

# Treating Refractory Epilepsy: An Updated Checklist

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## Classification

The ILAE 2017 Framework for the Classification of Epilepsy defines three diagnostic levels:<sup>1,2</sup>

1. Seizure type <sup>1-3</sup>			2. Epilepsy type <sup>1,2</sup>	3. Epilepsy syndrome <sup>1,2,4</sup>
<b>Focal onset</b> 2.99 cases per 1,000 people*	<b>Generalised onset</b> 4.33 cases per 1,000 people*	<b>Unknown onset</b> 0.81 cases per 1,000 people*	Focal	Focal
Aware	Motor	Motor	Generalised	Generalised
Impaired awareness	Tonic-clonic	Tonic-clonic	Generalised & focal	Generalised & focal
Motor onset	Other motor	Other motor	Unknown	Syndromes associated with DEE or progressive neurological deterioration
Non-motor onset	Non-motor	Non-motor		
Focal to bilateral tonic-clonic		Unclassified		

## Other considerations

Aetiology <sup>1</sup>			Comorbidities <sup>1</sup> (list not exhaustive)		
Structural	Genetic	Infectious	Learning difficulties	Intellectual disability	Autism spectrum disorder
Metabolic	Immune	Unknown	Depression	Motor deficits	Movement disorders

\*Estimated prevalence



## An epilepsy syndrome:<sup>1,4</sup>

- Represents a cluster of features that tend to occur together
- May have distinctive comorbidities and specific findings on EEG and imaging
- May have associated aetiological, prognostic, and **treatment implications**

## Actions:<sup>1</sup>

Where possible, define a patient's epilepsy at each diagnostic level

Consider the aetiology of the epilepsy and the presence of comorbidities

## Comorbidities



Roughly 50% of adults with active epilepsy have at least one comorbid medical disorder, many of which are associated with poor long-term outcomes<sup>5-7</sup>



Comorbidities can significantly impact HR-QoL, seizure frequency and severity, and may affect response to ASMs<sup>8</sup>



Epilepsy is associated with a 53% increased risk of cardiovascular events, and active epilepsy is associated with a 5.8-fold increased risk of sudden cardiac death versus matched controls.<sup>9,10</sup>

## Increased prevalence of:<sup>\*11</sup>



**Mental health conditions**  
e.g., depression, anxiety



**Neurodevelopmental comorbidities**  
e.g., ADHD, ASD



**Higher risk of suicide**



\*Versus general population

## Actions:

Ask about comorbidities as part of routine patient care<sup>12</sup>

Regularly screen patients to identify any mental health problems<sup>11</sup>

Evaluate patients who report cardiac complaints, or are receiving medication potentially targeting the heart, for cardiovascular comorbidities using a 12-lead ECG<sup>13</sup>

## Side effects of ASMs



Long-term use of some ASMs is associated with decreased **bone mineral density** that may lead to osteopenia, osteoporosis, and increased fractures<sup>14,15</sup>

- Supplements should be considered for patients at risk<sup>11</sup>



Some ASMs can cause **weight gain**, leading to metabolic disturbances<sup>16</sup>

- Aside from an impact on physical fitness and QoL, weight gain can also affect medication compliance, and may affect the response to ASMs in patients with refractory epilepsy<sup>16,17</sup>



ASMs are associated with an increased risk of **major cardiovascular events**<sup>9</sup>

## Actions:

Regularly review the potential adverse effects of ASMs with patients<sup>12</sup>

Monitor patients who report cardiac complaints, or who are receiving medication that may affect the heart, with a 12-lead ECG<sup>18</sup>

## Contraception

The use of some types of ASM during pregnancy has been associated with a range of **harmful effects to the baby**, including major congenital malformations, adverse effects on neurodevelopment, and fetal growth restriction<sup>19</sup>

These ASMs are therefore contraindicated in people of childbearing potential, unless a **pregnancy prevention programme** is in place<sup>19</sup>

## Actions:<sup>19</sup>

At each annual review for females with epilepsy, discuss the risks associated with ASMs and with untreated epilepsy during pregnancy, and review treatment according to their clinical condition and circumstances

Urgently refer any patient currently taking ASMs for specialist advice if they are planning a pregnancy, or if they are pregnant



## Adherence

- Adherence to medication among patients with epilepsy is **suboptimal**<sup>20</sup>
- Poor adherence to ASMs is associated with increased mortality, emergency department visits, hospitalisations, fractures, and head injuries<sup>20</sup>

## Action:

Support patients with epilepsy to take their medication as prescribed to reduce seizures, and explain that uncontrolled seizures increase the risk of epilepsy-related death<sup>11</sup>

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## Abbreviations

ADHD: attention deficit hyperactivity disorder; ASD: autism spectrum disorder; ASM: anti-seizure medication; DEE: developmental and/or epileptic encephalopathy; ECG: electrocardiography; EEG: electroencephalography; HR-QoL: health-related quality of life; ILAE: International League Against Epilepsy; QoL: quality of life.