

Overcoming challenges or barriers to establishing a career in ME/CFS research for early career investigators and those new to the field

The major barrier to establishing a career in ME/CFs research is that it is not considered a serious illness by the masses and most physicians. Why would a researcher devote a career to an illness that is not serious. Most people think patients are "tired". The barrier is that ME/CFs was once named the "Yuppie Flu" and not taken seriously.

Only 1/3 of medical schools even TEACH med students about ME, and the caliber of that content is dubious. *All* medical schools should be required to teach information about ME (given that it's a major disease more prevalent than Parkinson's or Multiple Sclerosis). The content of that education should be in line with what experts have been saying for decades. Consult the experts, rather than pretending that we don't know anything about it. Make it clear that it is physiological, not a result of depression or deconditioning. Make it clear that GET/CBT are NOT appropriate or helpful treatments and often harm patients.

An avenue to consider is to make factually correct information about ME on boards exams for med students. If it's on the boards exams, med schools will have to teach it.

The negativity of the medical profession - continuing to dispute its existence is bound to put people off.

so also is the confrontation researchers can experience from the ME community as well as medical personnel.

The University of Minnesota in November 2018 held a "ME/CFS Medical Educational Event". I have heard great returns of interest from this event. Holding this at all medical schools.

<https://www.youtube.com/watch?v=kp1TSEdsHZ0> (presentation)

Name power is key - get the Mayo Clinic to become a participant in ME/CFS research and thus, get the Midwest to become an active participant.

Open up funding. Increase public awareness.

Ditto

Targeted new investigator, RO1, RO2 and R21 grant RFAs.

Targeted outreach to medical students; predoctoral support to students via their medical school administration.

We need funding commensurate with the burden of this disease and to overcome past underfunding.

Meet the patients. ME is not CFS. Let the patients tell you why.

The main barrier seems to be abuse directed at researchers who engage in psychological treatments, which is a shame because these seem to be the most helpful approaches for patients.

<p>This needs to be part of the medical curriculum taught in medical schools. Currently only 6% of schools teach about it. Most physicians are not knowledgeable on it. Some even don't believe it.</p> <p>Requirements by current physicians for training on information we know now, testing, and treatments for symptoms</p>
<p>Data, Data, Data, make us track, we can give info for these student projects.</p>
<p>Fund preceptorships---can young investigators shadow at the NIH with some of the scientists working on ME? They should have a full day of didactics and then shadow. There are many models on preceptorships around the country including the AETC (AIDS Education Training Center; this is HRSA funded) and the New York State Department of Health clinical education initiative. (ceitraining.org)</p>
<p>ME/CFS needs to be introduced, emphasized and recognized in effort to be infused into medical curriculum</p>
<p>Fund this area of research commiserate with the disease burden</p>
<p>Adjust the pay line to early career investigator-initiated proposals.</p> <p>Invite junior researchers into ME/CFS-related committees.</p>
<p>Develop and implement further training for medical school students and post-graduate researchers by documenting the widespread existence of this disease, as well as the crippling effect on sufferers, their families, and the economy as a whole based on loss of productivity in the workforce.</p>
<p>Funding, funding, funding. And publicity about these opportunities.</p>
<p>make more noise (same as above) by giving cfs/me sufferers and their families access to spaces, meeting places, information and to mobilize, students become aware and interested.....if the spaces are in the hospitals, all the better</p>
<p>IF THE GOVERNMENT AND THE MEDICAL ESTABLISHMENT TAKES THE DISEASE SERIOUSLY THEN INVESTIGATORS WILL BE INTERESTED.</p>
<p>It's absence from GP educational curriculum, where it is taught eg in neurology it is still labelled as FND or Somatic disorder etc category based on the out of date perception from PACE of being a psychological condition not a biological one.</p>
<p>Teach ME in medical schools.</p> <p>Establish ME as a challenging intriguing specialty.</p>

Study Chinese Acupuncture & Herbs: there are currently NO doctors on the frontlines who know how to deal with ME/cfs or viral epidemics, because viruses are not studied in western medical schools & anti-virals are not recommended as early treatment.

Education - most won't know much about ME/CFS so the NIH needs to proactively educate people, including potential PhD supervisors. There aren't many centres of ME/CFS research so it might be hard for graduate students wanting to enter this field to find a knowledgeable supervisor. Also funding. You need to commit to funding ME/CFS research at a rate commensurate with the prevalence and disease burden, and advertise widely to university medical schools, bioscience, biology and health science departments that you are doing so. Proactively invite grant applications. Create ME/CFS specific doctoral scholarships to encourage new people to do a PhD in this area - advertise these scholarships widely. Fund attendance for early career researchers, graduate students, and final year undergraduate students at national and international ME/CFS research colloquiums (travel, accommodation, conference fees), and advertise these grants widely. Proactively educate the public and academics and medical professionals to correct misperceptions and myths that might be putting people off showing an interest in this field. Let people know how important this is.

-Increasing general awareness about ME/CFS and opportunities for new researchers go get involved. Although this a highly complex disease, precisely because so little is known about the etiology and treatment of ME/CFS, research in this area is ripe for huge discoveries

-Provide incentives (i.e, grants) - researchers will often “follow the money”

Just tell them not to bother, ME/CFS is not an illness the NIH, CDC or Pharma will forgive you for making your career

Increased funding

Increase required teaching in medical schools

Make it a priority to educate them in medical schools while they are considering their options. Too many leave school with little to no knowledge of me/cfs or the exciting arena of research happening today. ME/CFS offers research that crosses all disciplines and affects multiple disease spectrums. How can they choose this field without the proper Introduction?

Consider actually publicizing the career; a Google search turns up a few bits about existing research teams, but nothing with regard to those interested in entering the field.

Offer significant financial incentives for new investigators. Put out frequent RFAs.

Talk to Ron Davis at Open Medicine Foundation, talk to the patients. We are desperate for your help.

again you need to fund the field. If there is one for the research, people will work in the field

We need to improve the education of all healthcare professionals in ME so that they are more familiar with this condition early in their career and natural medical curiosity is ignited.

- more funding! No young researcher goes into a field with such a financial scarcity.
- change curricula so the disease is known and accepted and the studying of it gets a better reputation.
- Build up high-quality research centers.

Don't call it as Psychosomatic. There is more to MECFS. Funding is much needed for various studies.

As stated above, disease must be legitimized. Second, the numbers of patients suffering must be clarified; right now, the population is largely invisible. Building on the second point, researchers must be shown to what extent the disease is life-altering. Since it is not life-threatening in the conventional sense (though the community has lost many to suicide), it can easily be minimized.

Access to labs and biomedical facilities

Funding of PhDs

Ensure illness is not misrepresented as primarily fatigue

Emphasize huge patient involvement in donating to research funding and in volunteering for clinical trials

Endowing Positions at R1 Research Universities for Chronic Fatigue.

EDUCATION

Money.

Mentoring from high profile scientists such as Ron Davis, collaboration with excellent Australian & global scientists currently working in the field.

More funding.
Need to inform all states, medical schools that ME/CFS biochemical, immunological illness
-find money to pay them so they can do this work -correct misconceptions about CFS to attract people to the field
Validate the disorder to give credibility to professionals seeking a career to study cfids.
Providing medical textbook companies with information. Assurance for fellowship money of several years
Engage in a more robust educational campaign for physicians, researchers, academics, and the general public about the legitimacy of the disease and its devastating effects. Given the general state of ignorance and misinformation about ME/CFS, is the paucity of early career investigators any wonder? How is the field going to attract new researchers if the disease remains in the dark?
First and foremost there should be a least a minimal med school and/or medical science rotation of 4-6 wks of an introduction to this illness since millions are inflicted w/ this illness.
I think the biggest thing a doc could want to from doing something like this is notoriety, their name in print to boost them up after they leave. A boost to their practice and their name. A promise of notoriety for just being involved in the research for a limited time, like 3 years of their career. Especially if they find something of value. Docs just starting out would have this on their records and it would introduce them to a lot about the legal side and advocate side as well. It would also be good for those interested in law as well. Their name in print and in the field early in their career. Maybe offers of paying off student loans for them. I know we have very limited funding, and that is a main issue in getting docs in research, but it is also linked to many other kinds of research. So it is an open door for whatever their specialty would be and also a chance to work in something they feel passionate about. Offers made to med student in their final year of school to come aboard, fresh knowledge. Also to get those who have the most experience, the promise of their papers being published into the medical journals, their names being prominent. What the carrot would be for each person is very individualised and maybe find the person you want and ask them what they want the most. I know you can not give them a huge salary, but maybe there is something else they would want. Ask them what that is.
This goes back to public awareness leading to a strong call to action for the ME/CFS community. Awareness generates donations and donations fund research.
Offer fellowships and transitional-training to medical Doctors who developed ME/CFS themselves to shift from clinical practice to go into research and afford to do so. Run a campaign on the web at low cost targeted at medical students to inspire them to go into this arena. Go abroad. Medical researchers in India can be found for a fraction of Western costs.

Funding. The interest is there if the money is there. Educating new scientists about ME/CFS and the exciting potential to make a difference.
Stop funding research groups investigating the periphery.
Same response as Potential research resources above.
I firmly believe that without identifying the source of the illness, it will be impossible to truly overcome barriers.
Again, only a massive increase in funding will encourage early career researchers into the field.
Increased funding.
Offering education in several areas will help that involved in ME/CFS, since it involves so many bodily systems. Mentoring by seasoned medical physicians, scientists, and other medical professionals will be beneficial. Those experienced in research will help as well in general to help. I am a caregiver of a family member with ME/CFS and experienced working in coordinating in clinical trials, so feedback I can share for example will be beneficial to help educate those new to research and ME/CFS. Both education and compassion are needed for those wanting a career in ME/CFS research.
Again, the more money spent on informing the public, current uniformed GP's and internists and specialist medical professionals, and incooperating ME as a serious health condition taught in medical schools would in all likelihood help early career investigators overcome many barriers they currently face.
Establishment of VISTA like compensation to trade work in this field against Loans for the costs of Medical Education.
Again, more ring fenced funding. It's been said over and over. Inadequate funding is our largest obstacle.
-
/
Communicate that it is a major opportunity to contribute and research results can be useful for other diseases.
Breakthrough results in this area will contribute to future disease avoidance. Hold a game prize competition.
clearly alerting investigators that \$\$\$\$ is available so that they can pursue this area. Also NIH needs to help young investigators get freed from the institutional constraints on that exist on their applying for grants and upward mobility.
-Increasing general awareness about ME and opportunities for new researchers go get involved. Although this a highly complex disease, precisely because so little is known about the etiology and treatment of ME, research in this area is ripe for huge discoveries
-Provide incentives (i.e, grants) - researchers will often "follow the money". I would like to see Dr. Collins take action on the words he spoke at the recent NIH meeting/conference

Reliable funding to research teams. Dr Ron Davis has repeatedly complained of the difficulty of recruiting early career investigators and those new to the field because he cannot guarantee funding for ongoing employment.

FUNDING

Distribution of knowledge to medical schools. Harvard Medical School barely teaches about CFS/ME. Why isn't this happening at ALL medical schools.

Find ways to get across three facts: a) that this field provides young investigators the rare opportunity to make a major difference in a major disease; b) gets across that this is a growing, exciting field and c) that it is possible to be successful in it. Don't waste your time going after conservative minded young researchers; target adventurous young researchers who are burning to make a difference.

Have Jarred Younger communicate how he managed to successfully create an ME/CFS/FM research center

Have Nancy Klimas and Ron Davis communicate the interest they've seen from young researchers

Have Francis Collins and Walter Koroshetz continue penning blogs emphasizing their support for ME/CFS and the opportunities present

Provide funds for successful senior researchers such as Ron Davis, Ian Lipkin and Nancy Klimas to bring young researchers into the field.

Of course, fund successful senior researchers who will naturally attract younger researchers into this field - no magic pill needed - just fund them!

Provide funding for current ME/CFS researchers to add new researchers to their team

N/A

Find ways to get across three facts: a) that this field provides young investigators the rare opportunity to make a major difference in a major disease; b) gets across that this is a growing, exciting field and c) that it is possible to be successful in it. Don't waste your time going after conservative minded young researchers; target adventurous young researchers who are burning to make a difference.

Have Jarred Younger communicate how he managed to successfully create an ME/CFS/FM research center

Have Nancy Klimas and Ron Davis communicate the interest they've seen from young researchers

Create an "Innovation Reward" for young and/or new researchers who provide the most innovative ideas for work in ME/CFS

Have Francis Collins and Walter Koroshetz continue penning blogs emphasizing their support for ME/CFS and the opportunities present.

Provide funds for successful senior researchers such as Ron Davis, Ian Lipkin and Nancy Klimas to bring young researchers into the field.

See more \$ and schooling for all medical professionals above.

Stable funding along with compelling stories of the many devastated by this disease. Pull on their heart strings!

Stop vilifying physicians and investigators for trying to help patients. Put the patient's treatment back with whom it belongs - their physicians and providers (not the government or others who do absolutely nothing in regards to these types of illnesses, diagnosis or multiple diagnosis)

Wow - are medical field university students even taught about ME/CFS? Who even knows there's a huge need? We need WAY more exposure.

If one of the barriers is a feeling that there's not enough of a need / that the medical community is still largely in denial, have career investigators billet at patients' homes for at least a few days to see 1st hand how a patient's life is impacted

Educate the educators at medical schools.

What are the current barriers? I'm assuming money and the visibility of the disease. Making it more visible via all types of media will make people more aware, and the more visible the disease, the higher the likelihood that fundraising will be more successful.

Education so that researchers know this an option, and an exciting and groundbreaking one.

Funding, publicity...perhaps opening a CFS center at a medical school for medical students to learn about it. Continue to pursue promising scientists to find who may be interested. Make sure doctors who are starting in the field of CFS get to work or talk to doctors who treated it for a long time like Dr. Cheney and Peterson. Contact scientists studying CFS and suggest they offer an internship each year for a young doctor or scientist to learn about the field.

The only reason there is challenges is because there is not enough money spent on the illness for scientists to feel they could see changes in the illness, it's 50 years since who recognized the disease and not one treatment is available

Make people proud of engaging with those that have and care for those with ME. There has been a concerted effort by the establishments all over the world to trivialise and belittle those with ME. Doctors and medical professionals have been allowed to discriminate against those with ME and it will take the profession to collectively to stand up and say enough is enough we support those with ME. Once that has started researchers will flock to be the first to find all there is to know about ME, it is in their nature.

I suggest you listen to the OMF foundation and the SMSCI organizations and listen to respected ME/CFS researchers, like Nancy Klimas, etc.

The word needs to be gotten out that ME/CFS research has made huge strides in the last several years and is not the small, infrequent study backwater it used to be. Encourage web postings such as the recent one about the NIH meeting on Medscape, and discourage publication of horrible nonsense such as the Medscape reposting of those two terrible Reuters articles. Can the NIH write up such articles and distribute them to the news media?

Teach this in medical schools

See all of the above - include a small bit of funding to aid showing Unrest at colleges et al.

Challenges and barriers ! any patient knows all about those. And the long long long history of this disease being denied, minimized, misrepresented and even made fun of...well who would want to enter that field of study. This disease needs to be culturally accepted so patients and researchers will not be stigmatized. Fortunately and unfortunately, some researchers and physicians actually have experienced ME/CFS in someone they know and have stepped up, or just find the mystery fascinating and jump in. Meanwhile, the cultural stigma is still there and it needs to go.

as does this. Even having to ask this question reveals the strategies which for 30 yrs have attempted to cover up and/or discourage interest in finding a cure.

It's crucial that incoming researchers be made aware of the scope of the problem and the ways the medical community often fails patients with ME/CFS. A uniform international set of standards and diagnosis criteria will help new researchers identify which previous studies/research directions have value and which are unhelpful.

I'm just a patient, so consider the source, but there is a brand new Medical School in Austin that publicizes that they are pioneering new strategies for training med students. The head of this school is a Neurologist. Shouldn't SOMEbody be in touch with this school as they are getting off the ground and propose a program for training specialists in ME/CFS?

I think those blessed few who are pursuing this field have more of a calling than most . . . they really want to help relieve the real suffering they see. Many don't really "believe" until they have seen someone lose their life and health to this illness. Researchers motivated solely by money just not interested in CFS I fear.

Funding

<p>look at those who have managed to attract new researchers into the field</p> <p>fund incentives and/or scholarships</p>
<p>Funding, obviously. Lack of glamour - it's a condition that is very rarely terminal. However, the cost to the economy is very high due to serverely reduced capacity for productivity.</p>
<p>open mindedness to the impact of RF pollution</p>
<p>Recognition of Environmental Physicians.</p>
<p>This illness is still tainted with stigma, ignorance and misunderstanding. Most investigators enter the field by accident, not design. There is little prestige associated with this field and often researchers face the same legitimacy challenges as patients as they struggle to overturn strongly entrenched stereotypes of this illness. As Jose Montoya said of his supervisor early in his career on a visit to Paris when they passed a homeless man on the street "that is how you will end up if you continue to study chronic fatigue syndrome". Hopefully views have changed since then.</p> <p>Young investigators need to understand that this is a fascinating field full of opportunity. Patients are so incredibly grateful to all of the wonderful human beings who have chosen to dedicate their energy and gifts to unraveling this debilitating illness.</p> <p>Forty years ago, there was no diagnositic tool for Multiple Sclerosis. My uncle, as a young PhD student, helped pioneer the use of the MRI scanner as a tool to identify the brain lesions now associated with this illness. He has had a fascinating career in this field and more recently was awarded the John Dystel prize outstanding contributions to research in the understanding, treatment, or prevention of multiple sclerosis. There absolutely should be similar national and international prizes in the ME/CFS field that recognise the outstanding contributions so many researchers have made to our understanding of ME/CFS and the efforts they have made to give us visibility and appropriate support. They are our angels.</p>
<p>Because the majority of patients are women, I suggest going to women's colleges and speaking to those who are looking at a career in biology or medicine to pique their interest in the ME research field. If we make today's students aware of a disease that effects women's health and is a field on the verge of expansion, they may show an interest and choose a graduate program that relates to that field of study. Get them before they have committed to another field of research.</p>
<p>Government needs to authoritatively release patients by making the disease know and understood front and center. No more gagging the media because you made a mistake with the vaccines. Start really forcing the CDC to review the vaccine schedule or so many people are going to be I'll that we won't have a country.</p>
<p>Grow credibility.</p>
<p>Funding</p>
<p>More funding.</p>

Scholarships for med students and researchers may help. Conferences or lectures for doctors to receive CEUs to learn about ME/CFS. Make it available online to reduce cost and make it more flexible time wise. Because it is a lot to learn. Putting together ME/CFS clinics with the necessary specialists and offering time-in-clinic CEUs for health professions willing to learn more. Med students could also participate, especially if these clinics were attached to or near medical schools.

Visibility of funding would help to attract many new researchers to the field. At the moment, a new researcher would surely look at ME/CFS and wonder whether they would be able to obtain future grants. Perhaps fund all new researchers for a minimum of 3-5 years, with specific targets to be achieved during this time.

Proactively convince new researchers that ME/CFS is an exciting and rapidly advancing field of medicine, and that researchers can really make a significant difference. As Prof Ron Davis has said: ME/CFS is the last branch of medicine about which we know very little. This is clearly not a good situation for patients, but is potentially very exciting for new researchers i.e. emphasise that they can really make a difference by entering the field of ME/CFS.

Ignore the haters - it's a real condition that needs research.

Hold Dr. Collins accountable for directing significant NIH money to ME/CFS. Much time has passed and much more funding and resources are required.

Adequate funding for researchers to get into the field.

Recognition for researchers in the field.

Early education to this new research

Clear statements (followed by actions and funding) from up high that biomedical ME research is a priority and will be funded reliably into the future.

Legitimize the disease, by educating the medical community and the research funding community about its history and current scope. Integrate ME/CFS awareness into every U.S. medical degree program. Request that upon doing so, every medical program issue a press release to its community and local journalist contacts, as well as posting the news to its own website.

- research grant money for young/new researchers in ME/CFS.

- advertising of grant money in major related field research publications.

- mentoring winners of young/new grant money with established and passionate researchers in ME/CFS

- ensuring young/new researchers access to established patient populations.

- encouraging young/new researcher participation in ME/CFS conferences, money to attend said conferences

Funding.

See "approaches to strengthen..."
Finances are lacking
Money?
<p>Education</p> <p>NIH making it clear this is an important area by taking special measures, putting in money and setting up centres etc will help convince the skeptics this is worthy of their time.</p> <p>The name chronic fatigue syndrome is both belittling and hugely stigmatized</p>
<p>I don't know but imagine new ideas are often squelched. We need a return to thinking in medicine.</p> <p>We can't assume all Enviromental variables are safe until they are proved guilty. That approach is a recipe for illness, and in the US 50% o fun have at least one chronic illness..</p>
<p>ME/CFS should be branded as the new AIDS. If the disease is seen as a widespread epidemic and a very severe illness, then there will be much more prestige associated with doing research in the field. It will attract more money and more research minds</p>
<p>Fund research big time, like AIDS research was funded!</p>
<p>Focus groups of the current post docs, research associates and research assistants can provide insight regarding how they became involved and elicit their suggestions for recruiting more colleagues. It appears that many are working in the research labs of senior ME researchers e.g., Dr. Hanson or senior scientists new to the ME field e.g., Dr. Oaklander. New ME investigator awards will attract young scientists, who need to secure external funding as part of their faculty appointment.</p>
<p>I would advise any early career investigators to avoid the current politicized "ME/CFS" field and instead do ungently needed research on actual ME as described in the ME-ICC and in the medical literature by such experienced clinicians such as ED Acheson, AM Ramsay, Elizabeth Dowsett, and Byron Hyde.</p>
<p>Do not allow anyone to establish a career in ME/CFS research as this will inevitably again do tremendous harm to ME patients.</p> <p>Instead, allow the few ME researchers that we have left to instruct new investigators before their knowledge and skills disappear forever.</p>
<p>Ensure financing for long periods, so that careers can be built in ME research. ME needs its place in training so that young researchers have heard about it already during studies and can find interest. More money! More money will increase research projects, and high number of advertized research projects suggests there is money, and money (safe jobs) will attract young researchers; increase PhD projects. Stop the stigma about ME so that young researchers dare to choose ME research. Establish Graduiertenkollegs (young researchers groups that work on a certain topic over several years).</p>

Attitudes of disbelief, ignorance, dismissal

More funding, eliminate any suggestion that ME is psychological rather than physical.

The very first barrier will always be knowledge and awareness of the disease itself. There will not be very many newly interested researchers if they are not familiar with the disease, its severity, and epidemiology, and might be influenced by the ever-prevalent stigmas associated with ME/CFS. This issue also applies to the Peer Review process when it comes to grants, since the review committee, as of 2018, consisted of a mere 37% of actual ME/CFS experts leaving the remaining members of the committee unprepared, biased, or under-educated with regard to the disease, thus impeding the committee's overall ability to make scientifically sound decisions, and as a whole being much more likely to reject a proposal that the actual ME/CFS researchers and community might deem as an absolutely necessary first step forward or as a potential breakthrough. Knowing how difficult it is for ME/CFS grants in general to gain approval is not exactly an invitation to a well-supported or financially stable career. Many researchers already pursuing ME/CFS research were left to come up with their own creative funding ideas as their research proposals received absolutely nothing from the NIH. A lot of currently occurring research has been initiated with zero assistance from any appropriate agency, which does not make the line of ME/CFS research sound particularly enticing or even possible in some cases for many new scientists who need to earn a living wage. The fact that the NIH chose to set up this working group/committee for ME/CFS rather than establish a full 28th Institute for ME/CFS is also not encouraging and insinuates that the disease is of less importance than most others, which is not conducive to recruiting newly interested scientists/researchers seeking a well-established, honorable, and stable career in medical research. The entire bureaucratic, biased system that ME/CFS researchers must endure is a serious issue that deters many new professionals who are in fact otherwise intrigued by the mystery of the disease.

The most significant barrier associated with doing research on ME/CFS is stigma.

In a 2017 interview, former Scientific Director of Solve CFS, Dr. Zaher Nahle, relates the stories of both a student and professor studying CFS. (Source: <https://tinyurl.com/y2twhcwl>)

-A graduate student [is doing a] thesis. When they have their departmental meeting they make fun of him because he is not working on fancy diseases it is the commitment from NIH, it's investment that is serious, that is tractable from the NIH and other institutions that that will allow that individual to hold their head high and do one of the most exciting work in ME/CFS.

-A professor at one of the most prestigious universities in the US...he must keep one foot in seeing patients with infection arenas and one in CFS because his institution will not support him if he only does ME/CFS these are really issues that we have to confront and the way we confront them is investing in this field as much as we can because we are operating in a 30 year deficit that is why this problem is so huge now."

When a friend of mine was in medical school, she mentioned my illness to a professor. He replied, - ah the 'nebulous' Chronic Fatigue Syndrome", with the emphasis on nebulous. Then, he laughed. This was in 1998.

Physicians and researchers in medical institutions have been laughing at ME/CFS for 20 years. It is obvious that a stigma exists which impairs the perception of ME/CFS as a serious, disabling illness.

Ron Davis highlighted the need to have medium term funding in order to attract/retain researchers. Funding e.g. for a relatively long period (5 - 10 years) will be necessary to attract/retain researchers.

ME/CFS is not taught in science classes or medical schools other than as an incidental nod. This has to change. There needs to be courses on immune disorders with CFS for at least a semester. Sometimes it's better to get new eyes on the research. Host lectures either from Patient Advocates for physicians in towns like Houston where there is only one doctor who treats the disease. Dr. Patricia salvato. Dr. Teitelbaum. Patience like myself who are knowledgeable and can answer questions. The videos and lectures need to make the lecture fun and scientific at the same time in lay and medical terms. When I watch many presentations are too clinical, non engaging, and boring. The information is sometimes overly expounded on, long, and tedious. The information is awesome but presentation is poor. We need to get medical boards in every state via the NIH to promote continuing education courses for the diseases.

Again, very important. The experienced doctors are retiring. A huge incentive would be NIH or CDC endorsed investigations and funding.

1) Offer early career investigator (ECI)-specific funding opportunities (e.g., R21s for ME/CFS or related illnesses).

2) Convene ME/CFS-focused review panels so that ECIs are not continually penalized by working in a less-recognized area.

3) Ensure that review panel members are rotated and supplemented with ME/CFS-friendly - outsiders that includes a broad representation of relevant ME/CFS related disciplines and related research areas.

Increase funding for research and education programs regarding the illness are necessary to attract researchers.

Need to establish well-funded post-doc funding for new researchers and clinicians and pair them with people such as Peterson and Bateman, etc. Need at least 12 such positions nationally. At a salary that would support a family.

WORKFORCE DEVELOPMENT

NIH ADMINISTRATIVE STRUCTURE, GRANT SUBMISSION & REVIEW

RESEARCH FUNDING

CLINICAL EXPERTISE

PATHOBIOLOGY DISCOVERY

BIOMARKER

ARTIFICIAL COHORT HETEROGENEITY

INTRINSIC BIOLOGICAL HETEROGENEITY

EPIDEMIOLOGIC KNOWLEDGE

INTERDISCIPLINARY COLLABORATION

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!!!

That we all stop calling ME chronic fatigue syndrome / cfs. As Dr Klima says: "The name is a really big deal, and I and everyone else in this field regret that we didn't chase it (cfs) away faster". This chronic fatigue syndrome-name is damaging the patients so profoundly. It gives the disease a credibility problem. A lot of people think it is a joke, and perceive it as chronic lazyness syndrome. We need to insist myalgic encephalomyelitis aka ME is the correct name.

-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 early career researchers to the field and encourage established researchers to focus their expertise and techniques on this disease.

Medical school students must first receive enough education about this area to even know that ME/CFS exists!

As noted above, mentoring/training, and a stable funding source. T15 training grants.

Most important: Present up-to-date published research articles to medical school INSTRUCTORS, so they are aware that ME/CFS is a disease, and do not teach otherwise. Start with exercise intolerance data.

2) Provide funding and facilities

Lack of research funding is the biggest barrier. Until funding for ME is at least close to being commensurate to the disease burden, most investigators are not going to be willing to risk their livelihoods on this important research.

By making clear decisive statements using the ICC, we could turn the tide today of patients being abused by family members and society because of the narrative that behavior changes are all that is needed to "overcome" ME.

Education in and outside of medical schools about this illness so that researchers are even aware of the reality of this illness (see my experience with the endocrinologist above), and also adequate funding - there will be no careers without money.

The negative, and misinformed, stigma is by far the biggest barrier to establishing careers. Most medical professionals have a very distorted understanding of the disease and most of the established researchers say they have been strongly warned against doing so, that it is a waste of time with little to no funding or purpose.

Early researchers have to know that this is a problem worth solving, something that is currently almost impossible to know without personally knowing someone suffering from this disease.

The issue is not so much to clarify that it is -real- but that it is much, much more severe than people understand. This misconception is so profound that even the psychosocial researchers behind the current cognitive-behavioral paradigm do not have a proper understanding of the severity of this disease despite selling themselves as leading experts.

Researchers and clinicians specialized in both ME and AIDS all testify that their ME patients are worse off. This is a shocking reality that the vast majority of medical professionals are wholly unaware of, would scoff at the very idea of. This is a presently insurmountable barrier without a paradigm shift, but one that is easily fixed by simply communicating what is already known and expanding on the epidemiology of the disease.

The success of any early career researcher depends on whether s/he finds an important result that can be published in a high impact journal. However, even the most brilliant researcher cannot choose which results exist, and whether current technology is advanced enough to find them. The best strategy for building a successful research career is to pick important sounding fruits that have recently become low hanging fruits. However, ME/CFS is still a high risk field with high hanging fruits, which means that only established researchers who can afford the risk will enter. But there are few of those, because they are already happy in their other field, which is not ME/CFS.

* I would suggest to introduce early career researchers via method development: metabolomics, lab on a chip, recent advances in in vitro optical microscopy, etc., where ME/CFS is intended to be the prime target for the method, but the method is of independent interest. But perhaps that is the physicist talking.

Scholarships, grants, fellowships

The biggest challenge is the dearth of funding. You prioritize this with rich funding, and educate university researchers and I GUARANTEE you that researchers will flock to the opportunity. People flock to where the RESOURCES ARE. Shame on NIH for leaving this field for decades grossly underfunded, leaving millions of Americans suffering, committing suicide and in a crisis of no medical care. SHAME ON NIH. This is politics, and not leaders of scientific objectivity.

Make a AIM FOR A Treatment/CURE research initiative for this disease.

Try to seed fund some ME research at our strongest medical research universities.

Use money from the arts to write and portray the Americans afflicted (of so many outstanding, productive brilliant people and careers lost) , saturate media

When early career investigators see established ones fail to be funded and no RFAs being issued for a field, and look as the dismal amounts of money for this disease vs other fields such as MS, opioid and alcohol abuse research, and AIDS, they are not encouraged to enter the field. The issue of samples for those new to the field is discussed above.

Engaging New Researchers & Researchers in Alternate Fields

I think one of the most compelling ways to get scientists excited about researching ME/CFS is to present them with the true stories of how ME/CFS has impacted the lives of the people who live with it.

Beyond that, presenting them with the constellation of physiological processes that make up the disease would seem to me to be an exciting puzzle for any researcher to solve.

As a researcher, I suppose I would like to see what kind of logistical support I would have, in terms of previously established researchers in the field, funding sources, patient advocacy groups and other types of infrastructure organizations, as well as their past accomplishments and future plans.

*I think Silicon Valley would be a great place to scout. Yes, I know money is always an issue, but sometimes people will help with projects just because they are passionate or personally connected.

1. The biggest barrier may be simply not never being exposed/ educated about ME/CFS ever. Since less than a third of medical school even superficially mention ME/CFS, the chances medical or scientific students/ trainees have ever heard of ME/CFS are are slim-to-none. If NIH were able to put together a short brochure/ e-fact sheet introducing the condition and share it via their numerous contacts, that may be helpful. A multi-prong approach is likely needed, e.g. having the brochure at tables during conference, sharing it via NIH Intramural Newsletters, etc., so that students/ trainees are exposed to ME/CFS repeatedly via different methods.

2. Establishing a virtual network like that mentioned above might help younger/ new scientists find mentors and collaborators. Often students/ trainees find their research passion and mentors through the classes they take, the research groups they rotate through, or people they meet. Historically, since ME/CFS was not taught in most schools, these mentors simply may not exist in their institutions or even region.

3. Leadership, management, and business skills related to running an independent research group, which are in some ways like running a small business. Most scientists appropriately focus their efforts on the science but there are many skills involved in creating and operating a successful independent research group which are not traditionally taught in graduate or professional school. Some may learn these skills through instruction from/ observation of their mentors but not everyone is so lucky.

4. A virtual network, e.g. a webinar, which meets regularly - .e.g once a month or every 2 months -- where young/ new investigators can discuss their work, ask questions, hear from more senior investigators about their career paths, and discuss the latest research papers/ trends might be helpful. Such a network may provide emotional and practical support, expose young/ new scientists

to work/ mentors outside their groups/ institutions, and promote collaboration. An effort to invite senior or well-known scientists outside the ME/CFS field (but who may study overlapping issues like sleep) to such a webinar to speak is not only helpful to the attendees but also educates the speaker about ME/CFS (i.e. at least they will know the name and some may look it up a bit to prepare for their talk).

Career investigators are reluctant to study ME because they have not received proper education about ME in medical schools.

They should be trained on:

Myalgic encephalomyelitis: International Consensus Criteria -- 2011 research and clinical definition improving on the Canadian Consensus Criteria and distinguishing ME from CFS

<https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2796.2011.02428.x>

ME International Consensus Primer for Clinical Practitioners -- how to understand, diagnose and manage the symptoms of ME. This primer is superior to information on the CDC website

https://d3n8a8pro7vhmx.cloudfront.net/meadvocacy/pages/2292/attachments/original/1554817421/Myalgic_Encephalomyelitis_International_Consensus_Primer_2012.pdf?1554817421

Additionally, the little that is heard about the disease myalgic encephalomyelitis in regards to definition and symptoms comes from questionable sources full of misinformation such as the CDC, NIH ME/CFS page, as well as the following sources:

UPTODATE (a well known doctor resource): <https://www.uptodate.com/contents/treatment-of-chronic-fatigue-syndrome-systemic-exertion-intolerance-disease>

MERCK - <http://www.merckmanuals.com/professional/special-subjects/chronic-fatigue-syndrome/chronic-fatigue-syndrome>

HEALTHDAY: <http://consumer.healthday.com/diseases-and-conditions-information-37/misc-diseases-and-conditions-news-203/two-treatments-for-chronic-fatigue-syndrome-may-offer-long-term-relief-704953.html>

GOOGLE - https://www.google.com/?gws_rd=ssl#q=Chronic+Fatigue+Syndrome

WEBMD - http://www.webmd.com/chronic-fatigue-syndrome/news/20151123/chronic-fatigue-therapies-provide-some-with-long-term-relief?src=RSS_PUBLIC&ecd=soc_tw_newsbot

<http://www.degruyter.com/view/j/reveh.2015.30.issue-4/reveh-2015-0026/reveh-2015-0026.xml?format=INT>

MEDICINENET.COM: <http://www.medicinenet.com/script/main/art.asp?articlekey=192078>

WIKIPEDIA https://en.wikipedia.org/wiki/Chronic_fatigue_syndrome

TREATO <https://treato.com/Myalgic+encephalomyelitis/?a=s>

CMAJ - Canada - Page 7 says no contraindications for exercise
<http://www.cmaj.ca/content/early/2016/03/14/cmaj.150684>

Kaiser Permanente: <https://healthy.kaiserpermanente.org/health-wellness/health-encyclopedia/he.myalgic-encephalomyelitis-chronic-fatigue-syndrome.hw32907?kpSearch=myalgic%20encephalomyelitis>

MAYO CLINIC - <http://www.mayoclinic.org/diseases-conditions/chronic-fatigue-syndrome/basics/treatment/con-20022009>

University of Florida Health: <https://ufhealth.org/news/2017/study-points-possible-trigger-chronic-fatigue-symptoms-offering-hope-new-therapies> &

https://www.ahchealthnews.com/2019/02/04/cure-chronic-fatigue/?fbclid=IwAR2R2sna462xQj3SSekMnopSlaqwaClS__-h2qeQUH9B-Fm2DMMxJ5yCXc

Harvard Doctors Reveal The Best Ways to Manage Chronic Fatigue Syndrome:
<https://www.health.harvard.edu/promotions/harvard-health-publications/understanding-chronic-fatigue-syndrome?fbclid=IwAR1YpQwdJUwSb9zQJucmlsJvWkwIHIWU4owTBOncsQoF12TYUWUFAR2ujM>

The University Times: http://www.universitytimes.ie/2019/02/an-unhealthy-mind-can-lead-to-an-unhealthy-brain-lets-not-forget-that/?fbclid=IwAR3nfoHcx1c5UK3Nlju2k8z0VT6jxpMBdREyPu0uE53a-ZzvojKoo70nmvM&doing_wp_cron=1549671725.6050140857696533203125

Canada: Central Sensitivity Syndromes (CSS) helpful in explaining CFS and FM to patients
<http://thischangedmypractice.com/hope-for-patients-with-fatigue-pain-and-unexplained-symptoms/>

Treating Conversion Disorder: (Says CFS is a conversion disorder)
<http://pro.psychcentral.com/recovery-expert/2016/01/treating-conversion-disorder-psychosomatic-illness/> Specifically this statement in this article: "The patient needs to be instructed to not refrain from activities when symptoms are present, but to keep active -throughâ€ the pain. No damage will result."

Note: information based on this book:
https://www.goodreads.com/book/show/130610.The_Divided_Mind

The myth that ME is actually a syndrome comprising of several -fatigue conditionsâ€ and driven by psychosocial elements has greatly harmed the perception of the disease.

Young investigators do not want to get involved with a â€conditionâ€ which is only -fatigueâ€ in nature or psychosomatic.

Stop referring to ME as a mystery. No one refers to diabetes as a mysterious disease even though exact factors leading up to the diagnosis is unknown. Only a partial list of risk factors is currently known. There are many researchers who are interested in finding causes, treatments, and cures for

the disease. Researchers relate to and have compassion for the burden that diabetes has on an individual and society. Referring to ME as a mystery implies there is doubt that it is a disease at all, and solidifies belief that it is possible for the patient to control health outcomes solely with psychosomatic treatments or lifestyle changes.

HHS has not properly campaigned to educate the populace or the medical community on the reality of this disease, and the destructive nature it has on the patient, the caregivers (or lack of caregivers), and society.

There should have been a warning to the medical community of the removal of CBT and GET from the CDC website as treatments for ME that they can be harmful or just completely ineffective. GET should have a black box warning for anyone with ME.

Mentoring is a good idea, young researchers coming into the ME/CFS field (assuming they overcome the lack of funding and institutional support) are starting from scratch and several of the researchers who have spent much of their career working on ME/CFS could help guide new entrants into promising research areas.

As mentioned the stigma against going into ME research is a big problem. Most medical students are not taught a great deal about ME/CFS or have been taught the discredited and no longer recommended CBT/GET. Virtually nobody will go into a field that they know nothing about or have been taught falsehoods about hence it needs no research since its a psychosomatic disease. This will need addressing before early career investigators will be interested in moving into ME/CFS research.

Interestingly the most success in this area thus far was achieved by turning the Oscar shortlisted film Unrest into a CME¹, done by the patient advocacy organization MEAction

¹<https://www.meaction.net/unrest-ce/>

A big problem currently is the stigma. Need a public relations program and education program raising the awareness of the scientific and medical communities as to the reality and severity of ME/CFS as a crippling disabling disease of equal importance to already "acceptable" diseases.

Find ways to raise awareness that this field provides young investigators the rare opportunity to make a major difference to a diverse population and revolutionize thinking about a major disease; that this field is growing and has tons of unanswered (and unasked!) questions; and, via a stable infrastructure, that it is possible to make a successful career in it.

Money!! Money!! Money!! Find ways to get across three facts: a) that this field provides young investigators the rare opportunity to make a major difference in a major disease; b) gets across that this is a growing, exciting field and c) that it is possible to be successful in it. Don't waste your time going after conservative minded young researchers; target adventurous young researchers who are burning to make a difference.

Have Jarred Younger communicate how he managed to successfully create an ME/CFS/FM research center.

Have Nancy Klimas and Ron Davis communicate the interest they've seen from young researchers.

Create an -Innovation Reward- for young and/or new researchers who provide the most innovative

ideas for work in ME/CFS.

Have Francis Collins and Walter Koroshetz continue penning blogs emphasizing their support for ME/CFS and the opportunities present.

Provide funds for successful senior researchers such as Ron Davis, Ian Lipkin and Nancy Klimas to bring young researchers into the field.

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.

Increase overall funding for ME

NIH and stakeholders must develop a fully funded outreach program to eliminate stigma associated with being in this field (as clinician, researcher, etc) and/or having a diagnosis of ME

Appropriate training about ME in all healthcare education

Work strategically to significantly increase the number of 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

Pathobiology 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.

Clinical Intervention Trials

Artificial Cohort Heterogeneity

Intrinsic Biological Heterogeneity

Epidemiologic Knowledge

-inclusion of pediatric patients

Interdisciplinary Collaboration

- Motivate Early Career Researchers to Explore MECFS - young researchers may be hesitant to choose a disease that is not well known, well-funded and with a limited number of leading experienced researchers to work under. To address this, identify some areas of overlap with other established well-funded diseases/topics. Design grants that will attract involvement from Labs that research these diseases. This will draw in younger researchers that can focus on an overlap disease/topic whilst still having a home within an established research centre.

- Motivate senior researchers to pivot to MECFS from a related condition - matching funding/startup financing programs that will support the spin out and creation of dedicated MECFS labs/biotech companies by mid-career researchers

- Fund the creation of a Clinician/Researcher MECFS organisation - a body that will drive knowledge sharing, research publication, training and guidelines for clinicians and researchers.

This starts also at university, in medical schools.

The medical curricula need to be updated

Perhaps NIH should specify in an RFA that a team needs to employ a new PhD in the research project, in addition to those applying. This might encourage many new researchers into the field.

MEICC criteria

Expansion of the number of Centers for Excellence, increase in their individual funding, and an extension of the number of years they will receive dedicated funds. Ideally, there should be one or more NIH funded Centers of Excellence in the western United States.

In order to encourage early career investigators, it is essential to show them that there is a future in ME/CFS research. Increasing the funding potential will generate career stability and having increased funding will also allow early career investigators to become leaders in an underdeveloped field. These early investigators will eventually be seen as those who entered the field early and will benefit from this recognition as their career progresses. Focusing solely on -early career- events is somewhat short-sighted since the primary issues of limited funds, and few established ME/CFS researchers are not addressed by early career-centric efforts.

Funding!!!

Some ideas presented here at the following

<http://www.me-ireland.com/scientific.htm>

<http://www.me-ireland.com/research2.htm>

<http://www.me-ireland.com/bogus.htm>

<http://www.me-ireland.com>

-NIH should push ME/CFS curriculum in medical schools (currently, advocacy groups holding 'Unrest' screenings is about as good as it gets).

-Mentoring and shadowing programs

-Understanding that training many new clinicians to know more about this condition is a better and more sustainable approach than hoping new people will specialize in this condition specifically. There is a bit of a 'desperate' vibe; most diseases are not asking young clinicians "please focus your career on this disease."

I am too sick to participate in in-person studies and have repeatedly been turned down for studies that don't require me on-site because I am too sick to show gains.

First they have to have the disease be treated as a real discipline by the NIH and the CDC; not an offshoot of psychiatry.

With a proper systems biology approach, I believe this challenge can be met. The primary barrier to attracting talent is motivation. If ME/CFS is presented as I have described above, there should be applicants who want to be part of the next generation of bioinformatical approaches to medical research. Researchers who commit to ME/CFS as a systems biology field would then be able to move laterally into cross-over conditions, and come back to ME/CFS as they choose. I think the key is to tie ME/CFS research into systems biology, as that is a growing field with over \$400 Million in funding pledged by major institutions (Harvard, Stanford, Institute for Systems Biology, etc).

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/liasing 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

RESEARCH FUNDING

Barriers:

Lack of set-aside RFAs, program announcements, administrative supplements
Lack of year-over-year growth trajectory funding
Inconsistent, insufficient contributions from other institutes
Insufficient commitment from Office of the Director
Paucity of investigator-initiated applications, including those from senior researchers at major academic centers
Lack of meritorious applications
Lack of committed, multi-year funding disincentivizing researchers, especially senior researchers from risking their career and entering this field

Strategies:

Issue disease-specific FOAs for investigator-initiated applications
Issue multiple, multi-year, disease-specific RFAs to ensure stability for newcomers (senior and junior investigators) to the field and enable a secure dedicated career path
Supply, at minimum, an initial \$50MM infusion to fund RFAs that will accelerate the field. Thereafter, implement consistent year-over-year growth trajectory funding increases (minimum 40%), including commitments from all trans-NIH WG institutes and a substantial commitment (e.g. 10% of the total NIH ME funds) from the Director's Common Fund, until funding is commensurate with disease burden.

Issue and advertise the availability of interdisciplinary administrative supplements enabling grant recipients to recruit outside expertise, prompting established investigators to find expert collaborators in overlapping fields and construct joint approaches
Solicit and fund high-risk, low-data exploratory and hypothesis-driven R21 applications
Increase the payline for all ME grant applications
Engage in targeted outreach and solicitation of applications from senior investigators at major academic centers whose domain expertise is relevant to ME

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

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

ARTIFICIAL COHORT HETERO/HOMOGENEITY

Barriers:

Lack of standardized research case definition, or agreement on core features required in all ME research cohorts

Lack of validated, standardized objective measure(s) and/or biomarker(s) for cohort selection

Lack of clarity, consensus, and transparency in defining and reporting cohort selection methods

Deficiencies in disease-specific instrumentation, methods and guidelines to fully characterize and report disease features

Lack of representation of severely ill in many studies

Sex, race, age, socioeconomic, biases in existing data and research cohorts (males, minorities, youth, poor underrepresented)

Strategies:

Encourage research selection criteria requiring PEM during grant application/review process

Encourage transparency in reporting cohort composition metrics, including: definition(s) met and how this was determined; debility (KPS); severity definition and scale (by future disease-specific scale); duration; onset type; age; and sex

Reach consensus on core inclusion/exclusion criteria and methods used for all ME research cohort selection to facilitate cross-study comparability and reproducibility

Reconvene a methodological working group to identify deficiencies in CDE guidelines, further standardize assessment methods and measures, and recommend areas of need for development of novel tools

Issue RFA for development and validation of disease-specific instrumentation and methodological practices to enable consistency in cohort selection, descriptive cohort reporting, comprehensive disease characterization, phenotype subgroup stratification, and sensitive capture of change in

disease status, including: severity instrument, scale and standardized terminology; PEM instrument; fatigue instrument; sleep instrument; orthostatic intolerance instrument; pain instrument
Review and refine CDE recommendations to include: require cohort reporting and data stratification by PEM status; PEM instrument; severity instrument, scale and standardized terminology; disease-specific fatigue, sleep, OI, pain instruments
Develop and disseminate strategies for engaging severely ill and very severely ill in studies
Overcome the sex, race, age, socioeconomic biases in existing data and research cohorts; account for males, minorities, youth, poor underrepresented (and underdiagnosed)

INTRINSIC BIOLOGICAL HETEROGENEITY

Barriers:

Complex disease, multisystem involvement

Multiple triggers/etiologies

Disease provocation, spontaneous fluctuation

Disease progression, remission, relapse

Diversity of severity

Diversity of symptomology

Confounding comorbidities, overlapping syndromes

Lack of validated, standardized objective measure(s) and/or biomarker(s) for cohort selection

Deficiencies in disease-specific instrumentation, methods and guidelines to fully characterize and report disease features

Strategies:

Issue FOA with set-aside funding for diagnostic tests

Develop and disseminate strategies for engaging severely ill and very severely ill in studies

Develop and disseminate strategies, methods and ethical guidelines for capturing baseline versus provoked states

Encourage longitudinal data capture

Large data and biorepository for comprehensive study of disease landscape

Encourage and support identification of subjective-objective correlates

Encourage and support subgroup stratification analyses:

Define prominent clinical phenotypes by: leveraging existing (and imminently expiring) clinical expertise, conducting large-scale data analysis in a comprehensive database

Encourage researcher data stratification analyses and reporting by: definition, severity, debility, onset type, exposure/trigger, duration, progression, recovery/remission, symptoms, age, sex

Encourage transparency in reporting cohort composition metrics, including: definition(s) met and how this was determined, debility (KPS), severity (by future disease-specific scale), duration, onset type, age, sex

Reconvene a methodological working group to identify deficiencies in CDE guidelines, further standardize assessment methods and measures, and recommend areas of need for development of novel tools

Issue RFA for development and validation of disease-specific instrumentation and methodological practices to enable consistency in cohort selection, descriptive cohort reporting, comprehensive disease characterization, phenotype subgroup stratification, and sensitive capture of change in disease status, including: severity instrument, scale and standardized terminology; PEM instrument; fatigue instrument; sleep instrument; orthostatic intolerance instrument; pain instrument

Review and refine CDE recommendations to include: require cohort reporting and data stratification by PEM status; PEM instrument; severity instrument, scale and standardized terminology; disease-specific fatigue, sleep, OI, pain instruments

EPIDEMIOLOGIC KNOWLEDGE

Barriers:

Lack of basic epidemiologic assessments characterizing disease landscape precludes informed construction of subgroup cohorts for exploratory and clinical research

Given that CDC's plan for epidemiologic research is BRFSS, which is self-report phone survey based, there is a need for NIH to lead comprehensive epidemiologic studies that adequately capture this disease population

Lack of patient engagement with medical care/survey capture due to stigma, uninformed practitioners, psychosomatic narrative polluting literature/medical practice

Lack of centralized patient registry portal for engagement with research data capture efforts
DMCC only includes CRC data and omits many large cohorts with extensive phenotyping data
Sex, race, age, socioeconomic biases in existing data and research cohorts, males, minorities, poor, youth underrepresented (and underdiagnosed)

Strategies:

Conduct exhaustive, comprehensive epidemiologic study, using appropriate patient selection methods, to define: demographics; prevalence; natural history, onset types, triggers, environmental exposures, risk factors; breadth of symptomology; spectrum of severity, establishing foundation to develop disease grading metric and instrumentation; exertional and cognitive provocation/PEM triggers; duration, fluctuation, progression, remission/recovery, relapse; comorbidities and overlapping syndromes (e.g. POTS, EDS, FM, MCAS, SFN, endocrine dysfunction, SIBO, MCS); functional and mobility impairment, disability.

Assess and rectify age, sex, race, socioeconomic biases in diagnostic capture and prevalence estimates
Overcome the sex, race, socioeconomic, age biases in existing data and research cohorts; account for males, minorities, poor, youth (underrepresented and underdiagnosed)

Support appropriate community-based epidemiological strategies to help medical practitioners in underserved areas recognize ME in their patient populations

Include ME-targeted components in existing broad epidemiological initiatives like the All of Us Research Program and the Environmental Influences on Child Health Outcomes Program

Establish a large data and biorepository for comprehensive study of disease landscape, implementing exceptional rigor in data collection, construction, and design; and incorporate other large cohorts (e.g. UK Biobank, Klimas, Stanford) into the DMCC

Fund establishment of a patient registry portal for data capture

Fund targeted data aggregation efforts

Fund retrospective analyses utilizing pooled existing cohort data and clinical histories

Fund/initiate prospective longitudinal studies

INTERDISCIPLINARY COLLABORATIVE APPROACHES

Barriers:

Investigators with expertise in overlapping domains are ignorant about ME

ME research is currently being conducted in silos

Need mechanisms to link clinicians and researchers

Role of comorbidities, overlapping syndromes understudied

Clinical subtypes undefined

Strategies:

Targeted outreach soliciting proposals from relevant domain experts (senior PIs) (e.g. energy metabolism, neuroinflammation, autonomic dysfunction, mechanisms of central/peripheral asthenia)

Issue FOAs for collaborative projects to facilitate engagement of outside expertise with established ME researchers

Issue FOA for collaborative supplements to existing projects (i.e. NIGMS Supplements for Collaborative Science (SCS))

Issue FOA for interdisciplinary collaborative project proposals (i.e. NIGMS Glue Grants)

Sponsor NIH conferences annually to disseminate findings, facilitate collaborations

Facilitate representation at society conferences, encourage block symposium to elevate disease profile, invite high-profile scientists to leverage star power

Engage in targeted outreach soliciting proposals from relevant intramural and extramural domain experts (senior PIs)

Facilitate matchmaking between domain experts and clinical expertise/bioresources

Compile and disseminate a disease primer/educational video(s) for new investigators of biologic knowns, clinical resources, crash-course on disease-specific issues

Program Officers perform matchmaking between applicants and outside domain experts during grant submission/revision

Issue dedicated disease-specific RFA to entice researchers and clinicians with outside expertise

Create a large data and biorepository for comprehensive study of disease landscape. Leverage the integration database created for the current Centers to store research from present and future ME-related projects. Make data integration a requirement for NIH-funded research on ME. This could include structured and unstructured data with all PII masked to safely protect patient data. Solicit data from other agencies to get a baseline sample set for research. Department of Veteran Affairs has a very large health database, for example.

Exhaustively publicize new disease findings, CRC results

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

Support development of in vitro/in vivo disease models

To be a better patient advocate, I audit graduate-level courses at Rice University and notice a distinct trend in today's student body toward high-multiple degrees and very specific specialization, to stand out. Looking across universities, I also see increasingly creative interdisciplinary joint degree programs and fellowships, as well as programs offered by two institutions where students toggle between campuses.

Informative Analogies: the combined Internal Medicine/Psychiatry residency at Duke University, Emory et al. that has populated a small professional association and the pages of a niche journal; EnMed, Texas A&M University's innovative Engineering Medicine school, developed in concert with Houston Methodist Hospital, to educate a "new kind of physician" for transformational change; and the M.S.L. degree program at Yale Law for a small number of non-lawyers who want to master basic legal understanding, to explore in-depth the relation of law to their different native discipline.

I would recruit a major academic institution to play host and seat an advisory board of otherwise inaccessible “stars” to create curriculum, ponder how to build seamlessly continuous career ladders, etc. Interdisciplinary training reduces perceived dependence on scarce ME/CFS funds and prepares acolytes and influencers alike to write the stories that fire the imagination of successive generations of students.

Though your task order emphasizes “early,” do not overlook mid-career candidates, even from non-science backgrounds. The revolution in free or low-cost, high-quality education online makes it more realistic than ever for older, returning students to discipline-hop. Speaking from personal experience, those students will tend to have creative fires, perspective, and the determination to walk through walls, turning skeptics into believers.

Give a thought, too, for business school students who are hugely motivated to find ideas in the life sciences and whose numbers include more and more devotees of social enterprise. Their energy is infectious, and they are cross-pollinators who may plant the spark and set alight a young science team. I consider MBA students a secret weapon for designing vehicles to render “impossible” obsolete – music to the ears of ME.

As noted in my response to a previous question, the nomenclature has long stood as an impediment. It is high time for CFS to be retired. ME is a practical and worthy replacement.

Again, public, medical professionals and Ph.D. level programs that KNOW about the disease. Education. Information. Data. The NIH acknowledging to the public that ME/CFS exists and is a national and worldwide problem that needs to be addressed. Plus, make it easy for investigators to find all research regarding this disorder so that it can stimulate them to take the next logical step. Advertise that the world needs this mystery to be solved. I can just imagine being "the one" who solves the puzzle.

Virologist ,
Think about fail in our immunization.