

Addressing the Challenges of Clinical Research Participation Among Populations Disproportionately Impacted by Lupus

*Findings and Recommendations of the Inaugural
Lupus Multi-Cultural Engagement Partnership Meeting*

December 11 - 12, 2017

A Collaboration of

the **Lupus Research Alliance** and the **National Minority Quality Forum**



February 2019

Dear Colleagues,

The Lupus Research Alliance and the National Minority Quality Forum are pleased to present this final report of the inaugural meeting of our Lupus Multi-Cultural Engagement Partnership, which was held on December 11-12, 2017 in New York City in the offices of the Lupus Research Alliance. Over the course of these two days, nearly 40 experts took up the gauntlet and grappled with two thorny, interrelated objectives:

- Clear-eyed articulation of the challenges that serve to impede progress in creating clinical trial cohorts that more accurately reflect the diverse populations who are affected by lupus; and
- The development of actionable recommendations to answer those challenges that can be implemented in different settings and have a high potential for success.

We are immensely appreciative of the commitment that compelled the participants from around the country to venture to New York City in mid-December to work with us on what some have defined as an intractable problem. However, we need engagement from those participants and beyond. The recommendations presented in this report are suggested ways that different groups can get involved. As you review this report, we ask you to give consideration to how your organizations can engage with us to achieve what we believe is a shared objective: the creation of new science that can lead to innovative, safe, and effective therapies to manage, and perhaps cure, the complex disease of lupus in all of its manifestations.

We would also like to recognize our sponsors. Without their support, this meeting and the initiatives that it has already stimulated would not have been possible. Our thanks to: Bristol-Myers Squibb, EMD Serono, GSK, and Mallinckrodt Pharmaceuticals.

We look forward to hearing from you on how we can work together toward our ambitious goal of pushing the limits of scientific exploration and shepherding new discoveries into potential treatments to ultimately help ease the burden of people living with lupus.

Sincerely,



Kenneth M. Farber
President and Chief Executive Officer
Lupus Research Alliance



Gary A. Puckrein, PhD
President and Chief Executive Officer
National Minority Quality Forum



TABLE OF CONTENTS

Introduction.....	1
Recommendations.....	4
Recommendations Matrix.....	5
Actions to Date.....	8
Presentation Highlights.....	10
Highlights from Breakout Group Discussions.....	16
Strategies to Overcome Identified Challenges and Barriers.....	21

APPENDICES

Appendix A - Participant Roster.....	25
Appendix B - Agenda.....	28
Appendix C - Discussion Group Assignments.....	30
Appendix D - Briefing Document.....	31

Introduction

The Lupus Research Alliance (LRA) and the National Minority Quality Forum (NMQF) formed the Lupus Multi-Cultural Engagement Partnership (Lupus MCEP) in 2017 to address the causes and potential solutions for the lack of inclusion in clinical trials of populations that are at greatest risk for and have the highest prevalence of Systemic Lupus Erythematosus (SLE or lupus).

Lupus predominantly affects women, and disproportionately affects women of color who identify as African American, Hispanic, Asian and Native American – population cohorts that are historically underserved and undervalued by the American health services research, financing and delivery complex. Further, after diagnosis with lupus, these populations are more likely than Caucasians to experience multiple comorbidities such as cardiovascular disease and diabetes, as well as worse health outcomes related to quality of life and three times as high mortality rates.

Lupus is a complex, difficult-to-diagnose and incurable disease that causes the immune system to inexplicably and randomly attack the body's own tissues and vital organs, including the heart, brain, kidneys, lungs, skin, joints, and blood. Persons with lupus are most often diagnosed between the ages of 15 and 44. The delay in confirmatory diagnosis after the initial onset of a lupus-related symptom can be up to five years. Over time, this chronic disease damages organs, increasing morbidity and mortality. Responses to the few available medications to treat lupus symptoms and co-morbidities vary by race and ethnicity.

Clinical trial participation among the diverse population groups affected by lupus is critical for statistically significant evidence needed to support the development and prescribing of targeted, effective therapies. However, efforts to increase engagement of these populations in lupus clinical research must be implemented within a broader environment that has not traditionally been welcoming of their involvement. LRA and NMQF created the Lupus MCEP to address concurrently the barriers to engagement that exist within all sectors of health services research, delivery and financing to develop a clinical research model that, in order to be successful, must engage populations who have historically been marginalized.

The inaugural Lupus MCEP meeting featured presentations from researchers, clinicians, people with lupus, and patient advocates who described the complexity of the Lupus MCEP charge through their



particular lenses. Following the presentations, each participant was assigned to one of three breakout groups:

- Patients, their Families, and Social Networks
- Employers, the Faith Community and Educational Institutions
- Physicians, Hospitals, and Researchers

The breakout groups were tasked with focusing with more precision on the challenges for their communities of concern, brainstorming on strategies that can be developed to overcome these challenges, and reaching consensus on strategies that can be accomplished in a one to two-year period as opposed to macro-level systemic changes. The questions presented to the breakout groups to facilitate discussion were:

- What are the major challenges faced by your target sector in engaging traditionally underserved populations to participate in research?
- What are existing assets of your target sector to address the key challenges identified? What assets are needed?

The report starts with the Recommendations Matrix which presents strategies that various sectors can implement based on the discussions in the breakout sessions. The strategies presented are near-term and longer-term items that can be done with partners through combining resources and collaborating to achieve our joint goal. This is followed by Actions to Date which are activities that LRA and NMQF have undertaken since the meeting. The information shared by each speaker is then encapsulated in the Presentation Highlights. This is followed by Highlights from Breakout Group Discussions, which includes key overarching system issues that surfaced during the question and answer sessions following the presentations. The report concludes with Strategies to Overcome Identified Challenges and Barriers.

The roster of attendees, the full agenda for the meeting, the breakout group assignments, and the briefing document that was disseminated prior to the meeting are included in the report appendices.

Some of the issues and highlights are beyond the scope of the Lupus MCEP either by virtue of the magnitude of the human and fiscal resources required to design and implement solutions, or because the issue is endemic to the American clinical research system and not unique to lupus. However, all issues raised are included in this report because their resolution is critical to the success of sustainable clinical trial reform.



The recommendations in this report are the basis of a road map to help lead us toward representative participation in research and ultimately better treatments for people with lupus. Lupus is a multi-faceted disease that requires an equally diverse approach to research and treatment. This includes collaboration from many sectors beyond the typical groups involved in lupus. The goal of this report is to help foster that collaboration and to encourage and engage groups interested in the health of populations disproportionately impacted by lupus to take action.



Recommendations

The following Recommendations Matrix presents opportunities various groups can undertake to help improve recruitment and retention in clinical trials for people with lupus. The Matrix is divided into three main issues that emerged in the meeting:

- Recruitment and Retention
- Economic and Financial Considerations
- Education and Awareness that Lead to Behavior Change

Each issue is divided into activities that can be directed at different target audiences, and each recommendation includes a suggested lead noted by a number in parentheses at the end of the recommendation. For example, the first recommendation, “Increase awareness of the value added by participating in clinical trials, and to create realistic expectations of the clinical trial experience. (1, 4)” falls under the issue, Recruitment and Retention with a target audience of Persons with Lupus and Family and a suggested lead of (1) Advocacy Groups and (4) Principal Investigators.



Recommendations Matrix: Recruitment and Retention

Target Audience				
Persons with Lupus and Family	Community-Based Organizations	Health Care Providers (Not conducting research)	Investigators (Conducting research, may be practicing physicians)	Study Sponsors (Pharmaceutical Companies, Contract Research Organizations)
<p>Increase awareness of the value added by participating in clinical trials, and to create realistic expectations of the clinical trial experience. (1, 4)</p> <p>Provide clinical trial participants and other people with lupus with complete and accurate information about trial outcomes to be fully transparent about risks and rewards of participating in research. (3, 4)</p>	<p>Increase awareness of the value added by participating in clinical trials. (1, 2)</p>	<p>Develop educational programs, such as CMEs and grand rounds, for primary care physicians and other primary care providers and their staff in screening and diagnosing all forms of lupus. (5)</p> <p>Use electronic medical records (EMRs) to identify and prescreen potential trial participants. (3, 4)</p> <p>Provide education on HIPPA to increase the understanding of what can and can't be done under HIPPA around recruitment and retention activities. (5)</p>	<p>Design research studies/clinical trials to be participant-friendly and supportive, including maximizing the use of technology and other mechanisms/services to reduce logistical and economic barriers to patient recruitment and retention. (3, 4)</p> <p>Develop mechanism for developing clinical trial career roadmaps in rheumatology. (5)</p> <p>Create a research mentoring program between principal investigators and younger clinicians. (5)</p>	<p>Streamline the enrollment process, such as enabling volunteers to securely and conveniently complete enrollment paperwork at home, to view their personal data, and to understand and authorize informed consent. (3, 4)</p> <p>Create online consent forms with easy-to-understand icons and a dictionary of technical and clinical terminology. (3)</p> <p>Identify site-specific barriers people with lupus face and create customized support options by site or geographic region. (3, 4)</p>
KEY - Suggested Lead:	1. Advocacy Groups 4. Principal Investigators	2. Government Agencies 5. Professional Medical and Nursing Societies	3. Pharmaceutical Industry	



Recommendations Matrix: Economic and Financial Considerations

Target Audience				
Persons with Lupus and Family	Community-Based Organizations	Health Care Providers (Not conducting research)	Investigators (Conducting research, may be practicing physicians)	Study Sponsors (Pharmaceutical Companies, Contract Research Organizations)
Identify the financial and logistical challenges associated with participating in clinical trials. (1)	Explore options for developing and supporting people with lupus, families and caregivers with services that will alleviate the burden of trial participation. (1)	Develop/identify reimbursement or other incentives for screening and referral of people with lupus for clinical trials. (3, 4)	Explore options to support research sites that are in proximity to the clinical trial participants, using technology to develop remote monitoring and communications options. (3, 4)	Allow extra time and resources needed to implement new recruitment efforts in order to be inclusive of diverse populations representative of people with lupus. (3)
KEY - Suggested Lead:	1. Advocacy Groups 4. Principal Investigators	2. Government Agencies 5. Professional Medical and Nursing Societies	3. Pharmaceutical Industry	



Recommendations Matrix: Education and Awareness that Lead to Behavior Change

Target Audience				
Persons with Lupus and Family	Community-Based Organizations	Health Care Providers (Not conducting research)	Investigators (Conducting research, may be practicing physicians)	Study Sponsors (Pharmaceutical Companies, Contract Research Organizations)
<p>Create online resources to enable people with lupus to review frequently asked questions (FAQs), to find tools that will help them discuss lupus with their families, engage in moderated discussions with other lupus patients, and function as informed and empowered advocates for their care with clinicians, investigators and payers/insurers. (1, 2, 3)</p> <p>Convene working groups of primary care clinicians, researchers, and people with lupus to develop and test messages to increase interest among people with lupus for participating in clinical trials. (1, 2, 3, 4, 5)</p>	<p>Increase awareness and education about lupus and the value of participating in clinical trials to a wide range of stakeholder groups including communities of color, employers, unions/organized labor, sororities/fraternities, and faith-based communities. (1, 2, 3)</p> <p>Develop messages and tool kits for use in K-12 schools to enable them to increase awareness of lupus through multiple available media channels, including, for example, school newsletters and morning announcements. (1)</p>	<p>Review and revise graduate medical education curricula and diagnosis and treatment guidelines to reflect informing patients of research options as a component of quality care. (3, 5)</p> <p>Convene organized research, clinical, and graduate medical and nursing education leadership to reach consensus on the role of the primary care provider, clinical specialists, and investigators as part of the care team that supports people with lupus. Issue a joint statement discussing the ramifications of this forward looking, patient-centric paradigm shift. (1, 3, 5)</p>	<p>Increase awareness among investigators and clinicians that addresses the assumptions and inherent biases that interfere with researcher and clinician outreach to people with lupus who are potential clinical trial participants - incentives to address bias. (1, 5)</p> <p>Develop CME programs to train Research Fellows in Rheumatology, Nephrology, Dermatology, and other specialties regarding clinical trials in lupus as a component of quality care/standard of care. (5)</p> <p>Develop an information campaign that includes clear, accessible messaging about the importance of increasing diversity in lupus clinical trial cohorts. (1, 5)</p>	<p>Education on patient perspectives on understanding of disease and clinical research participation (Patient-Focused Drug Development initiative, Patient Reported Outcomes, Real World Evidence). (1)</p>

KEY - Suggested Lead:

- | | | |
|----------------------------|---|----------------------------|
| 1. Advocacy Groups | 2. Government Agencies | 3. Pharmaceutical Industry |
| 4. Principal Investigators | 5. Professional Medical and Nursing Societies | |



Actions to Date

Since the meeting in December 2017, the LRA and NMQF have been working on and/or have completed several initiatives that emerged as a result of discussions and in collaboration with some attendees and/or sponsors.

Issue	Activities and Collaborators
Recruitment and Retention	<ul style="list-style-type: none"><li data-bbox="509 562 1511 741">• The Lupus Clinical Investigators Network (LuCIN) has included Patient Advisory Boards that reflect the lupus population in the review of clinical trial protocols to help ensure that trials are designed with patients in mind.<li data-bbox="509 814 1446 951">• The LRA is exploring the design and pilot of an avatar program that answers questions on informed consent in non-technical terms to facilitate transparency and realistic expectations.<li data-bbox="509 1014 1520 1455">• The NMQF, in collaboration with and support from the LRA, has begun development of the Lupus Index which will be used as a key resource to help target provider outreach and education, and inform outreach and education strategies. The Lupus Index will be a geographical information system that houses, analyzes and publishes health statistics on lupus in the United States. It will combine data from public and private sources - starting with public information (payor data such as Medicare and Medicaid), not currently integrated or available in a central location, with an accessible format specific to lupus.



Issue	Activities and Collaborators
<p>Education and Awareness that Lead to Behavior Change</p>	<ul style="list-style-type: none"> • The Balm in Gilead shared two Sunday Morning Health Corners on lupus during Lupus Awareness Month and interviewed LRA staff and a person with lupus on a podcast. The LRA and GSK participated in the Balm in Gilead’s annual Healthy Churches 2020 conference. • The LRA developed an African Americans and Clinical Trials brochure that was reviewed by members of its Multi-Cultural Outreach Task Force and is distributing it through various outreach opportunities. • The LRA collaborated with Janssen to organize panel discussions on lupus at two Delta Sigma Theta regional meetings. • A Lupus Community Education Toolkit was developed with content from the LRA, input from the NMQF and support of Mallinckrodt. The Toolkit is a full suite of materials needed to conduct lupus community awareness and education. The materials are designed to help individuals recognize the signs and symptoms of lupus, encourage individuals to connect with health care providers who are knowledgeable about lupus, and provide information on the importance of research participation. The Toolkit can be used by persons with lupus, healthcare professionals and lay health educators to educate lay audiences. • The LRA is working with the National Kidney Foundation to determine how to bring together nephrologists and rheumatologists since lupus nephritis is one of the most severe manifestations of lupus which disproportionately impacts minority groups. • The LRA has a collaboration agreement with Black Nurses Rock to promote lupus disease and clinical trial awareness and education with their chapters nationwide.



Presentation Highlights

Welcome and Opening Remarks

Joseph Mauriello

Lupus Research Alliance Board of Directors

On behalf of the Board of Directors of the Lupus Research Alliance, Mr. Mauriello expressed his gratitude to the attendees for their time, commitment, and willingness to share their expertise.

The Lupus Multi-Cultural Engagement Partnership: A Collaboration of the Lupus Research Alliance and the National Minority Quality Forum

Kenneth M. Farber, President and CEO, Lupus Research Alliance

Gary A. Puckrein, PhD, President and CEO, National Minority Quality Forum

Albert Roy, Executive Director, Lupus Therapeutics

Mr. Farber set the stage for the meeting by noting that the Lupus Research Alliance has one ambition – the realization of new, better and safer treatments to prevent, treat and cure lupus. One way to do that, he stated, is through collaborations like this with many stakeholders who can bring their expertise to the table to help conquer lupus. Dr. Puckrein further emphasized the importance of this collaboration and the need for research and researchers to establish a presence in the communities that are home to the populations of concern. Mr. Roy provided an overview of the Lupus Clinical Investigators Network (LuCIN), a major initiative of Lupus Therapeutics, an affiliate of the Lupus Research Alliance, that is comprised of leading experts at top research centers across the U.S. and Canada. He noted that LuCIN was created to accelerate the identification and development of new therapies to treat lupus.

Understanding Lupus: The Clinical Perspective

Anca D. Askanase, MD, MPH

Founder & Clinical Director, Lupus Center, Columbia University Medical College

Dr. Askanase provided an overview of Systemic Lupus Erythematosus (SLE) that covered incidence and prevalence, racial differences in disease and response to treatment, diagnosis and classification criteria, current treatment options, and the factors that can complicate clinical trials for people with lupus. She noted that studies funded by the Centers for Disease Control and Prevention estimate an incidence of 5.5/100,000 and prevalence of 75/100,000, with 1 in 537 Black females having been diagnosed



with lupus. Some of the racial and ethnic differences in manifestations are stark, with Hispanics and African Americans experiencing much higher rates of renal disease than Caucasian non-Hispanics, and studies showing there are different responses to treatment. The goal of treatment is to initially decrease disease activity and then to maintain low disease activity/remission. This includes preventing flares and chronic irreversible damage. A patient who is diagnosed with lupus at age 20 has a one in six chance of dying by 35 years of age, most often from lupus or an infection. There are two major obstacles to drug development for lupus: the nature of the disease and the heterogeneity of how it manifests, as well as insufficient numbers of patient participants for all the studies as they are currently designed. Clinical trials are complicated. Better trial design is needed, and researchers need to make sure that enough patients of different races and ethnicities are represented in the trials so that differential responses to the therapies can be identified and studied. To date, only one drug has been successfully developed specifically for lupus.

Inherent Biases as Challenges to Engagement in Clinical Research

Ana E. Núñez, MD

Associate Dean for Diversity, Equity and Inclusion; Professor of Medicine

Drexel College of Medicine

Dr. Núñez introduced the concept of the value of recognizing and addressing implicit bias as key to improving our healthcare system and reducing health care and health status inequities. She then led the group through an exercise on bias, highlighting that we all have some implicit bias - we don't know what we don't know. While biases can help us survive, unconscious biases present challenges. The exercise also enabled the group to become more aware that there is a trade-off between speed and accuracy when processing new information. Too often, Dr. Núñez cautioned, we may lose situational context, and good intentions may result in actions and outcomes that have negative consequences for all parties. She shared some examples of health-equity models and discussed the imperative to increase health literacy and cultural competence. She concluded by emphasizing that exposure to more inclusive participant cohorts expands the hypothesis-generation skills of researchers.

The Lupus Index: Filling in the Picture

Gary A. Puckrein, PhD, President and CEO, National Minority Quality Forum

Dr. Puckrein set the stage for how big data can be used to help target services for people with lupus by discussing the connection between community health and collaborative networks, where all members in a society contribute to and inform population health. Health care and health status disparities are



the result of the failure of these community-based collaborative networks to operate optimally for particular cohorts. To better understand this, performance indicators can be developed to determine how well these networks function collectively or how well an individual component is operating. To better understand these issues, the NMQF maintains a comprehensive database of over 2 billion patient records that can be linked by zip code. The database can be used to define disease prevalence, costs and outcomes for demographic and geographic population cohorts. The database supports the generation of geomaps that display information about acute and chronic disorders at the zip code level that can be segmented by age, sex, gender, race and ethnicity. Using zip code linked data and predictive analytics, these geomapped indices help researchers, policymakers, and patient advocates define where unmet needs exist and forecast trends. Dr. Puckrein shared a preliminary vision of the data that will be available through the planned Lupus Index, which will enable LRA, LuCIN and the Lupus MCEP partners to identify geographical variations in treatments, outcomes, and cost, as well as to target activities and monitor impacts with precision.

Understanding Lupus: The Patient Perspective

Insights into Lupus and the Patient Perspective on Clinical Trials:

Diane Gross, National Director of Advocacy and Programs, Lupus Research Alliance

Ms. Gross shared the results of a series of small discussion groups that were conducted to better understand the perspective of people with lupus about clinical research. Only one-third of the participants had ever been asked by their doctor about participating in a trial, and none of the people had ever broached the subject with their doctor. Participants reported that after their doctor, the main sources they would use for finding out about trials are lupus trials sites, newspapers, magazines, lupus groups, others with lupus, flyers, pharmaceutical companies, and healthcare institutions. The sources they trust most are their doctor, foundations, and others in a trial. Participants reported that their biggest concerns around trial participation were questions about side effects followed by interaction with current medications, whether the medication would actually help, the possibility of getting sicker, having full disclosure as to what is being done and why, and the commitment of the group conducting the trial. Physicians were noted to be a key impediment to trial participation because they are not asking patients; yet patients report their doctor would be the most trusted source for trial information and would be highly influential in their decision making.



The Lived Experience:

Kaamilah Gilyard, Person with Lupus/Lupus Advocate

Ms. Gilyard spoke candidly about living with lupus and the challenges she faces, stating that every day is a battle since your body is fighting itself. She was diagnosed at age 17 during her senior year of high school after numerous emergency room and doctor visits and has been living with lupus for over 20 years. Once diagnosed, she found it challenging to find anyone who knew about lupus and could serve as her support system. Initially diagnosed with systemic lupus and subsequently diagnosed with both discoid lupus and lupus nephritis, her disease has progressed and has affected almost all her organs. Ms. Gilyard takes more than 30 pills per day and numerous injections to combat lupus, co-morbid conditions, and side effects of the medications. To manage her disease, she sees multiple medical specialists – her “ologists”.

Ms. Gilyard described her experience participating in clinical research and how it made her feel empowered. After several years, it took the death of her aunt with lupus to lead her to the decision to try a trial. Participating in clinical research, she believes, helped her save her own life and benefits the community. Even though the medication being tested was not found to be efficacious, she knows her participation was important, and it gives her hope for the future. Ms. Gilyard noted that current treatments leave a lot to be desired, and young women shouldn't have to make decisions about their fertility in their teens. Despite all this, she remains optimistic, stating that lupus causes you to rearrange your dreams, but it doesn't mean you must stop dreaming.

The Lived Experience:

Leah Crocker, Person with Lupus/Lupus Advocate

Ms. Crocker also spoke about her journey with lupus and the other conditions she suffers from. She was not healing well after carpal tunnel surgery, went to the doctor, and was then diagnosed with lupus and Raynaud's syndrome while in graduate school pursuing a Master's in Education. Because of her diagnosis, it was strongly recommended to her to not be in an environment such as a school system because of the germs and the body's inability to effectively fight off illness. Living with lupus has changed what she does and how she does it. Although she completed her degree, she has not been able to use it. Because of the severity of her Raynaud's, her rheumatologist recommended that she move to a warmer climate. She now resides in Atlanta, GA where the warmer climate agrees more with her diseases. Like Ms. Gilyard, she battles lupus every day and does not know what the day will bring when she wakes up. She knows her limitations and has learned how to live within them. She participated in a clinical trial because her doctor asked and



because she feels that participating is an important contribution for the lupus community. Ms. Crocker noted that she has been a participant in several trials and feels it is the responsibility of patients to help to educate and reach others.

Improving Global Public and Patient Engagement in Clinical Research

Mary Jo Lamberti, PhD

Senior Research Fellow, Tufts Center for the Study of Drug Development

Dr. Lamberti shared results from various studies conducted by the Tufts Center for the Study of Drug Development. One study of 755 physicians found that only an estimated seven percent of physicians report that their patients have asked to be referred into a clinical trial. Similar results were found in a study specifically looking at lupus and engaging African Americans in clinical trials in which an overwhelming majority of physicians indicated that lupus patients rarely inquire about clinical trials. The study also found that the most effective approach to outreach to the African American community by physicians is through the church. Key insights to consider are the need to foster communication between healthcare providers and patients to create more awareness and education about clinical trials; encouraging learning at places which promote effective channels of communication including the church or educational organizations; and that people in the lupus community generally have a positive outlook on clinical trials and are ready to learn more about the process of participation.

Getting to Yes: Engaging People with Lupus in Clinical Research

Nadine Spring, MPH

Manager, Lupus & Antiphospholipid Syndrome Center of Excellence, Hospital for Special Surgery

Ms. Spring addressed the needs of patients regarding participation in clinical trials. Patients must be helped to understand that they can change their minds and withdraw from a study at any time, that they are not guinea pigs, and that there are potential benefits for them. Healthcare providers must be helped to understand that lupus brings many challenges to daily life and that adding a trial can be viewed as another burden. Patients want providers to know that they are concerned about their level of energy and cognitive function. They want to take fewer medications and they want more effective drug options with fewer side effects and lower costs. They want an increased quality of life and fewer long-term side effects. There are numerous reasons people with lupus don't participate in clinical research: the option is not offered; their lupus is stable and they do not want to risk getting worse; they are newly diagnosed; it can be a big time commitment in an already burdened life for someone suffering from chronic fatigue; they are anxious because of the experience of others and the uncertainty of the investigational product; there is some



mistrust of the research community; and there are family planning concerns. Some key things to consider in getting patients to say yes to clinical trials are establishing good rapport between patients and staff, not pressuring anyone to join a trial, clearly explaining the risks and benefits, thinking about how people are asked to take part in a trial, and educating staff who talk to patients about common concerns.

Closing Remarks

Elizabeth Ofili, MD, MPH, Director & Senior Associate Dean, Clinical Research Center & Clinical and Translational Research, Morehouse School of Medicine

Dr. Ofili described the work that she and her colleagues at Morehouse School of Medicine are doing with African-American communities to fight cardiovascular disease and in managing a cardiology registry. Lessons from this work, she believes, can be applied to the challenge of improving clinical research for people with lupus. The long-term goal for the registry is to become the most comprehensive patient registry for minority patients with cardiovascular disease and co-morbid conditions, including lupus. She provided an example of a health coach program at a church that is much better in engaging the community than are the primary care physician sites, and how the church program is able to collect better data, achieve lasting positive health results, and identify areas where African Americans are not being recruited. A community advisory board was created to provide input into the design of their protocol. This strengthens the partnership and creates an incentive for board members to go out and promote the protocols in their community. Additionally, a smart app is being developed that will allow everyone involved to see the data being collected. Physicians will be encouraged to work with patients to download the app. Engaging community physicians and making sure that the app doesn't create more work for them is a key to participation and success. This collaboration can serve as a model of community and academic institutions working together to improve recruitment of patients too often considered hard to reach. Dr. Ofili said that the challenge to the Lupus MCEP is to find ways to use referral networks that are useful to the investigator, community physician, and patients.



Highlights from Breakout Group Discussions

There was generally consensus that clinical trials should become part of the standard of care for lupus. For many reasons, they are not. First, the average primary care physician does not see many lupus patients. Second, few rheumatologists are interested in clinical trials. And third, medical school curricula do not usually prepare physicians to consider experimental therapies for treating disease. Thus, clinical trials are not top of mind for most physicians and therefore not the standard of lupus treatment and care. In addition, for the patient and their families, living with lupus can be daunting. Because it is a multi-system disease with symptoms that wax and wane, and often mimic those of other diseases, it is difficult to diagnose and evaluate. It is also difficult to determine the best source of treatment or if a treatment, experimental or otherwise, is effective or safe. Treating lupus also requires a level of care coordination that makes case management time and labor intensive. Thus, adding clinical trial participation to patients already complicated lives is, for many, untenable. Following are highlights from the breakout group discussions that are responsive to the two discussion questions. The three breakout groups were asked to think about the questions from the following target sectors:

- Patients, their Families, and Social Networks;
- Employers, the Faith Community and Educational Institutions; and
- Physicians, Hospitals, and Researchers.

Appendix C lists the participants in each group.

What are the major challenges faced by your target sector in engaging traditionally underserved populations to participate in research?

Lack of minority participation in clinical trials is not unique to lupus. A variety of challenges contribute to lower-than-desirable participation in clinical trials by populations defined as minorities in the United States. These challenges are not unique to lupus, and to some degree are not unique to minorities. Systemic participation barriers in the clinical trials continuum include:

- Lack of commitment or incentive by sponsors of research to construct clinical trial cohorts with diversity of enough statistical significance that it may bring undesirable complexities to the FDA review and approval process.
- Misperceptions, biases and hidden beliefs by investigators and potential participants.



- Economic and social constraints that may compromise the ability of willing participants to engage in clinical research.
- Lack of transparency regarding how clinical trials work and the benefits of participation, such as receiving better and more frequent medical care. Trial protocols are often incomprehensible, reflecting sponsors' perspectives while not addressing patients' needs and concerns. They are also frequently written using clinical and technical terminology that is not readily comprehensible, even for potential participants who are literate and competent in other fields. Materials are often written at a reading level that is too high for patients, especially those whose primary language is not English.
- Community physicians often lack awareness of the availability of clinical trials. In a recent Lupus Research Alliance study, two-thirds of participants said their doctors had never mentioned a trial. The study also found that patients trusted their doctors most as a source of information about clinical trials, and as the most influential person in helping them decide whether to participate.
- Many community physicians worry about the effects that investigational treatments may have on their patients' physical and psychological wellbeing. They also worry about losing control of their patients' care. The potential loss of practice revenue, either from the non-reimbursable time it takes to educate and talk with patients about a trial, or from 'losing' patients to the trial process can discourage physicians from making referrals.
- Many physicians regard clinical trials as huge investments with little pay-off. Physicians who do refer their patients to trials may encounter a lack of infrastructure and support.
- Trials often lack the research coordinators needed to identify, screen and enroll potential participants. Eligibility screenings aren't always accurate.
- How patients are recruited can be a barrier. For example, patients (perhaps most people) may not consider participating if it requires them to call an information line and provide personal details to a stranger.
- The fear of being a 'guinea pig,' or the possibility that an experimental treatment will either disrupt the stability of a current medication or make a patient worse may make them unwilling to participate.



- Trials may pose financial strains for patients as well, especially those who cannot risk lost work time, or afford the childcare, or transportation required to travel to distant sites. Indeed, trials commonly take place in areas that are far from the communities where underserved and minority populations live. For patients who work, are juggling responsibilities to family and home, and are generally challenged with the demands of daily living, trial participation can be dismissed as an unwelcomed burden without sufficient benefit.
- The possibility that investigational treatments could lead to infertility or death, interact negatively with drugs that patients are already taking, or result in other side effects that could worsen their condition also can prevent consideration of trial participation. These fears may become especially pronounced when a patient's current medications are working, or if they are relatively "okay" before a trial begins.
- Some patients may fear that receiving a placebo drug will bar them from accessing new therapies when they have active disease, which has historically occurred among people of color who have participated in clinical trials.

What are the existing assets of your target sector to address the key challenges identified? What assets are needed?

- The Lupus Clinical Investigators Network (LuCIN) is a clinical trials network comprised of nearly 60 academic research centers throughout North America and is supported by the Lupus Research Alliance's affiliate, Lupus Therapeutics. LuCIN provides a coordinated framework for testing potential new treatments quickly and cost-effectively, while upholding the highest scientific standards. LuCIN works with biotechnology and pharmaceutical companies to accelerate the development of new therapies for lupus, promote collaboration throughout the lupus community of scientists, healthcare providers, patients and families, and advance the quality of lupus research by attracting and training new investigators. LuCIN also tests existing drugs for possible repurposing for the treatment of lupus.
- The Patient Advocates for Lupus Studies ("PALS") program, which is scheduled for implementation in the first quarter of 2019, will coordinate with LuCIN healthcare teams to provide individuals diagnosed with lupus opportunities for peer-to-peer communication with an individual who has the condition and understands the challenges of managing it. PALS is under development and will



provide information about the need to advance lupus drug development, the importance of clinical trials and the critical role of lupus patients in research.

- The LRA's Multi-Cultural Outreach Task Force (MCOTF), a nationwide group of volunteers who have lupus or a close connection to someone with lupus, undertakes education and awareness efforts designed to increase appropriate and accurate diagnoses by increasing clinical trial engagement. MCOTF provides proactive and informative messages about the present and future of lupus research to audiences that include African-, Hispanic-, Asian- and Native-American patients and their families, as well as corporate executives and leaders of community and faith-based organizations.
- The Lupus Patient-Focused Drug Development Initiative (PFDD), a collaboration of the Lupus and Allied Diseases Association, the Lupus Foundation of America and the Lupus Research Alliance, was a way to bring the voice of the patient to lupus therapy development and to inform FDA regulatory decision-making on new drugs. *Lupus: Patient Voices*, a report summarizing feedback from an in-person meeting held in September 2017, online participation, and a survey of more than 2,000 people with lupus, was released in March 2018. The report includes data and personal accounts from people with lupus on symptoms, daily disease impacts, current treatments, and views on clinical trials.
- Existing patient and provider educational materials are an asset. CME programs, particularly those developed by The Lupus Initiative, a national program of the American College of Rheumatology (ACR) that is dedicated to reducing health disparities in lupus, include topics such as the epidemiology of lupus and implicit provider bias. In addition, The Lupus Initiative has developed a program called Materials to Increase Minority Involvement in Clinical Trials (MIMICT) to aid in increasing and improving referrals from community-based providers to clinical trial centers.
- Existing research infrastructure that has research coordinators to solicit potential trial participants and to facilitate the enrollment process. Some sites have mobile units for screening, and some study sponsors pay for participants' transportation, childcare and food costs.
- Electronic Health Records (EHRs), which can be used for prescreening patients who may be eligible for specific trials, including patients who may not yet have been diagnosed with lupus but may be exhibiting several indicators of the disease. Some hospitals are starting to implement this with assistance from companies with software to help screen EHRs.



- Provider referral networks have been effective in other disease states and can teach us how to develop effective networks for lupus.
- Patient Reported Outcomes and Real World Evidence are rapidly growing and developing fields. Instruments such as the those that assess health-related quality of life such as the Patient Reported Outcomes Measurement Information System (PROMIS) and LupusQoL are being reviewed and evaluated for their ability to capture patient outcomes in a way that can be used to facilitate shared decision making and improve quality of care.



Strategies to Overcome Identified Challenges and Barriers

Increasing Education and Awareness

Increasing education and awareness among patients, families and physicians was one of the most frequently mentioned themes in all three breakout groups. Education is key to correcting misperceptions about clinical trials -- the risks, commitment, costs, and benefits -- and, in turn, to eliminating unconscious biases and hidden beliefs among physicians and patients.

Groups stressed the importance of targeting information about lupus and clinical trials to the widest possible range of communities -- especially young adults, women of childbearing age, and of color -- those at greatest risk for the disease. They noted that educational materials, to be effective, must be accessible, linguistically, and culturally appropriate; show understandable and meaningful clinical data; explain the aims, risks, and benefits of trial participation; and address patient concerns and questions.

Using media in all its forms, including print, radio, television, internet, videos, webinars, and social media platforms like Facebook and Twitter, is the best way to disseminate information to multiple populations. Other recommended strategies for increasing education and awareness about lupus included reaching out to students at historically black colleges and universities; having social workers bring educational materials to neighborhoods where people live; or, presenting information at places where community members gather, such as barber shops, beauty salons, night clubs, churches, sororities, community centers, unions, town hall meetings, and public schools. Since the messenger is as important as the message, lupus patients who have firsthand knowledge of community services and clinical trials might be the best sources of education and information for the public as well as physicians.

Raising awareness about lupus also requires reaching critical stakeholders in business, faith (not only Christian) communities, and educational institutions. One proposal featured a person-centered strategy that starts small by recruiting elders, clergy, union representatives, human resource managers, parent-teacher association members, and sorority/fraternity leaders, and then expands as volunteers share lupus education through their respective networks. Thus, what may begin with one-on-one contact could potentially evolve into an expanding conversation throughout many communities. Groups also suggested peer-to-peer storytelling as a mechanism for educating patients and families and reducing isolation by providing a sense of shared experience and community.



Groups emphasized the need to bring educational campaigns to community physicians, including rheumatologists and primary care providers, who might block access to trials if they don't support or understand them. Making clinical trials "top of mind" for these physicians, as well as medical students, and providers-in-training will accustom them to considering clinical trials as standard of care. This will most likely require a cultural shift in health care, health research and academic medicine, such as augmenting medical school curriculum with modules on clinical trials, or providing physicians, investigators, and research coordinators with low-cost incentives such as cell phones, iPads, gift cards, or rewards to travel to meetings where they can promote trial participation. Such incentives may change views of clinical trials from a major investment of time and money to sources of financial reward or career development.

As part of the medical culture shift, healthcare settings could adopt technological improvements, such as apps or software that interface with EHRs to help identify potential trials and trial participants, pre-screen them and make sure they meet eligibility criteria. There must also be a shift in the way research teams provide patients with information about clinical trials. While it is important to provide potential participants with complete and accurate information about trial outcomes, it is equally important to highlight encouraging stories with positive outcomes to embolden patients to participate.

Building Trust is Essential

All breakout groups agreed that trust is essential to increasing minority participation in clinical trials. Building trust requires increasing engagement and strengthening relationships among patients, families, and the medical, and research communities. One way to accomplish this is to generate a list of support and advocacy groups, and then form coalitions that can work together to create clear, accessible messaging about the importance of minority participation in clinical trials. These coalitions must include lupus patients as partners in educational outreach, research, and all decision-making, which will help them understand every aspect of a trial. As partners in lupus research, patients need assurance that they will receive full emotional support through regular phone contact with peers and research staff, as well as support for expenses involved in participation such as transportation, childcare, and food.

Meeting patients where they are is essential to building trust. This means that every member of the research team must understand that patients' experiences begin as soon as they reach the trial site. How does the parking attendant of the clinical trial facility treat them? The security guard? The front desk administrator? Every step of the research process must be customer-service friendly and regard patients as top priority, not second-class citizens. Meeting patients where they are also means that physicians and investigators must demonstrate understanding and empathy for cultural differences. They should receive



cultural relevancy training for help in shedding unconscious biases, hidden beliefs, or stereotypes. And, they should learn to demonstrate caring and respect by overcoming any hesitancy to conduct physical exams.

To meet patients where they are, physicians and investigators must also provide trial information in patients' native languages. They must honor different gender norms, as well as the necessities of special needs communities, including deaf or hard-of-hearing individuals. And, they must build a healthcare team that is not only ethnically, culturally, and racially representative of the patient population, but one that also includes a health coach, social worker, mental health professional, and individuals with lived experiences of lupus.

Physicians and investigators should not pressure patients to behave according to their expectations and needs but accommodate patients' needs and values by structuring trials flexibly (e.g. allowing nurses to draw blood at patients' homes) so that participation does not complicate or burden their lives.

Groups said that it is equally important for research coordinators to secure patients' trust so they can fulfill their responsibilities of identifying and contacting potential trial participants, arranging and conducting screenings, and ensuring that participants meet all eligibility requirements. Coordinators would also benefit from monetary incentives and, more important, from better training to help them balance the competing demands of multiple trials.

Creating a Cultural Shift and Utilizing Technological Enhancements

All groups advocated the use of technology to increase minority participation in clinical trials. Technology can simplify trial participation. Telemedicine, for example, can streamline the check-in process, and allow nurses more flexibility in scheduling visits for at-home blood draws. Other online resources can allow patients to securely view their personal data, review FAQs, find tools that will help them discuss lupus with their families, or engage in moderated discussions with other lupus patients. (e.g. The Kelly Fund has chat rooms with restricted access for patients to talk).

Slide decks can be used to explain informed consent. Posting informed consent forms online so patients can download and complete them in the privacy of their home could reduce the stress of filling them out. Also, creating online consent forms with easy-to-understand icons and a built-in dictionary at a third-grade reading level which patients can use to look up unfamiliar terms, will make filling them out less confusing and frustrating. Groups also expressed strong interest in apps or software that could interface with EMRs to



identify potential trial participants, and pre-screen them to make sure they meet eligibility criteria.

Finally, groups voiced overwhelming support for creating a culture of research. Such a culture would make it instinctive for primary care physicians to refer lupus patients to clinical trial centers and ensure feedback to the referring non-researcher provider. A culture of research would provide necessary support to hire, train, and incentivize research coordinators to call generated leads to increase trial participation. Such a culture would make community physicians and rheumatologists part of the research team and would support clearer communication between them and investigators. Without clear and continuous communication with investigators, community physicians may not refer patients to trials. Thus, there must be a feedback loop that allows investigators and community physicians to share information about trial participants. Finally, a culture of research would encourage doctors, medical students, providers, and providers-in-training to regard clinical trials as standard of care when thinking about treatment options.



Appendix A

LUPUS MULTI-CULTURAL ENGAGEMENT PARTNERSHIP MEETING

DECEMBER 11-12, 2017

PARTICIPANT ROSTER

Anca D. Askanase, MD, MPH

Founder and Clinical Director, Lupus Center
Columbia University Medical Center
New York, NY

Brenda Blackmon

Founder, The Kelly Fund for Lupus
Englewood, NJ

Stephanie Cogan

Vice President, Corporate Relations
National Kidney Foundation
New York, NY

Leah Crocker

Person with Lupus/Lupus Advocate
Atlanta, GA

Daniel E. Dawes, JD

Co-Founder, Health Equity Leadership and
Exchange Network (HELEN)
Fort Lauderdale, FL

Kenneth M. Farber, JD

President and CEO
Lupus Research Alliance
New York, NY

**Sheldon D. Fields, Ph.D., RN, FNP-BC, AACRN,
FNAP, FAANP, FAAN**

National Black Nurses Association
Dean and Professor of the School of Health
Professions
New York Institute of Technology
Old Westbury, NY

Christy M. Gamble, JD, DrPH, MPH

Director of Health Policy & Legislative Affairs
Black Women's Health Imperative
Washington, DC

Owen Garrick, MD

National Hispanic Medical Association
President and CEO
Bridge Clinical Research
Oakland, CA

Kaamilah Gilyard

Person with Lupus/Lupus Advocate
Queens, NY

Cary L. Goodman

National Program Director
The Balm in Gilead, Inc
Midlothian, VA

Diane Gross

National Director of Advocacy and Programs
Lupus Research Alliance
New York, NY

Henrietta Ho-Asjoe

Health Care Consultant
New York, NY

Catherine Jackson, RN, BSN, MPH

Director of Advocacy
Mallinckrodt Pharmaceuticals
St. Louis, MO



Beverly John

Vice President of Finance
WomenHeart
Washington, DC

Kim Kaiser

Special Consultant-Industry Relations
Lupus Research Alliance
New York, NY

Helen Kellar-Wood, PhD

Immunoscience Lead, Diversity and Patient
Engagement
Bristol-Myers Squibb
Princeton, NY

Andrea Kott

Public Health Writer & Editor
Sleepy Hollow, NY

Mary Jo Lamberti, PhD

Senior Research Fellow, Tufts Center for the Study
of Drug Development
Tufts University
Boston, MA

Sam Lim, MD, MPH

Professor of Medicine,
Division of Human Immunology and
Rheumatology
Emory University School of Medicine
Atlanta, GA

Niva Lubin-Johnson, MD, FACP

President-Elect
National Medical Association
Chicago, IL

Joseph Mauriello, CPA

Treasurer, Board of Directors
Lupus Research Alliance
New York, NY

Sheryl McCalla, JD

Director, Lupus Initiative
American College of Rheumatology
Atlanta, GA

Cassandra McCullough

Executive Director
Association of Black Cardiologists
Arlington, VA

Martha Nolan, JD

Senior Director of Government and Strategic
Affairs
Academy for Radiology and Biomedical
Imaging Research
Washington, DC

Ana E. Núñez, MD

Professor of Medicine
Drexel University College of Medicine
Philadelphia, PA

Elizabeth Ofili, MD, MPH, FACC

Professor of Medicine, Director & Senior
Associate Dean, Clinical Research Center &
Clinical and Translational Research
Morehouse School of Medicine
Atlanta, GA

Damemarie Paul

Bristol-Myers Squibb
Lawrence, NJ

Bonnie Pobiner, PhD

Director US Medical Affairs,
ImmunInflammation
GlaxoSmithKline
Research Triangle Park, NC

Gary A. Puckrein, PhD

President and CEO
National Minority Quality Forum
Washington, DC

Jillian A. Rose, LCSW, MPH

Assistant Director, Community Engagement,
Diversity & Research
Hospital for Special Surgery
New York, NY



Albert T. Roy
Executive Director
Lupus Therapeutics, LLC
Arlington, VA

Suz Schrandt, JD
Director, Patient Engagement
Arthritis Foundation
Atlanta, GA

Nadine Spring
Manager, Lupus and APS Center
Hospital for Special Surgery
New York, NY

Teodora Staeva, PhD
Research Director
Lupus Research Alliance
New York, NY

Dayani Tipple
Director, Disease Awareness
GlaxoSmithKline
Media, PA

Christina Vazquez Mateo, PhD
Clinical Research Scientist
EMD Serono
Quincy, MA

Gretchen Clark Wartman
Vice President for Policy and Program
National Minority Quality Forum
Washington, DC

Edith Williams, PhD
Assistant Professor
Medical University of South Carolina
Charleston, SC

Liou Xu, PhD
Senior Statistician
National Minority Quality Forum
Washington, DC



Appendix B

LUPUS MULTI-CULTURAL ENGAGEMENT PARTNERSHIP MEETING

The Lupus Research Alliance Board Room

275 Madison Avenue, New York, NY 10016

DAY 1: MONDAY, DECEMBER 11, 2017 (Lunch will be available at 12:30 PM)

1:00 PM	Welcome and Opening Remarks <i>Joseph Mauriello, Lupus Research Alliance Board of Directors</i> Statement of Purpose and Anticipated Outcomes
1:15 PM	The Lupus Multi-Cultural Engagement Partnership: A Collaboration of the Lupus Research Alliance and the National Minority Quality Forum Remarks: <ul style="list-style-type: none">• <i>Kenneth M. Farber, President and CEO, Lupus Research Alliance</i>• <i>Gary A. Puckrein, PhD, President and CEO, National Minority Quality Forum</i>• <i>Albert Roy, Executive Director, Lupus Clinical Investigators Network (LuCIN)</i>
1:45 PM	Introduction of all Discussants and Overview of the Day <i>Diane Gross, National Director of Advocacy and Programs, Lupus Research Alliance</i> <ul style="list-style-type: none">a. Day 1 Topic: Understanding Lupus and the Need for Participation of Populations that are Under-Represented in Biomedical Researchb. Overview of the Structure of the Day
2:15 PM	Understanding Lupus: The Clinical Perspective <i>Anca D. Askanase, MD, MPH</i> <i>Founder & Clinical Director, Lupus Center, Columbia University Medical College</i> <ul style="list-style-type: none">a. Epidemiology, etiology, current standard of careb. Clinical research and drug development
3:15 PM	Inherent Biases as Challenges to Engagement in Clinical Research <i>Ana E. Núñez, MD</i> <i>Associate Dean for Diversity, Equity and Inclusion; Professor of Medicine</i> <i>Drexel College of Medicine</i>
4:00 PM	The Lupus Atlas: Filling in the Picture <i>Gary A. Puckrein, PhD, President and CEO, National Minority Quality Forum</i>
4:30 PM	Summary of the Day: Thoughts for Tuesday <i>Diane Gross, National Director of Advocacy and Programs, Lupus Research Alliance</i>
5:00 PM	Group Photo & Reception
6:30 PM	Dinner on your own



DAY 2: TUESDAY, DECEMBER 12, 2017 (Breakfast will be available at 8:00 AM)

8:30 AM	Opening Remarks <i>Gretchen C. Wartman, Vice President for Policy and Program, National Minority Quality Forum</i> <ol style="list-style-type: none">Day 2 Topic: Addressing Barriers to Clinical Research Participation in Under-Represented PopulationsOverview of the Structure of the Day.
9:00 AM	Understanding Lupus: The Patient Perspective <ol style="list-style-type: none">Insights into Lupus and the Patient Perspective on Clinical Trials: <i>Diane Gross, National Director of Advocacy and Programs, Lupus Research Alliance</i>The Lived Experience: <i>Leah Crocker, Person with Lupus/Lupus Advocate; Kaamilah Gilyard, Person with Lupus/Lupus Advocate</i>
9:45 AM	Improving Global Public and Patient Engagement in Clinical Research <i>Mary Jo Lamberti, PhD</i> <i>Senior Research Fellow, Tufts Center for the Study of Drug Development</i>
10:15 AM	Getting to Yes: Engaging People with Lupus in Clinical Research <i>Nadine Spring, MPH, Manager</i> <i>Lupus & Antiphospholipid Syndrome Center of Excellence, Hospital for Special Surgery</i>
11:00 AM	Break and Reassemble in Concurrent Discussion Groups
11:15 AM	Concurrent Discussion Groups: Engagement Challenges and Strategic Responses (Lunch will be available) <ul style="list-style-type: none">Patients and their Families and Social Networks <i>Facilitator: Henrietta Ho-Asjoe, Health Care Consultant</i>Employers, the Faith Community, Educational Institutions <i>Facilitator: Daniel Dawes, JD, Co-Founder, HELEN</i>Physicians, Hospitals, and Researchers <i>Facilitator: Owen Garrick, MD, President and CEO, Bridge Clinical Research</i>
1:15 PM	Break: Conclude Concurrent Discussions and Return to Board Room
1:30 PM	Discussion Group Output <i>Facilitator: Diane Gross, Lupus Research Alliance</i>
2:30 PM	Closing Remarks <i>Elizabeth Ofili, MD, MPH, Director & Senior Associate Dean, Clinical Research Center & Clinical and Translational Research, Morehouse School of Medicine</i>
2:45 PM	Thank you and Next Steps <i>National Minority Quality Forum</i> <i>Lupus Research Alliance</i>
3:00 PM	Adjournment



Appendix C

Lupus Multi-Cultural Engagement Partnership – Discussion Group Assignments

Discussion Group A: Patients and their Families and Social Networks	
Facilitator:	Henrietta Ho-Asjoe
Scribe:	Diane Gross
Participants:	Brenda Blackmon Stephanie Cogan Christy Gamble, PhD, JD Kaamilah Gilyard Helen Kellar-Wood, PhD Mary Jo Lamberti, PhD Suzanne Schrandt, JD Christina Vazquez Mateo, PhD Liou Xu, PhD

Discussion Group B: Employers, the Faith Community, Educational Institutions	
Facilitator:	Daniel Dawes, JD
Scribe:	Gretchen Wartman
Participants:	Sheldon Fields, PhD Cary Goodman Catherine Jackson Beverly John Cassandra McCullough Damemarie Paul Dayani Tipple Edith Williams, PhD

Discussion Group C: Physicians, Hospitals and Researchers	
Facilitator:	Owen Garrick, MD
Scribe:	Kim Kaiser
Participants:	Anca Askanase, MD Andrea Kott Sam Lim, MD Niva Lubin-Johnson, MD Sheryl McCalla, JD Martha Nolan, JD Elizabeth Ofili, MD Bonnie Pobiner, PhD Nadine Spring



Appendix D

Background Information for the Lupus Multi-Cultural Engagement Partnership Meeting

Outcomes

The desired outcomes of the inaugural meeting of the Lupus Multi-Cultural Engagement Partnership were to 1. develop national and local strategies that can be piloted to break the barriers and expand patient advocacy efforts around clinical research and awareness of lupus, and 2. form new alliances that will result in new education and awareness programs around clinical research specifically for under-represented populations.

Problem Statement (Background Document Shared with Participants)

Systemic lupus erythematosus (SLE or lupus) is a complex, multisystem autoimmune disease predominantly affecting women and diagnosed during childbearing years (ages 15-44).ⁱⁱⁱ In lupus, the immune system inexplicably and randomly attacks the body's own tissues and vital organs, including the heart, brain, kidneys, lungs and blood. Lupus is a leading cause of premature cardiovascular disease, heart attack, stroke, and kidney disease among young women. The disease is characterized by periods of more severe symptoms and disease activity called "flares" and remissions. The chronic nature of lupus leads to organ damage accrual over time, and increased mortality and morbidity when compared to the general population. Lupus can impact any organ, some of the most severe and debilitating forms of lupus include lupus nephritis, a kidney inflammation that can result in kidney failure, and central nervous system disease causing seizure, brainstem dysfunction, stroke or psychosis.

Lupus affects an estimated 200,000-500,000 people in the United States with some claiming the figure may be as high as 1.5 million. One of the difficulties of diagnosing and treating lupus is that no two cases are alike; the disease affects everyone differently. In addition, there is no one test to diagnose lupus. Lupus has been referred to as the great imitator because the symptoms vary widely, and it is often mistaken for other diseases. Therefore, a diagnosis can take months, even years, from symptom onset. Lupus patients often report it takes 4-6 years and an average of 3 doctors to get diagnosed. As the ten-year survival rate decreases from 80-90% to 60% with advanced stage disease,ⁱⁱⁱ early detection is critical.

Some of the symptoms of lupus include a red rash on the face often in the shape of a butterfly across the nose and cheeks, painful or swollen joints, unexplained fever, swollen glands, extreme or prolonged fatigue, hair loss, sensitivity to the sun, fingers turning white and/or blue in the cold, and memory problems. When a person experiences these symptoms, it is called a flare. Flares can be triggered by ultraviolet light, infections, stress, and changes in medication.



There is no known prevention or cure for lupus. Current treatments address the symptoms but not the underlying disease and have problems with efficacy and toxicity. Only four treatments have been approved for lupus and only one of these, belimumab, was developed specifically for lupus. For the most feared complication of the disease, lupus nephritis, there are no approved treatments.

Disparities in Lupus

Lupus disproportionately affects women at a rate of 9:1. It disproportionately affects traditionally underserved populations - African American, Hispanic, Asian, and Native Americans. These women of color have two to three times higher risk for developing lupus than Caucasians.

Five-year survival in people with lupus has improved from 50% in the 1950's to over 90% currently,^{iv,v} but mortality remains high and is on the rise compared to the general population. Mortality rates among traditionally underserved populations with lupus are over 3 times as high as Caucasians, and they are more likely to experience multiple comorbidities such as cardiovascular disease and diabetes, and worse health outcomes and related quality of life.^{vi,vii,viii,iv,x} The reasons for these health disparities are complex, and include genetics, comorbidities and socioeconomic challenges. Access to healthcare and active engagement of the patient in their own care are particularly important factors.

To better understand the prevalence and incidence of lupus, particularly its impact on people of African American, Hispanic, Asian, and Native American descent, the Centers for Disease Control and Prevention has funded development of 5 lupus registries in Georgia, Michigan, New York City, California and the Indian Health Service. Results published to date continue to show the disproportionate impact of lupus on traditionally underserved populations.^{xi,xii,xiii} According to the US Census, the total non-Caucasian population is expected to rise to 56% in 2060 compared to 35% in 2014,^{xiv} so it can be expected that the burden of lupus will significantly increase.

Cost to Society

The cost of lupus has a significant impact on our society. Chronic diseases with early onset, like lupus, have a negative impact on earnings and the ability to accrue for retirement. Since lupus tends to impact women in their prime earning years, many people with lupus end up relying on public assistance. A study of people employed at the time of lupus diagnosis found that by five years after diagnosis, 15% had stopped working, by 10 years, 36% had stopped working, and by 15 years, 51% had stopped working. On average, these individuals were diagnosed in their mid-thirties; therefore, almost none were employed to the normal retirement age.^{xv} A study of employment and work disability for people with SLE found that 33% of SLE patients were on work disability, while 47% were employed. Work disability was related to "a variety of psychosocial and disease related factors, including age, race, sex, SES [socio-economic status],



education, disease activity and duration, pain, fatigue, anxiety, and neurocognitive involvement.^{xvi}

The annual cost per SLE patient, including medical, work absence, and short term disability, is higher than for diabetes, chronic obstructive pulmonary disease, and heart disease. A study using a database of patients with employer sponsored medical coverage found that direct medical expenses in one year for people with lupus was \$19,502, 2.7 times greater than matched controls without lupus.^{xvii}

Lack of Safe and Effective Therapies

Because of the complex nature of lupus and the fact that there is no cure, treatment is focused on preventing flares, managing symptoms when they occur, and reducing organ damage and other problems. A variety of medications are used to treat lupus, many of which have side effects including hair loss and weight gain. In addition to medication to treat lupus symptoms, patients may be on medication to treat conditions related to lupus such as high blood pressure, osteoporosis, or blood clots.

Medications used to treat the disease, such as corticosteroids or immunosuppressants, can cause increased susceptibility to infection or osteoporosis, and can lack efficacy and cause toxicity in some patients.^{xviii,xix,xx,xxi} The unpredictable nature of the disease, need for long term treatments, and the effects of disease activity and treatment can severely impact quality of life.

Only four FDA-approved medicines are available to lupus patients - belimumab, the antimalarial hydroxychloroquine, prednisone (a corticosteroid), and aspirin. In 2011, belimumab was the first drug in over 50 years to be approved for lupus and the first ever developed specifically for lupus. However, belimumab does not remove the need for other treatments. Standard of care continues to rely on corticosteroids combined with immunosuppressant and chemotherapeutic agents approved for other indications. These treatments can be effective in alleviating symptoms but have toxicities and harmful side effects (including osteoporosis, sterility, and infections) that can be as debilitating as the disease itself.

For lupus nephritis, which affects up to 60% of patients, there are no FDA approved treatments. Despite the adoption of immunosuppressant medicines and new treatment regimens there has been no reduction in the percentage of patients progressing to end-stage renal disease (ESRD). Worryingly, and for reasons that are not understood, the incidence of ESRD among lupus nephritis patients may in fact be increasing.

Although lupus is more severe and more prevalent in non-white populations, recruitment of these traditionally underserved populations to participate in clinical trials has proved particularly challenging. For example, belimumab Phase 3 trials did not include enough African American patients to determine if the drug is effective in this population. As a result, the FDA has mandated a post approval trial in black race patients. New initiatives are needed to understand the reasons for the failures to include diverse patients in lupus clinical trials and develop evidence-based remedies.



Lupus clinical trials are highly challenging due to the extreme heterogeneity of the disease and the demographics of the affected population. Only one drug has been approved specifically for lupus. However, owing to advances in understanding the biological basis of the disease there are now more lupus therapeutics in preclinical and clinical development than ever before. There is also tremendous investment at the federal level, the National Institutes of Health and industry have committed \$27 million to validate new targets in lupus as part of the landmark Accelerating Medicines Partnership.

Lupus Research Alliance Efforts to Advance Drug Development

The Lupus Patient-Focused Drug Development Initiative (PFDD) is a collaboration of the Lupus and Allied Diseases Association, the Lupus Foundation of America, and the Lupus Research Alliance. A day-long meeting to advance lupus therapy development and inform Food and Drug Administration (FDA) regulatory decision-making on new drugs for lupus was held in September 2017.

The meeting featured two panels of people with lupus and family members and speakers that included clinicians, representatives from the FDA, and a community representative. Audience members also provided input throughout the day on symptoms and treatments. Meeting participants spoke about the difficulties of managing treatment for this heterogeneous and unpredictable disease, including the side effects of many medications. Throughout the meeting, attendees demonstrated their resilience in the face of lupus and expressed the urgent need to develop new treatments. A comprehensive Lupus: Patient Voices report was sent to the FDA in March 2018 summarizing all the feedback from the meeting, online participation, and surveys from more than 2,000 people with lupus.

The Lupus Research Alliance launched the Lupus Clinical Investigators Network (LuCIN) to accelerate the identification and development of new therapies to treat lupus. Comprised of leading lupus experts at 58 academic research centers throughout North America, LuCIN provides a coordinated framework to test potential new treatments quickly and cost-effectively while upholding the highest scientific standards. Investigators are committed to the Network, working together to determine which new treatments and approaches to conducting clinical trials are most worth pursuing, as well as to involve patients as active members in the research process.

The goals of LuCIN are to: conduct safe and reliable clinical studies on new lupus treatments; facilitate sharing of clinical and biological data to better understand lupus; and enlist patient input and participation in clinical studies. Another primary objective is to identify leadership and promote collaboration throughout the lupus community of scientists, healthcare providers and patients and families.

The Network is also designed to advance quality lupus research by helping attract and train new researchers in the field. Experienced scientists mentor junior investigators at each center, encouraging the next generation of top talent to pursue lupus research as their career path. In addition, the insights gained



by a consistent group of highly experienced investigators working on the same studies is expected to improve tools used to measure the effectiveness of potential treatments.

LuCIN was originally created as an outgrowth of a project initiated by the Lupus Research Alliance to test drugs that have been approved for other diseases by the U.S. Food and Drug Administration (FDA) for their potential in lupus, known as drug repurposing. Testing existing drugs for their possible use in lupus can bring new treatment options to patients faster. LuCIN will also pursue lupus clinical trials of investigational drugs in partnership with biotechnology/pharmaceutical companies.

-
- ⁱ Ward M, Access to Care and the Incidence of End Stage Renal Disease Due to Systemic Lupus Erythematosus. *J Rheumatol.* 2010 June; 37(6): 1158-63.
- ⁱⁱ Yazdany J, Feldman C, Liu, J, et. Al. Quality of Care for Incident Lupus Nephritis Among Medicaid Beneficiaries in the United States. *Arthritis Care Res.* 2014 April; 66(4) 617-624.
- ⁱⁱⁱ Lateef A, Petri M. Unmet medical needs in systemic lupus erythematosus. *Arthritis Research and Therapy.* 2012;14(suppl4)s4:1-9.
- ^{iv} Urnamoto KM, Michet CJ Jr, Thumboo J, Sunku J, O'Fallon WM, et al. Trends in the incidence and mortality of systemic lupus erythematosus, 1950-1992. *Arthritis Rheum.* 1999;42(1):46-50.
- ^v Lim SS, Drenkard C, McCune WJ et al. Population-based lupus registries: advancing our epidemiologic understanding. *Arthritis Rheum.* 2009;61(10):1462-1466.
- ^{vi} Alcaron GS, McGwin G, Rosman JM et al. Systemic lupus erythematosus in three ethnic groups. XIX. Natural history of the accrual of the American College of Rheumatology criteria prior to the occurrence of criteria diagnosis. *Arthritis Rheum.* 2004;51(4):609-15.
- ^{vii} Alcaron GS, McGwin G, Uribe A, et al. Systemic lupus erythematosus in a multiethnic lupus cohort (LUMINA)xvii. Predictors of self-reported health-related quality of live early in the disease course. *Arthritis Rheum.* 2004;51(3):465-74.
- ^{viii} Costenbader KH, Desai A, Alcaron GS et al. Trends in the incidence, demographics, and outcomes of end stage renal disease due to lupus nephritis in the US from 1995-2006. *Arthritis Rheum.* 2001;63(6):1681-88.
- ^{ix} Hanley JG, Urowitz MB, Su L, et al. Seizure disorders in systemic lupus erythematosus results from an international, prospective, inception cohort study. *Ann Rheum Dis.* 2012.
- ^x Feldman C, Hiraki L, Liu J. et al. Epidemiology and Socio demographics of Systemic Lupus Erythematosus and Lupus Nephritis Among US Adults with Medicaid Coverage, 2000-2004. *Arthritis & Rheumatism.* 2013;65(3):753-763
- ^{xi} Lim S, Bayakly A, Helmick C, et. al. The Incidence and Prevalence of Systemic Lupus Erythematosus, 2002-2004. The Georgia Lupus Registry. *Arthritis & Rheum.* 2014;66(2):375-368.
- ^{xii} Marder W, Somers EC, Lewis EE, et al. (2010) Michigan Lupus Epidemiology & Surveillance Program (MILES): Patients presenting with cutaneous lupus as first symptom have delayed progression to SLE. *International Congress on Autoimmunity.*
- ^{xiii} Dall'Era M, Snipes K, Cisternas M, et Al.(2014) Preliminary Population- Based Incidence and Prevalence Estimates of SLE: The California Lupus Surveillance Project. *American College of Rheumatology Scientific Meeting.*
- ^{xiv} US Census Bureau (2013). Projections of the Size and Composition of the US Population: 2014-2060. Accessed May 12, 2015 at: <https://www.census.gov/content/dam/Census/library/publications/2015/demo/p25-1143.pdf>
- ^{xv} Yelin E, Trupin L, Katz P, Criswell L, Yazdany J, Gillis J, et al. Work dynamics among persons with systemic lupus erythematosus. *Arthritis Rheum* 2007;57:56-63
- ^{xvi} Baker K, Pope J. Employment and work disability in systemic lupus erythematosus: a systematic review. *Rheumatology* 2009; 48(3):281-284.
- ^{xvii} Carls G, Li T, Panopolis P, Wang S, Mell AG, Gibson TB, Goetzel RZ. Direct and indirect costs to employers of patients with systemic lupus erythematosus with and without nephritis. *J Occup Environ Med.* 2009;51(1):66-79.
- ^{xviii} Gladman DD, G. C. (2000;27(2)). The Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus international comparison. *J Rheumatol,* 373-376.
- ^{xix} Calvo- Alen J, McGwin G, Toloza S, et al. Systemic lupus erythematosus in a multiethnic US Cohort (LUMINA);XXIV. Cytotoxic treatment is an additional risk factor for the development of symptomatic osteonecrosis in lupus patients: results of a nested matched case control study. *Ann Rheum Dis.* 2006;65(6)785-790
- ^{xx} Haque S, Gorden C, Isenberg D et. al. Risk factors for clinical coronary artery disease in systemic lupus erythematosus: there lupus atherosclerosis evaluation of risk (LASER) study. *J Rheumatol.* 2010, 37(2):322-329.
- ^{xxi} Zonana-Nacach A, Yanez P, Jimenez-Bladeras FJ et al. Disease activity, damage and survival in Mexican patients with acute sever systemic lupus erythematosus. *Lupus.* 2007;16(12):997-1000.





LUPUSRESEARCH.ORG



NMQF.ORG