Key input from patients to EMA workshop on generating clinical evidence for Long Covid

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Long Covid

- **Prevalence**: WHO Europe (2023): 36 million people affected in Europe, 1 in 30
- **Definition**: persistent symptoms >3 months after infection leading to functional impairment (WHO) ***define it as 6 months of symptoms?***
- **Prognosis**: **majority of people with chronic long Covid do not recover after 24 months and more** (>90% if symptoms >12 months; SARS1, MERS, ME/CFS)
- **Up to 50% fulfil** criteria for **ME/CFS** with poor quality of life and underfunded research
- **Gaps: therapies, biomarkers, definitions, evidence/data** (non-hospitalised patients, children, women, elderly; related conditions, risk factors, diagnostic tools, therapies), **registries/cohorts** (prevalence, progression), **consistency, standards, funding**

Recovery and symptom trajectories up to two years after SARS-CoV-2 infection: population based, longitudinal cohort study | The BMJ
Is 'Long Covid' similar to 'Long SARS'? | Oxford Open Immunology | Oxford Academic (oup.com)
The Health-Related Quality of Life for Patients with **Myalgic Encephalomyelitis / Chronic Fatigue Syndrome (ME/CFS)** | PLOS ONE
Research update: The relation between ME/CFS disease burden and research funding in the USA - PubMed (nih.gov)

Outcome measures

- **Focus on most debilitating (specific) cardinal (major) symptoms** such as exertion intolerance, post-exertional malaise, orthostatic intolerance, neuro-cognitive dysfunction, in line with **consensus diagnostic criteria for ME/CFS**
- **Target core biomedical mechanisms** including inflammation, vascular damage, hypoperfusion, autoimmunity, immune dysregulation, viral persistence & reactivation.
- **Define clinical phenotypes** & promote application of phenotype categorisation in research settings
- **Develop objective biomarkers** for social security, insurers and labour markets
- **No research centered on psychosomatic theses** as underlying cause of disease. They are inadequate, waste resources, impair social and financial security & harm patients.

Coordination, design, methods, infrastructure

- **Use, adapt, & validate existing research infrastructures and adaptive trial platforms** to study multiple interventions in parallel based on predefined algorithms
- **Use and adapt instruments validated for related conditions** such as ME/CFS
- **Data from hospitalised patients is a flawed basis for studies on long Covid**
- Better **coordination** across Europe (UK, Switzerland) and globally (US)
- Yes, we need RCTs to generate robust data ***but***, while we wait, **we also need proof-of-concept interventional studies based on existing and experimental marketed and shelved pharmaceuticals and procedures** for treatment!
- Yes, there are concerns about the off-label use of prescription drugs and other approaches lacking an evidence base, as well as DIY drugs/biohacking, online product, but patients **have no alternative**!

Patient and Public Involvement (PPI) and inclusion

- **Involve patients before and throughout trials**
- **Favour patient-initiated & co-created trials** to select **relevant** endpoints and outcome measures
- **Focus on those who need solutions most and not on the easy trials to conduct**
- **Focus on non-hospitalised patients** & **women**
- **Include most severely affected patients, housebound, bedbound.** They require innovative solutions incl. decentralised treatment studies, telemedicine, digital recruitment, house visits, mailing of medication
- **Consider children and older patients. Their phenotypes are not that different!**

Take home messages

Sense of urgency: 4 years and no treatment, no biomarker, no clear definition, no reliable data for a so far incurable disease affecting millions of people

1. **Focus** on core **biomedical mechanisms** (immune and vascular dysregulation) to develop **objective biomarkers** for and **treatments** of specific **cardinal symptoms**
2. **Use, adapt & validate existing assessment tools, definitions, research infrastructures** for related conditions such as ME/CFS
3. **Facilitate off-label use of approved drugs in related indications** (anti-coagulants, antivirals, immune-regulators, anti-inflammatory drugs) as long as there is no treatment
4. **Facilitate targeted funding** for research into post-infectious conditions & s**upport and facilitate private-public partnerships** to foster R&D
5. **Involve patients and the public** in research, healthcare, policies and funding decisions

Thank you for your attention.

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