

# Medical Therapies Commission

## Members

### Chair

Kimford J. Meador (USA)

### Members

Dong Zhou (China)

Patrick Kwan (Australia)

Emilio Perucca (Italy)

Sanjeev Thomas (India)

Tim Welty (USA)



Kim Meador

### Management Committee Liaison

Emilio Perucca (Italy)

## Aims and 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. Goals of the individual task forces of our commission are below.

### Access to Treatment

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 TF 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

Expand website with listing and description of multiple botanicals. Explore information on traditional medicines.

### Dietary 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.

### Elderly

Define the scope of the problem, select educational goals, and identify areas needing research.

### Emergency Treatment

The goals of the TF on emergency Treatment is to 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

1) Review literature related to generic substitution of antiseizure medications. 2) To review issues related to safety and reliability of generic drugs in various countries, especially resources limited countries. 3) Develop products that inform and assist ILAE members in making decisions about generic substitution of antiseizure medications.

## Psychology

1) Present and discuss pathways that illustrate how psychological services (addressing depression, anxiety, and suicidality) can be integrated into epilepsy care. 2) Collaborate with Psychiatry Commission to develop educational input for international epilepsy curriculum that relates to psychological and psychiatric topics.

## 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 seizures 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

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.

## Commission Activities and Accomplishments:

Activities and accomplishments of the individual task forces of the Medical Therapy Commission are presented.

### Access to Treatment

#### Members

Federico Vigevano (Italy), **Co-Chair**  
Ornella Ciccone (Zambia), **Co-Chair**  
El Hadji Makhtar Ba (Senegal)  
Ching-Shiang Chi (Taiwan)  
Edward Kija (Tanzania)  
Kurnia Kusumastuti (Indonesia)  
Hazel Paragua-Zuellig (Philippines)

Archana Patel (USA)  
Pratibha Singhi (India)  
Nana Tatishvili (Georgia)  
Viviana Venegas (Chile)  
Dong Zhou (China)  
Ken Koskela (USA)

1. **Global survey on access to ASMs:** The Task Force completed the global survey on Access to ASMs which included availability of 35 ASMs in different formulations, availability of rescue medications and drugs for the management of status epilepticus, problems in prescription and distribution of AEDs, presence of projects to improve access to ASMs, general barriers to access ASMs. *Replies from 101 countries were analyzed. The TF is completing the manuscript for international publication.*

2. **Survey on ASMs prices** (integration to the Global Survey): the TF conducted a specific Survey aimed to assess and compare differences in the pharmacy retail price of 5 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.

**3. Parallel Survey on Access to ASMs in Africa:** In order to fill the gap of info from African Continent (LMIC/LICs), a specific survey for Africa using a slightly modified version of the survey questionnaires was sent in March and September 2020 to epileptologists/neurologists/other professionals involved in the treatment of epilepsy (also out of ILAE/IBE network) of 28 countries in Africa. Probably due to the additional burden of the COVID pandemic, the reply rate was very low: we had 11 answers from 8 countries. In total (with the data of the Global Survey) we reached 29 answers from 22 countries in Africa.

It was not possible to have the face-to-face TF meeting in Genève in July 2020 due to the cancellation of the Congress due to the COVID Pandemic.

## Botanicals & Traditional Medicines

### Members

Steve Schachter (USA), **Co-Chair**  
Siegward Elsas (Switzerland), **Co-Chair**  
Chumbo Zhang (China)

Nicholaus Sucher (USA)  
Dana Ekstein (Israel)  
Elisabeth Ngo Bum (Cameroon)

The task force continues to work on expanding its website information which has listings and descriptions of multiple botanicals and traditional medicines. They are now working to get approval of the website information by the ILAE and have it linked to the ILAE website.

## Dietary Treatments Task Force

### Members

Heung Dong Kim (Korea), **Co-Chair**  
Jong Rho (Canada), **Co-Chair**  
Stéphane Auvin (France)  
Mackenzie Cervenka (USA)  
Derrick Chan (Singapore)

Tove Hallböök (Sweden)  
Sehee Kim (Korea)  
Katherine Megaw (South Africa)  
Beth Zupec-Kania (USA)

To achieve the task force aim to promote the use of the ketogenic diet, the task force had planned to hold 3 workshops in 2020, but all were cancelled due to COVID-19 Pandemic. The 7th Global Symposium for Medical Ketogenic Dietary Therapies moved to 19<sup>th</sup> to 23<sup>rd</sup> October, 2021.

## Epilepsy in the Elderly

### Members

R. Edward Faught (USA), **Chair**  
Naoki Akamatsu (Japan)  
Ettore Beghi (Italy)  
Benjamin Cretin (France)  
Monica Dhakar (USA)  
Giorgia Guissani (Italy)

Guenter Kraemer (Switzerland)  
Patrick Kwan (Australia)  
Ilo Leppik (USA)  
Rebecca O'Dwyer Vourganti (USA)  
Loretta Piccenna (Australia)

The task force on Elderly and Epilepsy conducted an initial review of content epilepsy-related websites and found that content on epilepsy in the elderly was either minimal or hard to find.

The group is also conducting a literature review collecting and sharing of references in order to prepare a review manuscript.

## Emergency Treatment

### Members

Eugen Trinkla, **chair**

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.

## Generic Medications

### Members

Tim Welty (USA), **chair**  
Michelle Bell (USA)  
Damian Consalvo (Argentina)  
Charles Hammond (Ghana)  
Ho Wan Leung (Hong Kong)  
André Palmieri (Brazil)

Jim Polli (USA)  
Melody Ryan (USA)  
Thanarat Suansanae (Thailand)  
Kiran Thakur (USA)  
Jo Wilmshurst (South Africa)  
Dong Zhou (China)

The TF has reviewed the literature related to generic substitution of antiseizure medications including issues related to safety and reliability of generic drugs in various countries, especially resources limited countries. The TF has been working to finalizing the report on the survey findings with plans to publishing an article.

## Psychology Task Force

### Members

Rosa Michaelis (Germany), **chair**  
Kette de Valente (Brazil)  
Milena Gandy (Australia)  
Laura Goldstein (UK)  
Janelle Wagner (USA)

Kirsty Donald (South Africa)  
W Curt La France Jr (USA)  
Avani Modi (USA)  
Markus Reuber (UK)  
Venus Tang (Hong Kong)

1. **Online survey of barriers to psychological treatment in PWE published:** The Psychology TF successfully ran and analyzed an international survey to investigate barriers to psychological treatment in PWE. The results of the survey have been published in *Epilepsia Open*: 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*. Accepted Author Manuscript. <https://doi.org/10.1002/epi4.12455>

Based on the results the Psychology TF plans to present and discuss pathways that illustrate how psychological services (addressing depression, anxiety, suicidality) can be integrated into epilepsy care.

2. **Update of Cochrane review “Psychological treatments for PWE” published:** This Cochrane review was a priority review due to the update of the British NICE guidelines on epilepsy. The Psychology TF has therefore updated the review and presented the results to the NICE committee: 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. Psychological treatments for people with epilepsy. Cochrane Database of Systematic Reviews 2020, Issue 8. Art. No.: CD012081. DOI: 10.1002/14651858.CD012081.pub3.  
  
This update includes a recategorization of psychological interventions and the risk of bias assessment has been expanded by putting an emphasis on risk of bias categories that are of particular importance when investigating psychological interventions (i.e. fidelity, competence assessment, selective recruitment). A brief version of this review will be published in a league-associated journal soon, preferably – like the previous version – in *Epilepsia*.
3. **IEC 21 session proposal accepted:** The IEC 21 session proposal entitled “*Suicide and Seizures - Suicide management in routine clinical epilepsy care*” has been accepted.
4. The TF submitted a nuanced **comment on proposed clinical practice guideline for treatment of depression in adults with epilepsy**
5. **Input to online case-based International Epilepsy Curriculum:** Christian Brandt (Chair Disability TF, Psychiatry Commission) and Rosa Michaelis (Chair Psychology TF) continue to co-coordinate input addressing psychosocial and psychiatric issues (e.g. counseling of anxious parents, screening for depressive symptoms etc.).

## Regulatory Affairs Task Force

### Members

Jackie French (USA), **Co-Chair**  
Michel Baulac (France), **Co-Chair**  
Alexis Arzimanoglou (France)  
Emilia Bagiella (USA)  
Dennis Dlugos (USA)  
Sunao Kaneko (Japan)

Russell (Rusty) Katz (USA)  
Rima Nabbout (France)  
Terrence O’Brien (Australia)  
Emilio Perucca (Italy)  
Eugen Trinko (Austria)

This year we continued our focus on extrapolation during the “virtual” research Roundtable for Epilepsy. We presented arguments to FDA and EMA on how to handle infant epilepsy, and whether extrapolation of efficacy to 1 month of age was appropriate. The FDA is taking this under advisement, and should reach a conclusion in the near future.

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 to be published by ILAE in *Epilepsia Open* and *AES* (in *Epilepsy Currents*) to assist clinicians in interpreting the warning. The advisory is now finalized and soon will be submitted for joint publication

We also addressed the issue of regulatory requirements for seizure diaries, and clarified these during the Research Roundtable for Epilepsy (RRE).

## **Women/Pregnancy Task Force**

### **Members**

Torbjörn Tomson (Sweden), **chair**

Dina Battino (Italy)

Rebecca Bromley (UK)

Silvia Kochen (Argentina)

Page Pennell (USA)

Sanjeev Thomas (India)

The global survey of existing guidelines and recommendations for the management of women with epilepsy during pregnancy was completed. The results were presented at a session on pregnancy organized by the TF at the Bangkok IEC in June 2019. At the same session, members of the TF also gave an update on neurodevelopmental outcomes after exposure to antiseizure medications and on the practical management of epilepsy in pregnancy in resource limited settings. The results of the global survey was published in *Epilepsia Open* in August 2020. The TF has published a full length expert opinion report in *Epileptic Disorders* on the management of epilepsy in pregnancy. An executive summary of the same report was published in *Epilepsia*. The publication in *Epileptic Disorders* has been transferred to ILAE's Wikipedia team and an agreement has been made with the publisher to make it available on Wikipedia. The Wikipedia team has agreed develop a specific Wikipedia posting based on the publication in *Epileptic Disorders*. In December 2019, the TF had a full day meeting in conjunction with the Annual AES meeting in Baltimore setting the goals for its activities during 2020. The TF work during 2020 has been through e-mail communication between the members, and has focused on a systematic review of breastfeeding during treatment with antiseizure medications.

## **Recommendations for Future Work:**

Plans for the individual task forces of the Medical Therapy Commission are presented.

### **Access to Treatment**

1. The Task force plans to publish the data on the Global Survey on Access to ASMs in an international journal within 6 months.
2. The Task Force is considering producing a separate publication on Prices of 5 common ASMS at global level in collaboration with the TF on Generics.
3. The Task Force will analyse the answers from the 22 African Countries and consider a separate publication on Access to ASMs in Africa.
4. An online TF Meeting will be held in February or March to finalize the manuscript on the Global Survey and discuss the other two possible publications
5. A conclusive "face to face" TF meeting will take place with the TF members present at IEC in Paris or, in case of a virtual congress, an online TF Meeting will be organized at the end of August.
6. 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**

The task force will continue its work on expanding its website information which has listings and descriptions of multiple botanicals and traditional medicines. They are now working to get approval of the website information by the ILAE and have it linked to the ILAE website.

### **Dietary Task Force**

To contribute to the aim of the task force to promote the use of the ketogenic diet, the 7th Global Symposium for Medical Ketogenic Dietary Therapies has been moved to 19<sup>th</sup> to 23<sup>rd</sup> October, 2021 due to the Covid pandemic. Members of the TF are also working establishing on a new professional society devoted to metabolism-based therapies for neurological disorders

### **Elderly**

The task force plans to continue a systematic review of websites to identify good content on Epilepsy and the Elderly in order to offer better content to pertinent websites, and promote publications on this topic.

### **Emergency Treatment**

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**

The TF has reviewed the literature related to generic substitution of antiseizure medications including issues related to safety and reliability of generic drugs in various countries, especially resources limited countries. The TF is finalizing the report on the survey findings on generic substitution of antiseizure medications including issues related to safety and reliability. They plan to publishing an article, which they will pre-submit it to the Publications Committee for their review prior to submission to a journal for publication. Additionally, they will be working on a white paper with recommendations to consider to improve the quality of and confidence in generic products.

### **Psychology**

The Psychology Task Force will collaborate with the Identification, Treatment and Prevention TF (Psychiatry Commission) on the development of specific strategies to address barriers to the delivery of psychological care in patients with epilepsy in different nations. The Psychology TF and Psychiatry Commission plan to offer ongoing input to international epilepsy curriculum informed by the results of the survey.

### **Regulatory Affairs Task Force**

Because of the postponing of the EMA guidelines activities due to their move, these discussions and their outcome must be followed-up. It is unclear if they have accepted the new infant protocol proposed by the task force. We hope to have another meeting with them in 2021. In regards to the FDA, the annual research Roundtable for Epilepsy (April 2021) is our only opportunity to meet with FDA; thus, we will focus on seizures types and epilepsy syndromes, and how to classify patients in studies to make them more representative of the general populations.

As in the past, we remain ready to address regulatory concerns as they arise.

### **Women/Pregnancy**

The TF will continue to develop new expert opinion papers on relevant topics for Epileptic Disorders and subsequently for Wikipedia. For 2021, we plan to deliver a similar manuscript on breastfeeding and antiseizure medications. To facilitate these goals, TF teleconferences will be conducted and if circumstances permit a final face-to-face meeting in conjunction with ICE for those members attending the conferences. For the next term, we suggest development of an expert opinion educational paper on contraception for Epileptic Disorders with a related Wikipedia version.

Submitted by KJ Meador consolidating reports from Task Force Leaders