National
Multiple Sclerosis
Society

FUNDING ANNOUNCEMENT

Health Care Delivery and Policy Research Program
CONTRACT PRIORITIES for Fiscal Year 2016

Eligible applicants include private non-profit and for-profit entities, and government organizations. Applicants who wish to apply for more than one of the following priorities must submit a separate application for each using the Society's Web-based proposal preparation and submission system: **https://nmss.fluxx.io**

1. **What are the factors related to cost-escalation of MS DMT's and how does the cost of DMT's, particularly out of pocket costs, relate to access to DMT's, payer's policies concerning coverage, initiation of and adherence to therapy, and the ways in which people with MS view the value of treatment? The Society would like to fund this priority in two phases with the cost component on a fast-tracked basis and the value component as a longer-term component.**

2. **What is the extent to which people with MS utilize complementary and alternative medicine? To what extent is this utilization part of an integrative medicine approach that combines mainstream medicine and CAM? What are the policies followed by payers for coverage of CAM independently and as part of integrative medicine?**

3. **What are the barriers preventing access to rehabilitation services, particularly maintenance services among people with MS and what are some of the potential solutions to these barriers?**

Deadlines:

A letter-of-intent is *required*; authorization to submit a full application will be contingent upon an invitation from the Society following review of the letter-of-intent. All letters of intent must be submitted through the Society's Web-based proposal preparation and submission system: https://nmss.fluxx.io

- **Our receipt online of your two-page letter(s)-of-intent 10/7/2015**
- **Approval e-mailed to selected investigators to submit full applications (projected) 11/10/2015**
- **Our receipt online of your full application 1/14/2016**
- **Peer review committee meets 4/2016**
- **Notification of approval, conditional approval, or denial (projected) 6/2016**
- **Contract start date will be determined through negotiations with the Society**

For more information contact:

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All letters-of-intent and full applications are reviewed by a peer-review panel consisting of scientists and clinician-scientists drawn from a variety of relevant specialties, including health policy, neurology, epidemiology, and others. This peer-review panel operates in a way very similar to NIH peer-review study sections. Proposals are evaluated on the basis of scientific merit and relevance to multiple sclerosis. Detailed reviewer's comments are provided to all investigators submitting full applications, whether or not they are recommended for funding. Funding recommendations are made without geographic bias and neither the National Board of Directors of the National MS Society nor donors play a role in the process. All funding recommendations are reviewed by the Society's Research Programs Advisory Committee (RPAC), a panel similar to a NIH council. Review by the RPAC helps to ensure the fairness and integrity of the Society's peer review process, which has been in place for more than 60 years.

Priority 1: What are the factors related to cost-escalation of MS DMT's and how does the cost of DMT's, particularly out of pocket costs, relate to access to DMT's, payer's policies concerning coverage, initiation of and adherence to therapy, and the ways in which people with MS view the value of treatment? The Society would like to fund this priority in two phases with the cost component on a fast-tracked basis and the value component as a longer-term component.

The goal of the proposed study is to acquire, analyze, and interpret data in order to understand the factors driving the significant increase over time in the cost of MS disease-modifying drugs as well as the impact of these costs on people with MS. Of particular interest are the ways in which these costs are passed on to people with MS, both indirectly through coverage restrictions and directly through out-of-pocket costs such as co-pays and co-insurance. A second goal is to explore "value metrics" concerning DMT's in order to develop a better understanding of how people with MS view the value of DMT's and how the perception of value is affected by cost.

The National Multiple Sclerosis Society invites qualified investigators to submit two-page letters-of-intent through our Web-based system describing a proposed study to assess the factors responsible for the high cost of DMT's and the continuing escalation of these costs. Such a study should also explore how DMT costs result in payer strategies designed to control costs which restrict access to therapies. In addition the proposed study should examine the ways in which people with MS may respond to high drug costs by delaying the start of treatment, failing to adhere to treatment regimens, taking drug holidays, stopping treatment altogether, or diverting funds from other important life activities. An additional component of the study would explore how people with MS perceive the value of DMT treatment and how those perceptions are affected by cost.

Background:

Individuals with MS are fortunate to have more than a dozen options in terms of disease-modifying drugs that have been approved by the FDA. These DMT's range widely in terms of: mechanism of action, route of administration, dosing, benefits, and side effects. However they are similar in terms of their cost and in terms of a history of cost escalation in spite of increased competition from newer drugs. Insurers have responded to the issue of DMT costs with a variety of cost-management strategies such as specialty tiers, step-therapy, and others. These cost-management strategies have complicated access to DMT's. In addition, both anecdotal and pharmacoeconomic data suggest that the out-of-pocket costs of these drugs weigh heavily on people with MS and may result in failure to start therapy, deviation from prescribed dosing schedules, or stopping therapy altogether. While some studies have examined the issue of out-of-pocket costs, there has not been a study that comprehensively examined not only the effects of high cost and cost escalation but also the forces driving them. At this point in time we lack current, systematic, comprehensive, and scientifically sound data concerning the issues related to the costs of DMT's and their impact on people affected by MS. The proposed study would address these gaps. Having such information would greatly assist efforts to address and ameliorate the adverse effects of these issues.

The issue of cost is related to the issue of value as perceived by people with MS. Although there are many treatment options for people with MS and many studies have

examined the clinical and paraclinical outcomes of such treatments, there has been less research focused on understanding the ways in which people with MS perceive the values of these treatments and how those perceptions are influenced by cost factors. The proposed study would develop a set of value metrics that incorporate the perspectives of people with MS and how these are affected by cost.

Timing:

The Society intends to fast-track the cost phase of this priority owing to the pressing nature of cost-related issues both for PwMS and the health care system. In this case fast-tracking may affect several of the milestones connected with the submission, review, and implementation of the proposed project. This might include:

- Notification of eligibility to submit a full application
- Deadline for submission of a full application
- Date for review of the full application
- Date for notification of award
- Start date of study
- End date of study
- Deadline for submission of final report

Full details concerning the above dates will be provided following review of the letter-of-intent.

Priority 2: What is the extent to which people with MS utilize complementary and alternative medicine? To what extent is this utilization part of an integrative medicine approach that combines mainstream medicine and CAM? What are the policies followed by payers for coverage of CAM independently and as part of integrative medicine?

The goal of the proposed study is to acquire, analyze, and interpret data in order to determine the extent to which complementary and alternative therapies are utilized by people with MS; the extent to which CAM is utilized independently, alongside traditional medicine, and/or as part of an integrated approach combining CAM with traditional medicine; and how payers handle claims for CAM either as stand-alone therapies or as part of overall coverage for MS and primary care.

The National Multiple Sclerosis Society invites qualified investigators to submit two-page letters-of-intent through our Web-based system describing a proposed study that would address the extent, patterns, and coverage of complementary and alternative therapies among people with MS.

Background:

Many studies have attempted to examine the extent to which people with MS use CAM as part of their response to MS. However in recent years the lines between mainstream medicine and CAM have shown signs of blurring. The American Academy of Neurology recently published a review on the subject and some treatments traditionally considered somewhat outside the mainstream have gained traction with both patients and practitioners, e.g., Vitamin D supplementation and mindfulness. At the same time, CAM has begun to acquire increased legitimacy as part of a trend toward integrative medicine which seeks to incorporate the best of many approaches to healing. This trend is particularly appealing in MS where there are many treatments available that are partially effective but which do not totally alleviate the myriad symptoms of MS. Moreover as more people with MS explore the potential benefits of a wide variety of treatment strategies, there is increasing pressure on insurers to incorporate many of these in their coverage.

The proposed project would take an innovative approach to the study of CAM, its relationship to mainstream medicine, and the extent to which coverage for it is available. Pragmatic trials of CAM-related interventions are on the rise and as we learn more about the benefits and risks of CAM interventions it is important that we develop a better understanding of the utilization of these interventions and how they fit in with the overall landscape of medical care. Data from the proposed study could be used by the Society to help drive programmatic priorities and to inform advocacy efforts regarding appropriate access to worthwhile interventions.

Priority 3: What are the barriers preventing access to rehabilitation services, particularly maintenance services among people with MS and what are some of the potential solutions to these barriers? Barriers may include cost, insurance coverage, architectural barriers, transportation, distance, membership in underserved populations, lack of information concerning services, lack of qualified providers, age, and inadequate documentation, among others.

The goal of the proposed study is to acquire, analyze, and interpret data in order to gain a better understanding of the extent to which people with MS have access to appropriate rehabilitation services, what barriers stand in the way of such access, and how those barriers can be overcome.

The National Multiple Sclerosis Society invites qualified investigators to submit two-page letters-of-intent through our Web-based system describing a proposed study to investigate what are the barriers preventing access to rehabilitation services, particularly maintenance services among people with MS and what are some of the ways in which those barriers can be overcome? Barriers may include cost, insurance coverage, architectural barriers, transportation, distance, membership in underserved populations, lack of information concerning services, lack of qualified providers, age, and inadequate documentation, among others.

Background:

MS is a complex, multi-faceted, and lifelong condition that requires comprehensive attention by health care providers to myriad symptoms and functional limitations. While DMT's and symptomatic treatments have improved the picture for people with MS, functional limitations that compromise independence remain a significant issue, especially among those with a progressive course. Rehabilitation offers a wide and increasing array of strategies to improve function where feasible, maintain function in other cases, or slow further loss of independence. However anecdotal reports suggest that access to needed rehabilitation services can be a significant challenge for many. This is particularly true for those in need of "maintenance" therapy, i.e., treatment geared not to improvement so much as stemming the tide of deterioration. Access to maintenance therapy among Medicare recipients was the subject of a recent decision in a class action suit that successfully affirmed coverage for maintenance therapy for Medicare recipients. Unfortunately access to maintenance therapy and, to some extent, restorative therapy remains a challenge for many. Results of the proposed study would provide the Society with critical information to help drive advocacy efforts to expand the benefits of rehabilitation to a larger segment of the MS population, particularly those in need of maintenance therapy to help preserve their independence.

Methodological Considerations for Priorities 1 – 3

The proposed study could combine a variety of research methodologies including qualitative research methods (e.g., focus groups), survey methods (e.g., mail, phone, and/or face to face interviews), and analyses of existing datasets, or other methods, although it is anticipated that some primary data collection will be needed. Qualitative research should include adequate methods for structured scoring and analysis of data. Novel means of data collection are encouraged, where appropriate. Collection of data in whatever form should be undertaken in such a way as to maximize, to the extent feasible, that the results can be generalized to the target MS population or subpopulation (for example pediatric patients, patients living in rural areas, etc.).

If surveys are implemented, particular attention should be paid to the proposed samples, including how they will be drawn, how subject selection will be conducted, and what steps will be taken to ensure that they are as broadly representative as possible of the target population. Applicants should present a plan that justifies the proposed sample selections and minimizes selection biases to the extent that it is feasible and economically possible to do so.

If existing datasets are utilized, the investigators should ensure that such datasets are reasonably representative of the target populations that are the subjects of this announcement and include key variables needed to accomplish the study's aims that are aligned with this announcement.

Study design and data collection should be planned so as to ensure the validity and interpretability of the resulting data. The protocol should include procedures to ensure data collection is implemented in a consistent way and that all data are complete.

The protocol should emphasize the use of standardized techniques with recognized reliability and validity. Measures should be both comprehensive and parsimonious, i.e., variables of interest should be thoroughly and soundly assessed and unnecessary and redundant measures should be avoided. The selection of measures should be adequately justified and the measures themselves described in reasonable detail.

The data analytic plan should include a strong justification for the proposed sample size(s) along with a detailed plan for the analysis of the data. It is strongly suggested that a statistician with experience in the type of study proposed be included as an integral member of the investigative team. Where appropriate, a health economist with experience relevant to the proposed study should also serve as a member of the team.

Where appropriate, applicants are encouraged to consider scientifically rigorous designs such as randomized controlled trials. Control groups could take various forms such as treatment comparisons, wait-list groups, placebo conditions, etc.

Dissemination Plan:

In collaboration with the Society, the proposed project must develop **and implement** a comprehensive dissemination plan. The purpose of this plan is to ensure that the findings derived from the study will be utilized effectively to publicize the implications of

the study to a wide audience. The dissemination plan may include a variety of components including: 1) publication of results in appropriate refereed journals; 2) integration of findings into the various programs of the Society; 3) materials and programs for both client and professional education; and 4) other approaches such as Web-based material, etc. Implementation of the dissemination plan will in all likelihood involve appropriate departments of the Society in collaborative efforts. The proposal should include the broad outlines of a dissemination plan. The exact details will be worked out in collaboration with the Society once the project is underway. To facilitate collaboration with the Society, the PI will meet with the Society project officer and other members of the Society staff during the first year of the project to discuss implementation of the dissemination plan. Funds for this purpose should be included in the proposed budget.

In order to facilitate dissemination of findings to the scientific community, the final payment on the contract will be retained until 1) the final research report is received and approved by the Society and 2) the investigators have submitted an article reporting the findings to a peer-reviewed journal of their choice.

Full implementation of the dissemination plan, particularly those components that involve the Society, may extend beyond the term of the project. However, the contractor will only be expected to assume operational responsibility for components of the plan implemented during the term of the project.

Organizational Considerations:

Applicants should provide evidence for their ability to organize and manage all phases of the proposed project. Applications should include letters verifying willingness to participate on the part of any proposed collaborators.

Applicants should provide evidence for their ability to organize and manage studies of the type proposed, recruit the required number of subjects (if applicable), and analyze and disseminate the results of the study. The application should describe how study procedures will be standardized and coordinated across participating locations. If appropriate, applicants should provide evidence of expertise and experience in conducting and interpreting the results of qualitative research. Such expertise may reside with the applicant or it can be provided in the form of a subcontract to an appropriate co-investigator.

Applications should include a detailed timeline with specific milestones and indication of the deliverables that will be provided at each milestone to verify accomplishment of objectives. The deliverables will be described in detail in the contract and will be the result of negotiations between the Society and the contractor. These deliverables will include periodic reports of progress in the study along with a final comprehensive report.

The final report should include a detailed data analysis along with a discussion of the findings of the study and their implications. It should also include specific recommendations based on the findings of the study. These recommendations should point to future measures that go beyond the dissemination plan developed and implemented as part of the study, e.g., specific strategies that the Society could

implement in order to address the issues identified by the project. These recommendations could encompass further research, advocacy, programs, educational efforts, etc. While the length of the final report will depend on the nature of the study and its findings, based on previous contracts funded by the Society, applicants should anticipate preparation of a report encompassing 200-300 pages or more.

Study Dataset:

Subsequent to the completion of the study and if feasible, the investigators will deliver to the Society a complete set of all data collected as part of the study in machine readable form with appropriate format statements based on a widely used statistical analysis package such as SAS or SPSS. The dataset will be accompanied by sufficient documentation (e.g., detailed data dictionaries, etc.) to allow the staff of the Society and their consultants to utilize the data with minimal consultation with the investigators. Alternatively the investigator and the investigator's institution may, with the approval of the Society, develop and implement an alternative plan to make the study data available for public use. In most cases, data collected as part of the study are the property of the Society. However, the Society realizes that under certain circumstances institutional rules or conflicting contractual arrangements will necessitate a modification in the aforementioned policy. In addition, the Society strongly encourages investigators to utilize these data for the preparation of scientific articles, conference presentations, and other materials as appropriate to a prescribed dissemination plan.

After appropriate privacy safeguards have been implemented, the study dataset will be made available to outside investigators. Outside investigators will be required to submit a detailed proposal to the Society describing how they intend to utilize the data. The proposal will be evaluated by a peer-review group and data will be released only to those investigators whose proposals pass the peer-review and have been reviewed and approved by the institutional review board from the institution of the investigator submitting the proposal.

How to apply:

A letter-of-intent is *required*; no full application will be considered unless the application is in response to an invitation from the Society following review of the letter-of-intent.

1. Read the funding cycle timetable on page 2 of this announcement for a list of important milestones.
2. Register at our apply online site, if you have not already done so: **https://nmss.fluxx.io**
3. Once you are registered, log in to our apply online site and complete and submit your two-page letter-of-intent using the pre-application facility and following the instructions on the next page.
4. Optionally, contact Dr. LaRocca to discuss your research idea before submitting the letter-of-intent.
5. Your letter will be reviewed by the Health Care Delivery and Policy Research Advisory Committee
6. You will be informed of the decision of the Committee concerning whether or not you are invited to submit a full proposal.
7. If invited to submit a full application, log in to our apply online site and begin preparation of your full application.
8. You must submit your invited, full-length proposal **in electronic form only** by 11:59 PM, Eastern Time, January 14, 2016.

GUIDELINES FOR THE LETTER-OF-INTENT

Investigators wishing to apply for funds should submit a **letter-of-intent**, up to a maximum of two single-spaced pages, for each priority for which they seek support. The letter(s)-of-intent ***must be in Adobe Portable Document Format (PDF)*** and must be prepared using our apply online facility: **https://nmss.fluxx.io**. Instructions for use of the Web site appear on the next page. Letters-of-intent that are e-mailed to the Society or mailed in paper form will not be considered and will be discarded. Investigators should **not** submit full proposals at this time. **The deadline for our receipt of letters-of-intent is 11:59 PM, Eastern Time, 10/7/2015**. An applicant who submits a letter-of-intent will receive an e-mail indicating that the Society has received the letter.

Letters-of-intent should include the following information in summary form:

- Priority to be studied. For investigator initiated proposals, list "Investigator Initiated" as the priority. (A separate pre-application with a single letter-of-intent should be submitted for each priority addressed.)
- Project objectives.
- Brief statement of the methodology to be used, including sample, measures, and design.
- Estimates of the timetable and budget for completion of the project.
- Identification and resources of the applicant organization(s) and a brief statement of the qualifications of the main project staff.

- Name, title, address, telephone and FAX numbers, and e-mail address of the proposed principal investigator for the study.
- **Do not include** any of the following: cover letters, biographical sketches, CV's, or attachments of any kind. Your submission should include only those elements indicated above and on the apply online site.

Based on a screening of the letters-of-intent by the HCDPR Advisory Committee, invitations to submit full applications, together with instructions for submitting the application, will be e-mailed to selected investigators on or about 11/10/2015. **The deadline for our receipt of full applications is 11:59 PM, Eastern Time, 1/14/2016.**

All proposals will be reviewed by an independent, multi-disciplinary, volunteer peer review committee. Award notification will be sent on or about June 2016. In some cases, based upon the review committee's recommendations, an application may receive a "conditional approval," pending negotiations involving staff of the National Multiple Sclerosis Society, our advisors, and the applicant, concerning aspects of the proposal. Approved applications -- including applications that were initially conditionally approved and have subsequently been successfully negotiated -- will be funded to begin on a date to be determined by the Society.

Letters-of-intent must be submitted through our apply online site **https://nmss.fluxx.io** by 11:59 PM, Eastern Time, **10/7/2015**. Letters submitted after that date, letters submitted by e-mail, and letters submitted in paper form ***will not be reviewed***.

INSTRUCTIONS FOR USE OF THE APPLY ONLINE WEB SITE - MSGrants

The following changes to the Society's application procedures have been implemented:

- A ***new*** grants management system called **MSGrants** has been implemented for preparation and submission of research proposals to the Society. MSGrants can be found at **https://nmss.fluxx.io**
- Compatible browsers include **Chrome, Firefox,** and **Safari.** Internet Explorer is not fully compatible and should be avoided. Check with your IT department for information on installing one of these browsers if you do not already have one.
- Passwords for accessing the site never expire and a new password will not be needed for each cycle.
- Submission of proposals is exclusively electronic for **all** parts of the proposal, including institutional approval and appendix materials, and no paper copies of any part of the proposal will be sent to the Society.
- In place of the former coversheet, institutional approval by your organization to submit your application will be made electronically using the same online system. Institutional approval is not needed for the pre-application (letter-of-intent), only for the full application.
- The application process itself consists of two parts, a short pre-application (which includes the letter-of-intent described above) and the full application.
- The basic elements of the application remain largely unchanged but have been re-ordered and reformatted.

If you have already been issued a password for MSGrants, you can skip the next two sections.

Registration for New Users

If you did not have a password for our previous system, mssocietyapplyonline, you will need to register and be approved for access to the new system. Go to **https://nmss.fluxx.io** and click on **Register Now.** Complete the online registration form and submit your registration by clicking on the words **Submit Request.** Society staff will review your registration information to verify that you are qualified to apply for funding. If approved, you will receive an automated e-mail message containing your login credentials within ***two business days***.

Registration for Existing Users

If you have a password for our previous system, you do not need to register again, however you will need to reset your password. Go to **https://nmss.fluxx.io** and click on **Reset or Create Password.** At the next screen, enter the e-mail address that you used in the old system and click on **Submit.** The system will send you an e-mail with a link to reset your password. If the system does not recognize your e-mail address, you will need to register as if you are a new user.

A Word about Passwords

When you create your new password it will need to contain at least one:

- Uppercase letter (A through Z)
- Lowercase letter (a through z)
- Number (0 through 9)

Once you have obtained a user id and password, go to **https://nmss.fluxx.io** and log in. Once you log in, you will be able to see which funding opportunities are active along with the deadlines for each. You will also be able to begin the preparation of your pre-application, which includes the letter-of-intent.

In the system your password never expires and you will not need to obtain a new password in order to apply for other funding programs or subsequent cycles. You will be using MSGrants for a variety of purposes in addition to preparation and submission of proposals, including, viewing proposals that you have prepared on the system, and preparing and submitting progress reports.

It is important that you not share your password with others and it is not possible for two different people to apply for funding opportunities using a single password.

The Pre-Application (Letter-of-Intent)

In the past prospective applicants were required to contact a member of the Society's Research Programs staff to obtain clearance before submitting a proposal. While the Society still encourages personal contact and discussion of possible ideas for proposals, in the current system this process has been formalized somewhat through the use of a "Pre-Application" step. For each funding opportunity, there is a pre-application that must be completed and submitted to the Society before the applicant can prepare a full application. For the HCDPR program, the pre-application includes the letter-of-intent described above and is reviewed by a peer review panel. If your letter-of-intent is approved, you will receive an e-mail message stating so and you will be able to begin preparation of the full application.

How to Complete the Pre-Application (Including the Letter-of-Intent)

Once you are logged in, click on **Funding Opportunities** to see a list of available funding opportunities, along with information on the application deadlines. Scroll down to **Health Care Delivery and Policy Research Contracts** and click on **Apply Now.** This will open the pre-application. Your **Organization** and **Name** should be prepopulated. If not, select them from the drop-down lists. Enter a title for your pre-application (this can be changed later) and complete the **Eligibility Quiz.** The Eligibility quiz will establish whether you are eligible to apply for that funding opportunity. If you pass all of the eligibility criteria, the rest of the pre- application will open and you can begin to complete this step. If you fail one or more of the eligibility criteria, you will not be able to prepare and submit a pre-application for that program.

- **Brief Project Summary:** Provide a brief summary of the study that you are proposing.

- **Project Zip Code:** In the **Project Zip Code** field enter the zip code (U.S. applications) where the work will actually be done. If more than one site is going to be used, this should be the Zip code of the primary or lead site.
- **Estimate of Amount Requested:** In the **Estimate of Amount Requested** field, enter your best estimate of the total cost of your proposed project in U.S. dollars. This figure will allow Society staff to gauge the overall amount of funding that is likely to be requested during a given cycle. This figure will not be used to evaluate whether or not to approve your pre-application and you will be able to change this figure later.
- **Currency:** Make sure you select U.S. Dollars.
- **Letter-of-Intent:** Prepare your letter-of-intent off-line, convert it to PDF format, and upload it to this section.
- Once you have completed all sections of the pre-application, click on **Save** to save your work. At this point you can log out and return later to revise your pre-application by pressing the **Edit** button, or you can click on **Submit** to submit your pre-application for review. Saving your application does not send it to Society staff. You must click on **Submit** in order for it to be considered for approval.
- Once you press **Submit**, you will no longer be able to make changes, although you will be able to see your pre-application.

When you submit the pre-application, it will automatically be sent to Dr. LaRocca to begin the review process. Once your pre-application is submitted, it will appear in the grantee portal under **Pending Approval.** While it is pending approval it cannot be edited.

How to Complete the Full Application

If and when your letter-of-intent has been approved, you will be notified and you can log in and begin to prepare the full application. When you log in, click on **Open Applications** then on the title of your application. Click on **Edit** to begin the preparation of your full application. Detailed instructions for completion of the full application will be provided to applicants approved to prepare and submit a full application and will also be available online. Please read these instructions carefully before preparing your full application.