

# Osteoporosis and fractures in institutionalized patients with refractory epilepsy and intellectual disability

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## IMPACT

### **Thesis**

In this thesis we focused on bone mineral density and fractures in a group of patients with epilepsy and intellectual disability, residing at a long-stay care facility in the Netherlands. In 2009 and 2016, patients underwent dual-energy X-ray absorptiometry scans to assess their bone mineral density. About 67% of the children and 80% of the adults, were revealed to have a low bone mineral density. Forty-two percent of the children, had a history of fractures, of which half had suffered a major osteoporotic fracture. Over seven years of follow-up, 59% of the adults sustained one or more (non-) vertebral fractures, of which 35% had at least one major osteoporotic fracture.

### **Target groups**

The care for institutionalized patients with epilepsy and intellectual disability is complex. General practitioners, intellectual disability physicians, neurologists, internist-endocrinologists, physiotherapists, occupational therapists, nurse specialists, nurses, nurse assistants, caregivers (parents/family) etcetera; all play a major role in the multidisciplinary care for these patients. The results and implications of this thesis may be of interest for all of them, but mostly for the patients themselves. In Table 1 we summarize groups involved in the care for patients with epilepsy and intellectual disability, topics they should pay special attention to and (realized) related activities.

### **Relevance**

Current guidelines for diagnosing and treating osteoporosis (Dutch Society of Neurology on Epilepsy and the Dutch protocol Osteoporosis and Fracture Prevention) are limited to patients over the age of 50.

In our study, 56% of the participants were under the age of 50 and, therefore, falling outside the scope. In addition, the guideline of the Dutch Society of Neurology on Epilepsy is limited to the use of carbamazepine, phenobarbital, phenytoin, primidone and valproate. In our study, a wider variety of antiseizure medication had been prescribed. The current guidelines are therefore not completely relevant to the majority of our patients.

Based on the results of this thesis, we recommend (regular) bone health assessments in residential care according to the most recent protocol 'Osteoporosis and Fracture Prevention' and to initiate anti-osteoporosis medication if needed.

Table 1. Target groups and (realized) related activities

	<b>In patients with refractory epilepsy and intellectual disability, special attention is needed towards:</b>	<b>Realized</b>	<b>Activities</b>
<b>Patients</b>	<ul style="list-style-type: none"> <li>· Lifestyle intervention analysis including physical activity, nutritional intake, sunlight exposure (yearly, as part of the care plan)</li> <li>· Fall prevention</li> <li>· Assessment of medication use (regularly, as part of the care plan)</li> </ul>	<ul style="list-style-type: none"> <li>+</li> <li>-</li> <li>+</li> </ul>	<ul style="list-style-type: none"> <li>· (Inter)national presentations</li> <li>· Thesis</li> </ul>
<b>Healthcare professionals</b>	<ul style="list-style-type: none"> <li>· Lifestyle intervention analysis including physical activity, nutritional intake, sunlight exposure (yearly, as part of the care plan)</li> <li>· Fall prevention</li> <li>· Assessment of medication use (regularly, as part of the care plan)</li> <li>· Screening for BMD and VFs (regardless of age and type of antiseizure drug(s))</li> <li>· Diagnosing of low BMD and (subclinical) VFs</li> <li>· Laboratory testing (concentrations of albumin, calcium, creatinine, 25-hydroxyvitamin D, thyroid stimulating hormone) (yearly, as part of the care plan)</li> </ul>	<ul style="list-style-type: none"> <li>+</li> <li>-</li> <li>+</li> <li>+</li> <li>+</li> <li>+</li> </ul>	<ul style="list-style-type: none"> <li>· Development of flowchart</li> <li>· Peer-reviewed articles</li> <li>· (Inter)national presentations</li> <li>· Thesis</li> </ul>
<b>Policymakers</b>	<ul style="list-style-type: none"> <li>· Development of guidelines for screening and treatment of low BMD and/or fractures</li> </ul>	<ul style="list-style-type: none"> <li>+</li> </ul>	<ul style="list-style-type: none"> <li>· Development of flowchart</li> <li>· Peer-reviewed articles</li> <li>· Thesis</li> </ul>
<b>Healthcare financers</b>	<ul style="list-style-type: none"> <li>· Financial resources for the prevention and treatment of fractures, including BMD, VFA and the prescription of calcium, vitamin D and anti-osteoporosis medication</li> </ul>	<ul style="list-style-type: none"> <li>-</li> </ul>	<ul style="list-style-type: none"> <li>· Peer-reviewed articles</li> </ul>
<b>Pharmaceutical industry</b>	<ul style="list-style-type: none"> <li>· Side effects of both antiseizure and anti-osteoporosis medication</li> <li>· Effectiveness of anti-osteoporosis medication in combination with antiseizure medication</li> </ul>	<ul style="list-style-type: none"> <li>+</li> <li>-</li> </ul>	<ul style="list-style-type: none"> <li>· Peer-reviewed articles</li> <li>· Thesis</li> </ul>

Table 1. Continued

	<b>In patients with refractory epilepsy and intellectual disability, special attention is needed towards:</b>	<b>Realized</b>	<b>Activities</b>
<b>Researchers</b>	· (Feasible) Alternatives regarding screening and monitoring BMD	+/-	· Development of flowchart
	· (Feasible) Alternatives regarding assessing fracture risk	+/-	· Peer-reviewed articles
	· Optimal treatment options and preventive measures in both children and adults	-	· (Inter)national presentations · Thesis

\*BMD=Bone mineral density, ID=Intellectual disability, VFs=Vertebral fractures

Unlike the abovementioned protocols/guidelines, we propose not to apply restrictions regarding age or types of antiseizure medication. Bone health assessments are recommended as part of each patients' care plan and would include DXA/VFA measurements, laboratory testing (blood serum concentrations of albumin, calcium, creatinine, 25-hydroxyvitamin D, thyroid stimulating hormone) and a nutritional intake analysis.

One of the current treatment options for osteoporosis is treatment with oral bisphosphonates; drugs that inhibit bone resorption. These medications are typically prescribed for three to five years. Based on the findings in this thesis and no reports of serious side effects in the study group, the use of bisphosphonates in the individual patient might be reconsidered to extend to a period of ten years. To date, no research has focused on osteoanabolic medication like teriparatide or romosozumab in patients on chronic antiseizure medication. Especially in patients with a low BMD in combination with one or more vertebral fractures, osteoanabolic medication may be considered. Further research should focus on optimal treatment options.

### **Activities**

Our recommendations are put together in a flowchart and implemented in the residential care department of Epilepsy Center Kempenhaeghe. Due to an update of the Dutch protocol 'Osteoporosis and Fracture Prevention' and expected changes (regarding the treatment of vertebral fractures), the flowchart is currently under revision and therefore not included in this thesis. The internist-endocrinologist, general practitioners, intellectual disability physicians and nurse specialists are informed and trained to apply the most recent, designed flowchart. In case of doubt, treatment is discussed with experts from the specialized Center of Metabolic Disorders of VieCuri Medical Center. Future plans include the development of educational materials on fracture prevention for health care professionals within our institution.

All studies in this thesis are published or submitted to peer-reviewed international journals and several extended abstracts appeared in a national peer-reviewed journal as well. Many of the findings were presented and discussed during oral and poster presentations at national and international congresses in the fields of epilepsy, intellectual disabilities, neurology and/or endocrinology. Among those congresses were the yearly congresses of Epilepsy Center Kempenhaeghe (2018, 2019), the European (2018) and International (2021) Congress on Epileptology, the World Congress on Osteoporosis (2019) and the European Congress of the Tissue Society (2020).