

Medical Therapies Commission

2022 Annual Report

MEMBERS

Lieven Lagae (Belgium), chair
Tony Marson (UK)
Kim Meador (USA)
Leonor Cabral (Phillippines)
Hassan Hosny (Egypt)
Page Pennell (USA)
Anita Devlin (UK)
Kate Riney (Australia)
Archana Patel (USA/Zambia)
Stéphane Auvin (France)
Dennis Duglos (USA)
Eugen Trinko (Austria)
Samuel Wiebe (Canada), MC liaison

ACTIVITIES

- Overviewing and coordinating different actions of the six task forces
- Global Commission projects:
 - Vit D supplementation in persons with epilepsy
The question to be answered is whether there is evidence that vit D (or Calcium) supplementation is needed in patients with epilepsy. The link between some ASDs and osteoporosis is clear. However, it is not known whether chronic vit D can prevent osteoporosis. In 2022 a literature review was performed showing very little evidence. The Commission is preparing a position paper to give guidance in this important topic.
 - Valproate toxicity in men
In the past , some reports already mentioned possible testicular toxicity after valproate exposure. Recent animal work did confirm this effect. In addition, there is a study showing transgenerational effects of valproate taken during pregnancy. There seems to be an increased risk for neurodevelopmental problems in children born to mothers whose mother took valproate during pregnancy. Although methodologically the data are not yet very convincing, this signal was taken seriously in the UK and new guidelines for use of valproate in men are being prepared. The commission wants to produce an informative statement paper about optimal diagnostic follow up of bone status in epilepsy and possible vit D supplementation.

PREGNANCY AND WOMEN

TASK FORCE

Paige Pennell (USA), chair

Cristine Cukiert (Brazil)

Rebecca Bromley (UK)

Bettina Schmitz (Germany)

Zeinab Kone (Mali)

Bruna Nucera (Italy)

Sanjeev Thomas (India)

Alison Pack (USA)

In 2022, this task force focused on 2 projects building further on work done by the previous task force.

Project 1 – VPA in Females

- VPA remains the most commonly prescribed ASM in pregnant females and females of childbearing age in many parts of the world, e.g. Western Cape, South Africa (Mehta U, Smith M, Kalk E, et al. Understanding and Responding to Prescribing Patterns of Sodium Valproate-Containing Medicines in Pregnant Women and Women of Childbearing Age in Western Cape, South Africa. *Drug Saf.* 2021;44(1):41-51) The evidence-based reviews and guidelines (to be published AAN/ AES/ ACOG) could be supplemented by a survey to the ILAE chapters about current prescribing practices in their regions.
- The Task Force is preparing a position statement, focused on decreasing the prescription rates for VPA to females of childbearing age. The goal would then be to work in conjunction with WHO and UN on implementing the recommendations, including looking at cost and if some alternatives need to be subsidized in some countries, such as LEV as it is reaching the time when the cost should be reduced globally. Targeted audiences include neurologists, generalists, pediatricians, obstetricians, psychiatrists, and APPs/nurses. Partnership with IBE to reach females with epilepsy would be helpful.

Project 2 – Contraception for Women with Epilepsy

Task Force survey of contraception practices for women with epilepsy globally was discussed: Discussion led to the practical decision that the time is not yet ripe for this as it takes a cross-disciplinary approach and a lot of effort to gain data that is not readily available. For contraception however there is still an educational gap. Discussion was started to write a practical guide on what the neurologist should do. Which interactions should be more careful than others? Which oral contraceptives should be suggested? Action is being prepared for 2023.

PLANT BASED THERAPY

TASK FORCE

Kate Riney (Australia), chair

KP Vinayan (India)

Cecilie Landmark (Norway)

Elisabeth Theile (USA)

Siegward Elsas (Switzerland)

Chunbo Zhang (China)

Shang-Yeong Kwan (Taiwan)

Ali Asadi Pooya (Iran)

Motlalepula Matsabisa (South Africa)
Finbar O'Callaghan (UK)

Najib Kissani (Morocco)
Boulenouar Mesraoua (Qatar)

The Task Force's initial work was to undertake an assessment into the feasibility of the ongoing maintenance and updating of the resource www.epilepsynaturapedia.com as an ILAE supported website/resource. This site was initially created in 2012 and last edited in 2016 as a resource of all natural products with potential antiseizure effect. It is in a Wiki format and publicly available on the internet with an ILAE logo but is not a Wiki page. After much discussion it was determined that this was not consistent with current ILAE publication policy and that it was not feasible to continue to support this site's updating and validation going forward through ILAE Task Forces though it was recognized that the site remains a very useful resource. The site's author Stephen Schachter was to be informed, so that the ILAE logo is removed from the site. The Task Force then moved onto generate a work plan for the term of the Task Force, including a proposal to:

- Undertake an in-depth critical appraisal (systematic review) of cannabinoids for treatment of epilepsy (evidence to date) to facilitate optimal current clinical use and research priorities, including in adults.
- Assess access and prescribing limitations in different regions and health systems in the world (physician survey)
- Assess prescribing culture for cannabinoids among physicians (physician survey)
- Assess consumer perspectives on access to cannabinoids, understanding of evidence and place in therapy.

This work plan for publications was approved by the Publications Committee in July 2022.

Lastly in 2022 the Task Force developed and submitted a proposal for a session at the IEC in Dublin, September 2023 which was accepted. This session explores the consumer demand for plant-based therapies, what we have learned from cannabinoid trials and regulatory approval, current plant-based epilepsy treatments used in different regions of the world, agents with potential anti-seizure effect, and challenges and solutions in bringing plant-based treatments to market.

DIETARY TREATMENTS

TASK FORCE

Anita Devlin (UK), chair
Heung Dong Kim (South Korea)
Jong Rho (USA)
Mackenzie Cervenka (USA)
Janak Nathan (India)
Mark MacKay (Australia)

Pauline Samia (Kenya)
Valentina De Giorgis (Italy)
Omnia El Rashidy (Egypt)
Marisa Armeno (Argentina)
Kath Megaw (USA)
Magnhild Kverneland (Norway)

- The addition of 4 new members to the Task Force to ensure full geographical representation and adult as well as paediatric dietetic representation on the Task Force. The additional members are as follows: Dr Marisa Armeno, Argentina; Kath Megaw, South Africa Omnia El Rashidy, Egypt and Magnhild Kverneland, Sweden.
- The delivery of a Ketogenic dietary therapy workshops
 - 1st in South Asia with the lead centre as Pakistan 2-day virtual ketogenic dietary therapy workshop based in South Asia 30th and 31st July 2022
 - Very well supported by ILAE team
 - 1003 registrations from 53 countries
 - 48.4 % of the attendees were practicing dietitian, 32.3% were doctors, 13.2% were students aspiring to become dietitian & 6.1% were caregivers.
 - Most registrations were from India, Sri Lanka, Malaysia, Pakistan Bangladesh & Egypt
- 2nd workshop face to face and virtual hybrid based in Vietnam
 - 28 October 2022 in the Children's hospital, Ho Chi Minh City, Vietnam
 - Hybrid in-person and on-line delegates with simultaneous translation into Vietnamese was broadcast live, both to those attending in-person and online
 - Translation by a Paediatric neurologist - scientific terminology was accurate.
 - Faculty - 3 child Neurologists and 3 dietitians from Egypt, Malaysia, and India (Two were ILAE Task Force members)
 - In-person registrations - doctors 50, dietitians 5, other paramedical personnel 10
 - Virtual registrations - doctors 55, dietitians 6, other paramedical personnel 27
 - Total attendees 153, Doctors 105 Dietitians 11, other paramedical personnel 37, from 5 countries
- The Task Force has supported UK initiative to establish KetoRegister. Delphi processes are underway for data domains for inclusion. The link to participate in the Delphi process went out in the December 2022 Newsletter and appeared as an ILAE news item – will appear in ILAE newsletter.

EMERGENCY TREATMENT

TASK FORCE

Eugen Trinka (Austria), chair
 Ji Yeoun Yoo (USA)
 Jae-Moon Kim (South Korea)

Ching Soong Khoo (Malaysia)
 Adam Strzelczyk (Germany)
 Yamile Calle-Lopez (Colombia)

- Clinical practice guidelines on Status Epilepticus in Adult: These Guidelines are joint Guidelines between ILAE and EAN as well as EpiCARE. The Guideline proposal have been submitted to the respective bodies of the EAN and the ILAE. We received feedback from both societies, which we worked in resubmitted the Guideline protocol. Due to COVID-related restructuring of Cochrane-Group and newly elected and formed Guideline-Groups in the ILAE, there was a considerable delay before we got functional in 2022

again. An agreement between EAN and ILAE for this Guideline has been signed and the Guideline Group has been formed accordingly.

- Consensus definition on acute prolonged seizures and acute repetitive seizures: The FDA recently defined acute repetitive seizures and several investigational drugs are undergoing clinical trials, especially in the U.S. The availability of acute acting antiseizure medicines, necessitates a clear definition of acute repetitive seizures, seizure clusters and acute prolonged seizures. An international Expert Group, including members of the Medical Therapies Commission and the Commission on Terminology started a modified Delphi Process on the definition on these conditions. The aim is to produce an ILAE Task Force Report by the end of 2023.

ACCESS TO TREATMENT/GENERICIS

TASK FORCE

Archana Patel (USA/Zambia), chair
Ornelia Ciccone, Sr (Zambia)
Merab Kokaia (Sweden)
Ching-Shiang Chi (Taiwan)
Viviana Venegas Silva (Chile)
Edward Kija (Tanzania)

Tim Welty (USA)
Charles Hammond (Ghana)
Damian Consalvo (Argentina)
Thierry Darcis (UK)
Satish Jain (India)
Leonor Cabral Lim (Philippines)

- The task force has met regularly during this past year to discuss and finalize potential project plans across two main subgroups of work:
 - Barriers in innovative therapies
 - Challenges of basic access.
- The first subgroup focused on innovations has developed a proposal to assess the process of novel epilepsy treatments from conception to patient, compare to other conditions such as cancer, and identify barriers both due to regional variabilities and in general. Funding commitments from industry partners has been obtained to allow data acquisition and analyses for this study. By January 2023, a finalized proposal will be completed and from January to August 2023, initial data review performed with presentation of work planned for IEC 2023 (parallel session). The final report will be completed in 2024.
- For the basic access subgroup, the main project will be development of country readiness for IGAP. The plan for 2023 is to develop a list of indicators and survey around this, with launch of survey aimed for end of 2023.
- Crossing over the two subgroups are two smaller projects. The first is work on education around Generics. Revision of the prior Task Force on Generics' paper is being revised into a commentary and a proposal for a webinar through ILAE/IBE is being developed. These will occur in 2023. The second is looking at the availability of ASMs for specific epilepsy syndromes: Infantile Spasms, Lennox-Gastaut, and Status Epilepticus. This will be done in the following manner: (1) Overview of ASMs on country EM lists – to be

assessed by pulling 25-50% of country EM lists from each region; (2) Reviewing the recommended treatments per upcoming ILAE guidelines for these conditions; (3) comparing this data to the prior Task Force survey done on availability/accessibility; (4) surveying pharmacists in these countries on availability of these medications (if listed on country EM list) for patients.

REGULATORY AFFAIRS

TASK FORCE

Stéphane Auvin (France), co-chair

Dennis Dlugos (USA), co-chair

Jackie French (USA)

Alexis Arzimanoglou (France)

Lieven Lagae (Belgium)

Kelly Knupp (USA)

Eugen Trinko (Austria)

Emilio Perucca (Australia)

- The task force was involved in the Research Round table for Epilepsy in May 2022 organized by the Epilepsy Foundation with the participation of the FDA representatives. This year's topics were 'disease modifying' treatments and time-to-event designs. A publication is being prepared on the latter topic.
- The task force organized a session during the European Congress on Epilepsy in Geneva (July 2022) on the topic "Evolution of trial designs to improve treatment availability for infants: a regulatory opportunity/challenge". This open workshop was combined with a closed workshop with representatives of the European Medicines Agency. We had the opportunity to discuss several topics including extrapolation of efficacy of ASM in children, the time-to-event designs, and the design for monotherapy.
- We completed the procedure to ensure that the European Medicines Agency continues to recognize the ILAE as a Healthcare professional eligible organization at the EMA. Stéphane Auvin attended the meetings of HCP/POG. He also contributes to the group work on surrogate endpoints.
- The task force has had several virtual meetings throughout 2022 to define the topic of the main work of the Task Force for the current ILAE term. Different topics were discussed, and the committee members decided to work on inclusion and exclusion criteria and outcome measure for clinical trials on idiopathic generalized epilepsy. This will be a scoping review associated with a consensus by Delphi.

HIGHLIGHTS

- The 2 ketogenic diet workshops organized by the Ketogenic Diet Task Force) in South Asia (virtual) / Pakistan (in person)
- Successful contracts with industry to start the project 'Barriers in innovative therapies'. Adequate funding was obtained. (Access to treatment Task Force)
- Session at IEC Geneva: "Evolution of trial designs to improve treatment availability for infants: a regulatory opportunity/challenge" (Task Force Regulatory Affairs)

MEETINGS

The team met on 9 May 2022, 22 October 2022, 2 December 2022 (in person)

Report submitted by Lieven Lagae