Lily Chu, MD, MSHS – US ME/CFS Patient Survey – April to May 2013

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During April 2013, I was invited by the FDA to participate in their Drug Development Workshop as a patient representative and Board Member of the International Association for CFS/ME. To answer some of the questions posed, Dr. Leonard Jason, Madison Sunnquist, and Suzanna So helped me design and analyze an online survey. We disseminated the survey through popular online ME/CFS sites/ e-mail groups and state/ local support groups; recipients were also encouraged to forward the survey to anyone they felt might be interested.

Preliminary results from 477 respondents were shared at the April meeting. This report summarizes results from all 623 respondents living in the US who reported a clinician-confirmed diagnosis of ME/CFS. Approximately 50% participated in the Workshop only through this survey. Overall, results did not differ substantially from what was presented in April.

Demographics:

86% of our subjects were female and almost all subjects were Caucasian. The average age was 51±13 years and the average duration of illness was 18±11 years. 67% had graduated with at least a Bachelor's degree. All 9 US Census Bureau regions were represented.

Symptoms:

The top 5 most significant symptoms patients reported, respectively, were fatigue, exhaustion after mild activity, memory/ concentration issues, increase in symptoms after mild activity, and pain. Many other symptoms including symptoms that haven't been studied as much (such as multiple chemical sensitivities, gastrointestinal symptoms, and orthostatic intolerance) were also deemed to be significant by over 50% of our subjects.

99% felt that their illness was not improving over time, citing worsening of existing symptoms and appearance of new symptoms. About a third believed that their health was getting worse over time.

Testing:

We asked about five tests that ME/CFS specialists commonly order to assess their patients – natural killer cell activity, repeated cardiopulmonary exercise test, brain imaging, neuropsychological testing, and tilt table. For each test, about 50% of respondents had never had the test before partly due to cost, insurance coverage, or physician ignorance and resistance to ordering a test.

Of those who had any of the five tests, 66% had at least one abnormal result. For natural killer cell activity, 73% noted an abnormal result; for tilt table testing, 77%.

Impact on Daily Life:

Using the SF-36 Physical Functioning subscale, we found our respondents to be more disabled than 95% of the general US population as well as the average patient with chronic lung disease, congestive heart failure, or osteoarthritis. Only 13% were employed, with almost all citing ME or CFS as the reason why they could not work. For even basic personal care, 89% had to change their pre-illness routine; at least a quarter needed assistance from another person or special equipment (e.g. shower chairs, wheelchair, etc.). On their worse days, 61% were bedridden. On their best days, 75% were primarily homebound and could only do some light housework or less.

Perspectives on Current Treatment:

The overwhelming majority of people felt current treatments were not helpful or only slightly helpful but not enough to improve their day-to-day functioning. Patients repeatedly wrote about the need for disease-modifying treatments and not only for treatments that helped control symptoms.

We asked about how well currently recommended treatments worked. These treatments were cited as helpful by more than 50% of subjects:

- for the overall illness - balancing rest with activity, restricting or modifying physical/ mental activities
- for sleep – CPAP, over-the-counter medicines (such as Benadryl/ Tylenol PM), zolpidem, eszoplicone, tricyclic antidepressants, trazodone, benzodiazepines
- for pain – short/ long-acting opioids, flexeril, ibuprofen, chiropractor, biofeedback/ meditation
- for cognition – behavioral measures such as reminder notes

Behavioral measures were cited as essential in helping subjects cope with symptoms and daily activities but were noted to neither alter the course of illness nor substantially improve symptoms. We asked about antivirals, antibiotics, and immunomodulators but clear answers were not forthcoming due to mixed effects from the drugs (including side effects), uncertainty about benefit, or low numbers of respondents.

Subjects were also given space to note any additional treatments that they found useful for the above symptoms. Following are some that were commonly mentioned.

- for the overall illness - 45% of those who wrote about Vitamin B12 (intramuscular or sublingual) found it helpful, others cited magnesium and various vitamins
- for sleep – gamma-hydroxybutyric acid, cyclobenzaprine/ flexeril particularly for those with nocturnal pain, and valerian
- for pain – 58% of those who wrote about massage found it helpful but noted that the type of massage or masseuse was important, otherwise it could cause increased pain; 64% found heat packs/ hot baths helpful

We also left space for respondents to write about any symptoms we did not target in this section and corresponding treatments. Gastrointestinal symptoms were mentioned by 130 subjects who treated this with a gluten-free/ dairy-free diet or probiotics; orthostatic intolerance was mentioned by 105 subjects who used salt and water loading, beta-blockers, and fludrocortisone with some benefit.

The main reasons cited for stopping a medicine were side effects followed by decrease in effectiveness over time, especially with sleep medications. For effective non-prescription or non-drug treatments, cost, insurance coverage, and availability were major reasons for discontinuation. Respondents were also concerned about being more sensitive to drugs and the dependency potential of some medications.

62% cited formal exercise programs as worsening their health. Respondents commented that clinicians were not well-educated about post-exertional malaise and activity limits; some reported long-term disability from incautious activity. Contrary to what has been reported in the literature, despite suffering symptoms, many subjects continued to try to exercise or maintain some level of physical/ mental activity. These respondents recognized the effects of sedentary behavior but at the same time wished healthcare workers understood the limiting aspects of their illness.

Themes From Patient Comments to FDA:

We asked subjects at the end of our survey if there was anything else they wanted to mentioned to the FDA. The following box summarizes common themes from the 244 comments submitted:

Other Comments (n=244)
ME/CFS is an extremely debilitating disease - many losing hope
Lots of elderly patients with ME/CFS who have been sick for many years
A few teen patients with ME/CFS - want research on pediatric ME/CFS
Some do not want the term "CFS" anymore - name change desired
Why hasn't there been a cure? Why is research money being wasted?
When will drugs be approved?
Want to try Ampligen
Don't focus on medications for individual symptoms
More research on treatment and drug development
Importance of supplements and possibility of insurance coverage
Drugs' effects on patients who also have multiple chemical sensitivities
More research on cause/biomarkers of illness - pathogens, autoimmune
Educate doctors and healthcare workers
Medications are too expensive and not covered by insurance or Medicare

Conclusions:

1) There is a clear need for effective disease-modifying treatments, especially illustrated by the long duration of illness and very low level of functioning suffered by the respondents of this survey. Although fatigue was the top significant symptom, exacerbation of symptoms with mild activity, cognitive symptoms, and pain (all part of the 1994 Fukuda definition) were also deemed to be important by subjects. If a drug is to be marketed for ME/CFS overall and not only for a specific symptom, improvement in more than just fatigue should be required by the FDA.

2) Symptoms not included in the 1994 Fukuda definition of CFS, such as those affiliated with orthostatic intolerance and irritable bowel syndrome were cited by many subjects. There are currently drug trials addressing these conditions; perhaps FDA can provide incentives for these trials to include a subgroup of CFS patients if they fit the trial inclusion criteria otherwise.

3) 61% of respondents were bedridden during the worst part of their illness. Since most drug trials involving CFS have been clinic-based, the most severely affected have likely not been included. FDA should encourage drugs companies to consider addressing this population when designing trials, .e.g. including mobile blood draws or home-based assessments.

3). Contrary to the idea that all tests are normal in CFS patients, we found that 66% of our respondents had at least one abnormal test out of five commonly given to patients by ME/CFS specialists. Such tests can be used by pharmaceutical companies to objectively assess symptoms for study inclusion criteria or as outcomes measures.

4) Although no particular drug listed by us or cited by respondents emerged as a surprising blockbuster drug that could be re-purposed for overall use in ME/CFS, our table does provide some information that certain drugs might be more effective or less harmful for treating specific symptoms than others. This information might be useful for patients and clinicians. Furthermore, there were not enough respondents/ unambiguous answers to address how effective specific immunomodulators/ antivirals may be.

5) Use of complementary/ alternative treatments ranging from vitamin/ supplements is common as is low tolerance for “normal” drug doses. These factors should be considered when designing drug trials to decrease the chances of drug interactions and adverse effects.

Limitations:

Since this was an online survey using self-reported clinician-confirmed diagnoses of CFS or ME, we were unable to personally confirm exactly who had CFS or ME. About 6% of respondents stated they were self-diagnosed or did not have CFS or ME and were not counted in the results. Similarly, with questions about objective testing, we relied on self-report and could not confirm test results.

The overwhelming majority of respondents to our survey self-identified as Caucasian and 67% possessed at least an undergraduate college degree, a much higher percentage than the general US population. This is likely a result of adequate access to care to obtain an accurate diagnosis, Internet access, and membership in support groups rather than an accurate reflection of the epidemiology of ME or CFS. In fact, multiple community-based studies suggest a higher prevalence and more severe morbidity in minority populations. We also believe that we captured a sicker population than most prior ME/CFS studies. With the exception of one, most CFS studies have been clinic/ community-based, not home-based, and have reported SF-36 functioning scores in the 40-60 range compared to our average score of 25. Since our survey was accessible online, even homebound and bedridden patients could participate. Dissemination through support groups might also have skewed our respondents towards those who had been sick longer. Thus, our survey results may not be generalizable to non-Caucasian, lower socio-economic, less severely affected, or shorter duration-of-illness groups.

Effectiveness of a treatment was based on respondent recall. Since respondents might have tried a treatment years ago and ME/CFS includes cognitive dysfunction as a symptom, these factors might affect how accurately respondents answered. We did not have access to medical records to confirm contemporary patient opinions of treatment.