



AWARENESS



ADVOCACY



ADVANCEMENT

May 24, 2023

via email

Gary H. Gibbons, MD
Director, National Heart, Lung, and Blood Institute
Walter Koroshetz, MD
Director, National Institute of Neurologic Disorders and Stroke
9000 Rockville Pike
Bethesda, MD 20892

Re: Advancing POTS Research

Dear Dr. Koroshetz and Dr. Gibbons:

On behalf of Dysautonomia International, I want to thank you for taking the time to meet with me and my colleagues on Monday, May 15th as a follow-up to our in-person meeting with Acting NIH Director Dr. Lawrence Tabak and Acting NIH Deputy Director Dr. Tara Schwetz on March 10th. We appreciate the continued dialogue and interest in working together to ensure more NIH resources are directed towards postural orthostatic tachycardia syndrome (POTS) research.

As you know, over six million Americans living with POTS, and their families, are counting on us to deliver effective FDA approved therapies and cures. To ensure our collaboration is successful, I have outlined several critical elements of our conversation below for your further review and consideration. Dysautonomia International looks forward to this moment becoming a turning point for patients, researchers, and the NIH in igniting profound change in the federal government's commitment to POTS patients through robust research initiatives.

We look forward to scheduling another opportunity to meet with you, and your colleagues, including Dr. Hugh Auchincloss, Acting Director of the National Institutes of Allergy and Infectious Diseases (as recommended by Dr. Tabak), in the next few weeks to maintain momentum.

NIH's Commitment to POTS Research To Date

During our recent call, Dr. Gibbons stated that the NIH had hosted multiple POTS expert meetings and had issued multiple POTS Research Funding Announcements (RFAs). Unfortunately, as we mentioned on the call, this is inaccurate. We are concerned that if the NIH and its staff are working under the false assumption that NIH has already completed this work on behalf of the POTS community, this will make the NIH less inclined to do the meaningful work needed to advance POTS research for our patients, so it's important to clarify what has transpired to date.

NIH has never issued an RFA seeking POTS research applications, but we would certainly welcome one. NIH did issue one Notice of Special Interest (NOSI) with no specific POTS research funding attached to it in March 2021, which expires in May 2024.

Additionally, after instruction from Congress in 2018, the NIH held one POTS expert consensus meeting to identify the top research priorities needed to advance clinical care for POTS patients, and to identify how much funding would be needed to pursue such identified research priorities. The meeting was held on July 29, 2019 at the NIH campus in Bethesda, Maryland.

Before the meeting, the POTS researchers were told by NIH staff they were not allowed to discuss certain topics, including any mention of how much funding may be needed to address the top POTS research priorities, even though Congress itself had requested this information. Following the meeting, the NIH published its own findings, which were not disseminated to or approved by the experts in attendance, including myself, prior to NIH publishing its report. Out of concern that the NIH's report did not reflect what was discussed during the meeting, the 30 POTS experts who attended the meeting sent a letter to former NIH Director Francis Collins in 2020 expressing concerns and requesting correction of the NIH's report. NIH issued a revised report, again publishing it without disclosing it to or seeking feedback from the POTS expert meeting attendees. The revised NIH report still did not reflect the scientific consensus of the experts in attendance at the POTS experts meeting and failed to respond to the Congressional request to provide an estimate on costs to achieve the POTS research priorities identified during the meeting.

As a result, the 30 POTS experts published their own two reports summarizing the meeting findings in 2021 as peer-reviewed journal articles. Part 1 focused on the state of science and clinical care and Part 2 focused on priorities for POTS care and research (see attached). Since NIH failed to respond to Congress's request to provide a cost estimate to achieve the top POTS research priorities, the experts provided this estimate for Congress, noting that an increase in NIH funding of \$10 million per year for the next five years would be needed to address the research priorities outlined in the expert consensus documents.

Unfortunately, a careful review of the NIH RePORTER database reveals that NIH has not increased its POTS research investment since 2014, which has remained stagnant at roughly \$2 million per year or less. Two million dollars is an inadequate investment to make substantial progress in any field, much less one affecting millions of Americans, especially as our POTS patient population continues to see rapid growth due to continued SARS-COV-2 infection.

Importantly, just as the POTS experts pointed out in their 2020 letter to Dr. Collins, in its online categorical spending report, NIH is counting research that has nothing to do with POTS in its tally of POTS research funding. For example, Dr. David Goldstein's intramural NINDS research on neuroimaging in Parkinson's disease is counted in NIH's POTS research funding tally, despite this research having no relationship whatsoever to POTS research or clinical care, as confirmed by Dr. Goldstein. Despite this concern being raised to Dr. Collins in writing by the POTS experts several years ago, NIH continues to claim this study and other research studies unrelated to POTS in its tally of POTS research funding. We ask that NIH updates its online categorical spending report to accurately reflect the amount of money NIH is actually investing in POTS research.

Congress Directives to NIH Regarding POTS Research

To date, Congress has included appropriations language in the Labor, Health and Human Services, Education and Related Agencies Appropriation bill for the past six years directing the NIH to pursue robust POTS research and stimulate the field to benefit the millions of Americans living with this debilitating disorder. With the support of patients, families, researchers and Congressional leaders, the following provisions in summary have been advanced by Congress.

Fiscal Year 2023: The agreement strongly encourages NIH to establish a new multi-Institute Notice of Special Interest to spur additional needed research addressing the identified gaps in knowledge.

Fiscal Year 2022: The agreement encourages NIH to ensure that the \$1,150,000,000 investment Congress has provided to NIH for PASC research is used, in part, to identify how viruses like SARS-CoV-2 result in autonomic nervous system dysfunction, such as POTS, and how we can most effectively treat PASC associated autonomic nervous system dysfunction, including PASC associated POTS. The agreement encourages NIH to leverage the expertise of research centers that have previously studied post-viral POTS in pursuing these important research questions.

Fiscal Year 2021: While NIH did convene a distinguished group of POTS experts in July 2019, many critical questions and knowledge gaps remain regarding the causes and mechanisms of POTS and potentially effective treatments. The Committee encourages NIH to continue a dialogue with the POTS experts who attended the June 2019 NIH meeting regarding the evolving state of science on POTS. The Committee directs NIH to: (1) update the January 31, 2020, report after further consultation with POTS experts and submit a revised report to the Committee; (2) implement the research priorities described in the revised report; and (3) provide a progress update to the Committee 90 days after enactment documenting progress towards implementation.

Fiscal Year 2020: NIH is directed to submit the report on Postural Orthostatic Tachycardia Syndrome (POTS) that was requested in Senate Report 115–289, now overdue, no later than 30 days after enactment of this Act. NIH is strongly encouraged to include an estimate of annual NIH funding allocated to POTS research in its publicly available RCDC report.

Fiscal Year 2019: The Committee directs NIH to provide a report to the House and Senate Committees on Appropriations 9 months after enactment of this act that reflects participants' findings on: (1) the current state of POTS research; (2) priority areas of focus for future POTS research through 2025; (3) a summary of ongoing or upcoming efforts by NIH to advance the scientific understanding of POTS; and (4) an estimate of the level of funding that would be needed annually to achieve objectives (2) and (3).

Fiscal Year 2018: The Committee expects NHLBI and NINDS to work with stakeholders to stimulate the field and develop strategies that will increase our understanding of POTS and lead to effective treatments.

POTS Researchers Requests of NIH

In addition to the two expert reports cited above, please find attached a May 8, 2023 letter from 41 leading POTS researchers and clinicians to Acting Director Tabak supporting additional NIH funding for POTS research and a request for the NIH to create a POTS informed review panel to review POTS grant applications, recognizing the lack of understanding amongst the research and medical community of the disorder.

Specifically, the authors requested “that NIH prioritize POTS research in FY2024 and beyond, so that we can deliver more effective treatments to this large and growing underserved patient community.”

Sharing Pertinent Information in an Open and Transparent Manner

As previously mentioned, the NIH website outlines the last three years of NIH funding for POTS, which we believe to be an overestimation and inaccurate. We hope to establish a clear understanding early in this dialogue to ensure our definitions and common terms are in concert to avoid the mischaracterization of relevant research to our field.

We have heard from NIH officials, including during our recent meeting, that the lack of POTS research funding is due to a lack of POTS research grant applications. We find ourselves in a situation unable to prove the negative without some level of transparent sharing of information pertinent to this NIH response. The leading researchers in the field maintain to Dysautonomia International that they are submitting high value worthwhile research projects equal to, or better than, submissions in other research fields that receive substantial NIH funding.

To address this discrepancy, we respectfully ask that the NIH provide information, not identified at the researcher level or the specific application title, but in the aggregate, to establish shared information for our continued conversations. Specifically:

- How many applications have been submitted referencing the POTS NOSI since it was issued in spring 2021?
- How many applications in response to the POTS NOSI were scored by NIH reviewers vs rejected administratively?
- How many applications in response to the POTS NOSI were funded to date?
- Outside of the NOSI, how many applications for POTS research have been submitted to NIH and its Institutes since FY 2018? How many of those applications have been funded?

Analysis of POTS Researcher Experiences with NIH Applications

We appreciate your recommendation to work with our research colleagues to better understand their experiences in submitting NIH grant applications for POTS research. In that regard, we have asked researchers to share summary statements included in their denied submissions.

We would welcome the opportunity for you to speak directly with leading researchers in the field and are happy to facilitate those discussions. It is our hope that we can all speak frankly about NIH's interest in receiving proposals under the pending NOSI, that there is real opportunity for funding when submitting in response to a NOSI, and that you both are personally committed to seeing your Institutes and colleagues working with the POTS community to advance more research for treatments and cures for patients.

Understanding the role of the Center for Scientific Research

We found the discussion around the NIH Center for Scientific Research (CSR) interesting. We have heard consistent concerns from the POTS research community that their proposals are rejected by review panels unfamiliar with POTS.

Understandably, many researchers find themselves in a difficult situation when a submission is rejected to either argue their case on appeal or simply move on without risk to their future NIH proposals. We look forward to working with you and the CSR to ensure the CSR study sections maintain a robust roster of well-informed and experienced professionals with a well documented understanding and appreciation for POTS.

We would welcome the opportunity to have a leading POTS researcher present a one-hour Grand Rounds style lecture for CSR reviewers who serve on panels that may be more likely to receive POTS applications, and NIH program staff who may receive POTS applications. Increasing the internal knowledge about POTS within NIH is important to addressing the challenges POTS researchers face in trying to get their applications reviewed fairly, by people who are knowledgeable about what is relevant and important in POTS pathophysiology and treatment research.

We also look forward to further dialogue with your program officers in coordination with each of you respectively to ensure that a clear understanding, appreciation, and commitment to fund POTS research is conveyed throughout your Institutes. Communication and ongoing dialogue will assist all of us in measuring our progress and reporting to the POTS community and Congress.

Next Steps

In review, we would greatly appreciate the following next steps to continue the momentum of our previous conversations to further support research for POTS patients. Specifically:

- Could you please provide an email introduction of Dysautonomia International, and myself, to Dr. Noni Byrnes, the Director of CSR?
- Dr. Gibbons, thank you for the reference to Dr. Goff at the NHLBI. Could you please provide an email introduction of Dysautonomia International, and myself, to Dr. Goff via email?
- On behalf of Dysautonomia International, I would like to invite both of you to join a private discussion with leading POTS researchers during the upcoming POTS Researchers Roundtable, which will take place during Dysautonomia Annual's 11th Annual Conference in D.C., July 15-16, 2023. We are more than happy to work with each of you prior to the conversation on the framework for the discussion and questions to be asked ahead of time to ensure a productive and informative dialogue with our research community.

In conclusion, we again want to express our appreciation for your commitment to POTS patients. We are actively working with leaders in Congress to direct \$50 million in new POTS funding for FY2024 (see attached). Working together, along with the leading POTS researchers, we can ensure this commitment of resources makes a difference. We look forward to continued conversations and to scheduling another conversation in the coming weeks to discuss our findings from a review of the POTS researcher summary statements.

Sincerely,



Lauren Stiles, JD

President, Dysautonomia International

cc: Dr. Lawrence Tabek
Dr. Tara Schwetz