
<td>Other medication</td>
<td>Proton pump inhibitors and diuretics</td>
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### CONCLUSION

Adults with ID and epilepsy are at high risk of bone harm due to a myriad of factors including their intrinsic genetic makeup, multimorbidity, and iatrogenic influences of polypharmacy including ASDs. As the longevity in people in this vulnerable cohort increases due to better treatments and support it is important to be mindful of the changes they undergo at a bone health level to achieve and provide optimum quality of life. Thinking of bone health in this population needs a holistic and systematic approach, which has not been achieved to date. It will remain neglected and thought to be ‘someone’s business’ leading to it being ‘no one’s business’, unless we make this ‘everyone’s business’.

### REFERENCES