

Medical Therapies Commission

2021 Annual Report

2017 – 2021 Members

Kimford J. Meador (USA), chair
Dong Zhou (China)
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Aims & Goals

The aims of the Medical Therapies Commission are to serve the goals of the ILAE related to medical therapies:

1. To advance and disseminate knowledge about epilepsy,
2. To promote research, education and training,
3. To improve services and care for patients, especially by prevention, diagnosis and treatment.

Access to Treatment Task Force: The Task Force of Access to Treatment aimed to analyze the current access to ASMs worldwide and to give possible recommendations to reduce the Epilepsy Treatment Gap in relation to access to ASMs. The global survey conducted by the Task Force pursued the wider scope to include all available medications and formulations, pricing comparisons of 5 most commonly used ASMs and to provide a broader view of the state of pharmaceutical access in epilepsy care across the world.

Botanicals & Traditional Medicines Task Force: Expand website with listing and description of multiple botanicals. Explore information on traditional medicines.

Dietary Treatments Task Force:

1. To promote and establish the use of the ketogenic diets, particularly in countries with limited resources.
2. To provide standardized guidelines regarding ketogenic diets and its variants.
3. To advance and disseminate knowledge about ketogenic diet.

Epilepsy in the Elderly Task Force: Define the scope of the problem, select educational goals, and identify areas needing research.

Emergency Treatment Task Force: Produce two evidence-based guidelines: (1) European Guidelines in conjunction with the EAN and (2) Guidelines for resource poor countries. Both will follow the GRADE Methodology.

Generic Medications Task Force: Assess the frequency and impact of generic substitution of antiseizure medications in various countries, especially resources limited countries. Disseminate these findings to assist the ILAE and others.

Psychology Task Force: Examine pathways that illustrate how psychological services (addressing depression, anxiety, and suicidality) can be integrated into epilepsy care. Publish these findings to inform the patients and clinicians. Collaborate with Psychiatry Commission to develop educational input for international epilepsy curriculum that relates to psychological and psychiatric therapies.

Regulatory Affairs Task Force

1. Reduce placebo exposure in AED trials, by implementing new endpoints (time to event).
2. Further develop the possibilities of extrapolating data from an age group to another.
3. Interact with the European medicine Agency in the elaboration of their new guideline for antiepileptic drugs.
4. Elaborate new study endpoints for epileptic encephalopathies and specific diseases.
5. Evaluate seizure types and epilepsy syndromes, and how to classify patients in studies to make them more representative of the general populations.
6. Engage in an ad hoc manner when new regulatory issues arise.

Women/Pregnancy Task Force

1. To improve our understanding of the availability globally of recommendations for the management of epilepsy in women of childbearing potential.
2. To provide women with epilepsy of childbearing potential easy access to updated information of relevance for their treatment.

Activities & Accomplishments

Access to Treatment Task Force

- Global survey on access to ASMs: A total of 123 ILAE Chapters and 137 IBE Chapters were contacted. To access and compare differences in the price of ASMs among countries between brand and generic formulation in the same countries, a second questionnaire was sent to the same Chapters.
- Survey on ASMs prices: (integration to the Global Survey): the Task Force conducted a specific Survey aimed to assess and compare differences in the pharmacy retail price of five commonly used ASMs (VPA, CBZ, PB, LEV, LTG) among countries and income levels, between brand and generic formulation in the same country and payback modality for each of them. Replies from 59 countries (Africa 12, Asia 17, Europe 22, Latin America 5, North America 3, *income level*: HICs 49.2%, UMICs 15.3%, LMICs 28.8%, LICs 6.7%) were collected and analyzed.

The data will be part of the main publication of the Global Survey on Access to ASMs. The possibility of a separate publication on this data is under evaluation. The results of this survey were published:

Pironi V, Ciccone O, Beghi E, Paragua-Zuellig H, Patel AA, Giussani G, Bianchi E, Venegas V, Vigeveno F; ILAE Task Force on Access to Treatment. Survey on the worldwide availability and affordability of antiseizure medications: Report of the ILAE Task Force on Access to Treatment. *Epilepsia*. 2022 Feb;63(2):335-351.

Botanicals & Traditional Medicines Task Force: The Task Force continues to work on expanding its website information which has listings and descriptions of multiple botanicals and traditional medicines. They are working to get approval of the website information by the ILAE and have it linked to the ILAE website. They have also been working Dr. Marc-Daniel Gutekunst on an epidemiological and ethnobotanical study of natural epilepsy treatment in Rwanda as soon as Covid conditions allow.

Dietary Task Force: To achieve the Task Force aims to promote the use of the ketogenic diet, the Task Force had planned to hold workshops, but all were cancelled due to COVID-19 Pandemic.

Elderly Task Force: The Task Force on Elderly and Epilepsy has completed two manuscripts:

“Management of epilepsy in older adults: a critical review” by Loretta Piccenna, Rebecca O’Dwyer, Ilo Leppik, and Patrick Kwan for the ILAE Task Force on Epilepsy in the Elderly (2017-2021).

“The Epidemiology of Epilepsy in Older Persons: A Selective Review and Recommendations by the ILAE Task Force on Epilepsy in the Elderly”, Beghi E et al.” These are being reviewed by the LAE Publications Committee.

Emergency Treatment Task Force: The Task Force has been working with EpiCARE (a European Reference Network for rare and complex epilepsies to identify areas where development of needed epilepsy guidelines and then to develop these clinical practice guidelines and monitor them to assess adherence and impact.

The Task Force developed Guideline Protocols for the Joint EAN - ILAE - EpiCARE Guidelines on four topics:

1. Status Epilepticus (SE)
2. Dravet Syndrome (DS)
3. Lennox-Gastaut Syndrome (LGS)
4. Infantile Spasms (IS).

Dr. Trinka who chairs the Task Force published an educational article on treatment of status: Trinka E, Leitingner M. Management of Status Epilepticus, Refractory Status Epilepticus, and Super-refractory Status Epilepticus. *Continuum* (Minneap Minn). 2022 Apr 1;28(2):559-602.

Generic Medications Task Force: The Generics Task Force completed a survey with questions addressing the understanding of bioequivalence, standards for generic products, experiences with substitution, and demographic data. The survey was web-based and distributed to ILAE chapters, their membership, and professional colleagues of Task Force members. Results have now been published:

Niyongere J, Welty TE, Bell MW, Consalvo D, Hammond C, Leung H, Patsalos PN, Ryan M, Suansanae T, Zhou D, Zuellig H. Barriers to generic antiseizure medication use: Results of a global survey by the International League Against Epilepsy Generic Substitution Task Force. *Epilepsia Open*. 2022 Feb 6. doi: 10.1002/epi4.12583. Epub ahead of print. PMID: 35124903.

Another manuscript has been completed entitled “Best Practices for Generic Seizure Medications: Recommendations from the International League Against Epilepsy Task Force on Generic Substitution” by Timothy E Welty, Michelle W Bell, Damian Consalvo, Charles Hammond, Howan Leung, Philip N Patsalos, Melody Ryan, Thanarat Suansanae, Kiran T Thakkur, Dong Zhou, and Hazel Zuellig. It is being submitted for publication.

Psychology Task Force: The Psychology Task Force successfully ran and analyzed an international survey to investigate barriers to psychological treatment in people with epilepsy. The results of the survey have been published:

Gandy, M., Modi, A.C., Wagner, J.L., LaFrance, W.C., Jr, Reuber, M., Tang, V., Valente, K.D., Goldstein, L.H., Donald, K.A., Rayner, G. and Michaelis, R. (2020), Managing Depression and Anxiety in People with Epilepsy: A Survey of Epilepsy Health Professionals by The ILAE Psychology Task Force. *Epilepsia Open*. 2021 Feb 8;6(1):127-139.

The Psychology Task Force also completed a Cochran review and published it.

Michaelis R, Tang V, Nevitt SJ, Wagner JL, Modi AC, LaFrance Jr WCurt, Goldstein LH, Gandy M, Bresnahan R, Valente K, Donald KA, Reuber M. Cochrane systematic review and meta-analysis of the impact of psychological treatment on health-related quality of life in people with epilepsy: an update by the ILAE Psychology Task Force, highlighting methodological changes. *Epileptic Disord*. 2021 Dec 1;23(6):803-811.

Christian Brandt (Chair Disability Task Force, Psychiatry Commission) and Rosa Michaelis (Chair Psychology Task Force) continued to co-coordinate input addressing psychosocial and psychiatric issues (e.g., counseling of anxious parents, screening for depressive symptoms etc.).

Regulatory Affairs Task Force: The Task Force continued their interactions with the FDA and EMA on regulatory assessments and rules.

In fall 2020 the FDA added a warning to lamotrigine labeling related to cardiac risks. The Regulatory Task Force convened a group to quickly create an advisory that was published by ILAE in *Epilepsia Open* and AES (in *Epilepsy Currents*) to assist clinicians in interpreting the warning.

French JA, Perucca E, Sander JW, Bergfeldt L, Baulac M, Auerbach DS, Keezer M, Thijs RD, Devinsky O, Vossler DG, Welty TE. FDA safety warning on the cardiac effects of

lamotrigine: An advisory from the Ad Hoc ILAE/AES Task Force. *Epilepsia Open*. 2021 Feb 25;6(1):45-48.

French JA, Perucca E, Sander JW, Bergfeldt L, Baulac M, Auerbach DS, Keezer M, Thijs RD, Devinsky O, Vossler DG, Welty TE. FDA Safety Warning on the Cardiac Effects of Lamotrigine: An Advisory From the Ad Hoc ILAE/AES Task Force. *Epilepsy Curr*. 2021 Feb 28;21(3):1535759721996344.

Members of the Task Force also published a systematic review on the topic:

Bunschoten JW, Husein N, Devinsky O, French JA, Sander JW, Thijs RD, Keezer MR. Sudden Death and Cardiac Arrhythmia With Lamotrigine: A Rapid Systematic Review. *Neurology*. 2022 Apr 26;98(17):e1748-e1760. doi: 10.1212/WNL.0000000000200164. Epub 2022 Mar 8. PMID: 35260442.

Women/Pregnancy Task Force: A report on the management of epilepsy in pregnancy was published:

Tomson T, Battino D, Bromley R, Kochen S, Meador K, Pennell P, Thomas SV. Management of epilepsy in pregnancy: a report from the International League Against Epilepsy Task Force on Women and Pregnancy. *Epileptic Disord*. 2019 Dec 1;21(6):497-517. doi: 10.1684/epd.2019.1105.

Tomson T, Battino D, Bromley R, Kochen S, Meador K, Pennell P, Thomas SV. Executive Summary: Management of epilepsy in pregnancy: A report from the International League Against Epilepsy Task Force on Women and Pregnancy. *Epilepsia*. 2019 Dec;60(12):2343-2345.

Then a survey on guidelines of management of epilepsy in pregnancy was published:

Tomson T, Battino D, Bromley R, Kochen S, Meador KJ, Pennell PB, Thomas SV. Global Survey of Guidelines for the Management of Epilepsy in Pregnancy: A report from the International League Against Epilepsy Task Force on Women and Pregnancy. *Epilepsia Open*. 2020 Aug 5;5(3):366-370. doi: 10.1002/epi4.12420. eCollection 2020 Sep.

The Task Force is now in the final phases of completion of a publication of a systematic review from the ILAE Women Task Force on “Breastfeeding while on treatment with antiseizure medications.”

A video symposium was held at the 34th IEC by members of the Task Force entitled “Case studies in pregnancy and epilepsy.”

Recommendations for Future Work

Access to Treatment Task Force: The Task Force will analyse the answers from the 22 African Countries and consider a separate publication on Access to ASMs in Africa. The Future Task Force on Access to Treatment may be able to utilise this baseline data on Access to ASMs to work more on possible interventions and other aspects of Access to Care.

Botanicals & Traditional Medicines Task Force: The Task Force will continue its work on expanding its website information which has listings and descriptions of multiple botanicals and traditional medicines. It will now come under the Task Force called Plant Based Medicine.

Dietary Task Force: The Task Force wants to continue to promote use of the ketogenic diet via workshops. Members of the Task Force are also working establishing on a new professional society devoted to metabolism-based therapies for neurological disorders.

Elderly Task Force: The Task Force seeks to finalize publication of its two prepared manuscripts.

Emergency Treatment Task Force: The Task Force will continue its work with EpiCARE to develop guidelines for the treatment of status epilepticus. After critical appraisal, new guidelines will be formulated and submitted to the ILAE ExCo and the EAN for final approval.

Generic Medications Task Force: This Task Force is to be merged with Access to Treatment. They will be submitting their completed manuscript entitled “Best Practices for Generic Seizure Medications: Recommendations from the International League Against Epilepsy Task Force on Generic Substitution.”

Psychology Task Force: The Psychology Task Force will now come under the Treatment and Prevention Task Force (Psychiatry Commission) on the development of specific strategies to address barriers to the delivery of psychological care in patients with epilepsy in different nations.

Regulatory Affairs Task Force: The Task Force will continue its interactions with the FDA and EMA to improve the regulatory process.

Women/Pregnancy Task Force: The Task Force is completing a publication on breastfeeding and antiseizure medications. They seek to have a Wikipedia version of information on women and pregnancy.

Submitted by Kimford J Meador