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Thirugnanam Umapathi
National Neuroscience Institute, Singapore

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EVIDENCE BASED MEDICINE SHOULD APPLY EQUALLY TO RESOURCE-LIMITED SETTINGS

Thirugnanam Umapathi¹

¹.Senior Consultant Neurologist, Singapore National Eye Centre, National Neuroscience Institute, Singapore

Correspondence Author: Thirugnanam Umapathi Senior Consultant Neurologist, Singapore National Eye Centre, National Neuroscience Institute, Singapore **Email:** umapathi@nni.com.sg

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Major disparities exist in the outcomes of common diseases between the developed and the developing world. For instance, the mortality of Guillain–Barré syndrome (GBS), the most common cause of acute flaccid paralysis globally with an annual incidence of 1-2 per 1000,000, is believed to be up to 10 times higher in developing countries such as Bangladesh.¹⁻³ This is largely because large segments of the population do not have access to standard, evidence-based medicine (EBM) treatments, namely plasma exchange and intravenous immunoglobulin (IVIg) to hasten recovery; and intensive care, which mitigates against respiratory failure and autonomic dysregulation.³⁻⁵ IVIg treatment costs 12,000-16,000 USD and plasma exchange 4500-5000 USD in Bangladesh; resulting in only 15% of the GBS patients receiving these treatment.⁶ The limited treatment and the lack of comprehensive rehabilitation services leads to a congruent increase in morbidity. One study from Bangladesh reported 29% of GBS patients were unable to walk at 6 months.²

The default “capitalist” panacea of waiting for a gradual “trickle-down effect” has obviously not resulted in the poor, living at the bottom of the economic totem pole, getting eventual access to the above-mentioned standards of care as these treatments have been widely available in the developing world for almost half a century. Perversely, the latest development in improving outcome of GBS has been the use of eculizumab a drug that costs about 100k USD.⁷ The unavailability of standard care for GBS in many under-resourced regions has therefore resulted in many doctors nihilistically and erroneously turning to corticosteroids. This is in spite of eight randomized studies showing no benefit; and oral corticosteroids causing possibly a negative outcome.⁸

Research to find evidence for effective treatments that is more applicable in the developing countries is therefore urgently needed. I believe this requires two key paradigm changes:

- A) Democratisation of evidence production: The continuation of therapeutic research for more widely accessible treatment-alternatives even after industry-driven trials have yielded a positive result. This is well-illustrated in the case described by Chowdhury et al.⁹ They argue for the need to continue research for cheaper and safer alternatives to an acute thrombolysis program that is predicated on the use of a costly drug like tissue plasminogen activator and on the availability of emergent imaging. Acute stroke treatment could potentially be made more accessible to the vast majority of the developing world by trialing low-cost streptokinase and cerebral hemorrhage predictive scores.⁹
- B) “Disruptive” Technologies (<https://hbr.org/1995/01/disruptive-technologies-catching-the-wave>)- the need to invent creative, medical diagnostic and therapeutic technologies that alleviate the health-care deficiencies at “CK Prahalad’s base of the economic pyramid” (<https://www.strategy-business.com/article/11518>). Instead of a “fortune” we have opportunities at the “base of the pyramid”! One such example is the development of small volume plasma exchange to replicate standard plasma exchange for treatment of GBS by doctors in Sri Lanka, Myanmar and Bangladesh.^{6,10,11} The technique basically requires repeated manual bleeding of the patient, re-infusion of the red cells, discarding the supernatant plasma and replacing it with donated fresh frozen plasma or commercial albumin. This procedure is repeated many times a day over the next 8-10 days. The technique has been shown to be safe and achieves a volume exchange of about 60% of standard plasma exchange.⁶ However, attempts to organize a multi-national/centre controlled trial to address its efficacy vis a vis standard treatment has been met with considerable logistical, economical and seemingly ethical challenge (personal communication), many of which pertain to the lack of systematic democratization of evidence production discussed in paragraph (A). Another example of solutions that creatively “disrupt” current care-models is the LiveWell Centre for Rehabilitation Medicine in South India (<https://poovanthire>

hab.com). By adapting the Aravind Eye Hospital model of training and employing young women from under-served communities to become mid-level ophthalmic personnel (<https://www.hbs.edu/forum-for-growth-and-innovation/blog/Pages/default.aspx?post=51>) (<https://hbr.org/2010/04/how-poor-countries-can-help-so>)(<https://m.economictimes.com/et50-india-can-lead-in-reverse-innovation/articleshow/5906439.cms>), LiveWell employs a large team of well-trained therapy assistants to support the handful of physical therapists and psychiatrists.¹² The centre is sited in a rural location, not at a metropolis. With these measures, it is able to keep cost down and rehabilitation accessible to poor patients who are living with considerable unattended disability in under-resourced, rural regions. Likewise, an NGO in Maharashtra India called SEARCH, deployed women of the villages as community health-workers, rather than rely on traditional hospital-based care, to lead an initiative called “Home-Based Neonatal Care”. It reduced case fatality of neonatal sepsis from 16.6% (163 cases) to 2.8% (71 cases) in an impoverished and malnourished rural-tribal population, at a cost of USD 5.3/neonate.¹³ Similarly, a low-cost, community-based treatment protocol for multi-resistant tuberculosis treatment at Peru achieved an 85% cure rate, comparable to an expensive and less accessible “standard treatment” at referral centers.¹⁴ The basic pre-requisites for these creative methods of health care delivery are, they have to be;

- 1) context specific, 2) culturally appropriate, 3) systematically studied to be effective, and
- 4) sustainable for the target population.

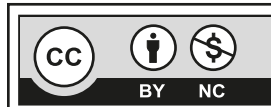
In this article I have laid out the importance of developing innovations and seeking systematic evidence of their efficacy so that therapeutic outcomes for people living in under-resourced parts of the world are not compromised and comparable to those in developed world - results similar, but the approaches need not be! The impetus for change has to come from collaborative research in low- and middle-income countries, with appropriate level of support from grant agencies, academia and the medical-industrial complex. The astrophysicist Neil Degrasse Tyson said, “The good thing about Science, is that it’s true whether or not you believe in it”. Allow me to paraphrase him- “The good thing about Science, is that it is not only true but is applicable to everyone, rich or poor”. How do we ensure evidence-based medicine, contextualized to resource-limited settings, remains the universal standard of care? That, I believe is one of the important challenges of the near future, that is seeing a greater rich-poor divide.

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