OPEN LETTER

A cascade of care for people with epilepsy: learning from “HIV/AIDS 90-90-90” [version 1; peer review: 2 approved with reservations]

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Abstract
Epilepsy is now more prevalent in many countries than HIV/AIDS. Building upon the successes of global policymaking for HIV/AIDS and creating a framework for countries and organizations to monitor progress in epilepsy care will help direct and justify much-needed novel programming. Given the clarity of the HIV/AIDS care continuum model and the UNAIDS 90-90-90 targets, I propose this same approach to the cascade of care could be used as a viable framework for people with epilepsy. In this model, the targets of success include (1) ensuring 90% of all people with epilepsy are aware of their diagnosis as a brain disorder, (2) starting 90% of people with epilepsy on quality controlled, appropriately chosen and well stocked antiepileptic drugs, and (3) achieving seizure freedom in 70% of those treated. At least 90% of all people with epilepsy must also be linked to and retained in appropriate care. Although the precise numbers may be debated, this cascade of care approach will assist in deconstructing the barriers to epilepsy care in populations better than the more familiar concept of the epilepsy treatment gap. These reflect concrete goals for health systems of epilepsy care that, if achieved, could lead to seizure freedom for the many people in lower income countries living with poorly controlled epilepsy.

Keywords
epilepsy, public health, child health, HIV/AIDS, health policy, health planning

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Background

Epilepsy is an important cause of chronic disability and a preventable cause of early mortality in low- and middle-income countries (LMICs). More than 1% of the population in LMICs, >60 million people, suffers from epilepsy. Phenobarbital, the oldest antiepileptic medication still in use today, was discovered in 1912. Phenobarbital costs 1 to 2 US cents per day or <5 USD per year and remains the drug of choice for several presentations of epilepsy. Four additional older antiepileptic drugs are commonly found on the World Health Organization’s Essential Medicines List and typically cost <50 cents per day.

Epilepsy is an exemplary disease for health systems planning for brain disorders. Epilepsy presents across the lifespan, with the predominance of first presentations in childhood and in the elderly. The stigma of epilepsy, including its formal and informal prohibitions on school attendance, employment, and marriage in some societies, emphasizes it as an important challenge for the global public health community. Medically, it represents a final common manifestation of a myriad of possible causes: genetic conditions, developmental conditions, central nervous system infections, head trauma, stroke, and sometimes defies clear explanation of its etiology. This is typical of several neurological disorders in which etiologies may reflect the so-called “triple burden” of communicable, noncommunicable, and traumatic disorders. Access to diagnostic services for epilepsy, such as electroencephalogram and neuroimaging, enhances the diagnostic clarity of epilepsy, but the absence of infrastructure in LMICs does not preclude antiepileptic medication treatment. Women of childbearing potential represent a special treatment group since some antiepileptic medications should be avoided during pregnancy, especially valproic acid, given the risk of this medication causing congenital malformations including neural tube defects.

Updating the approach to epilepsy treatment: a cascade of care

Prior framing of the global epilepsy challenge was through the epilepsy treatment gap, or the number of people with epilepsy (PWE) who are eligible for but not taking an antiepileptic medication. This gap reaches up to 90% in LMICs. Meanwhile, a “zero” treatment gap remains unattainable, even in high-income settings. In this way, “getting to zero” is not a realistic goal for epilepsy care as it would be for infectious diseases, which could be eliminated or even eradicated.

Using the treatment gap approach, essential steps in the care pathway of PWE have been overlooked. Since epilepsy is both a clinical problem and a matter of global policy, it requires metrics to optimize care and achieve population-based outcomes. Although countries may be meeting treatment gap goals, many PWE are not adequately diagnosed by seizure type. Some are treated with an inappropriate choice of antiepileptic medication. And in spite of adequate medication adherence, seizure freedom for many PWE may be difficult to attain due to inadequate dosing as well as limited quality and inconsistent supplies of antiepileptic medications.

As HIV prevalence rates drop in many countries, epilepsy may be more prevalent in many countries than HIV/AIDS. People living with HIV/AIDS have benefitted from global advocacy, political will, and dedicated and sustained financial investments. Private-public partnerships and supranational agencies have brought light to the extreme tragedy of the HIV epidemic. This was achieved in spite of the stigma of HIV/AIDS and the disproportionate burden of HIV/AIDS in resource-limited settings and vulnerable populations.

The same efforts have not been made in epilepsy, an ancient disease, that can learn from the progress of HIV/AIDS. Building upon the successes of global policymaking for HIV/AIDS and creating a framework for countries and organizations to monitor progress in epilepsy care will help organize and justify novel programming. It may not achieve the stature of HIV/AIDS programming, but a framework for thinking about progress in epilepsy care pathways can be realized. Given the clarity of the HIV/AIDS care continuum model and the UNAIDS 90-90-90 targets, I propose this same approach to the cascade of care could be used as a viable framework for PWE. In the HIV model, the targets of success include (1) ensuring 90% of all people with HIV infection know they are infected, (2) starting 90% of infected people on antiretroviral therapy, and (3) achieving viral suppression in 90% of those treated. At least 90% of all people with HIV are also linked to and retained in care.

1. Diagnosis of epilepsy allows patients to be successfully given their medical diagnosis, distinct from supernatural causes but also distinct from primary psychiatric behavioral events, cardiac dysrhythmias, symptomatic hypoglycemia, and related conditions.

2. Linkage to epilepsy care allows the establishment and organization of services for PWE - and the minimum standards for epilepsy care - including medication management, as well as access to neuroimaging, EEG services, and/or supportive laboratory studies such as antiepileptic drug levels.

3. Antiepileptic medication treatment enables the management of seizures through efficacious, appropriately chosen and prescribed, available, accessible, and affordable medicines.

4. Seizure control and freedom requires the antiepileptic medication or, in some cases, multiple medications to effectively reduce the number of seizures, ideally to zero in at least 2/3 of PWE, and increase the number of seizure-free days. Although not explicitly required, minimization of side effects such as sedation, would be optimal.

This cascade of epilepsy care should have globally agreed targets, likely 90% of PWE being diagnosed; 90% of PWE linked and retained in care for epilepsy; and 90% of PWE who need an AED receiving it. In addition, a reasonable goal of 70% of all PWE achieving seizure control should be targeted.
This provides a fair comparison for services across higher and lower income settings and may indeed reflect, like in HIV/AIDS, that lower income countries are better able to implement cascades of care for more of their population. Although these precise numbers may be debated by the global community, they are goals that reflect actual processes of epilepsy care.

There are several barriers to measuring and realizing these metrics.

1. **Diagnosis** of epilepsy can best be measured through community-based surveys in the population asking key survey questions. The lack of a distinct biomarker for epilepsy, such as a laboratory test, makes measurement often depend on semi-skilled providers.

2. **Linkage to epilepsy care** is perhaps the most difficult step in the care pathway since it requires functionality of the health care system that will not be overwhelmed by new referrals or under-prepared to deal with a potential influx of patients if diagnoses are made.

3. **Antiepileptic medication treatment** is realizable but there are insufficient efforts to make medications universally available, accessible, and affordable. Treatment of at least 70% of PWE will require non-governmental organizations, governments, supranational organizations, and patients. Barriers to realization of medication provision in 2019 remain common including out-of-date essential medicines lists, the variable quality of medication supplies in LMICs, lack of appropriate supply chains, excessive regulations on some medications, and high out-of-pocket costs to patients.

4. **Seizure control and freedom** are both scientific and educational challenges. Barriers to achieving this metric include expertise on dosing medications, choosing medications appropriately, and having the time and resources to adequately educate patients. It requires addressing causes of medication-resistant epilepsy including preventable causes such as neurocysticercosis, vaccine-preventable perinatal infections, and many cases of preterm birth. It includes changing the behavioral pattern of taking a drug temporarily, as is common for an infectious disease, to taking a medication constantly and potentially lifelong. Additional barriers include the lack of epilepsy surgery opportunities for many LMICs and lack of access to an expanded list of newer scientifically proven antiepileptic medications.

**Conclusions**

Epilepsy is a medically complex and historically poorly understood condition across cultures worldwide. In lower-income countries, neurologists are present in staggering low proportions. However, the metrics of achievement for epilepsy care can be made clearer and therefore can become achievable. Disaggregating the barriers to epilepsy treatment can inform the implementation of solutions and ultimately come full circle and “close” the more familiar “epilepsy treatment gap.”

**Data availability**

No data are associated with this study.

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**References**


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The author proposes a novel approach to the problem of getting appropriate treatment worldwide for people with epilepsy. There are parallels of epilepsy and AIDS and suggests an approach similar to that used to address the AIDS's epidemic. This involved global advocacy, public-private partnerships, political will, and most importantly, sustained financial support for the programs which were implemented with specific metrics to allow ongoing evaluation of success.

It seems that many of these strategies have been implemented through the Global Campaign Against Epilepsy - a collaborative project between WHO and two international epilepsy organizations. It seems that some discussion of the successes and failures as well as mention of the long term activities related to these initiatives in the People's Republic of China would be worth including in this comment along with a review of the 2015 WHO recommendations.

The treatment gap is at this point an ill-defined concept and I agree that it is a poor metric (without definition) to measure success of a program. I do not agree that it has been the sole metric used to assess interventions to improve care with epilepsy in the past. I don’t see the term mentioned in the guidelines. The development of a 90, 90, 90 metric to measure success is intriguing however and could be further developed although the actual measurement will be complicated.

A couple of minor points: I have difficulties identifying other neurological conditions that have the scope of antecedents of epilepsy. Can some be provided by the author?

It seems that the process starts with identification. This is not as easy as with AIDS. As pointed out a modicum of training is needed to identify cases; more if it is necessary to identify seizure type.

While the list of essential antiseizure medications may not include all of the latest drugs, there is little evidence that they provide a control advantage over the currently listed medications. They probably have fewer side effects but even if this is the case, (there are virtually no comparative studies) the cost differential may not be justified.
References

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Is the rationale for the Open Letter provided in sufficient detail?
Yes

Does the article adequately reference differing views and opinions?
No

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Yes

Is the Open Letter written in accessible language?
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?
Partly

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Neuroepidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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This is interesting and stimulating, to compare the success of the HIV/AIDS campaign, with possible strategies to treat patients with epilepsy worldwide.

Despite the success(es) at many levels, HIV remains a threat in many low income countries, and has not been resolved sufficiently. It may be misleading to celebrate this as a success, as in many countries, in particular in Africa have completely unmet needs.
The treatment of epilepsy also needs to break through many stigmata, misbeliefs and take the fact into consideration, that in Africa, only a small percentage of patients are seen by qualified health care professionals, and most (some estimate 80%) by healers.

Finally, and Dr Mateen points this out, there are 2 more important factors: 1) the work force of HCP, 2) and the drug costs, which seem minimal to us, but may be a large amount for persons in need. Culturally, and this may also be a point to consider, the acceptance of "western" medicine, is often considered with mistrust and afterthoughts of colonialization.

My summary is, that this paper is an important and interesting comparison, between the success of the HIV campaigns, and its possible use in epilepsy.

I recommend to relativize the HIV success and consider the low income countries, tackle the cultural aspects (which may be prohibitive in accepting treatment), and finally give more consideration on HP workforce, costs and coverage.

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Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Neurology, neuromuscular, neurooncology. education, global neurology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.