Potential research resources, tools, and/or materials that could help advance ME/CFS research or enable early career investigators and senior investigators new to the ME/CFS field to more easily conduct research
I think ME/CFS should be a reportable illness. Physicians should be required to contact the CDC to report victims. There would be more patients that could donate blood, etc for research purposes.
Talk to the people who have been studying this for decades and actually learn from them. Ask them what they need, ask them what absurd obstacles they've been up against. Reach out to them proactively, individually: A list, to start: Nancy Klimas Susan Levine Jose Montoya Anthony Komaroff Dan Peterson John Chia Byron Hyde Irma Rey Ron Davis Charles Lapp Lucinda Bateman
Ron Davis' nanoneedle biosensor seems like a promising and very useful device.
larger data sets of people suffering with ME - and ability of the medical profession to identify and record these. Centralised database of sufferers and symptoms
Teaching ME/CFS in Medical Schools
Outreach, education, advocacy, and collaboration are all important aspects of this. First we must educate doctors that this is a very real disease with very real suffering. When awareness spread around what HIV was actually doing to people, research funds opened up and help ease had. The same with any highly publicized disease. By raising awareness of the impact ME is having on individuals, families, and communities, I beleive there will be an outcry of support and help. Until the impact of the disease is widely publicised and brought into the public conciousness, I think we will continue to be at a stalemate in all of these areas.
Ditto
Access to free multplex and genome analysis. A readily accessible list and link to active researchers and clinicians.
Wearables are now cheap and worn by many patients.

Our body consists of 5 major systems that work together to keep we alive.

Circular, nervous system, digest system, respiration system, Musculoskeletal system.The 5 major system control by special systems.If one control system weak or sleep(same like low charge) , a major system related disease are expressed. If 5 major control system are weak or sleep, Fatigue condition may come
In my case, I can find the cause of CFS / ME disease by psychic ability and it is possible to treat within 1-2 hours. I have already recovered a few bottles and found a normal health condition. I would like to openly treat about 10 patients. If the treatment effect is confirmed, it would be good to verify the therapeutic effect by extending the patient population to about 100-200 patients. Once these treatments are identified, it will be good to study new directions for treatment.

Encephalitis and Encephalomyelitis are Acquired Brain Injuries.

Above. Also contact Ronald Davis of Open Medicine Foundation who is currently conducting me/cfs studies at Stanford. Harvard as well with Michael VanElzakker. Also me/cfs advocate Jennifer Brea who has started collecting data. Dr. Nancy Klimas Immunologist has been treating patients for years, has data

Limit the number of common issues. There are too many symptoms and variables. There has to be a range that connects to the nervous system, the brain neurons, the digestive breakdown.

Use those most commonly found, stay away from the hundred different symptoms, I have a different issue every other week, facial muscle spasms, weak limbs, itchy legs. Those don't matter, the number one is WHY can I not walk up and down the stairs like a normal person, why do I need to decline long trips, why do I need to sleep during the day regardless of stimulant treatment?, Sleep all day, all night? What are the common denominators, what are the main cases?

Look at bedridden, the housebound, the jobless with no 'disability' assistance. I can't find a job because I have to disclose my disease. And at that, it is not a simple definition. I'm okay one day but need the next three days off to recoup? I don't know when my brain signals are going to send a total gut dump mode, or vomit mode, or sleep mode. No one wants to hire that.

Create a survey, create a tracking system, there are such smart new students out there. There are seasoned doctors open to research. Tools need to be tracking tools, tests on brain activity. A campaign to get information out to the university communities for thesis projects, get the info out to the research departments. There are those that will want to look into it.

My best advice is to limit the symptoms to the most common, make us track our issues, then track the nervous system and the brain functions. Let's give them enough data to find the breakdown, find the solution. Get us involved, we are not whiners, or at least ween the whiners out, we want to be treated like we exist.

begin a mentorship program where they are paired with an already established respected ME researcher---someone who doesn't think GET and CBT is going to cure us. We need to get rid of those folks in field (i.e. Natelson, Friedberg). They are doing damage and are not helping the community. Stop asking them to be part of committees and review panels. It takes us in the wrong direction. We must train scientists under people who are working to cure and treat this biological disease and are serious about finding the root cause of the disease vs the belief that it is psychosomatic. The psychosomatic narrative is keeping us from moving forward and returning people back to their lives pre-disease.

Patient participation is critical. Patients with ME often cannot physically attend a research commitment appointment(s). Perhaps funding could create home-visit participation via RN or other, if not contraindicated per study rules.
ME patient registry and have fairs or something to diagnose people en masse-we do this for other diseases and illnesses. People who do not have the resources to go to specialist after specialist need to be reached and included in studies. We need a ramping up of diagnosing people yesterday! They shouldn't have to wait 20 years after symptoms start to be diagnosed and then they can't participate in studies because it's been too long. Disrupt this ridiculous and vicious cycle, please.
NIH could help in the recruitment and performance of clinical trials based on enhancing the ACE pathway. It could also pursue epidemiological features of community outbreaks of CFS-like illnesses and illnesses occurring among family members and among co-workers. Researchers should be encouraged to study CFS within a larger category of brain diseases. Animal inoculation studies, similar to those previously reported at Pathobiology. 1995;63(3):115-8. Acute encephalopathy induced in cats with a stealth virus isolated from a patient with chronic fatigue syndrome, by Martin WJ and Glass RT should be conducted. The structure and function of ACE pigments should be studied both in vitro and in vivo.
There are no faculty jobs on ME/CFS, which is discouraging to attract PHD students and postdocts to the ME/CFS field.
Walk-a-thons for research, symposiums which include all medical fields to be held in every city, making them a required CE. Handbooks on ME facts to distribute to medical and lay peoples to increase awareness and increase knowledge of ME.
Unknown
This would be better answered by reaching out to other organizations like MEAction and the OMF.
-collaborate with other research that may be linked, ie GMO, pesticides, pollution, agriculture research, construction materials, dentistry, -seek out the sufferers and create groups who can meet, hire spaces, help to organize..if they are in touch with each other, they can mobilise and create more noise, more noise means more funding etc
ATTENTION! FUNDING! MONEY! ATTENTION!
SEE ABOVE
1. Invite senior investigators who are not currently involved to attend research meetings.
Tap into viral mengingitis charities for longtitudinal studies and better understanding of who goes on to develop ME. Their after effects list is essentially ME. My disease progression could have been captured and studied via this route.
Communication and mentor ship. Communicating existing research and collaborating with research on related diseases

STUDY "The Spark in the Machine" by Dr Daniel Keown (a UK ER doctor) who explains how acupuncture works for western doctors & patients. Two other doctors to consult: DR Hyde in Canada at Nightingale Research Foundation who published a new book on ME in 2019 & Dr Chia in Torrance CA whose son had the disease & whom he successfully treated with Chinese herbs. DR Hng in UK is one of the few doctors who is open about having ME & has also written a small book on it: "ME & Me". Watch UNREST the documentary. Read "Dirty Genes" by Dr Dan Lynch in Bellingham WA. Speak to Judy Mikovits about her research on vaccinations spreading retroviruses: viruses jump from animals to humans especially in labs where they are processed in mouse brains & then made mandatory for humans - even those whose genetics make it impossible to fight off viruses from ANY source.
Biobancos de muestras, a las que podamos contribuir los enfermos y puedan ser utilizadas por todos los investigadores
It's best to ask researchers in the field this question - as a patient I am not sure but open accept to high quality, accurate information is really important. The Open Medicine Foundation have done a great job at building international collaboration and data sharing - you should speak to them.
-Considering use of the DePaul Symptom Questionnaire -CFS and ME primer for clinical practitioners, 2014 edition -2015 Nat'l Academy of Medicine report -Potential biomarkers begin explored by the OMF
Bring back Judy Mikovits and reinstate her research.
Take advantage of resources in places such as the University of Alabama's Medical Sociology program. Engage with these programs and have students assist with the collection of data, quantitative and qualitative data analysis, etc.
The IOM report. The OMF Symposium. The IAMECFS.
The work Open medicine foundation scientists The work of Dr Jose Montoya at Stanford who is doing a brain study The work of Dr Lawrence Afrin (MCAS expert, this disease is a comorbidity) mast cell activation effects the brain The work of Dr Peter Rowe (structural cause for the disease - cervical stenosis causes problems with nerves and blood flow, nerves, and cerebral spinal fluid flow) ME Action group The movie UNREST and activism of Jen Brea on Twitter - most patients who saw this documentary

cried because we saw ourselves in her We need more neurologists involved !!! Our brains are being destroyed. Neurologists are the worst doctors we go through. They don't believe there is anything wrong with us. Our symptoms are very similar to MS but a normal scan can not detect plaques so we are pushed away and marginalized. Neurologists need to invent new technologies to look for our inflammation. Dr Montoya is using a Tens MRI for instance
Diagnostic flow chart.
Make sure all researchers know and use the Canadian and/or International consensus criteria for cohort selection.
The narrative of much ME research has been dominated by psychosocial research which to my reading clearly demonstrates that this condition is not psychosocial. There is no education for healthcare professionals in training so as doctors (speaking for myself) the message received is that this is a lifestyle choice - it wasn't until I developed ME 7 years ago that I learnt the truth about this complex condition - since then I have been able to educate many of my colleagues who have been very receptive to education
- more funding - a collection of all biophysical findings from all studies (with proper criteria) over the decades - clearing the diagnostic criteria mess by promoting only the ICC
Connect with Dr. Ron Davis of Stanford and other organizations working for MECFS Research
Fund more PhDs for biomedical research More research funding on neurological aspects, less on fatigue Allow greater patient recruitment via international studies, eg use of Redcap to collect data, use of International resources for collecting / analyzing biological samples
Magnetic Resonance Imaging, Positron Emission Tomography, muscle biopsies, Nuclear Magnetic Resonance Spectroscopy, muscle strength testing, muscle fatigue testing, maximal oxygen consumption, fatigue index, time to fatigue tests.
Re-read all the CFSAC proposals - Fund CFSAC. Sign up for daily published journal articles using Stork <support@storkapp.me> - using all our various names, fully spelled out and using acronyms so you'll see them as soon as they're published, follow Cort Johnson's Health Rising <ME-CFS-FM-News@healthrising.org> follow MEAction https://www.meaction.net/news/research Study the research of privately funded M.E. organizations: the Open Medicine Foundation, Solve ME/CFS, Simmaron, and read the blogs and common data elements reports of people with ME/CFS. I

suggest you read all of Jennie Spotilla's posts from over the years and David Tuller's Virology Blog about the methodological problems of the UK's PACE study of 2011 - still - even this past month - feeding and disseminating long ago disproved disinformation about our illness. Read the history of the hijacking of our illness by the BioSocial field and the history of inadequate diverted funding. Get to know what the longest-term patients have dealt with to become aware of our 'trust' issues. Talk to patients about other co-morbid issues they might never have mentioned before.

For example: Long before I developed the EB virus in college, I had my tonsils and adenoids removed at 7, was a 'polio pioneer' when I was 8 - had three rounds of the injected Salk Vaccine (not the placebo), I had the Parvovirus B19 in 4th grade, had Herpangina at 15, developed hidradenitis suppurativa in my mid-20's after the birth of my 47 year old son and my worst M.E. flares often follow episodes of a few very painful bumps on one (or the other - but only one side at a time) on my hard palate, which burst and form holes (non-herpes virus ulcers) that take weeks to months to resolve. I had an episode of alopecia areata after cataract surgery in 2015 and sometimes general hair loss after intense periods of stress.

My swollen lymph nodes with Mono stuck far out of my neck (yes like the Frankenstein monster) for several years after the mono, finally receding after 2-3 years, never to return - but later (after a round of weeks of warm-water aquatherapy) I developed a swollen right side inguinal lymph-node which still returns during flares. In 2001 an immunologist suggested I have this node surgically removed for microbiology studies but the surgeon removed 5 from there (thinking he was looking for lymphoma) and sent them to pathology instead of microbiology (hadn't read my file). After recovering from an infection following this surgery, my ME/CFS symptoms disappeared entirely for 8 full months. I was fine for the first time since college - I could have a glass of wine with dinner without getting sick, go out dancing, care for my husband, children, mother and run my manufacturing business. All my previous symptoms including the swollen right inguinal lymph node returned full blast after 8 months - but it was a lovely and complete respite which changed my attitude towards my illness. For about 30 years I never caught a cold or flu (or if I felt a cold coming on, all symptoms disappeared within 15-30 minutes). AND THAT'S JUST ME!

TALK to us. Perhaps some sort of key-word search of other p/w ME's lists could mine similarities with others' histories that might help with sub-types.

Wearables are cheap and the data can be uploaded easily. Patients worlwide are a rich resource and companies making bioharnesses to measure physiology and activity are interested in research and some prepared to donate the equipment. We can put people on the moon and train elite athletes yet can't devise an effective physiologically guided activity program for a person with ME/CFS and its associated exercise intolerance . It is a huge whole in the research that would be extremely profitable to address .

Biobanks & Internation Research Symposiums such as the excellent 2019 event organised by www.emerge.org.au

Tech geniuses could write a program for sorting and matching all research and clinical trials - whether completed or in progress - a program to be made available internationally. As doctors from many countries have researched this illness, it could be a way to share information in real time.

Patient input - Lenny Jason had 1500 patients working with him on his PEM survey and he ended up with a robust survey document that captures the essence of the disease. So much research lacks patient input and the researchers go off on their own tangent that misses the bulls eye and often provides incomplete or misleading info as they don't know how to interpret the data in light of patient's lived experience. After Unrest: https://drive.google.com/file/d/1RDBbXcG4tg0WEzlH8xq-Fe69pwDhB2QV/view?usp=sharing https://www.youtube.com/watch?v=yKoheNZlqXg .
$200M/yr funding needed for ME at NIH
Campaign for cfids patients to participate to submit lab tests that they have already had done or paid for to a database that can be accessed by researchers.
Massachusetts ME/CFS & FM Association That this is such a systemic disease as a motivation to research so many areas
Embark on an educational campaign to let researchers and clinicians know that the doors of NINDS are open and that money for research is available or at least forthcoming in the near future. Start funding some of the worthy research that has already been started but was turned down for funding previously (OMF, for example).
See above
Just as cancer and/or stroke victims have the standard Flags of Urgency, so should ME/CFS urgent s/sx to be made available to all physician's offices.
I think patient survey are good, asking each patient to list all their symptoms and a computer program to pick out the ones that we have in common, but you may already do this. Also a huge area is why do we feel pain so much more than others. Do all patients feel this way? or it that the Fibro? Again, many patients may be able to offer some of their time to do work from home, as well as mothers etc that need a small income while being home with kids. Volunteers to do some of it. Again, set up credit for classes in college.It seems like having enough data would be key to research, so that again goes to more labs and more conversations with patients about their symptoms and the computer program to contain it all. Work from home and volunteers.You have a whole workforce at your fingertips, us ! Some of us can still spend an hour or so here and there doing stuff for you. Figure out what you need, and then ask. Many of us are disabled but we can have a small amount of income as well. Or gift cards.
I would suggest social media campaigns as outreach to locate and hear from more patients living with ME/CFS. I imagine many of us would gladly participate in order to further awareness and research. There is currently no platform (digital or physical) that brings the ME/CFS community together in a way we can share and learn from each other. You can’t solve something without data and that can’t be limited to small control groups but the investigators could learn so much from the masses of patients if there was a publicly advertised call to participate put out on various social media sites. I

was only able to access support by searching myself and too many have to work just to make it through the day before they can dedicate time to finding resources online. By blasting a callout on social media you could generate a larger response rate from people that can share their story of how they were diagnosed, what precipitated their initial onset and most importantly what treatments are working for them. We have to be able to talk collectively and share information. With that information patterns and identifying markers could be learned and diagnostic and treatment plans could be built.
Did you know? DARPA has funded a new innovative blood filter for viruses. A home CRISPR gene editing kit can be found for as little as $157.
Major increase in funding commensurate to other diseases of burden. Major grants to entice seasoned and new investigators.
Contact with Atara Biotherapeutics about their EBV treatments.
All Medical Schools should teach the students about this disease, both for informational purposes, new ideas and contributions from doctors who do not carry the prejudices and stigmas associated with this illness, which turns away many doctors from the desire to deal with it.
A Clearinghouse of information gathered is needed, and would need to provide access and info to researchers. Gather all current and past health info from patients to seek out anomalies and similarities of patients.
A massive increase in funding is the only way to encourage researchers into the field.
Nightingale Research Foundation criteria. Would Aperiomics testing be useful in chronic fatigue situations?
Increased funding.
Patient forums. Talk to the patients via these, read what they have to say. Especially via Science for ME, a forum especially set up to promote patient/researcher interaction. Use of biobanks are encouraged, where appropriate, to provide samples collected to a constant standard. Related, abandon use of Fukada criteria - any research criteria must include PEM as a defining symptom.
Advertising with posters, brochures, online media (LinkedIn, Facebook), etc... with the intent to educate not the just healthcare professionals, but the general public so that ME/CFS can be recognized, as well as promoting the importance of clinical trials helping people. Early career investigators and senior investigators can learn from the seasoned ME/CFS researchers and physicians, which can be done by conferences in person and online. Education and awareness is key, and stressing the importance of funding ME/CFS research.
The best way to attract new researchers to study ME is to advance the awareness of what ME is, how many suffer from it and establish a base that collaborates all results of research done in the past in order to direct researchers in the right future direction. Without improving the awareness of ME and incorporating it as a known illness taught about in medical schools, and increasing the knowledge

through public relation means of what ME is and does so that the public, and doctors, are educated about it, noone is likely to want to research it or to contribute to funding research for it unless they or loved one has been personally impacted by it.

Every medical specialty requires periodic re-certification. Offering a reasonable number of CME credits for watching Jen Brea's UNREST and/or Ryan Prior's 'Forgotten Plague' with appropriate questions that must be answered to receive the credits might be a reasonable way to spread awareness, reduce the stigma, and lead to more respectful interactions with all our health professionals. At the end of each session, requiring the download of a copy of the IOM's 2015 clinical guide to diagnosis and treatment might mean more of us diagnosed. This would expand access by identifying more people living with ME/CFS for studies. Most of us are too ill to risk studies that are likely to make us sicker, but expanding the base through broader diagnosis might help.

More knowledgeable doctors so patients can be diagnosed properly.

Read my proposal underneath.

RFA’s to break the cycle of inertia

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) has an estimated prevalence of 0,2% [1] to 0,4% [2], meaning it is more common than multiple sclerosis, AIDS or systemic lupus erythematosus. Patients with ME/CFS have been found to be more functionally impaired than those with other disabling illnesses, including congestive heart failure and end-stage renal disease. [3] The economic impact of ME/CFS in the US is estimated to be 18-24 billion dollars a year. [4]

Based on the estimated disease burden, equitable research funding for ME/CFS by the National Institutes of Health (NIH) would amount to 188 dollars million per year. [5] This is more than fifteen times the amount the NIH currently spends. [6] An enormous disparity exists between the research funding that is required and what is currently being done.

One of the main reasons for this is a lack of grant applications. Researchers are hesitant to jeopardize their career by entering a field where funding is uncertain. Research proposals in the field of ME/CFS could also be scarce due to the fear of being rejected on irrational grounds. Even internationally respected scientists such as Ronald Davis [8] and Ian Lipkin [9] have been rejected or ignored when they applied for research into ME/CFS. ME/CFS is a relatively new disease that suffers from stigma and prejudices, even within the research community and medical profession.

The result is a cycle of inertia where researchers are unwilling to enter the field as long as it remains underdeveloped. I believe the most efficient method to break this cycle is by earmarking funds for ME/CFS. By issuing requests for applications (RFA’s) the NIH could attract new researchers to study ME/CFS. This would reduce the disparity between the societal burden of ME/CFS and the dire lack of funding devoted to this illness. The use of RFA’s has been successful in the past in ME/CFS [9] and the development of other fields [10].

I would, therefore, recommend the NIH to increase the number of RFA’s to further research into ME/CFS.

References

[1] Reyes M, Nisenbaum R, Hoaglin DC, Unger ER, Emmons C, Randall B, et al. Prevalence and incidence of chronic fatigue syndrome in Wichita, Kansas. Arch Intern Med. 2003 Jul 14;163(13):1530-6.
[2] Jason LA, Richman JA, Rademaker AW, Jordan KM, Plioplys AV, Taylor RR, et al. A communitybased study of chronic fatigue syndrome. Arch Intern Med. 1999 Oct 11;159(18):2129-37.
[3] Institute of Medicine. Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness. Washington, D.C.: The National Academies Press, 2015.
[4] Jason LA, Benton MC, Valentine L, Johnson A, Torres-Harding S. The economic impact of ME/CFS: individual and societal costs. Dyn Med. 2008 Apr 8;7:6.
[5] Dimmock ME, Mirin AA, Jason LA. Estimating the disease burden of ME/CFS in the United States and its relation to research funding. J Med Therap, 2016;1(1):1-7.
[6] Spotila J. (2018, October 21). NIH Funding for ME Goes Down in 2018. occupyme.net. Available at: https://occupyme.net/2018/10/21/nih-funding-for-me-goes-down-in-2018/
[7] MEAction. (2015, 20 August). Ron Davis on why his NIH proposal was rejected. https://www.meaction.net/2015/08/20/ron-davis-nih-proposal/
[8] Interview with Dr. W. Ian Lipkin, ME/CFS Alert Episode 95. (December 2, 2017).
[9] Neuroimmune Mechanisms and Chronic Fatigue Syndrome. RFA-OD-06-002. https://grants.nih.gov/grants/guide/rfa-files/rfa-od-06-002.html
[10] Limited Competition of the MAPP Research Network (U01). RFA-DK-13-507. https://grants.nih.gov/grants/guide/rfa-files/RFA-DK-13-507.html

1. Cull from what other domestic and international research efforts on the brain, aging , nervous system, allergies , etc are using and bring the tools and results into this research.
2. Incorporate tools used for personal data collection (sports industry and health). Get the FDA CDRH folks involved.
3. Incorporate more high tech tools -
Invite IBM, Oracle , Apple, Microsoft, and others to a workshop focused on how their tools can help.
4. Review technology from NASA and DARPA and other military organizations.

video conferencing with bedridden patients- versus apps to forpatients to use, with local contacts to come to the house and get required specimens. Work hard with the advocacy organizations to recruit patients. PRovide more incentive for patients to participate. I have to fly from Boston to SLC to participate and spend at least one night in a hotel- and yet i get $50 for participating. It would be far easier for more people to participate if funding to get patients to travel were covered. Further, having patients from only SLC/Utah or Connecticut includes several environmental biases. Diet should be addressed head on- with testing- say with labs in the UK that are looking at diet and the microbiome.

-Considering use of the DePaul Symptom Questionnaire
-Grants for researchers in training to shadow more seasoned researchers at their centers
-CFS and ME primer for clinical practitioners, 2014 edition
-2015 Nat'l Academy of Medicine report
-Potential biomarkers being explored by the OMF

Fund the leaders in the field such as the Open Medicine Foundation and Dr Ron Davis's team at Stanford, to enable them to recruit more early career and senior investigators to the field.

https://drmyhill.co.uk/wiki/A_Regime_for_Antiretroviral_Treatment_of_Myalgic_Encephalomyelitis
I have no idea. I want to say surveys to gather information about health history and current symptoms, but honestly, as a sufferer of CFS, it's just so hard for me to concentrate most of the time so filling something like that out would be difficult. Maybe registering patients, and then sending one question at a time, say once a week? One example would be asking if a person with CFS has been treated for ADHD. Then sending another in a week's time, maybe asking if they've ever undergone chemotherapy. And so on.
Once again FUNDING! That's the reason nobody chooses to research this HORRIBLE disease! Also NIH needs to fund so ALL doctors in the USA have to be aware of ME/CFS education on this disease is real and how severe it is! Then when people are being seen and getting help the world will get a better idea as to what the cause or biomarkers could be. It's impossible to get help with this disease and there are only about 15 doctors in the USA who know and try to help us!!!! The waiting list to get into one is over 2-10 YEARS!!!! Don't you see why people with this disease kill themself??? We are in so much pain and agony and don't have a life outside of our bed! Absolutely ZERO support from anyone! The government should be HELPING!
Contact **[…]** in Manhattan NY. He is 82 years old and has been treating patients for 45 years. There are doctors out there who know this condition and can help, but no one believes them.
From what I understand, the biggest obstacles are a lack of funding due to how strict the guidelines are for granting funding to individuals or organizations who want to do this research. Increasing funding and green-lighting more of these projects would be a helpful first step.
N/A
Open access to the data. So much of the research was/is done as one-offs and should be replicated. Sometimes it isn't even found online.
Compile database and ask permission of those who reply to emails to retain their contact information for upcoming / future trials etc. Home studies and other considerations of those individuals who are severely ill making it nearly impossible to participate or travel.
Money. A massive investment of resources would make all the difference
Fund conferences. Encourage sharing.
Patient participation and forums which are easily accessible on the internet. This should not be limited to specific countries. A website with the ability for researchers to upload questionnaires for patients to respond to to assist with their research. Physicians and patients diagnosed with FM should be made aware of such a website and be encouraged to take part in any research posted.
Look up "Ramsay's Disease: Myalgic Encephaloyelitis (ME) and the Unfortunate Creatio of CFS" Book by Lesley O. Simpson and Nancy Blake Blood volume, malleability of red blood cells, and issue of non-malleable cells' inability to travel through microcapillaries thereby depriving organs that depend mainly on microcapillaries - brain, muscles, endocrine system - of oxygen and waste removal.

I have to admit I am not as aware of research tools. I have a suggestion though...find a group to study how people have improved with the illness. That would involve interviews...that might help. I still think the problem is we are too invisible. I think there needs to be more incentives to study it. A few years ago I gave blood to a company who promised to study it. All the blood samples using Next generation sequencing of Dr. Cheney's patients are still frozen since the company decided to work with cancer..not us. Dr. Naviaux has still not published his study for Dr. Cheney's patients, and it may be due to some statistical issues, but it makes me so mad I have given my blood twice, and nothing has happened with these studies. Dr. Naviaux had a lot of funding issues, but he may need some help with his statistical analysis. I think funding, funding, funding, and publicity would help the most.
Bring M.E sufferers together they provide so much information
Use Ron Davies , jarred younger
The patients themselves have done thorough research on the matter. Start with them and listen to them.
An app that records HE/BP, sitting up time, feet on the floor time, PAINSS/PEM duration
1) Work with clinicians and researchers who are already established in this field to piggy back onto their decades long work product
I suggest you listen to the OMF foundation and the SMSCI organizations and listen to repected ME/CFS researchers, like Nancy Klimas, etc.
Willingness of NIH to fund more out of the box studies. Meetings with broader topics that can attract researchers outside the field.
Grant money.
push the 5 year NIH study results to close and publish them!
Any investigations and tools that can further explain post exertional malaise
Positive publicity and scientific grant money.

Reach out to the communities of people living with ME/CFS! Some frequent online communities, but targeting friends and family members who may be aware of a loved one with the condition is also important. Many people with ME/CFS want to participate in trials and studies, but don't know how to go about being included and are too hobbled by their condition to make a powerful effort to speak up, be included, and submit their experiences. Building a website to centralize access to study/trial sign-ups as well as provide the results of studies/trials could go a very, very long way toward finding the people who not omly CAN participate, but also desperately want to do so.
Again, I wish there was a single communication pipeline for all physicians to report what they have tried and what has worked or failed. There's no research being conducted in Austin, TX that I'm aware of, but I'd be willing to cooperate with just about any of the testing going on. Could my doctor simply follow the protocols for one or more of the research, do the blood draws, etc. and report them back to researchers. I've already made arrangements to donate my brain to Stanford when I die. I would love to be of help while I'm still kicking (sort of).
Contact researchers such as Dr Klimas, the Batemen Horne Center, Dr Systrom, Dr Jared Younger. Dr. Ron Davis at the Open Medicine Foundation is a wealth of information as he is a caretaker for a severe patient as well as one of the most prominent researchers. Video conferences and webinars for primary care physicians would be a great asset and first line of defense for making diagnoses of patients. Create a database for researchers to share information and exchange ideas. Create a curriculum for this disease that would be required for all medical , NP, and RN students that includes symptomatology, diagnostic guidelines, prognosis,
More money and attention always seems to help . . .
exercise testing can help a lot, but with the caveat that some patients experience delayed PEM, so day two may not be sufficient to show the results of that delay, also it is really exertion of any kind (physical, cognitive, or emotional) that causes PEM, so solely using exercise may not be sufficient & other forms of stressing the body & brain need to also be used
Don't know.
Collaboration with Environmental health Trust, Bio-Initiative Report, Beatrice Golumb, Magda Havas, Marin Pall
Funding to universities.
Set up a database with links to all published research conducted to date and categorise by specialty? This may highlight any gaps in current knowledge or highlight themes and linkages.
It's always good to hear researchers are sharing expensive equipment, but wouldn't it be nice if all the ME centers were equipped properly. Research needs funds for cutting edge equipment if it's to be done properly.
Researchers should include Judy Mikovits. She is correct ...Al my blood tests prove it. Stop the cover-up. My 6 year old son had EBV cancer that almost killed him.

In the past, researchers were told to avoid ME/CFS study as it would ruin their career. Nowadays, ME/CFS is one of the biggest unsolved medical mysteries on the planet.
You know best
The wiki I mentioned is something I keep up to date and should serve as an effective way to get people up to date fairly quickly on the current microbiome research: https://old.reddit.com/r/HumanMicrobiome/wiki/
Viral load testing for all patients
Gather groups of patients. Monitor them ALL over time. Use them as a control group. Select a sub-set to take part in tests of any new technology - diagnostic tests, trails etc. Most would be happy to do anything if it helped.
I think we need to push medical schools to add ME/CFS to their curriculum.
Regular / annual conferences for ME/CFS, all with the backing of the NIH Fast-tracking for the publication of ME/CFS research studies in medical journals - or simply published online in an open, sharing way. Major journals (e.g. Lancet; NEJM etc) should be actively encouraged to publish ME research. Establish a ME/CFS research 'Tsar' to proactively encourage new researchers to enter the field. Ideally, an established and experienced ME/CFS researcher(s) could be assigned to visit and give talks at many universities in an attempt to attract new researchers to the field. Perhaps set annual targets for the number of new researchers that are to be confirmed as conducting studies in ME/CFS. Give reassurances that the NIH will look very favourably on new entrants to the field in terms of research grants.
Big data analysis. Common databases. Sharing of information. Widespread acceptance of the disease.
Funding!!!!!
Patient input
Biobank. Crystal clear definition of PEM as the core symptom (not fatigue!). Currently many researchers don't even know about the existence of PEM and of those that have read about it many confound it with plain exercise intolerance. Guidelines on studying patients in and out of PEM.

Develop clear and universal data-tracking for ME/CFS patients to be able to log their own metrics day-to-day, and make these accessible via both a smartphone app, an online, browser-based interface, and (for those unable to access a computer), weekly batches of printable data sheets. Encourage everyone who either has or suspects they have the disease to begin diligently tracking their own biometrics, diet, activity, symptoms and energy levels, and train them in how to do this (either via their healthcare provider(s), or better yet, via training materials directly available online). Also make these resources clear and accessible to patient advocates or support persons, who may occasionally need to be the ones actually asking patients the questions and/or doing the data entry (allow the data tracking system to note this, as well).
FLUORIDE: http://www.multibriefs.com/briefs/icim/nutrition.pdf EMF: https://emfscientist.org/index.php/emf-scientist-appeal AAEM: https://www.aaemonline.org/positionpapers.php
Primary to generating reasonable hypotheses would include consultation with physicians who have been working with this population since the first modern outbreaks in the US in the mid-80s - Incline Village, NV; Lyndonville, NY. Both Paul Cheney, MD, PhD, and David Bell, MD have volumes of valuable insight that would lead directly to research. Dr Cheney long predicted the Dauer metabolome results long before Naviaux was even thinking about that. His work on the cardiac patterns is central to our functioning, directly related to functional disability levels, and holds across 100% of his nearly 10,000 clients from over 30 years of specialized practice. He should be interviewed in depth for his working hypotheses before we lose him; he thinks outside the box in ways that are both creative and solidly grounded in the sciences of physics and biochemistry, and is a true researcher at heart who would be a rich lode of material for generating testable, relevant hypotheses. Please don't let us lose his knowledge and intellectual contributions!
A.I. Deep learning, machine learning, epigenetic sequencing, micro biome sequencing, blood spectroscopy research, genetic engineering, light based imaging: reach out to the company OpenWater run by Mary Lou Jensen, offer to connect willing participants in the form of patients for any trial of the imaging tech, if at all possible this may give the mecfs community a new way of looking at mecfs and it's effects in the body sooner then otherwise possible.
Please see this survey: http://emfsafetynetwork.org/wp-content/uploads/2019/03/EMF_Wireless-Study-2019_Final-1.pdf Perhaps you could use this survey for ideas to launch a new one. EMFs are reported to cause fatigue.
EMF-Portal; SaferEMR.com; Powerwatch (in the UK); Bioinitiative Report; Examination of research showing a overlap between electomagnetic and chemical sensitivity
Fit subjects with monitors that monitor every bodily function that can be monitored. Heart rate, bp, sugar, oxygen, Look for anomalies. Blood assays. Run everything you can think of and compare this to healthy controls.k
Are there severe ME samples in a biobank? Setting up specialist inpatient units for the severe can give drs access to this highly debilitated, unreached community

RF Engineers would be needed, also probably Electrical Engineers like William Bathgate, Michigan who understands these effects on health (RF is not the only issue, the smart meters put conducted frequencies on the household wiring , the effect of that on CFS should also be explored.)

CLEVELAND CLINIC CENTER FOR FUNCTIONAL MEDICINE (CCCFM)- involve Mark Hyman's team!!!! They are the best ever at this. I cannot say enough about what they did for me. The before photo of my sitting, holding my daughter age 4 because I was too fatigued to stand at Christmas, side by side with the photo of me skiing with her a few years later sums it all up. There is so much home for people with CFS, and Cleveland's CFM has got the answers.

Dietitians trained in Functional Medicine, especially the Wahls protocol or mitochondrial diets, honestly just use the Cleveland Clinic CFM's or an IFM certified nutritionist. IFM= Institute for Functional Medicine (www.IFM.org)

Know that not all Functional Medicine physicians are adequately trained. I'd also use the American Academy of Environmental Medicine as well, though they lack the Functional piece. A good physicians would be well versed in both. I do not use any Physicans anymore who are not trained this way since I got nowhere before despite being in some of the best centers, such as Columbia, Cornell, Penn, etc.

I think the effect of environmental sources of aluminum might be something to look at however, I am not well versed In this area.

1a. A national database that researchers can access that integrates patient questionnaires for location (city, state), age, sex, how long since first symptoms started, what they think caused the onset, whether symptoms have fluctuated, gotten worse, improved over time, anyone else in the family (immediate relatives or extended family) have it, previous other conditions before developing ME/CFS (hEDS, migraine, IBS, sleep problems, allergies), other conditions diagnosed after getting ME/CFS (same things as listed previously), list of what their symptoms are. - this might help to subdivide patients
1b. Database of doctors and office mailing addresses where people with ME/CFS have hone for diagnosis or treatment attempts (This would allow the government to make sure to update these doctors with a standardized definition of ME/CFS, future name changes of this disease, updated ICD code, testing protocols, treatment protocols, etc to make sure the doctors who are treating the patients are actually getting the updated info in order to better serve their patients)!!!!
1c. Database of all medical schools, nursing schools in the country to get these same updated info on this disease to those who are teaching and the future doctors and nurses being taught!!!!!
2. Database comparing all previously published work into categories, so researchers can easily see what has been looked at previously, what the results were, and where gaps need to be filled in or more extensive work done.
3. A database where current research (unpublished) can update results (good and bad), so other researchers can quickly amend their strategies for what had been most recently learned.
4. Planned collaborations between researchers, whether interdisciplinary or to best utilize different advanced technologies in the same field of study (perhaps one group has a more advanced seahorse machine and another has a more advance spectrometer another has a more advanced something else, etc)

Creating and funding training fellowships will attract early career investigators and senior investigators to the field. In my career as an HIV psychosocial researcher, I observed established researchers in other areas e.g., cancer, joining the HIV arena to take advantage of career opportunities. The complexity of ME is intellectually challenging and many researchers will be drawn to the field if sufficient funding is provided.

The recent conference highlighted the existing contributions of post docs and research assistants to the ME field. The professional generosity of senior researchers like Dr. Maureen Hansen, who had her postdoc present, will encourage others at the beginning of their careers to focus in this area. As Dr. Anne Oaklander noted, she was mentored by Dr. Tony Koroshetz and her current Validation of Mass General Neuropathy Exam Tool (MAGNET) for Initial Diagnosis of Length-dependent Small-fiber polyneuropathy will encourage others to become involved.

There were a number of tools cited during the NIH Conference that appear promising and funding to validate their use could advance the field. From the Institute of Medicine (now National Academy of Medicine) 2015 report to the present time, promising avenues for further research have emerged including standardized questionnaires, new uses of scans, identification & convergence on some of the biomarkers to be pursued.

The 2011 Myalgic encephalomyelitis: International Consensus Criteria (ME-ICC) published in the Journal of Internal Medicine. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2796.2011.02428.x

The criteria were developed for both the diagnosis and research of ME. These are the only contemporary research criteria that differentiate subjects with ME from subjects with other conditions producing their symptoms.

The 2012 Myalgic Encephalomyelitis International Consensus Primer for Medical Practitioners. https://d3n8a8pro7vhmx.cloudfront.net/meadvocacy/pages/2292/attachments/original/1554817421/Myalgic_Encephalomyelitis_International_Consensus_Primer_2012.pdf?1554817421

In regard to research. the IC Primer states on page iv:

"Research on ME: The logical way to advance science is to select a relatively homogeneous patient set that can be studied to identify biopathological mechanisms, biomarkers and disease process specific to that patient set, as well as comparing it to other patient sets. It is counterproductive to use inconsistent and overly inclusive criteria to glean insight into the pathophysiology of ME if up to 90% of the research patient sets may not meet its criteria (Jason 2009). Research on other fatiguing illnesses, such as cancer and multiple sclerosis (MS), is done on patients who have those diseases. There is a current, urgent need for ME research using patients who actually have ME."

Create and open many more Centers of Excellence all over the country staffed by people in every medical field and discipline. (Neurology, Gastroenterology, Infectious Disease, Rheumatology, Dermatology, Dentistry, Physical & Occupational Therapy, Nursing, Complementary Medicine, Social Services, etc.) with both newly minted and experienced General Family Practitioners for oversight and referrals.

-Jack Kruse, Neurosurgeion- https://www.jackkruse.com/emf-5-what-are-the-biologic-effects-of-emf/ -EMF Analysis- https://www.emfanalysis.com/ -The Baby Safe Project- http://www.babysafeproject.org/ -EMF Scientist- http://emfscientist.org/ -Human Radiation Effects Group, http://www.electric-fields.bris.ac.uk -EMF-L Archives- http://www.wave-guide.org/archives/emf-l -Swedish Association forElectroSensitive- http://www.feb.se -Council on Wireless Technology Impacts http://www.energyfields.org -Wave-Guide Archives, http://www.wave-guide.org/archives/emf-l -Health Canada, www.hcsc.gc.ca/ehp/ehd/catalogue/rpb_pubs/99ehd237.htm -Nick Pineault's youtube channel: https://www.youtube.com/channel/UCSNatlkDIyLFSBsrNwAzYSQ
Adapt and use ICC definition.
Utilize the in depth questionaires that we filled out a few years ago.
It is not possible to advance 'ME/CFS' research since a disease with that name doesn't exist. So-called 'ME/CFS' research has not, and will never, lead to interpretable results. Instead, use: State-of-the-art medical knowledge about ME and CFS as presented in Byron Hyde's upcoming book. The International Consensus Criteria for ME. Patient experience data about ME as collected by the Stichting ME research, with validated questionnaire.
As always, money, especially to pay for new technologies and to develop new technologies.

Requests for Applications - as many as possible, in addition to the regular grants. The NIH needs to issue Program Announcements for ME/CFS, as the last was issued in 2012 and that is beyond unacceptable and frankly, tragic. As I suggested above in my previous answer, all physicians need seminars, required online training, or some type of protocol to become familiar with even the existence of this disease in order to have any interest in it at all. Researchers will need to be given collaborative access within MANY of the NIH institutes as ME/CFS is systemic and affects nearly every organ. Lastly, as this goes without saying - increase funding overall and make special funding allowances for ME/CFS grant proposals since many researchers are not able to fiscally undertake their own proposed research yet are very eager to carry out the research. Additionally, all researchers MUST have access to investigate every and any potential treatment option, since there is currently not one effective palliative treatment option for ME/CFS. This includes all not-yet FDA approved drugs or those still in the pipeline (example: patients had to go on a hunger strike for Dr. Peterson in Nevada to gain access to Ampligen and conduct trials on patients. That is actually the literal definition of inhumane). QOL is so absurdly low that literally any drug with any hint of potential must immediately be investigated and researched to the fullest degree.
?
The NIH might consider making an exception of its refusal to fund pilot work. Early investigators are left to compete for a small pool of private money in order to establish data. Financial constraints caused by job loss, impairment, and disability status are challenges to fundraising in the MECFS community. The pot is very modest. Small grants for pilot work would help early investigators with funding, the most difficult area of research, and incentivize growth in the field.
One of the areas which requires resources is the analysis of exosomes in ME. E.g. to identify the micro-RNAs which are contained in the exosomes and to identify the cells these micro-RNAs come from. One of the ways to provide this is for NIH to provide a grant/run an internal (NIH) project to obtain this data; a grant to an external team with related experience may encourage that team to focus on ME. Once the data is available then this may encourage new teams, with related experience, to work on ME.
Patient identification and diagnosis Physician and health care provider education Epidemiologists
Stop redundant research studies and come up with some new things. Epstein-Barr is been disproved as a Cause, Etc as having many other suggested causes. ME/CFS is genetic and viral probably a a virus attached to a DNA strand causing the mutation. It says it's dormant until catastrophic injury - illness although some people have it from birth as active disease.
1) Tools that could be used to advance ME/CFS research include leveraging existing cohorts of healthy individuals (e.g., UK Biobank, Woman's Health Initiative, Nurses Health Study, Framingham) that serially collect blood and other biospecimens to identify cohort participants who developed ME/CFS at some time after enrollment. These data could be a rich source for comparing cell function and markers (e.g., cytokines, mitochondrial function) with each person serving as their own "healthy" control. It might even be possible to capture individuals pre and post potential initiating events such

as mono, pneumonia, or some other viral/infectious disease event. NIH could issue a Program announcement and consider grants that would use these pre-existing data with possible follow-up of participants if allowed or if reconsent were possible.
2) We are fortunate to have multiple means to interrogate the biological features of ME/CFS (e.g., neuroimaging screens, metabolomic profiles, gene expression assays, microbiome sequencing). However, there is a need for more tools to connect the results from different assay types. Ideally, these algorithms need to facilitate the interpretation of complex results to enable validation of findings across assay types and present a more comprehensive picture of the systematic disruption observed within cases. Such tools do not need to be phenotype specific, but the deep data sets generated by ongoing ME/CFS studies offer fertile ground for developing such tools.

It is rare today to have no treatment for a widespread debilitating disease, but that is the case for ME/CFS. There needs to be a higher number of research grants. There are insufficient studies to confirm or disprove any of the theories of the cause of ME/CFS. As a result, it is difficult to develop a cure.

We don’t need any more small n size studies. We do need physicians/researchers who are motivated to become familiar with the illness and past research. And who will do more investigative work into how to reduce symptoms and reverse the illness.

WORKFORCE DEVELOPMENT

NIH ADMIN & GRANT REVIEW

PATHOBIOLOGY DISCOVERY

BIOMARKER

CLINICAL EXPERTISE

STAKEHOLDER ENGAGEMENT

In order to bring in more researchers and gain the attention of doctors/hospitals, we need the full commitment of the NIH toward finding a cure for ME/cfs by investing $200 million a year in research funding through RFA's. This is similar to what is spent on Parkinson's and MS. When the NIH sends this signal to the research/medical community such as they have done with AIDS, the medical community will surely respond. Recently, my friend asked her niece who graduated with a PHD in medical research what area she would focus on, the niece responded: Alzheimer's! My friend asked why, the niece responded... well that is where the funding is!!!

1. Introducing ME students early on to ME, Fibromyalgia, and Gulf War Syndrome.

Postmortem

-Ramp up NIH funding for ME/CFS research to an amount commensurate with the burden of this disease, e.g., $100 to 200 million per year (Dimmock et al., J Med Therap, 2016). A significant increase in funding dedicated to ME/CFS research will attract new researchers to the field and

encourage the application of new techniques.

-Promote opportunities for funding ME/CFS research to develop diagnostic tests through the SBIR/STTR Program. More than 3% of NIH's extramural research budget goes to this program, amounting to almost $1 billion. In the current solicitation, ME/CFS is mentioned in passing in the Basic Immunology Branch topic in NIAID. NIAID could promote this topic with ME/CFS researchers and also make sure that the program manager supports funding research on this disease. Even better, NIAID could introduce a new topic for ME/CFS research, including clinical trials in Phase II (U44).

You could recruit, for instance, 5 new doctors or residents to train with known experts like Dr. Levine, Dr. Bateman, Dr. Kauffman, Dr. Klimas, and Dr. Rowe. Then send them to Dr. Clair Francomano and other Ehlers-Danlos experts to be sure they'll know how to recognize Ehlers-Danlos syndrome and associated disorders and complications. Also to Satish Raj and other dysautonomia experts to make sure they know how to diagnose and treat dysautonomia. Hopefully all these doctors are willing to train new doctors. I believe some of them do already.

Then send your new doctors to new cities and do population-based surveys to test prevalence and possibly set up longitudinal studies (and offer information about the NIH inpatient study to anyone who seems to qualify). Have them choose a city to practice in where there's not yet an ME specialist, preferably in a state where there's no recognized ME specialist (shouldn't be hard, as that's most places: there may be an existing grant for underserved populations that can be used for this purpose, or there may need to be new funding for this type of grant when directed at a condition rather than a geographic area which lacks basic healthcare. Medicare and Medicaid may be able to assist with educational grants as I believe they fund most physician education, but possibly an outreach to the public to inform them of this would be helpful for increasing funding to those organizations.)

NIH would help place the physicians in a multispecialty clinic if they wanted to join an existing clinic rather than setting up a private practice, and advertise the new doctors to local universities and primary care practices, so they will know when to refer to the ME doctor, and that this doctor is a source of patients for ME studies, which NIH wants to get applications for. Hopefully some of these new doctors would be MD/PhD's and be able to contribute to studies themselves.

Then keep repeating the training process with a new set of residents. Increase the throughput when practicable.

MRI

Exercise testing and invasive exercise testing labs

Spinal tap analysis

Easy access to biobank and data sharing.

First and foremost a compilation of the studies done that used patients who fit the CCC or ICC should be posted in one place. Someone is going to have to look at each study to clarify which patient population was used. The CFS or ME or ME/CFS or SEID labels have been used interchangeably which is inaccurate.

www.MEadvocacy.org has made an attempt to clarify what patient groups were chosen for specific studies. Someone needs to undertake verifying patient groups for every study labeled that may fit into this patient group. Link is to the work done by MEadvocacy volunteers.

https://d3n8a8pro7vhmx.cloudfront.net/meadvocacy/pages/22/attachments/original/1516736594/MEadvocacy_Website_ME_Science_Links_January_2018.pdf?1516736594

Adequate funding. Education, education and education of doctors and researchers about this illness and the devastation it causes. And no researcher is going to venture into this field if he or she does not believe they will be able to make a living at it. So money is the number one consideration here, and money won't be forthcoming unless the people at the top make it a priority, and to do that, they have to believe it's real. They have to give it the same sense of urgency as ebola. It is a health crisis, but the victims are invisible, mostly homebound, for years and even decades. The neglect feels criminal.

Centers of expertise, to provide sharing of resources, and stable, long-term funding.

Strategies used to kickstart research in AIDS likely provide a good outline. This is hardly a new problem and should not require entirely new bespoke strategies.

App/computer based pooled data collection from wearable devices that monitor heart rate, step count, etc., ME biobanks

Share NIH April 4/5 tapes.

Share Stanford symposium lectures.

This disease is a discriminated against disease-use special funding for this category if available.

The very severe are rare; get this in rare disease funding.

Boldly talk about MEcfs clinical crisis every possible opportunity. IT IS POLITICAL THAT THIS DISEASE HAS BEEN IGNORED. I have lost great respect for CDC and NIH as I've learned this history. Widely share videos of patients, CCC and ICC provider guides, the Pediatric Primer.

One of the most daunting aspects for someone who wishes to enter the field is access to quality samples that are accompanied with detailed clinical data. The UK biobank is helpful but will not be able to supply all projects. I believe that a US ME/CFS biobank is needed, developed by a specific project designed to collect no-strings-attached samples from subjects selected by ME/CFS expert physicians. The number of such physicians is rapidly dwindling as many who entered the fields during the ME/CFS outbreaks of the 1980s have retired or are at retirement age now.

I suggest that an RFA needs to be issued for collection of samples that would go into an NIH-sponsored repository, from which researchers could request samples by a non-cumbersome application process. For someone to enter the field now, it is necessary to make an arrangement with

one of the small number of physicians who see a large number of ME/CFS patients. Some of these physicians are at large medical centers, or near ones, while others are not. Because of their interest in advancing the field, some of these physicians have been working with researchers with inadequate compensation and inadequate staffing. It is actually often more difficult for such physicians to supply matched control samples than patient samples, but matched controls from the same geographical area would clearly be optimal. I believe a project manager salary needs to be provided to any physician who will be collecting samples and clinical data as part of a repository project, but small projects-such as R21s-often don't have an adequate budget for sample collection. Participating physicians will also need to be compensated adequately for their time.

Currently a number of ME/CFS researchers are collecting and maintaining a modest number of samples in excess of what was utilized in particular projects, in order to have samples to propose to use in future grant proposals. Such samples often have strings attached-an expectation on the part of the physicians who identified appropriate patients or controls and the PI who coordinated the project to be part of future research publications, especially when the physicians have not been appropriately financially compensated for their efforts and have entered into collaborations with an expectation of being involved in data analysis and publication production. In some projects, the samples were not collected with consent forms that would allow deposit of the samples into a repository.

To avoid complexity, I think that a biobank RFA should be issued with the clear understanding that the participating physicians and the PI should not have any expectation of automatic publication authorship from studies resulting from samples acquired from the biobank. Such individuals should be, of course, eligible to engage in a collaboration with a biobank user that results in their meeting the criteria for authorship as stated by the ICMJE, but such involvement should not be a requirement for investigators to be able to access the biobank. Otherwise, potential biobank users might be reluctant to use it if it means becoming involved in unwelcome collaborations. The individuals who provided samples or project management should be acknowledged in publications deriving from repository samples, but not have expectation of courtesy authorship or collaboration. The IRB approval and consent forms must be ones that allow deposit of samples in a repository for undefined future projects.

What would go into an ME/CFS biobank needs careful consideration. The UK biobank has various fractions of blood, stored in several types of preservatives. Availability of blood fractions will remain important for future studies, but it would usually not be difficult to acquire urine samples as well, and urine has been promising in some diseases for development of biomarkers. I think a second, likely separate effort also needs to be developed to get other types of tissue samples such as muscles biopsies and cadaver samples, especially brains, given the abundant evidence that brain function is altered.

That's the issue, there hasn't been enough viable research done.

1. International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis international conferences allow scientist to present their work, stay up to date on others' work, and network with potential collaborators. Researchers also get the chance to interact with clinicians, which they may only have limited access to otherwise.
2. Scientific journal Fatigue: Biomedicine, Health, and Behavior. 50% of articles in this journal focus on

ME/CFS or conditions related to ME/CFS (e.g other fatiguing illnesses, fibromyalgia). The journal also is another venue for researchers to submit their work to editors and peer reviewers familiar with ME/CFS for possible publication. Oftentimes, journals reject ME/CFS articles immediately due to unfamiliarity of editors with ME/CFS, lack of peer reviewers, or perceived disinterest by their journal's readers. In fact, articles about ME/CFS are often the most-viewed, downloaded, and even cited articles for some journals.
3. A running list on the Trans-NIH ME/CFS website of other potential funders, whether governmental, nonprofit, corporate or other.
4. JAMA Reading the Medical Literature series might be helpful for clinicians but also non-clinicians who may gain a better understanding of how study results are applied in clinical practice: https://jamaevidence.mhmedical.com/Book.aspx?bookId=847#69031456
5. EQUATOR network for study design, data reporting, and evaluation:: http://www.equator-network.org/
6. As was done in the April 2019 ME/CFS meeting at NIH, hold another one-day meeting for new, junior investigators with potential ME/CFS interest with the extensive outreach that was done. This brought in 70 people! Then follow-up with attendees to assess their ongoing progress with respect to their research interests. What had kept them interested or not interested in ME/CFS? What incentives do they need to stay involved with ME/CFS? IACFS/ME would be happy to host a similar event during our conference and also partner with NIH on other methods to reach/ retain new/ young researchers.

NIH needs to uniformly use the same research criteria (the ICC) in all NIH funded research. NIH needs to stop using an array of incorrect definitions such as Fukuda and SEID which result in co-mingled cohorts which muddies the results.

Brain Autopsy: brain bank must test for borrelia burgdorferi and other tick-borne associated diseases for those diagnosed

It comes down to funding and good faith. Dr Klimas has mentioned she can get funding to do research into Gulf War Illness but no funding for ME/CFS. The same researcher applies for funding for two diseases but can only get money for one. She also indicated that she found a way to get money for an ME/CFS clinical trial which was to do some work for a Parkinson's Foundation on the condition that they fund an ME/CFS trialÂ¹. This is good news but these examples show the bias against funding ME/CFS research.

It is worth establishing specific funding for new entrants into the field, say 25% of the allocated funds for new players, but this should be done after established players are already being funded so that ME/CFS research does not look like a dead end to who would potentially consider moving into this field. This is perhaps the biggest problem with attracting new talent, convincing them that this is an area worth spending their careers in and that its no longer a dead end. The aforementioned Parkinson's Foundation wanted Dr Klimas to move away from ME/CFS to Parkinson's research, thankfully she declinedÂ¹. We have lost talented people who needed to pay the bills so moved off to greener pastures. Two examples that come to mind are Zaher Nahle and Raeka Aiyar.

Â¹https://www.healthrising.org/blog/2018/10/10/cdc-roundtable-multisite-klimas-reset-chronic-fatigue-syndrome/

Establish enough stability of funding to build an infrastructure for researchers to more easily conduct research -- a longterm strategic plan with periodic signposts and achievement metrics is one strategy for same

See above!

Research Case Definition - Meeting after meeting, report after report have stated that there is a lack of consensus on the research case definition for ME as well as lack of operationalization of research definitions. To ensure proper selection of study participants and strengthen the science, this issue must be resolved as soon as possible.

To do so, NIH must sponsor a meeting of expert clinicians and researchers of ME to reach consensus on this issue as well as to specify methods to be used to select ME patients for participation. Note - see also the MEAction submission.

Post-exertional malaise - PEM is a hallmark of ME and according to some people in the field also occurs in other illnesses though it manifests differently. It seems that in ME , the triggers, onset, severity, frequency and duration are different than in other diseases/conditions. However, there doesn't seem a thorough scientific characterization of PEM which means that health care professionals and researchers may be missing patients with it or mislabeling patients without it. Therefore PEM needs to be carefully characterized in order to facilitate diagnosis, educate healthcare professionals (and stakeholders) and to elucidate what is same/different about PEM in all conditions in which it occurs. A thorough understanding of the physiology of PEM, the cognitive and physical impact of PEM in ME and of the cognitive and physical triggers of PEM is essential. This characterization should also be done by an NIH sponsored project of ME expert clinicians and researchers as well as researchers in the other conditions said to have PEM. This should be done immediately so as to ensure that the research definition and methods decided upon by ME expert clinicians and researchers will incorporate this characterization of PEM to accurately adjudicate ME patients.

Engage with these and other initiatives to spark interest in ME research

Next Generation Researcher Initiative

NIH Strategic Plan on Women's Health

NIH Loan Repayment Program

NIH Inclusion Across Lifespan

NIH Brain Initiative- many symptoms are similar to those of TBI, concussion

Cognitive issues are significant for many patients and the inability to engage in cognitive exertion without repercussions (PEM for instance), severely limits the ability of patients to feel meaningfully engaged in life. Research is urgently needed to find ways of enabling patients to (paraphrasing my sons) 'access their brain at will, without repercussions.' Being able to do so would be a huge

improvement in quality of life for many patients - possibly enabling them to resume their education, return to work and/or otherwise feeling meaningfully engaged in life.

Reminder - oftentimes caregivers observe things patients don't notice and or can more accurately describe what happens to patients, so whenever possible caregiver input should also be used.

A strategic plan is urgently needed - it must be a strategic cross-agency research plan that demonstrates urgency and commitment , including timelines, necessary funding, stakeholder involvement at every level, outcome measures etc, as well as the dedication and drive to get it done. NIH is well -positioned to sponsor the development of this place.

Issue multiple RFAs, PAs, administrative supplements and other funding mechanisms

INNOVATE --- Because current NIH funding mechanisms and programs do not adequately fund ME research or bring sufficient numbers of researchers into the field, NIH should promptly (within 1 year from today and with stakeholder involvement from start to finish) develop programs and mechanisms that WILL adequately fund ME research and bring in new researchers. (The benefits of these new programs/mechanism will likely extend to other diseases/conditions as they will probably also serve as templates for them.)

Work strategically to significantly increase the number or researchers and clinicians in the field. Increasing the number of clinicians who can accurately diagnose ME, will increase the number of accurately diagnosed patients which will increase the number of accurately diagnosed people available to take part in studies which will in turn lead to clearer signals in studies.

Pair researchers/clinicians with patients/advocates as mentors to help people new to the field learn how pervasively ME impacts lives.

Workforce training should include presentations by patients/advocate (live, video conferencing, etc) about real life with ME (school, work, SSDI, encounters with HCP, housing, food access, social, etc) to help them better understand the range of difficulties encountered by PwME and as a reminder of why the work they are doing is so important.

For conferences, working group meetings, workforce training etc. include presentations by patients/advocates (live, video conferencing, etc) about real life with ME (school, work, SSDI, encounters with HCP, housing, food access, social, etc) to help them better understand the range of difficulties encountered by PwME and as a reminder of why the work they are doing is so important. (In 2014 at the IACFS/ME conference, a long-time researcher from a Federal agency was shocked to learn that patients had trouble accessing food and/or had trouble preparing it (for instance could prepare it but then not be able to eat it). She'd been in the field for years but hadn't been "hit with" this detail about the limitations imposed by ME. How many other researchers who purportedly study ME are similarly unaware of the HUGE impact of ME?)

Ensure that (stakeholders patients, advocates, caregivers, etc) are part of all projects (from inception to completion to publication of results to follow-up) related to ME.

Note - see also the MEAction submission:

Workforce Development

with stakeholder participation as an integral component of the education process - Reminder - oftentimes caregivers observe things patients don't notice and or can more accurately describe what happens to patients, so whenever possible caregiver input should also be used.

NIH Administration Structure and Grant Submission and Review

Pathobiologiy Discovery

-include other illness groups as well as healthy controls to ensure that results are ME related and not simply an indicator of illness

Biomarker(s) Validation and Discovery

Clinical Expertise

Stakeholder Engagement

-must also include caregivers - Reminder - oftentimes caregivers observe things patients don't notice and or can more accurately describe what happens to patients, so whenever possible caregiver input should also be used.

- Large Scale Patient Registries of clinical and patient data

- Digital Marketing Outreach -

o Facebook ads to target and reach patients

o Facebook groups to recruit patients for studies

- Personal data platforms for patient's data

o Platforms that allow patients to securely upload a variety of medical data to share with clinicians/researchers e.g. blood results, activity data etc. something like these:

o https://www.healthbank.coop/

o https://pryv.com/

o http://www.myhealthmydata.eu/why-mhmd/

- Remote and Local Data Gathering Protocols - Patient Centric

o Use of digital patient devices for activity/heartrate/sleep monitoring, spirometry, lung/gastric inflammation etc.

o Use of digital patient apps for daily symptom recording e.g. fatigue, cognition, headaches on a VAS.

o Brain activity home testing using equipment suitable for mail and return (a very basic qeeg type test with online support for usage)

o Remote interviews using Skype or similar. Interview caregivers as a proxy if needed.

o Fluid collection - allow participants to use local clinics or home nursing services for blood draw and a courier delivery system to the relevant lab.

- Leverage existing advanced testing techniques e.g. brain imaging (SPECT, DAT scans), neurophysiology (QEEG etc.), vision neurology testing (example research).

Cross-site working and exchanges.

Network for young researchers (Thinking the Future network).

Sharing data and samples.

MEICC criteria

We believe that research resources, tools and/or materials that could help advance ME/CFS research or enable early career investigators and senior investigators new to the ME/CFS field to more easily conduct research should include:

- Funding multi-disciplinary researchers working within graduate programs, so that young researchers entering the field can be assured of sustained funding with a career in this field.

- A biobank with information from thousands of patients to include: blood, urine, and tissue samples; genetic info; images; and, data reflecting symptoms, disease progression, and treatment modalities used. Ideally, samples would be gathered at different times and states of disease progression, reflecting diversity of ages, sex, and ethnic background.

- A Voice of the Patient document, similar to the CDC's version, but different, that explains what patients were like before their illness, the ways they descended into illness (not everyone with ME/CFS developed it after contracting a viral infection), and the course of illness and what it looks like for people who are mild, moderate, or severe, and what top-of-the-line treatment looks like for various patients.

Funding!!!!

Educational materials, books, lectures and tools are listed on http://www.me-ireland.com/training.htm

-Replicate the National Database for Autism Research for this field. This is where subjects are given an anonymous identifier that can be tied to multiple studies. Actual data are uploaded and can be compared, correlated, etc. This is important because longitudinal studies are lacking.

Ron Davis's nanoneedle technology has compelling results & requires respect from NIH. Decades of neglect can be somewhat assuaged by urgent & intensive funding, participation & positive support from NIH.

1. Big Data Analytics
2. State-of-the-art imaging systems, including tissue immunoprofiling systems
3. Watson as an ME/CFS AI medical librarian

Use International Consensus Criteria and International Consensus Primer for Myalgic Encephalomyelitis as defined by the experts.

Support Dr. Ron Davis and his cohorts. This genius has a need: his step son is severely compromised by ME. His Nano whatever needs expansion to test more samples at a time. Support and help in any way in which we can. GET TO THE MEDICAL COMMUNITY each and every one to let them know that we are not out of our minds. Distribute materials to them that have been created by the Open Medicine Foundation-such as the continuing education from Indiana University- 2 hours and inexpensive-I have walked it into each of my providers. I think perhaps 1 has taken me up on it. This is imperative; the doctors are unable to help and treat this disease as hypochondria. If only they knew, and YOU HAVE the ability to bring it to them.

Again, an emphasis on Systems Biology and a Systems Sciences approach to systemic pathologies is imperative to make progress. We need to encourage young researchers and established as well to consider that these modern complex diseases are not linear failures of singular biologic factors. They are multi-systemic, complex conditions with multiple failures in communication and control mechanisms (cytokines, hormones, metabolomics, etc). An additional focus on cellular level problems is probably important, but this too is a hugely complex arena. The cell may be the most complex systems of all and is the number one candidate for competent systems biology. And by systems biology I don't mean simply adding computational data analytics to deal with the messiness. I mean starting from scratch with an 'emergent property of disease' approach to the systems involved. Starting with familiarity with Ludwig von Bertelanffy, and moving from there... See the 2002 Science article on Systems Biology for a start... (Science 01 Mar 2002: Vol. 295, Issue 5560, pp. 1662-1664, DOI: 10.1126/science.1069492)

WORKFORCE DEVELOPMENT
Barrier:
Ignorance about ME in academic community
Stigma/lack of disease validity in academic, medical community
Lack of senior mentorship support to young investigators, discouragement to enter field

Lack of evident funding stream to entice outside expertise, sustain a dedicated young investigator's career
Lack of accessible bioresources (lack of large biorepository, patient registry, paucity of clinical expertise)
Lack of in vitro/in vivo models to entice outside expertise, sustain a dedicated young investigator's career
High threshold of disease knowledge for entry into the field
Paucity of review materials in literature
Publications often relegated to niche/low impact journals
Psychosomatic narrative continues to pollute literature
Strategies:
Heavily leverage NIH intramural and extramural networks to actively promote disease awareness and scientific intrigue; actively bait interest in disease mystery, novel opportunities for discovery
Leverage Director Collins's and Koroshetz's megaphones, utilize every NIH media opportunity available to make the untapped scientific opportunities and plight of patients known within academia and industry
Engage a concerted campaign to rectify medical and scientific stigma
Sponsor NIH conferences annually to endorse validity, disseminate findings, facilitate collaborations; include dedicated day(s) and poster sessions for young investigators
Require publication of whitepapers out of NIH-sponsored events
Disseminate recorded materials out of NIH-sponsored events
Facilitate representation at society conferences, encourage block symposium to elevate disease profile, invite high-profile scientists to leverage star power
Exhaustively publicize new disease findings, CRC results
Targeted outreach soliciting proposals from relevant intramural and extramural domain experts (senior PIs)
Compile and disseminate a disease primer/educational videos for new investigators of biologic knowns, clinical resources, crash-course on disease-specific issues
Facilitate matchmaking between domain experts and clinical expertise/bioresources
POs perform matchmaking between applicants and outside domain experts during grant submission/revision
Issue dedicated disease-specific RFA to entice outside expertise, demonstrate capacity to sustain a dedicated young investigator's career
Improve perception of limited funds by e.g. broadcasting existing funding availability and SEP support across various institutes, via NIH communiques, Director's office
Issue administrative supplements to support interdisciplinary involvement of senior newcomers
Establish career training and mentorship program for young investigators
Develop and disseminate documentation encouraging young investigators to enter the field, ensure a viable career path
Further support a network of young investigators through the following initiatives: annual NIH young investigators conference; website; Program Officer availability for career growth; grant application support; proactive notification of applicable funding/fellowship opportunities, facilitation of collaboration and mentorship matchmaking dispersal of information on available bioresources; quarterly email updates on new resources/research findings targeted education on applicable funding opportunities; supplement awards to enable young investigator collaborations with established

PIs/CRCs; encouragement and sponsorship for society conference attendance; encouraging young investigators to evangelize about ME to their colleagues; and providing materials summarizing research knowns, needs and opportunities
Create a large data and biorepository for comprehensive study of disease landscape
Create a patient registry to support study recruitment and data/sample procurement
Support resolution of clinical expertise bottleneck to facilitate patient/data/sample access
Fund development of in vitro/in vivo disease models
Fund epidemiologic studies
Fund biomarker discovery, disease-specific instrumentation and methods studies
Utilize existing NIH programs and work with other federal and state agencies to incentivize specialization and research via loan forgiveness programs
Pair researchers with patients/advocates as mentors to help people new to the field learn how pervasively ME impacts lives and why work in this field is important
For conferences, working group meetings, e.g., include presentations by patients/advocates (live, video conferencing) about real life with ME (school, work, SSDI, encounters with HCP, housing, food access, social) to help them better understand the range of difficulties encountered by people with ME and as a reminder of why the work they are doing is so important

NIH ADMINISTRATIVE STRUCTURE, GRANT SUBMISSION AND REVIEW
Barrier:
No formal institute home, administrative ownership, institutional accountability
ME not listed on NINDS website list of diseases
No dedicated full-time program officer(s) focusing solely on this disease
Insufficient trans-institute coordination, institute participation, inconsistent funding commitments
Insufficient commitment across NIH to making tangible progress on this disease
In being handled exclusively by a Trans-NIH WG process, ME is not prioritized within any one institute; unclear how Trans-NIH WG recommendations translate into institute-specific strategies, goals, resource commitments, and actions
Lack of transparency and stakeholder engagement with the Trans-NIH Working Group
Ad hoc nature of Special Emphasis Panel not sufficient to ensure consistency in application review
Dearth of qualified, informed grant reviewers, confounded by COI as collaborators in small research community
Multidisciplinary representation required for each SEP review
Not every ME application is captured and channeled through SEP
Clinical trials applications not supported/reviewed by disease-informed reviewers across institutes
Lack of disease-specific FOA to entice new researchers, support career focus
Lack of ME researcher knowledge of availability of relevant RFAs in various institutes
Lack of meritorious applications (rigor, novelty, significance)
Strategy:
Develop a comprehensive outcomes-focused strategic plan that has the necessary funding, coordination, cross-institute commitment, stakeholder engagement, and NIH political leadership to aggressively address the challenges and barriers and truly “accelerate ME research”. This plan must leverage the numerous opportunities to deliver patient-focused outcomes while simultaneously building up foundational knowledge about ME.

Establish an Office of ME Research within the Division of Program Coordination, Planning, and Strategic Initiatives of the Office of the Director staffed with:
1) A director responsible for developing and coordinating a long term fully-funded strategic plan, integrating ME initiatives into every Institute and Center (including leading/liaising with the Trans-NIH WG), who functions as a trans-institute "czar" (as recommended by CFSAC) driving progress across institutes; and
2) At least one staff member responsible for outreach and coordination across all research priorities in each of the extramural and intramural grant programs, working with Program Officers in various institutes to facilitate informed review committees and ensure ample support to applicants during grant preparation.
Increase Trans-NIH Working Group transparency and stakeholder engagement
Hire multiple full-time Program Officers within ME's formal home institute focused exclusively on ME to support grant applicants, career development, study section composition
Periodically re-evaluate Special Emphasis Panel effectiveness, composition, reviewer knowledge of disease-specific issues
Bolster disease-specific grant writing support from Program Officers (e.g. regular grant assistance call-in "office hours" with NINDS and NIAID POs, invite junior/senior investigators as well as outside domain experts, listserv, website covering study design issues)
Engage a Program Officer in each of the Trans-NIH institutes with ME in their portfolio who knows how to navigate their institute
Issue FOAs including those with set-aside funding; RFA and/or Program Announcement would resolve uncertainty about where to send applications and streamline grant application process
Make guidelines and process very explicit and transparent to grant applicants (who to contact and when in considering submitting an application, whom to contact at various institutes and on the SEP)
Ensure grant applicants and reviewers are given disease-specific CDE guidelines, feedback, and guidance
Ensure clinical trials applications are handled by staff knowledgeable of ME issues
Overcome reviewer bias toward significance versus basic questions that are not necessarily novel but are essential for this field at this time; ensure field-informed reviewers know to defend the merit of addressing basic questions in this disease
Ensure grant reviewers understand and acknowledge the value of unbiased exploratory approaches versus standard hypothesis-driven proposals in this disease at this time

PATHOBIOLOGY DISCOVERY
Barriers:
Artificially heterogeneous cohorts due to variable research case definitions not requiring PEM
Lack of validated, standardized objective measure(s) or biomarker(s) for cohort selection
Intrinsically heterogeneous cohorts due to biologic disease variability (diversity of severity, diversity of symptomology, potential diversity of triggers/etiology, confounding comorbidities, overlapping syndromes, multisystem involvement, fluctuation, progression/remission)
Lack of dedicated disease-specific research funding opportunities
Lack of in vitro/in vivo model systems, reliance on primary biospecimens for all experiments
Dearth of clinical research resources: very few expert clinicians to support biospecimen pipeline; limits to properly diagnosed and characterized patients engaged with medical care (due to stigma,

misperception, psychosomatic narrative, absence in medical education, few expert clinician); lack of centralized registry to channel patients toward qualifying research studies
Paucity of aware, interested, capable, disease-informed researchers
Lack of/failed study replication efforts across multiple/larger cohorts
Spontaneously fluctuating and provoked disease state
Need for appropriate control and illness comparison groups to support specificity
Narrow focus of recent infectious acute-onset intramural study
Strategies:
Issue FOA with set-aside funding for exploratory etiology investigations
Issue FOA to develop in vitro and in vivo models (e.g. serum transfer studies)
Expand cohort sizes and define selection criteria for replication of prior findings
Encourage mitigation of artificial cohort heterogeneity by requiring PEM for all study participants
Clarify methodological definition reporting standards to support study reproducibility
Encourage use of sample sizes adequate to perform subgroup analyses on heterogeneous cohorts
Encourage all researchers to conduct subgroup analyses within their datasets, supply suggested stratification variables (e.g. definition +/- PEM, clinical phenotype, symptomology, severity, comorbidities), and establish reporting expectations
Solicit and fund "phase 0" exploratory trials in stringently-selected, enriched cohorts with the goal of pursuing exploratory outcomes, responder/non-responder and subgroup analyses rather than proving efficacy
Encourage systems biology approaches, aggregate dataset analysis
Utilize unbiased exploratory omics approaches with subgroup stratification analysis
Support large GWAS to identify risk variants, candidate pathways perturbed
Encourage accounting for baseline vs. provoked state with provocation studies
Account for spontaneous fluctuation with longitudinal data capture, utilize time interval assessments to capture fluctuations, do not assume static even when unprovoked
Survey and account for use of off-label pharmaceuticals, supplements
Define and utilize appropriate control populations/illness comparison groups (i.e. activity-matched, fatigued, inflamed groups); ensure healthy controls are free of ME symptoms; standardize methods for determining control appropriateness
Large data and biorepository for comprehensive study of disease landscape
Establish disease-specific autopsy tissue biobank
Support multi-disciplinary research studies that look at multi-system interactions
Funding mechanism to support writing up case reports and comparison group studies
Accelerate intramural infectious onset study; see multiple participants in parallel
Initiate design process of comprehensive intramural studies on other subgroups (e.g. long duration, severely ill)

BIOMARKER(S) DISCOVERY and VALIDATION
Barriers:
Heterogeneous cohort even when properly characterized with case definitions that require core features of the disease such as PEM
Lack of study reproducibility, incongruous findings across cohorts due to: intrinsic biologic heterogeneity, definition/selection criteria, specimen handling, laboratory methods
Lack of replication studies of prior findings in larger cohorts

Lack of comprehensive study of disease landscape to support subgroup analyses
Specimen handling issues (e.g. culture of tissues without donor serum)
Strategies:
Issue FOA with set-aside funding for biomarker discovery and validation
Large data and biorepository for comprehensive study of disease landscape
Expand cohort sizes and define selection criteria for replication of prior findings
Deploy systems biology approaches for aggregate dataset analysis
Support unbiased omics approaches with subgroup stratification analyses
Fund large GWAS to identify risk variants, candidate pathways perturbed
Encourage targeted subgroup stratification analyses defined by clinical phenotype, severity, comorbidities, symptom profiles
Define, disseminate and incorporate into grant review feedback disease-specific specimen handling specifications and encourage adequate methods reporting

CLINICAL EXPERTISE
Barrier:
ALL ME research currently relies on primary patient-derived data and/or biosamples
There are very few expert clinicians with substantial experience diagnosing, monitoring or treating this disease
The pool of diagnosed patients and the pipeline of patient-derived research resources are severely limited by the paucity of expert clinicians
These expert clinicians are overburdened with clinical care obligations and existing research efforts and do not have the bandwidth to participate in new research collaborations with newcomers to the field or young investigators
This small group of clinicians are nearing retirement, which will further diminish research capacity
The collective knowledge of this clinician group is not recorded or disseminated, which is a barrier to new and less experienced clinicians
ME diagnostic and treatment protocols are not incorporated into medical education curricula
Medicare only allows for a 15-minute meeting in ME, meaning this complex illness is financially impossible for clinicians to take on
Lack of objective testing/biomarkers poses an uncomfortable challenge to physicians in making an ME diagnosis by exclusion of other diseases and subjective symptom report
Strategy:
Fund, convene and maintain a clinical network leveraging medical and scientific expertise
Document, operationalize and encourage dissemination of clinical expert knowledge to researchers and the medical and patient communities
Leverage Director Collins' political capital to draw attention to the clinical care crisis and pressure other federal agencies and medical societies to resolve barriers in expert clinician workforce growth, medical education, medicare funding, and accessibility to clinical care
Provide leadership for a cross-agency structure to identify and tackle critical bottlenecks in clinical care and the clinical research pipeline
Utilize existing NIH programs and work with other federal and state agencies to incentivize clinical specialization and research via loan forgiveness programs
Pair researchers/clinicians with patients/advocates as mentors to help people new to the field learn how pervasively ME impacts lives and why work in this field is important

STAKEHOLDER ENGAGEMENT

Barriers:

Dissolution of CFSAC has left the ME community with no channel through which to communicate needs to NIH or other federal agencies

No specific venue within NIH for community engagement

Lack of transparency and community engagement with the Trans-NIH Working Group

Sparse disease-specific information and resources available online

Lack of venues for researcher engagement with patient/caregivers to understand disease features

Level of patient physical and cognitive impairment, disability and lack of financial resources

Not enough CRCs

Lack of clinical capacity within CRCs, dependent upon sparse, busy, distant outside clinical expertise

Not enough scientific and clinical outreach, lack of clinical education component

Not enough collaboration, data sharing

Strategies:

Leverage Director Collins's political capital to ask HHS to restore CFSAC

Develop a structured, NIH-led venue focused on advancing research that engages: ME patient, caregiver, and advocate communities; clinical communities; research communities; relevant NIH institutes; other federal agencies; academic institutions; medical and scientific societies; and the pharmaceutical industry in order to:

>> undertake a holistic approach to the wide-ranging problems impacting ME research

>> engage cross-agency collaboration in resolving interrelated and interdependent bottlenecks in growing the field

>> provide leadership and structure for a venue which facilitates movement on key issues that fall outside NIH's remit (e.g. HHS, Department of Education, SSA, VA) but impact the community and ultimately the capacity for growth in NIH-led research (such as diagnosis, clinical care, medical education, school accomodations, social security disability, and medicare).

Establish Trans-NIH Working Group transparency and stakeholder engagement

Proactively leverage Director Collins's and NIH Institutes' political capital and networks to increase disease awareness and active engagement among medical and scientific societies, academic institutions, and federal agencies

Leverage NIH intramural and extramural networks to promote disease awareness and scientific intrigue; actively bait interest in disease mystery, novel opportunities for discovery

Initiate a concerted academic awareness campaign to bait scientific interest

Leverage Director Collins's and Koroshetz's digital megaphones, utilize every NIH media opportunity available to make the untapped scientific opportunities and plight of patients known within academia and industry

Initiate a concerted public awareness campaign to rectify medical and scientific stigma

Fund additional CRCs

Encourage/require and support CRC education, clinical training, outreach efforts

Sponsor NIH conferences annually to endorse validity, disseminate findings, and facilitate collaborations; include dedicated day(s) and poster sessions for young investigators, and invite the patient and advocacy communities to attend and participate

Disseminate recorded materials out of NIH-sponsored events

Require publication of whitepapers out of NIH-sponsored events

Facilitate representation at society conferences, encourage block symposium to elevate disease profile, invite high profile scientists to leverage star power
Exhaustively publicize new disease findings, CRC results
Compile and disseminate a disease primer/educational video(s) for new investigators of biologic knowns, clinical resources, crash-course on disease-specific issues
Facilitate matchmaking between domain experts and clinical expertise/bioresources
Initiate and host digital roundtable events between researchers and patients/caregivers to facilitate discussion and brainstorming around key issues in ME research (e.g. barriers to study participation, what PEM feels like, triggers of PEM or long-term relapse)
Include ME in the list of diseases on the NINDS website
Expand the NIH digital space addressing ME research to include recorded materials (conference presentations, links to CDC resources), disease-specific educational materials for researchers and newcomers to the field, links to patient registries and available data/biorepositories, links patient support/advocacy organizations
Disseminate new research findings, funding opportunities, study recruitment opportunities, event notifications via listserv
Support a patient registry to facilitate study recruitment and data/sample procurement
Establish and maintain NIH-funded centralized data and biospecimen repositories, which can store anonymized clinical and research data including imaging data, and biospecimens collected from well-characterized patients in past, current, and future research studies, including existing repositories. Make accessible to outside researchers.
Fund epidemiologic studies
Support resolution of clinical expertise bottleneck to facilitate patient/data/sample access
Fund, convene and maintain a clinical network leveraging clinical and scientific expertise
Document, operationalize and encourage dissemination of clinical expert knowledge to researchers and the medical and patient communities

I would find it incredibly helpful to have assistance developing survey instruments, intake questionnaires for clinical practice, and screening tools unique to my subtype.

I also crave training/best-practice platforms (model: OPENPediatrics) to grow a stable of talent qualified for the ME trauma subtype and opportunity platforms to match talent with need. Even if his or her clinicians' interest is piqued, a lowly Patient Zero needs help to "flip" internal medicine practitioners and specialists with a gateway expertise (e.g., HIV/AIDS), to start offering ME/CFS care.

I have specific rock stars in mind who would be ideal beneficiaries of targeted funding for a pilot training module. They have Ivy League credentials, community bona fides by birth, and youthful energy, but long experience with community health and HIV/AIDS.

Their contributions to the field would be monumental but, as a patient advocate, I have needed help lighting the first match. (I started building my own institutional base to enrich the context for engagement, but I am thinking ahead here to other patient advocates in analogous scenarios who won't have the raw resources I had in a unique back story and a large medical center right outside my door.)

Conferences and forums should be transcribed, not just taped.

Use of CCC, ICCC and IOM frameworks to help create improved survey instruments; with awareness that different instruments will be useful for different purposes. Those useful in identifying persons with the disease will not necessarily be of much use in fostering compilation of the necessary detailed data needed to better understand underpinning mechanisms.

Many existing and proposed questionnaires and testing methods identified in studies, by clinicians, by patient advocate groups, and the various NINDSCDEs have strong components, and the studies done using them may yield fruitful findings. Other survey and testing instruments appear problematic. Yet the cogent point is that, until we have a more detailed map of the terrain, there is no way to validate or invalidate with assurance any particular investigatory method or determination.

Over a decade ago, ME Research UK Chairman Dr. Vance Spence made a presentation in the House of Commons at a hearing of the Group on Scientific Research into ME. Dr. Spence descried the absence of full clinical assessment and the conflation of patient populations due to overly vague criteria. He memorably described ME/CFS as a “diagnostic mess”. Some clarity is beginning to emerge to the diagnostic mess. But this begs the question: Now what?

We are advancing towards a much stronger understanding of the basic form, shape, and dynamic processes of this disorder. There appears to be general consensus that ME is a complex, multisystem, multi-symptom disorder involving profound dysregulation of homeostasis and characterized by dysfunctions of the central nervous system; autonomic system; immune system and cellular function/signaling. Unique features of the disorder include “crashing” phenomena; specific patterns of symptom presentation; specific types of negative feedback loops; recurrent feelings similar to a low-grade flu; and recurrent episodes of extreme loss of stamina. Yet neither these attributes nor the full panoply of reported common symptoms have been investigated in a manner which would allow the type of granularity needed to facilitate leaps in understanding of the underlying mechanisms or optimal therapeutic treatment.

Unless clinicians and research investigators are incentivized – or at least guided – by the HHS, and especially NINDS and CDC, to more precisely delineate symptoms and presentation dynamics, resources and time will be wasted as field participants wander and retread circles.

See above. Medical schools and nursing schools should have instructions on ME/CFS. How can investigators even have ME/CFS on their "radar" if they don't know it exists! I talked with a cardiac rehab nurse recently, and she had never heard of ME/CFS. I cannot tell you how many times I have had to explain this disease to medical professionals. How it's diagnosed (process of elimination of many other fatiguing disorders), etc. (you know the drill we go through).

Biopsie if all, blood test virus dna , check virus if you think virus