DOI: 10.1002/epi4.12500

#### COMMENTARY

# Does diagnostic delay impact on the outcome of epilepsy?

# Ettore Beghi 🕩

Department of Neuroscience, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan, Italy

Correspondence: Ettore Beghi, Department of Neuroscience, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan, Italy. Email: ettore.beghi@marionegri.it

Seizure recurrence in epilepsy poses the patient at risk of self-harm and can have a negative impact on his/her personal and social life. For this reason, the disease, when suspected, should be promptly diagnosed and treated. Unfortunately, this is not the case for several patients. Diagnostic delay in people with epilepsy has been the object of a number of studies that, even with differing results, showed that the disease might go undiagnosed for several years.<sup>1–4</sup> A delay in the diagnosis of epilepsy may occur preferably when the first seizures are focal or, if generalized, they present with inhibitory features or only mild motor signs. In those cases, the patient might seek medical advice even after several years.<sup>2</sup>

Along with seizure type, diagnostic delay can be explained by other factors, including patient's own poor awareness of the nature of his/her symptoms, doctor's misdiagnosis, and, not least, the rarity of some events and their modest impact on patient's daily life. However, seizure recurrence with strong impact on one's health and quality of life cannot be excluded even after mild events, particularly in untreated patients, and one cannot exclude that future seizures have a greater impact on patient's and public safety.

For these reasons, Laura Parviainen and co-workers<sup>5</sup> are commended for having addressed this issue in the intent to verify the impact of diagnostic delay on seizure outcome in patients with newly diagnosed focal epilepsy. The authors examined 176 adult patients who were eligible for inclusion in randomized trials of antiseizure medications. The choice of that sample was motivated by the accuracy of the medical records with specific reference to the history of seizures while untreated. Patients were followed for five years, and seizure recurrence was noted and classified in three categories: (1) Complete seizure freedom after treatment start; (2) Seizure freedom achieved after treatment changes; (3) No seizure freedom despite medication changes. The authors found that diagnostic delay alone did not correlate with treatment response at five years. However, seizure outcome was worse in patients with a higher number of seizures before diagnosis.

The results of this study confirm previous reports<sup>6</sup> in showing that diagnostic delay per se does not affect treatment outcome. However, the association between the number of seizures while untreated and treatment response during follow-up is at variance with previous studies that showed that the long-term prognosis of epilepsy (in terms of prolonged seizure remission during follow-up) is not affected by early treatment of seizures (in those studies, treatment of the first seizure).<sup>7</sup> The differences might be explained by the differing populations at risk (patients seen at the first seizure vs. patients with two or more seizures, the latter perhaps with more severe disease varieties) and by the length of follow-up (as poor treatment response proves to be a dynamic process when long-term follow-up is considered).<sup>8,9</sup> Then, having several seizures before treatment might be not only the result of diagnostic delay but also of an intrinsic greater severity of the disease at first manifestation.

This study brings to our attention another important problem, that is, if epilepsy should be diagnosed only after seizure relapse or even after the first seizure. The International League Against Epilepsy addressed this issue and concluded that in specific circumstances epilepsy can be diagnosed at the first seizure.<sup>10</sup> This definition helps reducing the diagnostic gap but requires that a comprehensive evaluation of the patient is performed and, for this reason, the diagnosis of epilepsy should be made by specialists who are well aware of the risk factors for seizure recurrence in a patient with a first seizure.

As the diagnosis of epilepsy is mostly based on an accurate history taken from the patient and, where present, from a witness, the diagnostic process is not easy and requires patient's awareness of the nature of his/her symptoms and

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skillness of the caring physician. We agree with the authors that public and healthcare workers should be made aware of the diversity of seizure types and the negative reflections of the recurrence of undiagnosed seizures.

### **CONFLICT OF INTEREST**

Ettore Beghi reports grants from Italian Ministry of Health, grants from Swedish Orphan Biovitrum, personal fees from Arvelle Therapeutics, and grants from American ALS Association, outside the submitted work. The author confirms that he has read the Journal's position on issues involved in ethical publication and affirms that this editorial is consistent with those guidelines. Read the winning article - https://onlin elibrary.wiley.com/doi/10.1002/epi4.12443

## ORCID

Ettore Beghi D https://orcid.org/0000-0003-2542-0469

#### REFERENCES

- Firkin AL, Marco DJ, Saya S, Newton MR, O'Brien TJ, Berkovic SF, et al Mind the gap: Multiple events and lengthy delays before presentation with a "first seizure". Epilepsia. 2015;56(10):1534–41.
- Jallon P, Loiseau P, Loiseau J. Newly diagnosed unprovoked epileptic seizures: presentation at diagnosis in CAROLE study. Coordination Active du Reseau Observatoire Longitudinal de l'. Epilepsie. Epilepsia. 2001;42(4):464–75.
- Hauser WA, Kurland LT. The epidemiology of epilepsy in Rochester, Minnesota, 1935 through 1967. Epilepsia. 1975;16(1):1–66.

- Gasparini S, Ferlazzo E, Beghi E, Tripepi G, Labate A, Mumoli L, et al Family history and frontal lobe seizures predict long-term remission in newly diagnosed cryptogenic focal epilepsy. Epilepsy Res. 2013;107(1–2):101–8.
- Parviainen L, Kälviäinen R, Jutila L. Impact of diagnostic delay on seizure outcome in newly diagnosed focal epilepsy. Epilepsia Open. 2020;5(4):605–10.
- Gasparini S, Ferlazzo E, Sueri C, Aguglia U. The relevance of "diagnostic delay" in epilepsy. Epilepsia. 2016;57(1):165.
- Leone MA, Giussani G, Nolan SJ, Marson AG, Beghi E. Immediate antiepileptic drug treatment, versus placebo, deferred, or no treatment for first unprovoked seizure. Cochrane Database Syst Rev. 2016;(5):CD007144.
- Sillanpää M, Schmidt D. Natural history of treated childhood-onset epilepsy: prospective, long-term population-based study. Brain. 2006;129(Pt 3):617–24.
- Beghi E, Beretta S, Carone D, Zanchi C, Bianchi E, Pirovano M, et al Prognostic patterns and predictors in epilepsy: a multicentre study (PRO-LONG). J Neurol Neurosurg Psychiatry. 2019;90(11):1276–85.
- Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475–82.

How to cite this article: Beghi E. Does diagnostic delay impact on the outcome of epilepsy? *Epilepsia Open*. 2021;6:470–471. <u>https://doi.org/10.1002/</u>epi4.12500