LRAN Lupus Research Action Network

by **Lupus Foundation of America**

Help Us Solve
The Cruel Mystery
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Why Lupus?
Clinical Trials 101

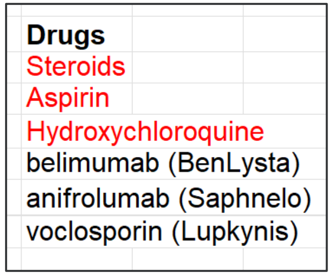
Joan T. Merrill, MD
Oklahoma Medical Research Foundation,
Professor of Medicine

Why Lupus?

or

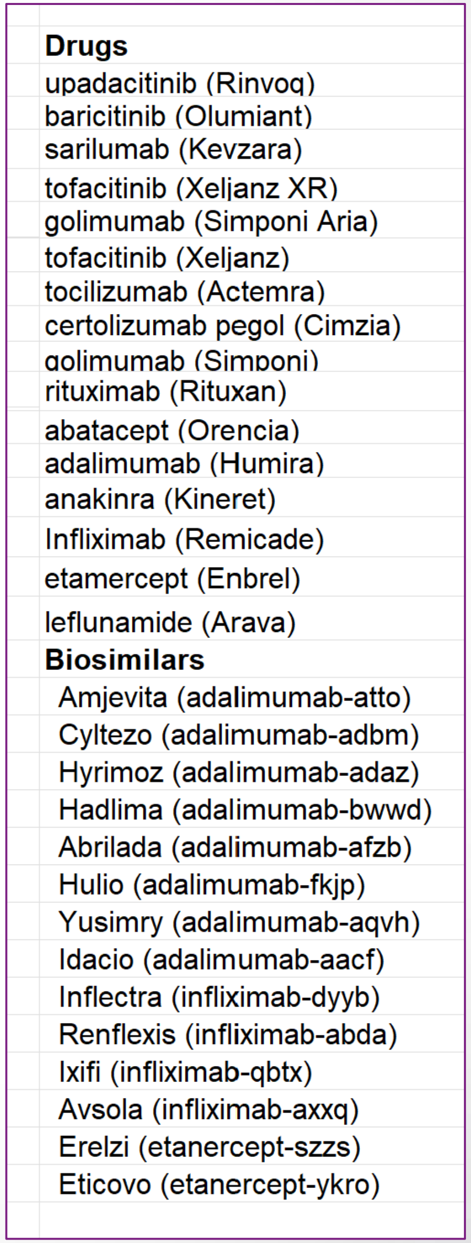
Why Not Lupus?

Lupus (SLE)



Drugs
Steroids
Aspirin
Hydroxychloroquine
belimumab (BenLysta)
anifrolumab (Saphnelo)
voclosporin (Lupkynis)

RA



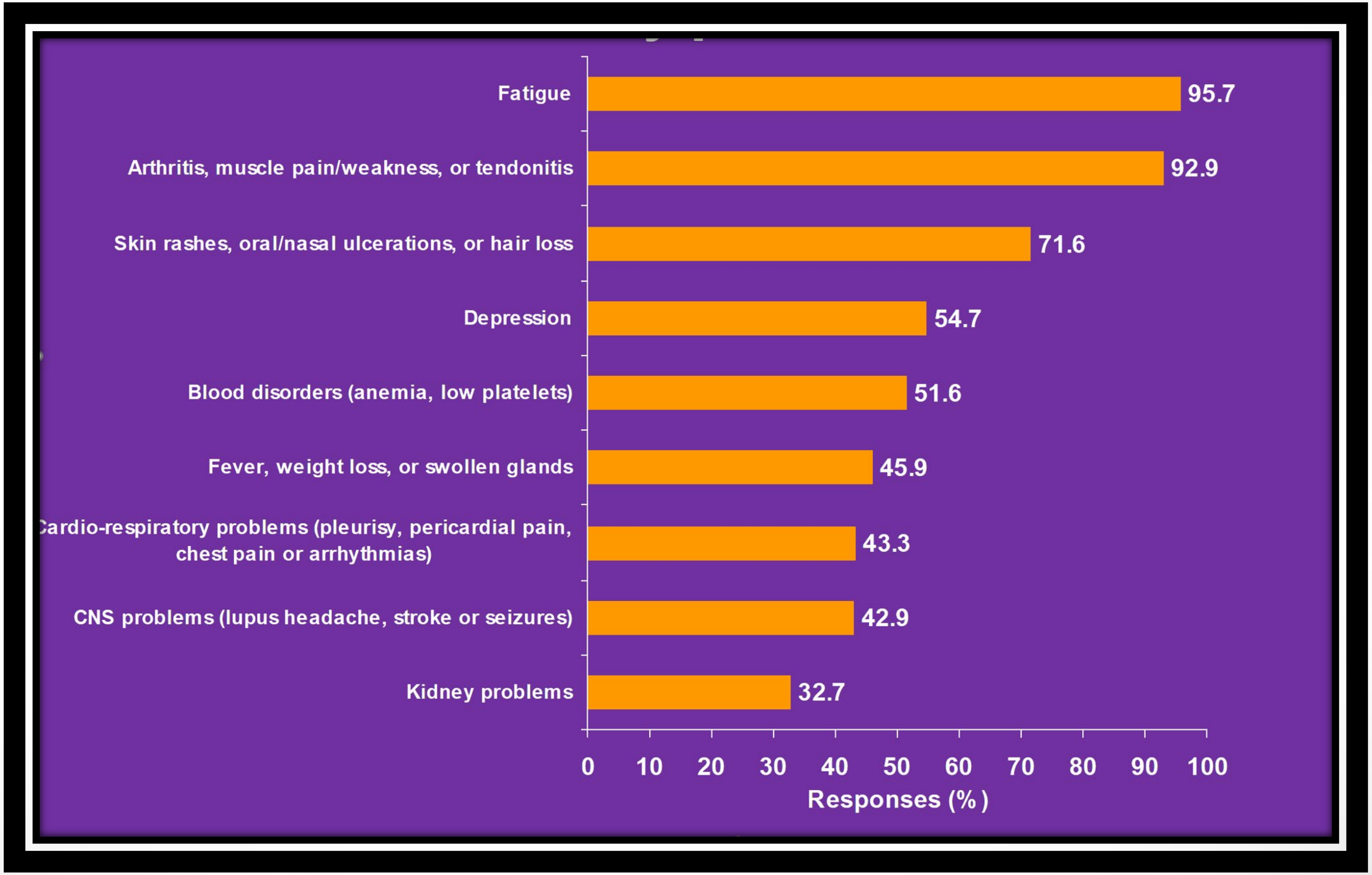
Drugs
upadacitinib (Rinvoq)
baricitinib (Olumiant)
sarilumab (Kevzara)
tofacitinib (Xeljanz XR)
golimumab (Simponi Aria)
tofacitinib (Xeljanz)
tocilizumab (Actemra)
certolizumab pegol (Cimzia)
golimumab (Simponi)
rituximab (Rituxan)
abatacept (Orencia)
adalimumab (Humira)
anakinra (Kineret)
Infliximab (Remicade)
etamercept (Enbrel)
leflunamide (Arava)
Biosimilars
Amjevita (adalimumab-atto)
Cyltezo (adalimumab-adbm)
Hyrimoz (adalimumab-adaz)
Hadlima (adalimumab-bwwd)
Abrilada (adalimumab-afzb)
Hulio (adalimumab-fkjp)
Yusimry (adalimumab-aqvh)
Idacio (adalimumab-aacf)
Inflectra (infliximab-dyyb)
Renflexis (infliximab-abda)
Ixifi (infliximab-qbtx)
Avsola (infliximab-axxq)
Erelzi (etanercept-szzs)
Eticovo (etanercept-ykro)

What is the impact of lupus on family, employment, and quality of life?

- There was limited information about this so the Lupus Foundation of America did a survey
- 531 people with lupus (each question was answered by at least 500 of these people
- 86% were between 20–50 years old
- 36% were married, 28% were single
- 31% were parents with children

M Crimmings,[1] K Lerstrøm,[2] M Govoni,[3] D Isenberg,[4] JT Merrill[5] [1]Lupus Foundation of America, Washington DC, USA; [2]LUPUS EUROPE, Romford, UK; [3]UCB, Brussels, Belgium; [4]University College London Hospitals, London, UK; [5]Oklahoma Medical Research Foundation, USA Presented at the World Lupus Congress Vancouver B.C. 2010

Most Common Features Reported by People with Lupus



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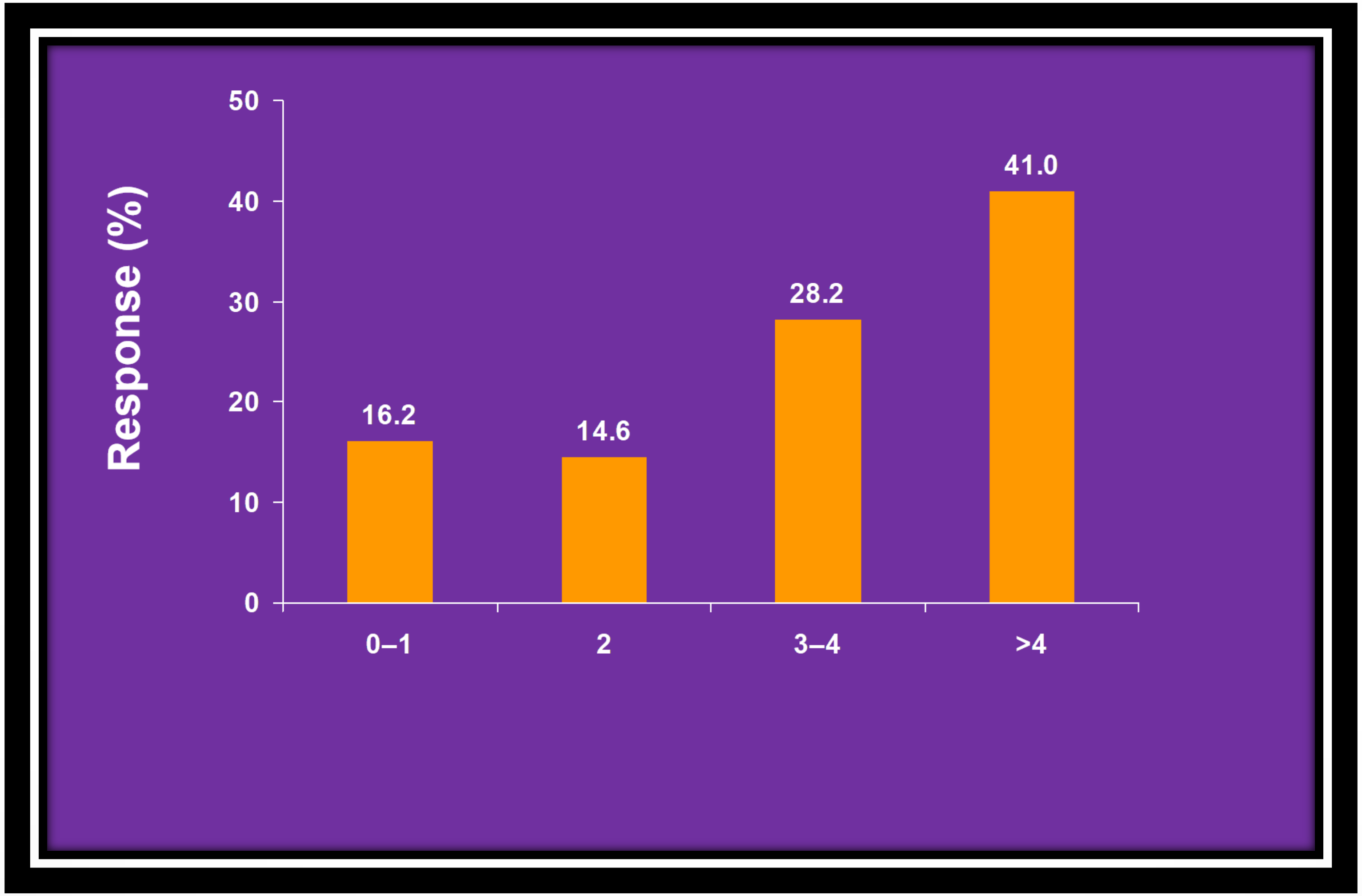
Number of Flares per Year



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How do people with lupus rate their current treatment?

‘satisfied’ or ‘very satisfied’ 44%

Neutral 42%

Very dissatisfied 15%

How do people with lupus rate their current treatment?

‘satisfied’ or ‘very satisfied’ 44%

Neutral 42%

Very dissatisfied 15%

Medications impair daily activities or work?
45%

Current State of the Art

How do we select the best treatments for each individual patient?

- We Don’t
- We Should
- We Will

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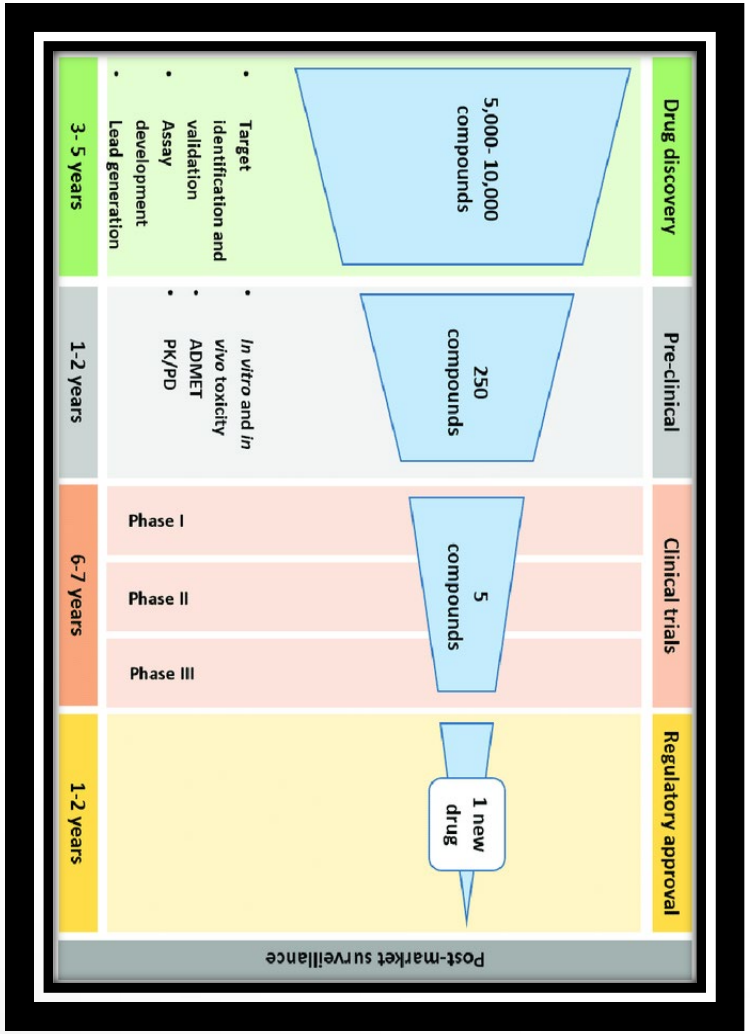
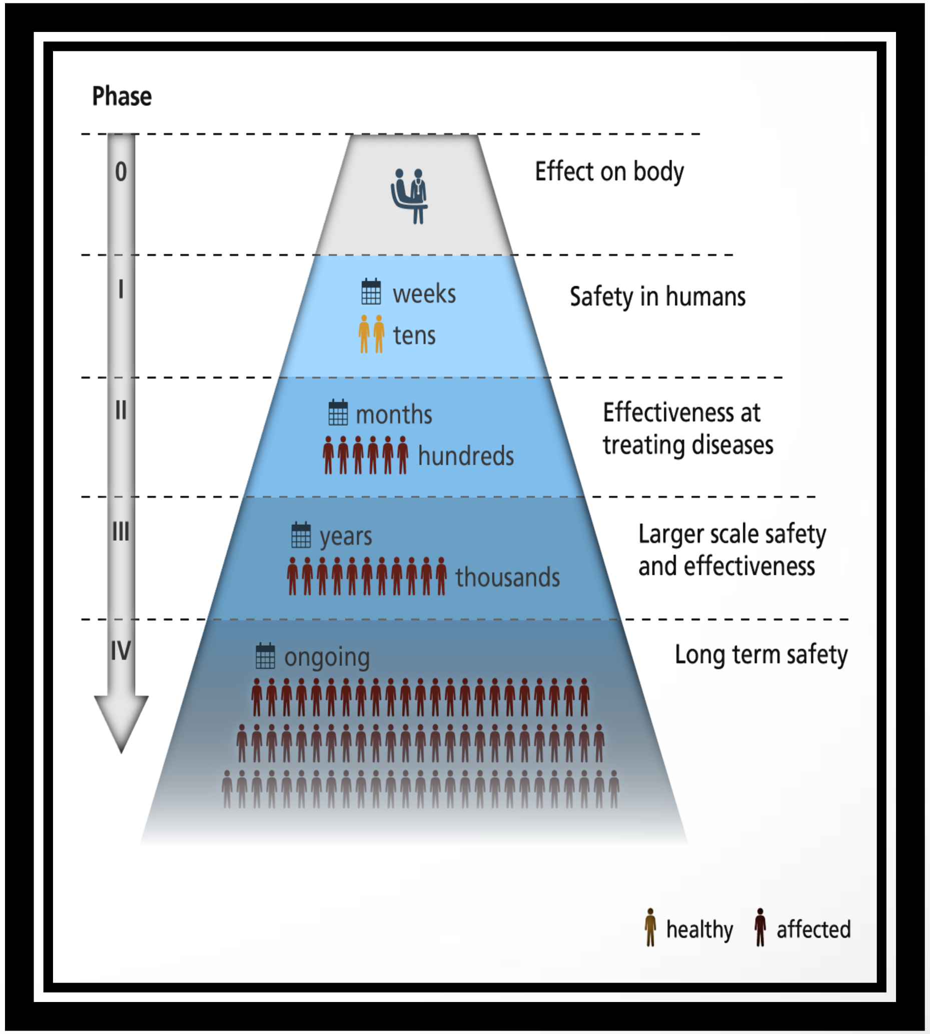
Types of Research

Subject	Types	Methods	Risk	Benefits
Test Tube			Minimal	Proof of Concept
Animal	Safety	Toxicity Studies	High	Dry Run
	Efficacy	Disease Models	High	Dry Run
Human	Observational	Retrospective	Minimal to Moderate	Testing of Disease Model for Relevance
		Cross Sectional		
		Prospective		
		Cohort		
		Case Control		
	Interventional	Clinical Trial:	Moderate to High	Potential Direct Benefits: Must outweigh Risks
		Open Lable		
		Placebo controlled + blinding		
		Randomized		

Drug Development: More and More People Exposed to Fewer andferwer Experimental Treatments





Participation in Clinical Trials

Benefits	Risks	Remediations
Treatment may help	Treatment might hurt	Informed Consent Close monitoring Access to Care Coverage of Expenses
Privacy (Names withheld)	Loss of Privacy	HIPPA Protections Violation Reporting
Access to Extra Care and State of the Art Monitoring	Costs/ Lack of communication with usual medical team	Rights to records No charge for study tests

Informed Consent

What to look for…

STUDY SAFETY:

- **What is the purpose of the study?**
- **Why do the researchers think that their approach might be effective?**
- **Who reviewed and approved the study?**
- **Is patient safety monitored throughout the trial?**
- **What happens if in the middle of the study, one group is doing much better (or worse) than the other?**
- **What are the short- and long-term risks and benefits?**

COORDINATING CARE:

- **Will you be able to continue your normal medications and treatment during the trial?**
- **Who will supervise your care, and where will the care occur?**
- **Will your doctor know exactly what you are receiving and the results of any tests that are done?**

Informed Consent (cont.)

What to look for…

STUDY COSTS:

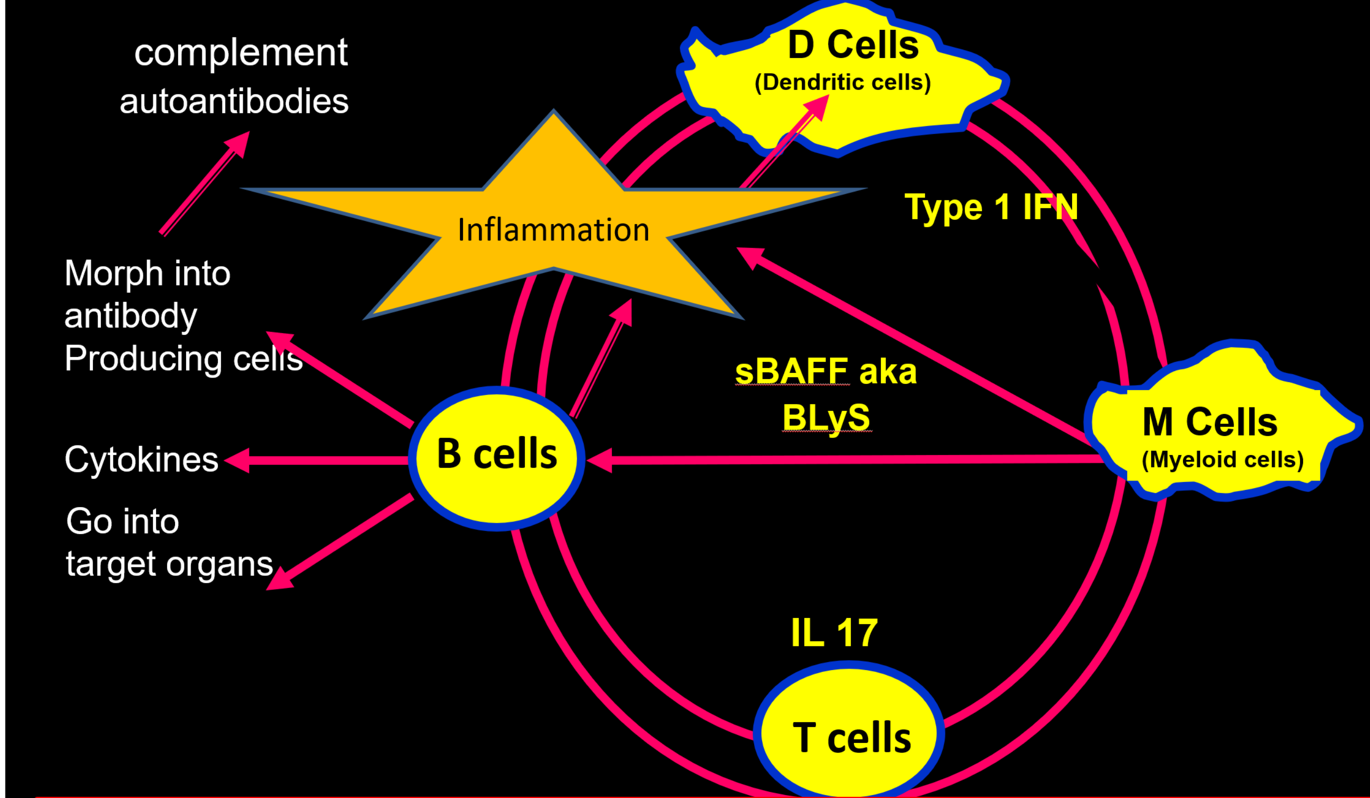
- How will the study affect your daily life?
- Will you have to pay for any portion of the trial, and how much will it cost?
- Is your parking or transportation reimbursed?
- How many extra visits will you have to make?
- Who can help you answer questions from your insurance company or health plan about the trial?

CONFIDENTIALITY:

- Who has access to your information?
- How will this information be protected?
- Will it be shared with anyone?
- Who can you contact with any questions, concerns, or side effects?

Issues in Developing Better Treatments for Lupus

Adapted from: Ramanujam M, Davidson A. Arthritis Research and Therapy 2004; 197



This is a cartoon of the immune system showing how the different immune cells interact with each other. When the immune system senses a threat from the environment, it starts the wheel turning. Because of the circular way in which it operates, this could turn into a perpetual motion machine if there is nothing to stop it. Fortunately most of us are equipped with ways to slow down the process once the threat is gone.

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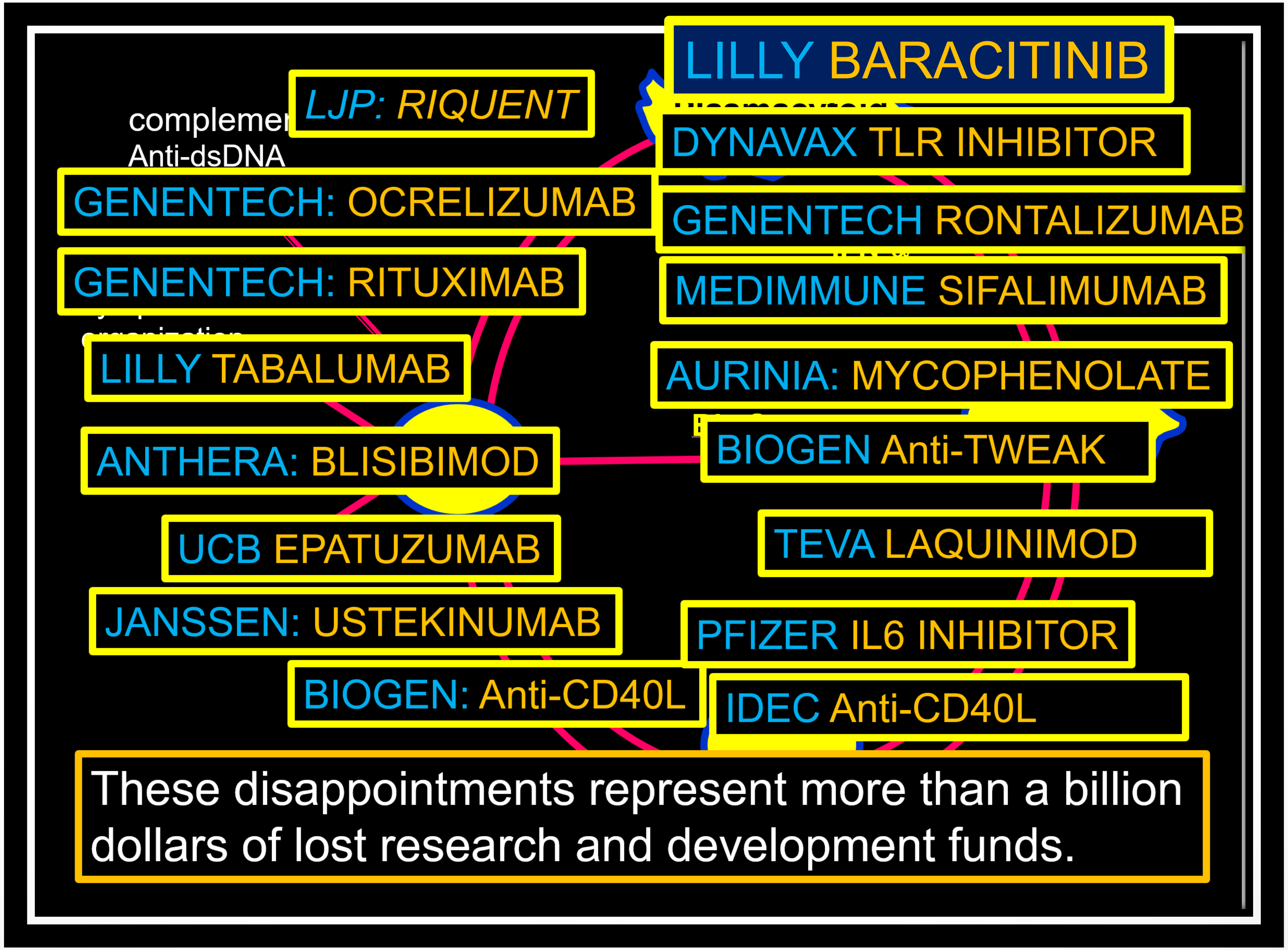
Completed Trials of Investigational Treatments for SLE



complemen
Anti-dsDNA

LILLY BARACITINIB

LJP: RIQUENT

DYNAVAX TLR INHIBITOR

GENENTECH: OCRELIZUMAB

GENENTECH RONTALIZUMAB

GENENTECH: RITUXIMAB

MEDIMMUNE SIFALIMUMAB

LILLY TABALUMAB

AURINIA: MYCOPHENOLATE

ANTHERA: BLISIBIMOD

BIOGEN Anti-TWEAK

UCB EPATUZUMAB

TEVA LAQUINIMOD

JANSSEN: USTEKINUMAB

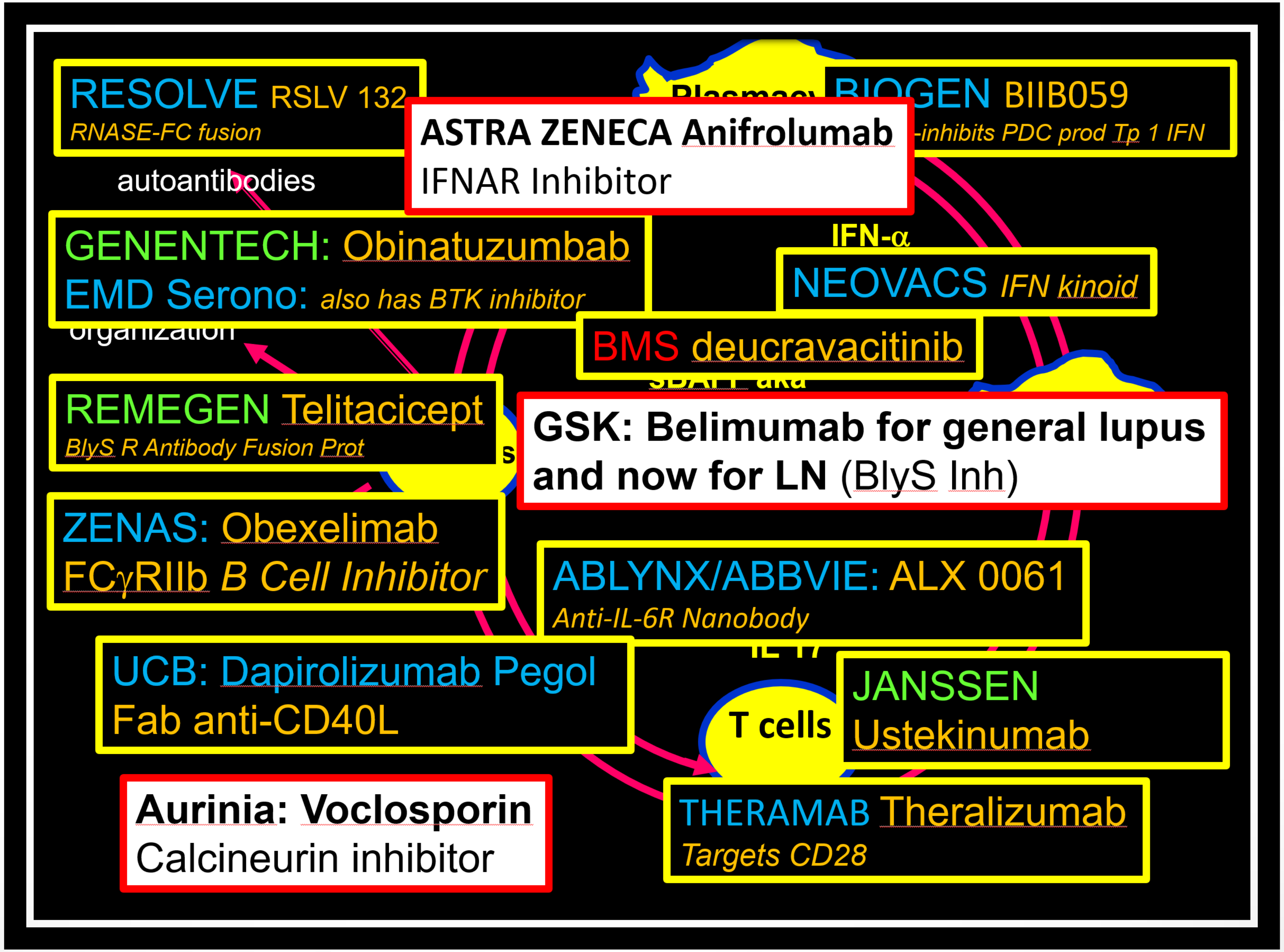
PFIZER IL6 INHIBITOR

BIOGEN: Anti-CD40L

IDEC Anti-CD40L

These disappointments represent more than a billion dollars of lost research and development funds.

Recent Developments



RESOLVE RSLV 132
RNASE-FC fusion

ASTRA ZENECA Anifrolumab
IFNAR Inhibitor

BIOGEN BIIB059
-inhibits PDC prod Tp 1 IFN

GENENTECH: Obinatuzumbab
EMD Serono: *also has BTK inhibitor*

NEOVACS *IFN kinoid*

BMS deucravacitinib

REMEGEN Telitacicept
BlyS R Antibody Fusion Prot

GSK: Belimumab for general lupus and now for LN (BlyS Inh)

ZENAS: Obexelimab
FCγRIIb *B Cell Inhibitor*

ABLYNX/ABBVIE: ALX 0061
Anti-IL-6R Nanobody

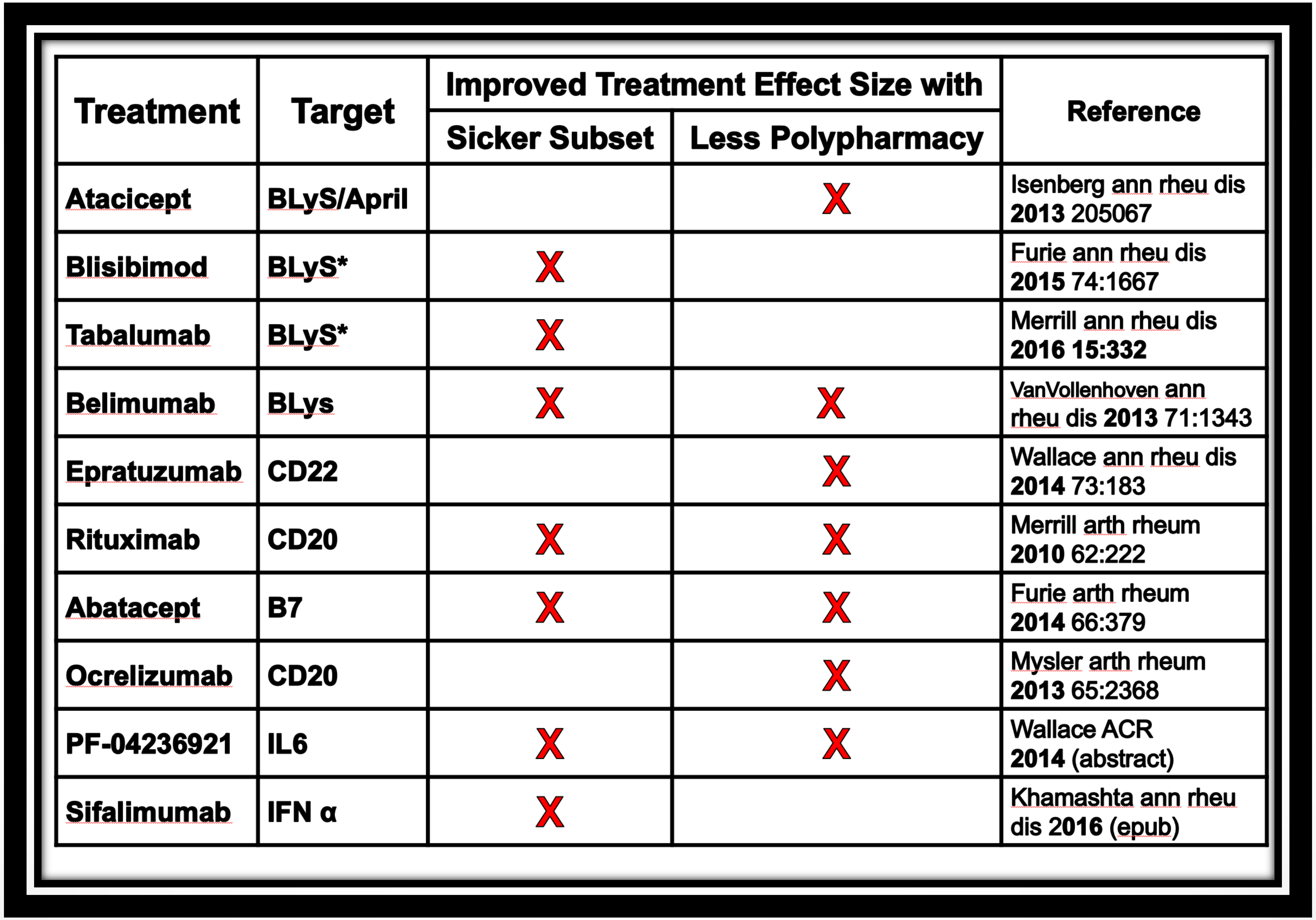
UCB: Dapirolizumab Pegol
Fab anti-CD40L

JANSSEN
Ustekinumab

Aurinia: Voclosporin
Calcineurin inhibitor

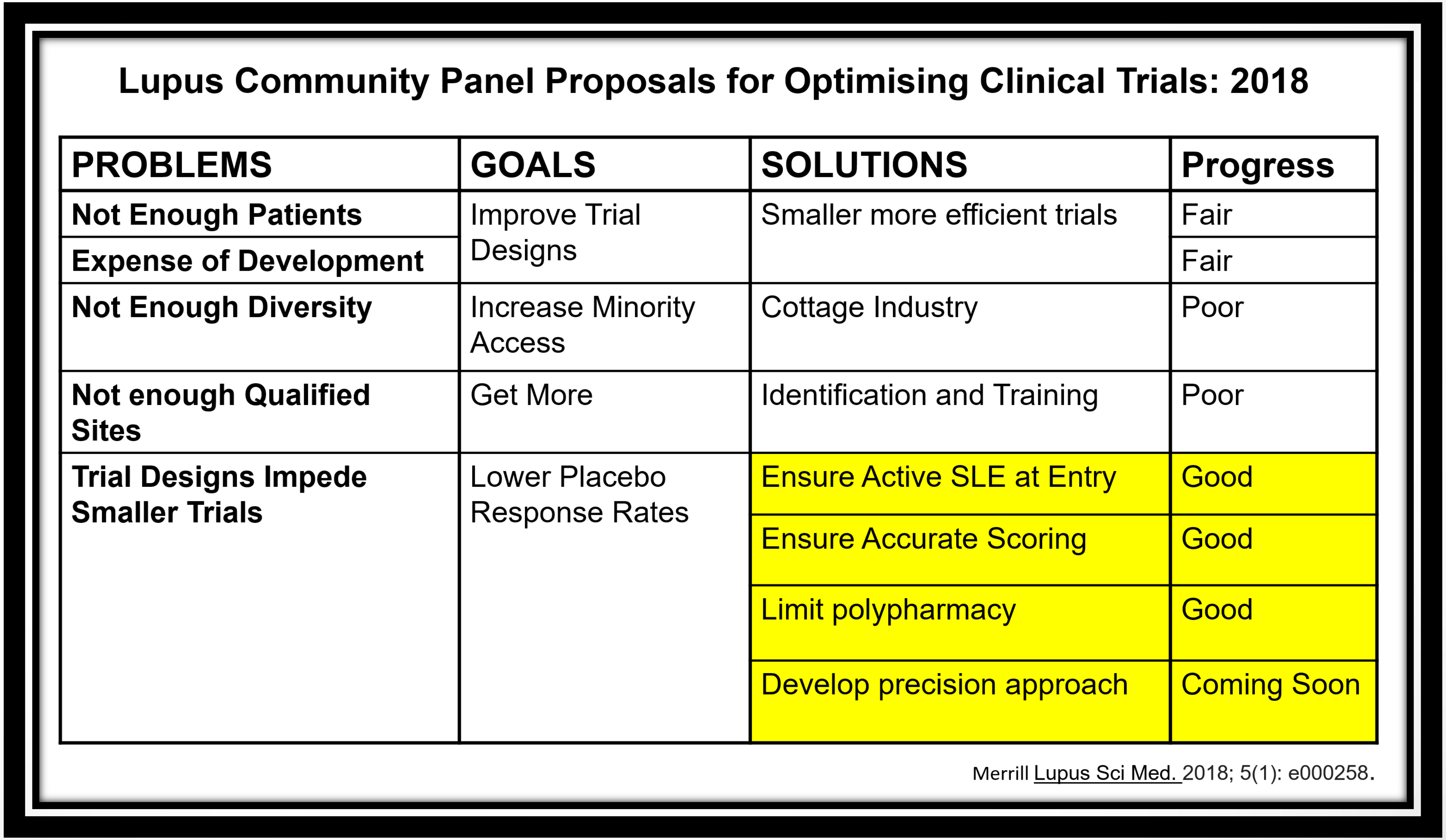
THERAMAB Theralizumab
Targets CD28

How Did This Happen?



Treatment	Target	Improved Treatment Effect Size with		Reference
		Sicker Subset	Less Polypharmacy	
Atacicept	**BLyS/April**		X	Isenberg ann rheu dis **2013** 205067
Blisibimod	**BLyS***	X		Furie ann rheu dis **2015** 74:1667
Tabalumab	**BLyS***	X		Merrill ann rheu dis **2016 15:332**
Belimumab	**BLys**	X	X	VanVollenhoven ann rheu dis **2013** 71:1343
Epratuzumab	**CD22**		X	Wallace ann rheu dis **2014** 73:183
Rituximab	**CD20**	X	X	Merrill arth rheum **2010** 62:222
Abatacept	**B7**	X	X	Furie arth rheum **2014** 66:379
Ocrelizumab	**CD20**		X	Mysler arth rheum **2013** 65:2368
PF-04236921	**IL6**	X	X	Wallace ACR **2014** (abstract)
Sifalimumab	**IFN α**	X		Khamashta ann rheu dis **2016** (epub)

How Was it Mobilized?



Lupus Community Panel Proposals for Optimising Clinical Trials: 2018

PROBLEMS	GOALS	SOLUTIONS	Progress
Not Enough Patients	Improve Trial Designs	Smaller more efficient trials	Fair
Expense of Development			Fair
Not Enough Diversity	Increase Minority Access	Cottage Industry	Poor
Not enough Qualified Sites	Get More	Identification and Training	Poor
Trial Designs Impede Smaller Trials	Lower Placebo Response Rates	Ensure Active SLE at Entry	Good
		Ensure Accurate Scoring	Good
		Limit polypharmacy	Good
		Develop precision approach	Coming Soon

Merrill Lupus Sci Med. 2018; 5(1): e000258.

Results from a Phase 2 Trial of Anifrolumab

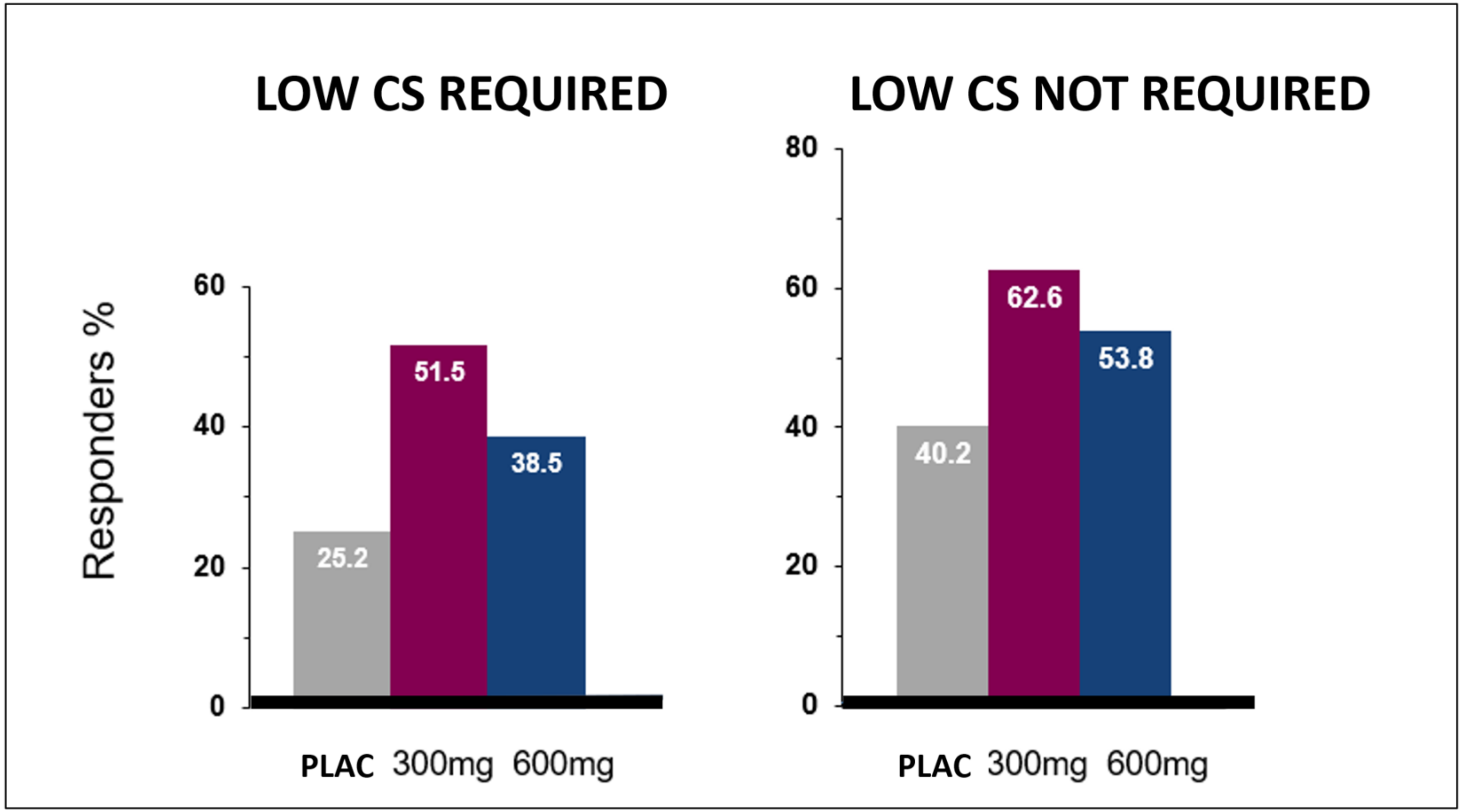


Figure from Furie ACR 2015
Full report in Furie Arth Rheum 2017 69:276-386

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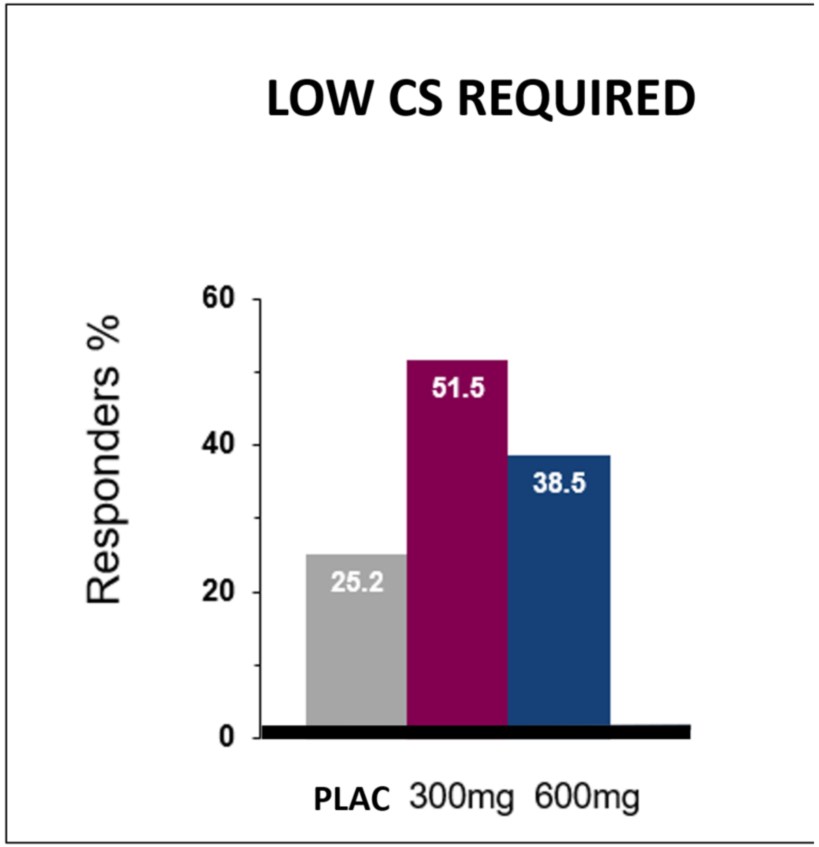
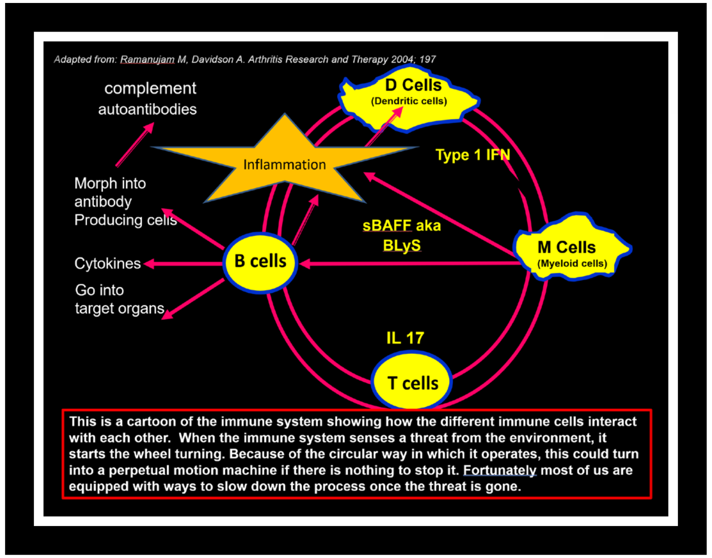
How Can We Do Better than a 50:50 Chance of Response?




Adapted from: Ramanujam M, Davidson A. Arthritis Research and Therapy 2004; 197

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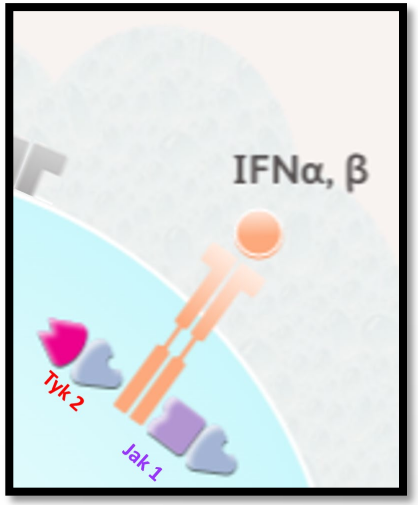

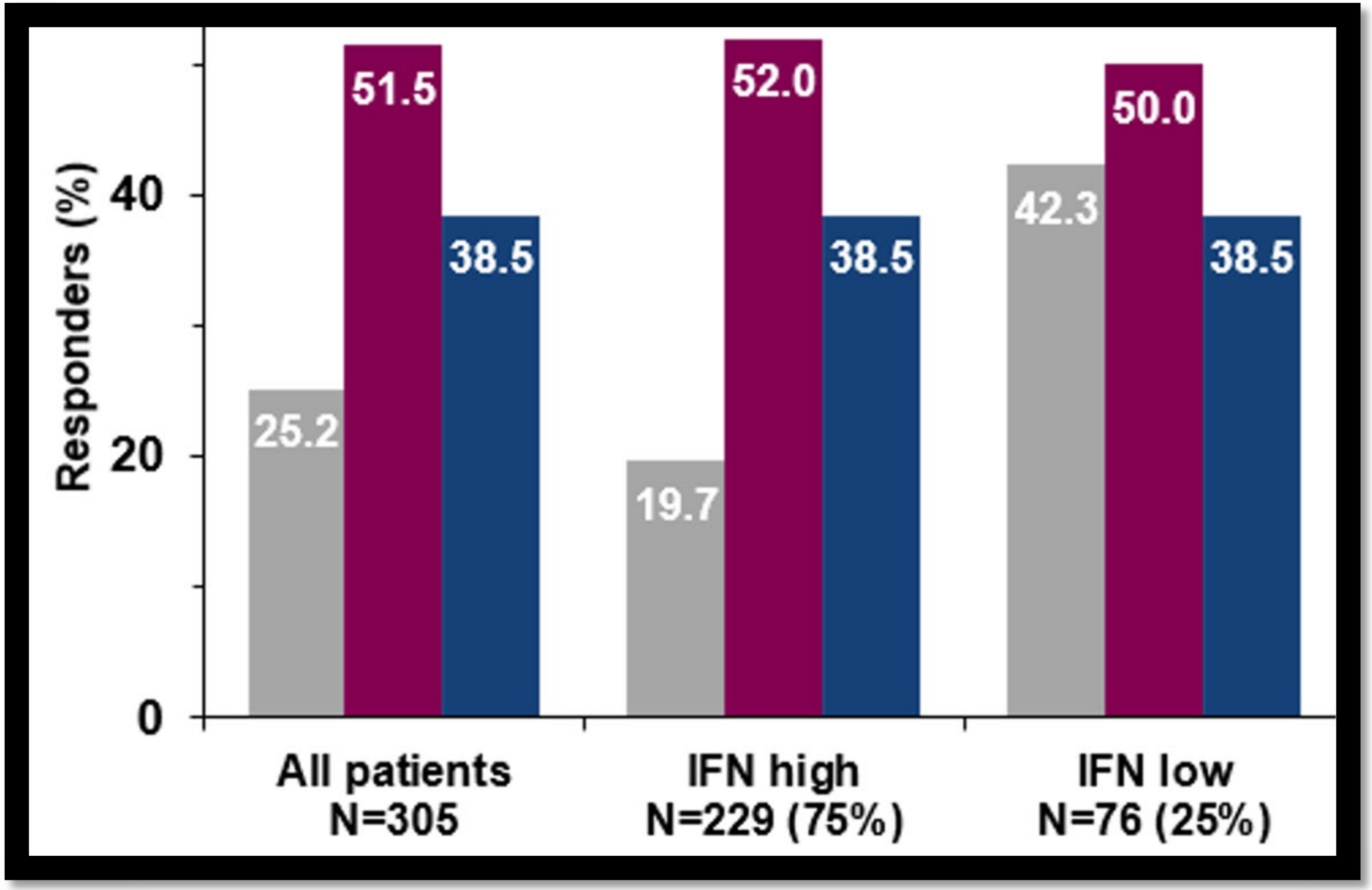

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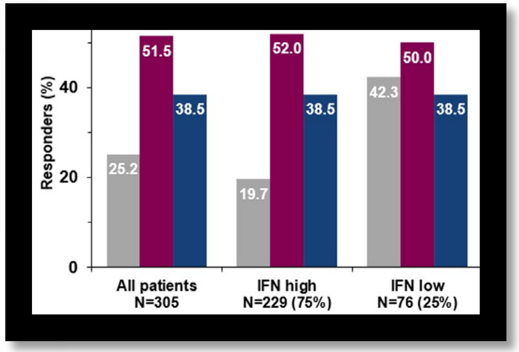
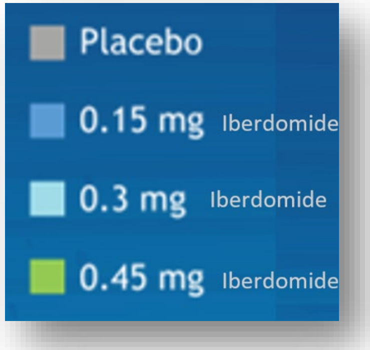
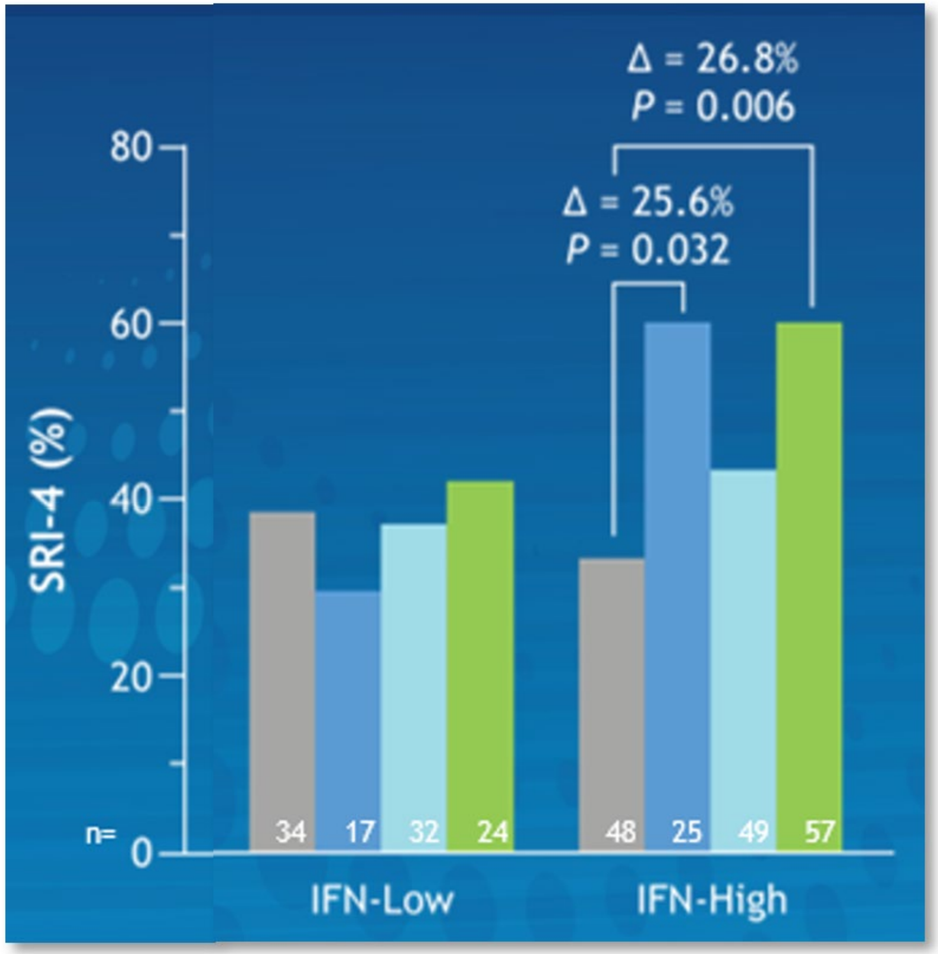
Iberdomide: Cereblon Ligand

Promotes Ubiquitination and Degradation of Transcription Factors Ikaros and Aiolos





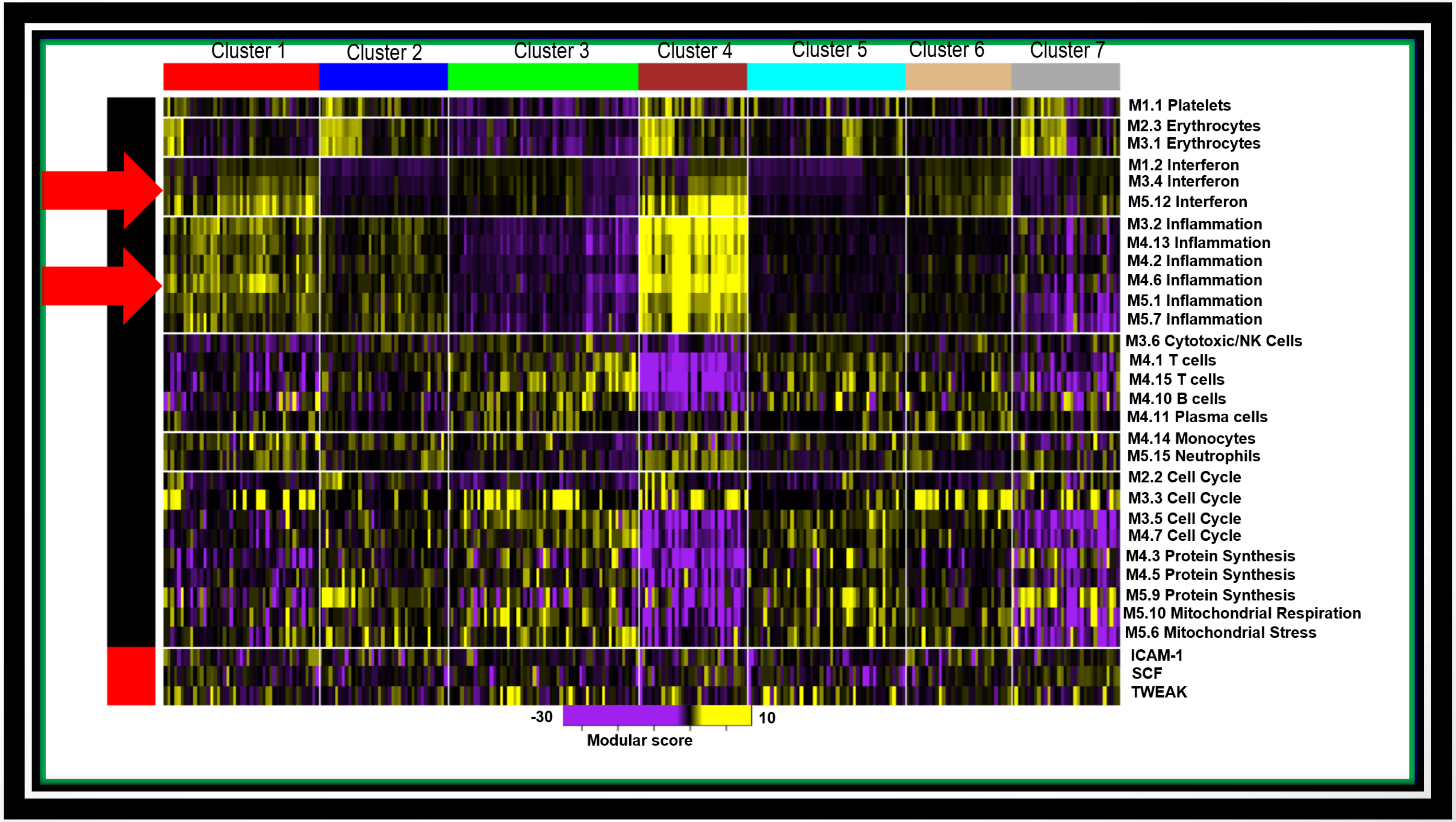


Type I IFN Panel from Dxterity

IFI27, IFI44, IFI44L, and *RSAD2*

Merrill NEJM 2022 386:1034-1045

What is Precision Medicine?



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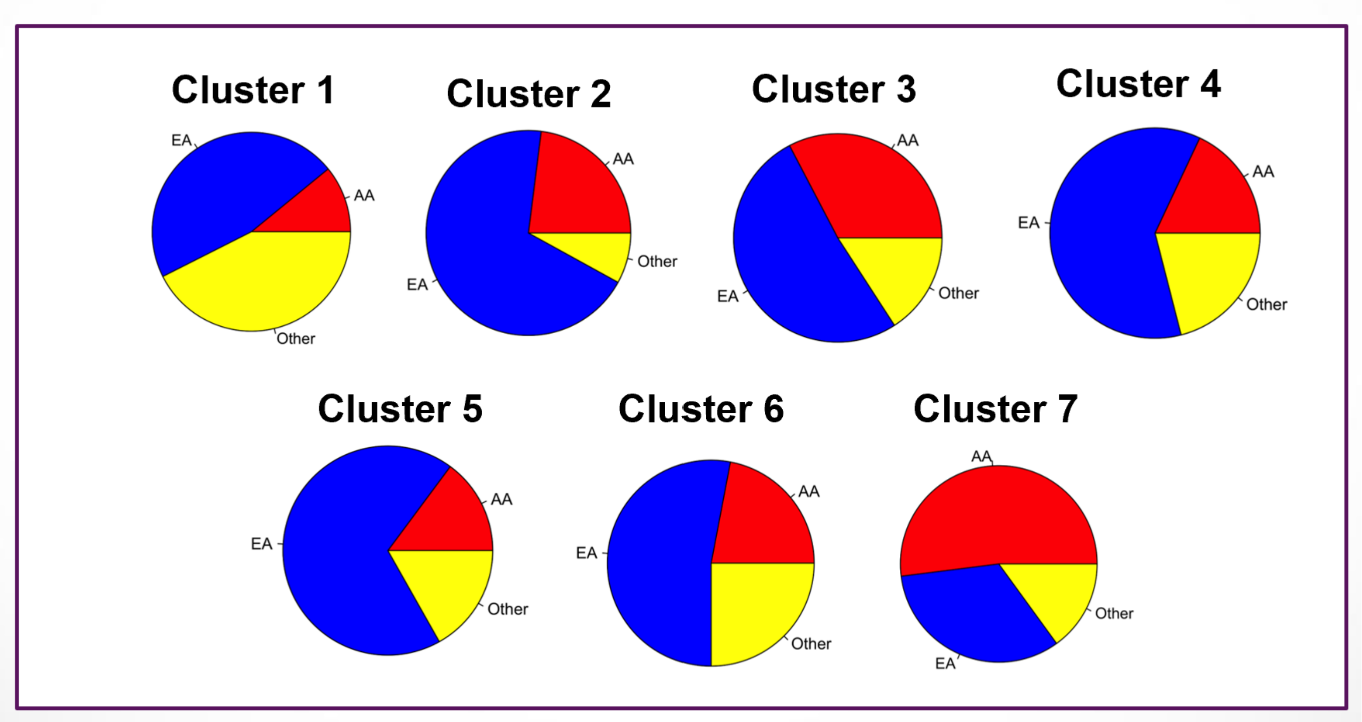
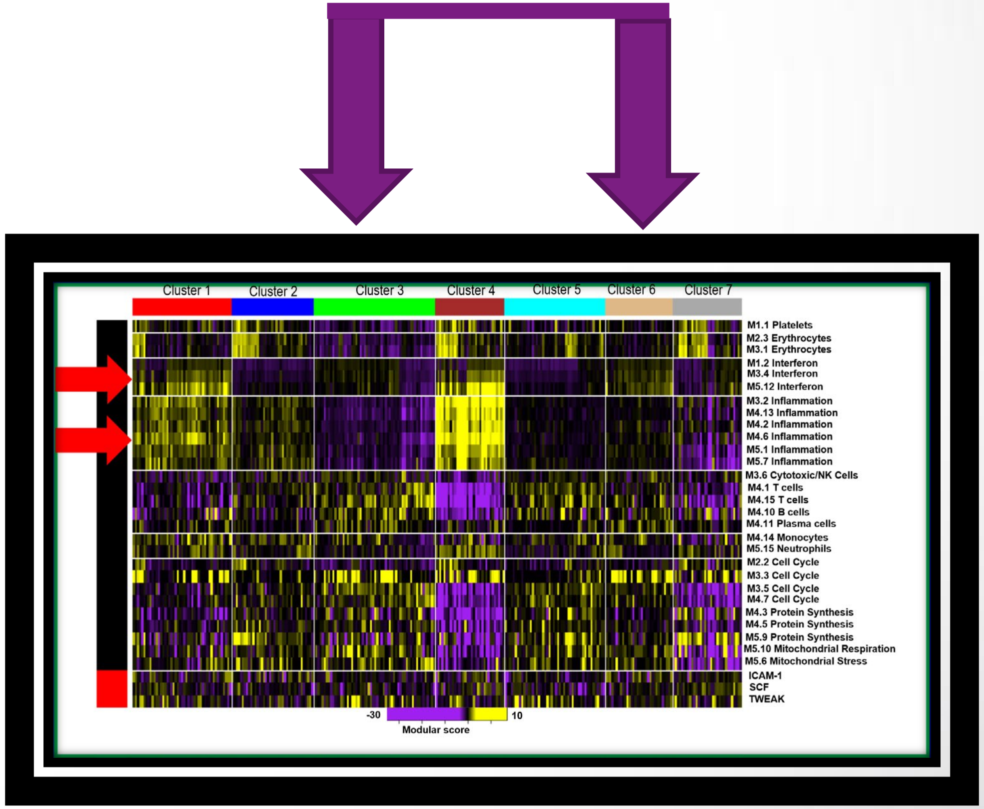
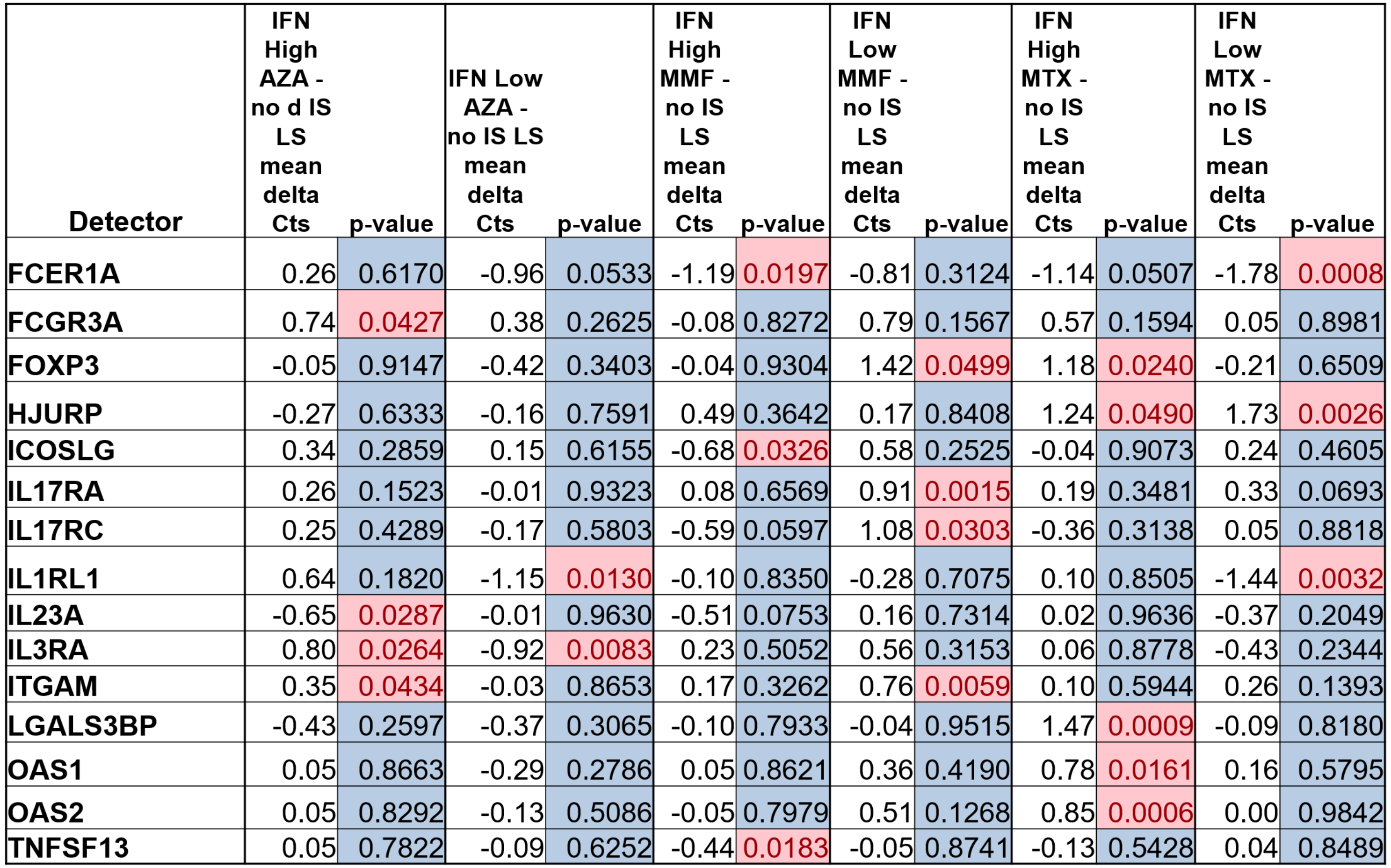
Racial Distribution in Each Molecular Phenotype Cluster



Importance of Clusters 3 and 6



How Can That Fancy Research Help us Pick Drugs More Scientifically?



Detector	IFN High AZA - no d IS LS mean delta Cts	p-value	IFN Low AZA - no IS LS mean delta Cts	p-value	IFN High MMF - no IS LS mean delta Cts	p-value	IFN Low MMF - no IS LS mean delta Cts	p-value	IFN High MTX - no IS LS mean delta Cts	p-value	IFN Low MTX - no IS LS mean delta Cts	p-value
FCER1A	0.26	0.6170	-0.96	0.0533	-1.19	0.0197	-0.81	0.3124	-1.14	0.0507	-1.78	0.0008
FCGR3A	0.74	0.0427	0.38	0.2625	-0.08	0.8272	0.79	0.1567	0.57	0.1594	0.05	0.8981
FOXP3	-0.05	0.9147	-0.42	0.3403	-0.04	0.9304	1.42	0.0499	1.18	0.0240	-0.21	0.6509
HJURP	-0.27	0.6333	-0.16	0.7591	0.49	0.3642	0.17	0.8408	1.24	0.0490	1.73	0.0026
ICOSLG	0.34	0.2859	0.15	0.6155	-0.68	0.0326	0.58	0.2525	-0.04	0.9073	0.24	0.4605
IL17RA	0.26	0.1523	-0.01	0.9323	0.08	0.6569	0.91	0.0015	0.19	0.3481	0.33	0.0693
IL17RC	0.25	0.4289	-0.17	0.5803	-0.59	0.0597	1.08	0.0303	-0.36	0.3138	0.05	0.8818
IL1RL1	0.64	0.1820	-1.15	0.0130	-0.10	0.8350	-0.28	0.7075	0.10	0.8505	-1.44	0.0032
IL23A	-0.65	0.0287	-0.01	0.9630	-0.51	0.0753	0.16	0.7314	0.02	0.9636	-0.37	0.2049
IL3RA	0.80	0.0264	-0.92	0.0083	0.23	0.5052	0.56	0.3153	0.06	0.8778	-0.43	0.2344
ITGAM	0.35	0.0434	-0.03	0.8653	0.17	0.3262	0.76	0.0059	0.10	0.5944	0.26	0.1393
LGALS3BP	-0.43	0.2597	-0.37	0.3065	-0.10	0.7933	-0.04	0.9515	1.47	0.0009	-0.09	0.8180
OAS1	0.05	0.8663	-0.29	0.2786	0.05	0.8621	0.36	0.4190	0.78	0.0161	0.16	0.5795
OAS2	0.05	0.8292	-0.13	0.5086	-0.05	0.7979	0.51	0.1268	0.85	0.0006	0.00	0.9842
TNFSF13	0.05	0.7822	-0.09	0.6252	-0.44	0.0183	-0.05	0.8741	-0.13	0.5428	0.04	0.8489

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Why Aren't We Studying The Standard of Care Treatments That We Use Most Often?

The DIVERT Trial: Examining **D**istinct **I**mmunophenotypes to **V**alidate and **E**nhance **R**ational **T**reatment in Systermic Lupus

Questions:
Who will respond to MMF?
Of those who don't who will respond if you add Voclosporin?
What seems to be going in in those who do not respond to both?

ClinicalTrials.gov Identifier: NCT05306873

Summary: Why Lupus?

- Not enough treatment choices for diverse patients
- We don't know how they work
- We have the technology to figure this out
- The more competition between companies, the better the technology that will be applied
- The next decade should be the tipping point

Questions?

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History of Racism and Clinical Trials

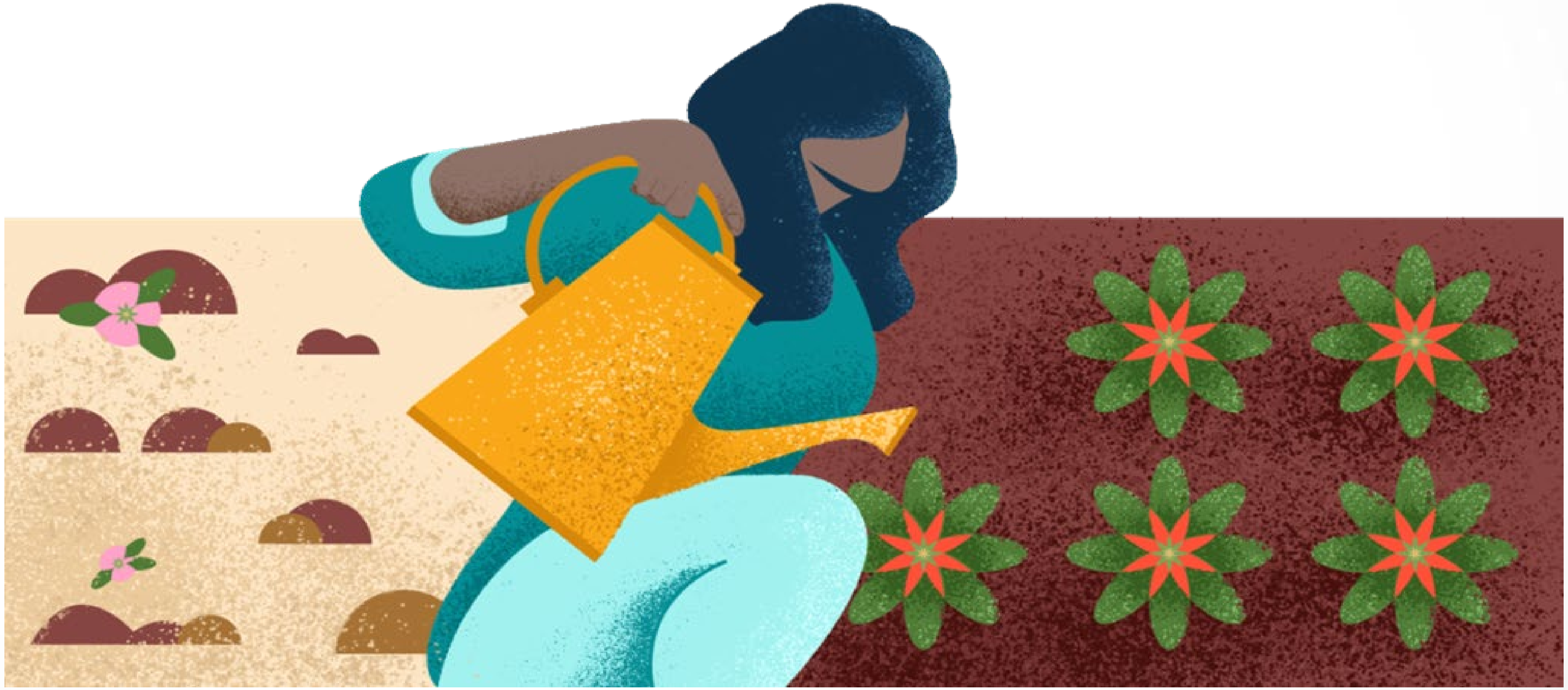
Rodlescia Sneed, PhD, MPH
Assistant Professor, Wayne State University

What is Race and Ethnicity?

- Race is defined as “a category of humankind that shares certain distinctive physical traits.”
- The term ethnicities is more broadly defined as “large groups of people classed according to common racial, national, tribal, religious, linguistic, or cultural origin or background
  - Race is often determined by society and culture, rather than physical traits
  - Example “one drop rule”

Source: Blakemore, E. (2021, May 3). Race and ethnicity facts and information. Culture.

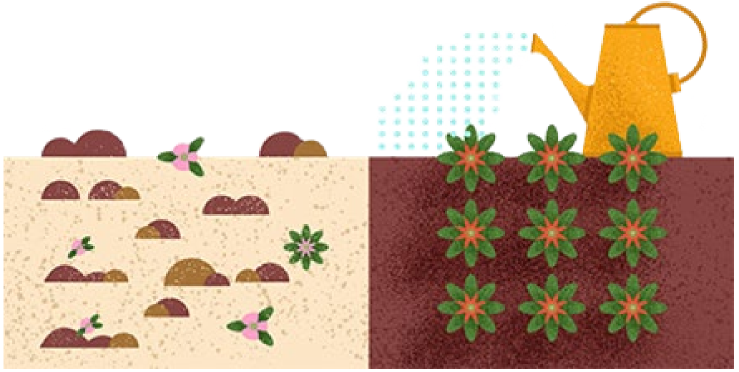
The Gardener's Tale: Allegory for Racism



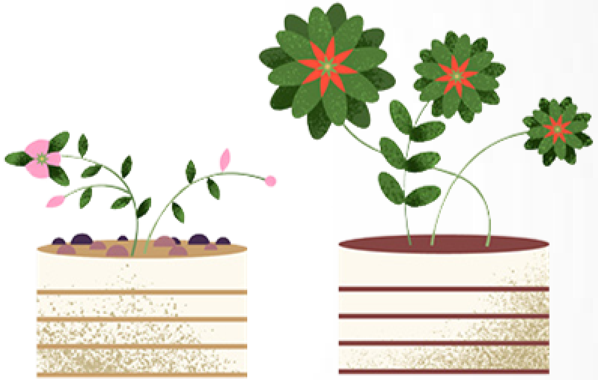
Source: Jones, C. P. "Levels of Racism: A Theoretic Framework and a Gardener's Tale," American Journal of Public Health 90 no. 8 (2000), 1212–1215.

The Gardener's Tale: Allegory for Racism

A gardener has two flower boxes, one that she knows is full of good soil and one that she knows is full of poor soil.



The gardener buys two packets of seeds for the same kind of flower — one packet for pink flowers and one for red flowers. She prefers the red over the pink, so she plants the red seeds in the good soil and leaves the pink flower seeds to be planted in the bad soil.



Of course, the red flowers flourish, but most of the pink flowers don't grow very high.

Jones C. Levels of Racism: A Theoretic Framework and a Gardener's Tale. AJPH 2000

The Gardener’s Tale: Allegory for Racism

- After years, the gardener returns and believes that her preference for the red flowers over the pink flowers. Failing to see that she doomed the pink flowers from the beginning by planting them in the poor soil in the first place.
- Who is the gardener? The gardener is the racism that is endemic in the United States. This racism is deeply rooted in the day-to-day mechanisms of life, from neighborhood segregation, discriminatory employment practices, and even gaps in discipline in education and the criminal justice system. All these factors exacerbate health disparities and create challenges to achieving health equity.

Does Racism Still Exist?

- Among Black women with lupus, unfair treatment and discrimination is associated with more severe disease
    - Discrimination may lead to increased stress which can increase inflammation and disease damage
- Black and Hispanic women with lupus who are pregnant have higher than expected rates of poor outcomes such as preterm birth
    - Likely related to decreased access to care, social determinants of health, and differential treatment by health care providers
- Black and Hispanic patients presenting to the emergency department with pain are less likely to receive pain medications than White patients presenting with pain
    - Likely related to racial biases regarding pain tolerance and communication/language barriers

Chae DH et al, Am J Public Health. 2015 October; 105(10): 2099–2107.

Clowse ME et al, Arthritis Care Res (Hoboken). 2016 Oct;68(10):1567-72.

Historical Context of Racism in Medical Research

- Racism is a process rather than a sequence of events. Therefore, the following examples provide a snapshot into how racist research projects in the U.S. have caused harm.
- Tuskegee Syphilis Study:
  - 600 Black men were followed from 1932-1972
  - Men were followed to understand the natural process of syphilis
  - Participants were not told that they had syphilis and were not treated even after treatment was available.

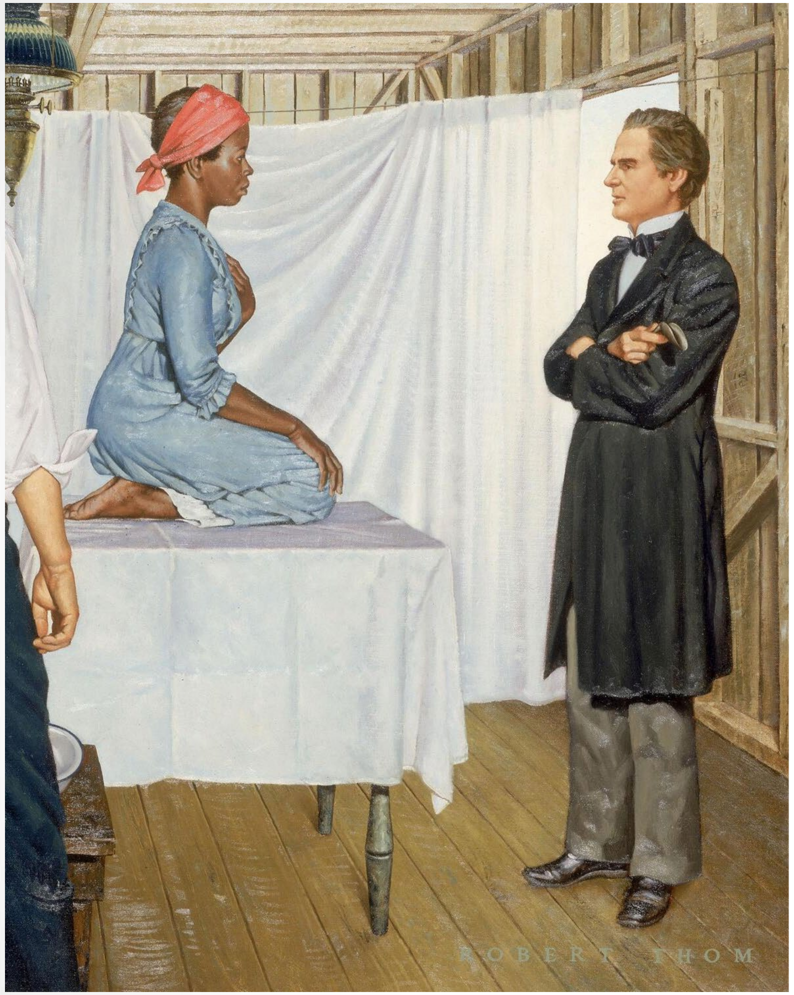
Historical Context of Racism in Medical Research: Tuskegee Syphilis Study:

- The study continued to observe the natural course of untreated.
- Effected men passed syphilis to their wives and children
- It wasn't until William Carter Jenkins, one of the first African Americans to be recruited to join the National Center for Health Statistics , a branch of the public health service, blew the whistle on the study with the help of fellow epidemiologist Peter Buxtun.
  - They contacted the Associated Press which ran the story on the front page of the New York Times: "Syphilis Victims in US Study went Untreated for 40 Years"

Historical Context of Racism in Medical Research: Henrietta Lacks

- 31-year-old Black women whose cervical cancer were removed in 1951 without consent or compensation
- Her cells were used to create the first immortal cell line for medical research use.
- Some applications of the HeLa cells have been to study the effects of radiation, poison, drugs, hormones, and viruses.
- HeLa cells were used in the development of the polio and COVID19 vaccines.

Historical Context of Racism in Medical Research (cont)



- J Marion Sims: born in 1813, this American physician became known as the father of gynecology.
- He is most well known for the surgical technique for the repair of vesicovaginal fistula, a severe complication of obstructed childbirth.
- Dr. Sims operated without anesthesia on enslaved black women. It was a common belief at the time that black people did not feel as much pain as white people.
- One enslaved woman, Anarcha, underwent at least 30 painful surgeries.

Clinical Trials Focus Groups: Thoughts on Race

"My friends always say "Don't do it. Don't forget your history…It haunts a lot of us…Any person of color."

"A lot of the clinical trials, we would like to do them, but a lot of times, we don't qualify…most of the time, with African American women, we don't qualify for a lot of the studies unless you lie."

"A lot of minorities, especially Black families, 'cause we don't go to the hospital, we wait until the very last minute, so when we do go to the hospital, we die. Then you'll have people say, "Don't go to the hospital. They kill you…"

Clinical Trials Focus Groups

Thoughts on Race

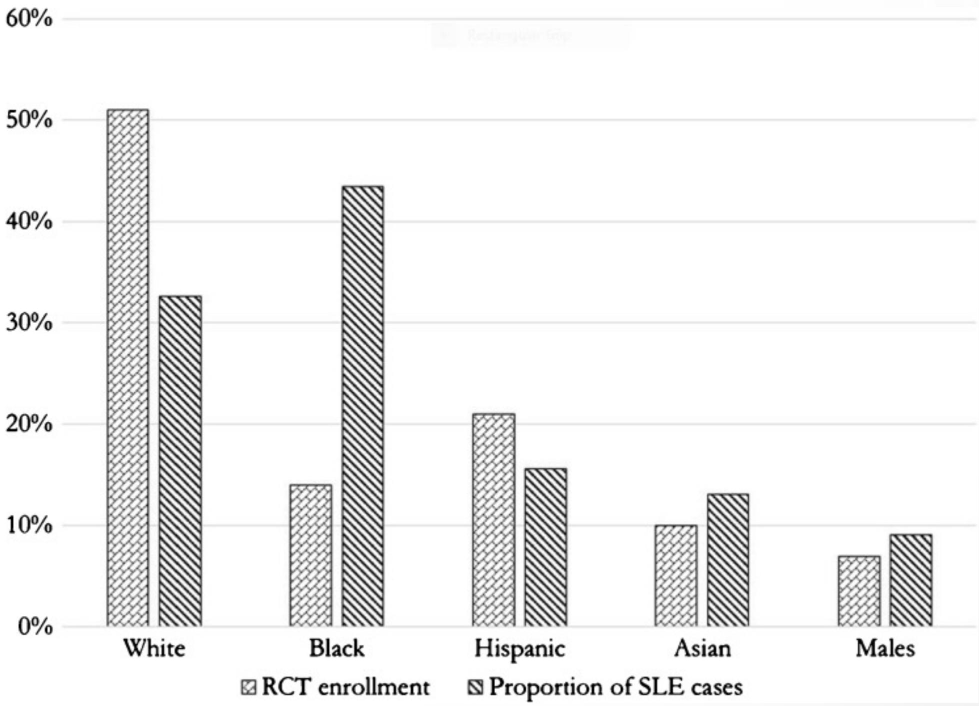
- “For me that [the race of the researcher] doesn’t matter. I just want to know that the person is truthful…if the person seems truthful and open and whatever, that’s fine.”
- “It’s needed. It’s needed. It’s needed. Because every time you look around, they’re always doing cancer research. Lupus is just as prevalent out there as cancer. It’s mainly in our community…the Black community.”
- “It’s a catch 22. We’re more predominantly affected. If we don’t participate in trials that benefit us, even more of us will be affected.”

How to Prevent Racism in Clinical Trials

- 1974 National Research Act: Created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
  - Voluntary informed consent must be obtained
  - Institutional Review Boards to maintain ethical standards
  - Federal Oversight: Presidential Commission for the Study of Biomedical Issues
- An Ethics Advisory Board was formed in the late 1970s to review ethical issues of biomedical research – resulting in the Belmont Report, which summarizes three ethical principles that should guide human research
  - Respect for Persons
  - Beneficence
  - Justice

What does this mean for clinical trials?

- Non-white people are under-represented in clinical trials
- 43% of people with lupus are Black, but only 14% of lupus clinical trial participants are Black
- Why is this the case?
  - Mistrust of physicians and researchers
  - Lack of authentic academic-community partnerships
  - Strict inclusion criteria



Falasinnu T et al, Curr Rheumatol Rep. 2018 Mar 17;20(4):20.
Lima K et al, Arthritis Care Res (Hoboken). 2019 Jul 26.

Why is Racial Diversity Important in Clinical Trials?

- To study new interventions across all populations that they will be used to treat
  - If differences are found by race/ethnicity, the reason why must be investigated so that EVERYONE benefits
- Certain conditions, such as lupus, are more common in people of color. We want to make sure that the people who are most affected by a disease are the ones benefiting from clinical trials, in order to get patients more effective treatments more quickly
- Unequal enrollment in clinical trials perpetuates systemic racism in healthcare

Questions?

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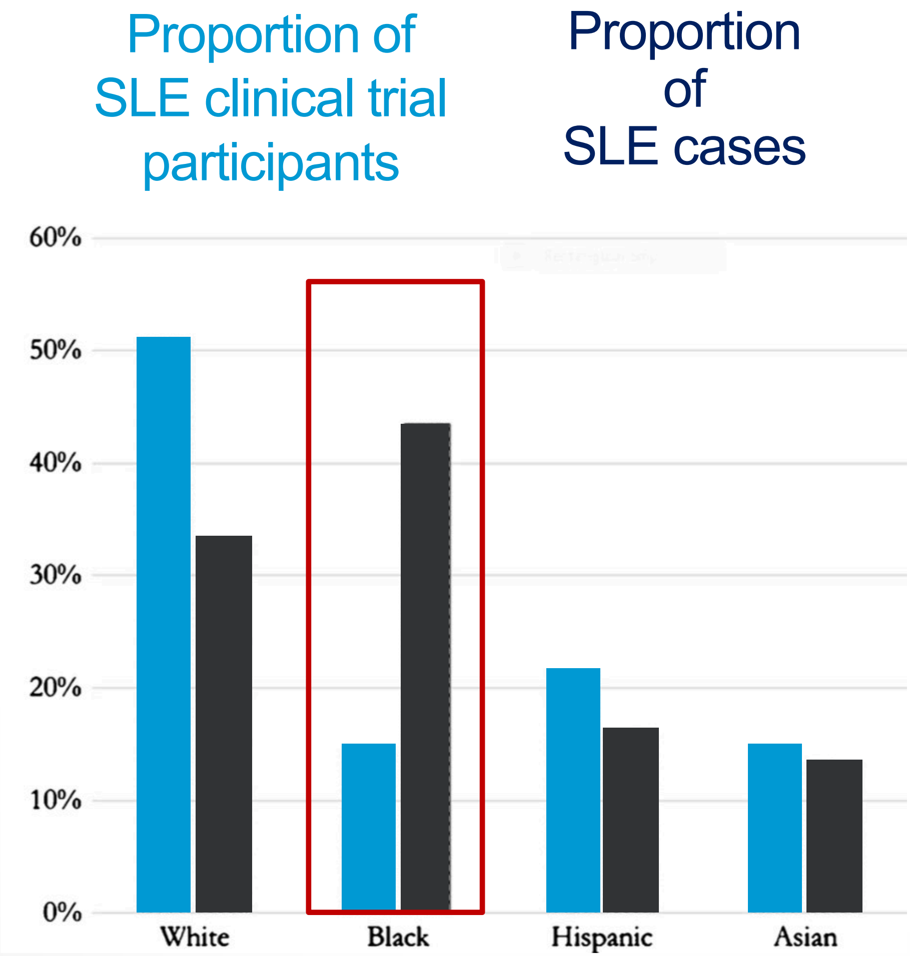
Clinical Trials: Barriers & Facilitators

Rosalind Ramsey Goldman, MD
Professor of Medicine, Feinberg School of Medicine, Northwestern University

Objectives

- Define problem: racial disparities in lupus clinical trial representation
- Working towards resolving the problem: including the patient's voice in the solution

Problem: Racial Disparities in Lupus Clinical trial Presentation



Falasinnu et al. *Curr Rheumatol Rep*. Mar 2018.

In the United States, Black individuals represent approximately 43% of lupus cases yet only 14% of lupus clinical trial participants.

White individuals comprise approximately 33% of lupus cases and 51% of lupus clinical trial participants.

What Do We Know Now: Review of the Literature

Only 7 studies evaluated factors associated with research participation of underrepresented populations (5 in SLE, 2 in RA, 5 in Black/African American patients, 1 in Hispanic)

Key themes included:

- Importance of trust in patient-provider relationship
- Understanding heterogeneity within and between racial/ethnic groups
- Need for authentic community-academic partnerships
- Implications of strict inclusion criteria on participant diversity

Key gap identified: **No study openly addressed experiences of racism or historical context**

Lima K, et. al. Arthritis Care Res (Hoboken). 2020 Oct;72(10):1481-1489

What Do We Need to Know?: Focus Groups

Goal: To explore barriers, mediating factors and motivators to clinical trial participation

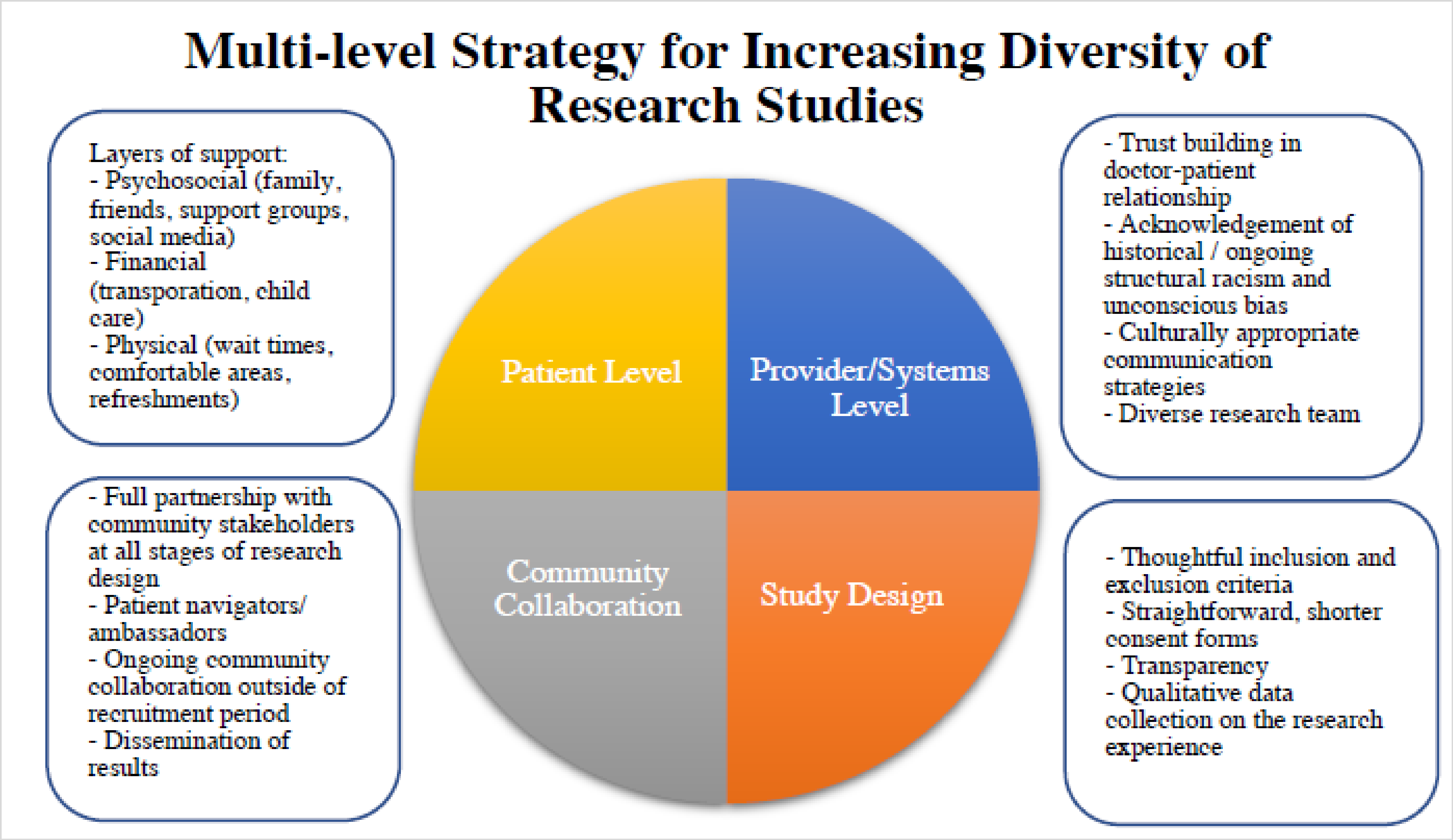
Held 4 focus groups, 2 in Chicago (N=16), 2 in Boston (N=15)

Mean age: 54, 90% female, all identified as Black

Twenty (65%) with SLE, 11 caretakers

Aspects of mistrust stemming from historical context and internalized and structural racism discussed repeatedly through the focus groups' discussions

Sneed RS et al. Arthritis Care Res (Hoboken). 2021 Oct;73(10):1387-1395.



Multi-level Strategy for Increasing Diversity of Research Studies

Patient Level

Layers of support:
- Psychosocial (family, friends, support groups, social media)
- Financial (transporation, child care)
- Physical (wait times, comfortable areas, refreshments)

Provider/Systems Level

- Trust building in doctor-patient relationship
- Acknowledgement of historical / ongoing structural racism and unconscious bias
- Culturally appropriate communication strategies
- Diverse research team

Community Collaboration

- Full partnership with community stakeholders at all stages of research design
- Patient navigators/ ambassadors
- Ongoing community collaboration outside of recruitment period
- Dissemination of results

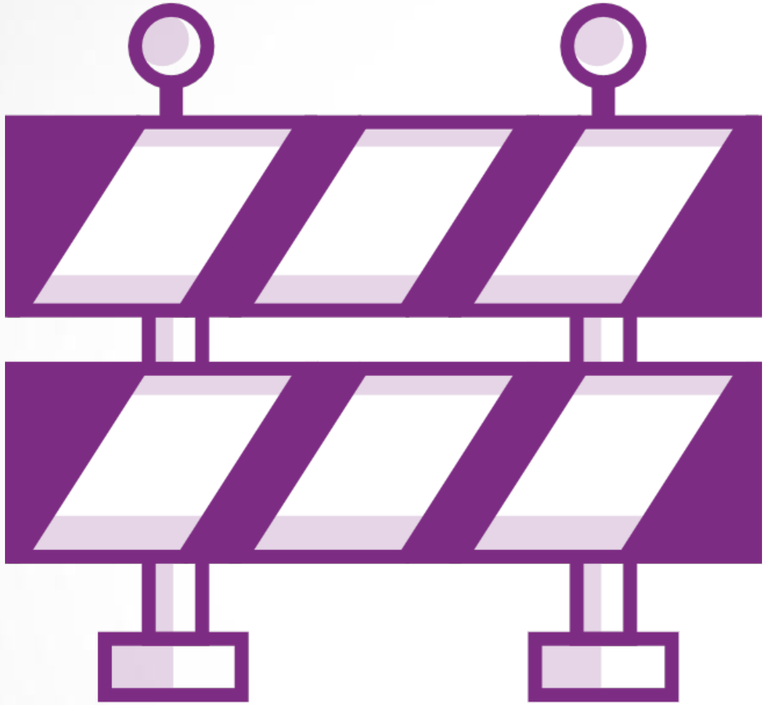
Study Design

- Thoughtful inclusion and exclusion criteria
- Straightforward, shorter consent forms
- Transparency
- Qualitative data collection on the research experience

Lima K, et. al. Arthritis Care Res (Hoboken). 2020 Oct;72(10):1481-1489.

What are Clinical Trial Barriers and Facilitators?

- Barriers:
  - Things that make it more difficult for eligible participants to enroll or participate in a clinical trial
  - Decrease the chance that an eligible participant will want to enroll
- Facilitators:
  - Make it easier for participants to enroll or participate in a clinical trials
  - Increase the chance that an eligible participant will want to enroll
  - Facilitators are helpful that increase the likelihood of enrollment



Barriers to Clinical Trials Enrollment

- Health Status
  - Patient may be too sick.
  - Patient may not have a confirmed diagnosis of lupus
  - Patient may have a history of prior withdrawal due to medical complications through the course of prior clinical trials.
- Confusing Research Materials
  - Unclear and lengthy consent forms
  - Inaccessible recruitment documents
  - Confusing explanations of the study's protocol

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Barriers to Clinical Trials Enrollment

- Lack of peer or family support
  - Family and friends seeing clinical trials as "unsafe"
  - Confusion about what a clinical trial is and what enrollment will mean
- Historical Injustice and Racism
  - Past and present experiences of discrimination and racism in healthcare and every day life may contribute to mistrust and limit participation

Barriers to Clinical Trials Enrollment

- Health Literacy Challenges
  - Descriptions of study drug or study protocol in overly-medical terms.
  - Meeting the participant at their literacy level
  - Linguistically-competent translation and adaptation to culturally-related concepts
- Financial and Time Constraints
  - Patients may not be able to take time off of work to go to study visits or have competing obligations.
  - Financial burden of paying for childcare, transportation, or parking to attend study visits

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Facilitators to Clinical Trials Enrollment

- Family, peer or partner support
  - Inclusion of patient’s support network as part of the clinical trial recruitment process and allow time to address their questions
- Supportive relationship with Healthcare Provider
  - Patients and Providers should be able to discuss the risks and benefits of a clinical trial, both before the patient is enrolled and during the study
- Discuss clinical trials study findings with participants
- Comments: The patient motivation or compelling stage of the disease that leads into finding “other” treatment solutions.

Facilitators to Clinical Trials Enrollment

- Clear Explanation of the Study’s Purpose and Goals
- Participants should understand why the study is being conducted and why they are eligible
  - Allowing Time for Informed Consent
    - Patients should be given enough information about the risks and benefits of enrolling in a study to make the decision that is right for them
  - Open Communication Between Patients, PI, and Study Staff
    - Patients should feel comfortable asking the study staff and PI questions, which will most likely be answered with multiple conversations

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Viewpoints on Trial Participation

Seekers

- Look for trial opportunities
- Self-advocate for care
- Savvy consumers that evaluate participation based on: study design, topic, researcher reputation

Refusers

- Remember your history
- Bad experience in a trial
- Lack of family support
- Religious reasons

Maybe

- Nothing else is working
- Stable health status
- No medications required
- Placebos used/Not used

* Research topic relevant to me
* Transparency
* Trust built with research
* Physician team agrees

Recommendations I:

Communicate Differently

- Focus on transparency
- Include study purpose
- Include researcher information
- Work with trusted community members
- Recruit through academic medical centers

Recommendations II:

Address Trial Design Issues

- Define exclusion criteria
- Use of placebos vs. current treatment
- Provide findings/updates throughout
- Show investment in participants health

Recommendations III:

Address Racism and Historical Context

- Discuss individual protections to prevent against unethical treatment
- Address the importance of diversity in trials directly with participants
- Recruit equitably across racial/ethnic groups
- Ensure culturally and linguistically appropriate materials

Questions?

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The Popular Opinion Leader Model

Dr. Rosalind Ramsey Goldman
Professor of Medicine, Feinberg School of Medicine, Northwestern University

Background and Introduction

- Improving Minority Participation and Awareness in Clinical Trials for Lupus (IMPACT+)
- Use of the Popular Opinion Leader (POL) Model to lead community education strategies
- Educate people living with lupus about clinical trials
  - In-person one-on-one interactions
  - Events
  - Social networks

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Popular Opinion Leader (POL) Model

- What is a Popular Opinion Leader?
  - These are individuals who are typically respected, well-informed, and trusted members of a social group
- Popular Opinion Leader Model
  - Multi-level intervention model, developed by the CDC, and successfully employed in a variety of public health contexts
  - Intervention designed to influence norms, behaviors, intentions and prompt actions at the community level

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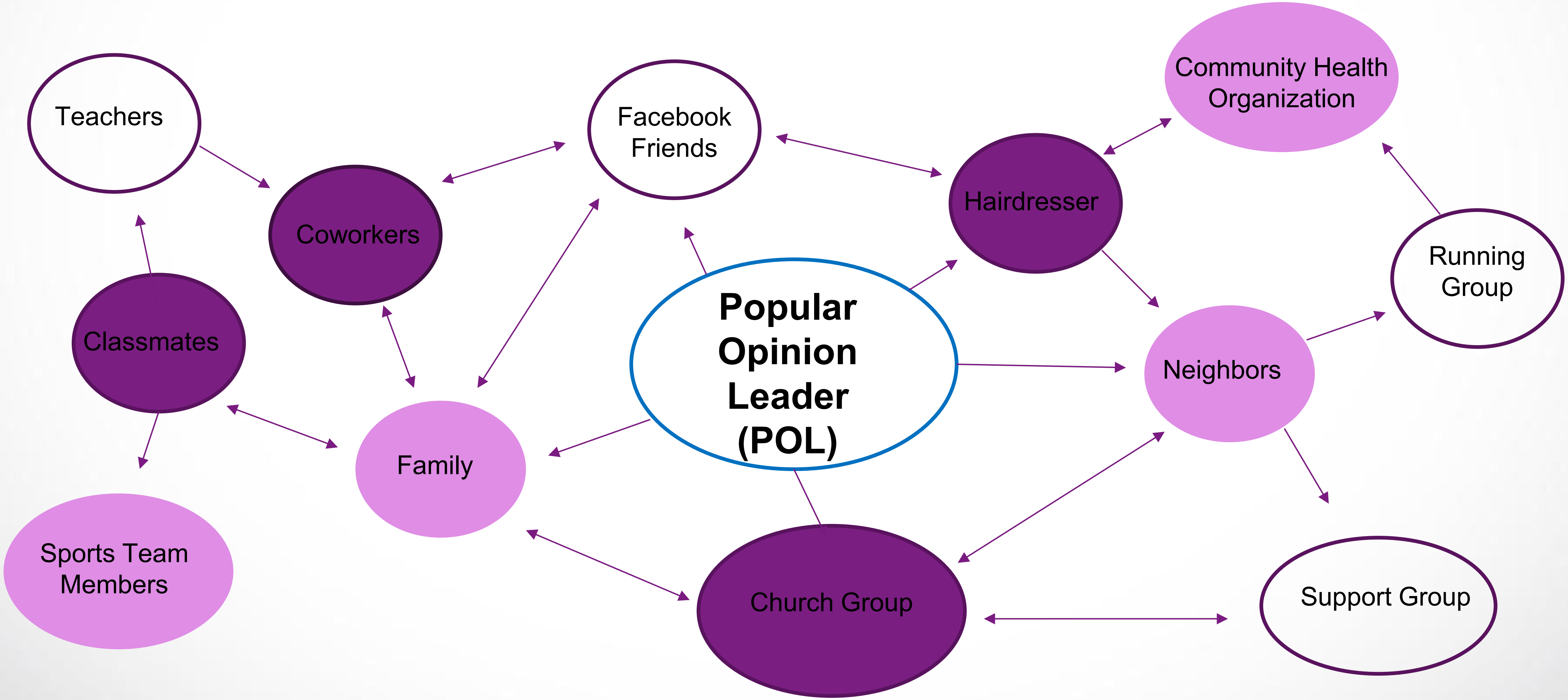
LRAN Participants as Popular Opinion Leaders

How will the POL Model work?

- As a Popular Opinion Leader, you will be sharing information on clinical trials throughout your community:
  - Communicate trust
  - Increase knowledge and awareness of clinical trials
  - Change perceptions of clinical trials,
  - Increase participation in lupus clinical trials
- POL model is based on the social diffusion theory; behaviors change in a population can be initiated and will then diffuse to others if enough opinion leaders within the populations are known to adopt, endorse, and support the behavior

Popular Opinion Leader (POL) Social Network



How Does a POL Influence Their Community?

- Social Network: a set of individuals or organizations who share common interests
- POLs can share information about health and scientific research through their social networks
  - Friends and Family
  - Fraternity/Sorority
  - Faith-based organizations
  - Social Media
  - Civic Group (Kiwanis club, Elks, Knights of Columbus)
  - Lupus support groups and other lupus events

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How POLs Help Their Communities

- By spreading information, POLs help to…
  - Increase awareness and understanding of lupus in a community
  - Help lupus patients reach specialists to help care for their lupus
  - Spread positive messages about science-based research and clinical trials
  - Build partnerships between researchers and the surrounding community

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How do POLs Spread Information?

- POLs spread the information they know by speaking with communities, congregations, and their own social networks
- Participate in round-table discussions or community forums
- Conduct surveys or ask others about their knowledge of lupus, clinical trials, and healthcare, and spread the information they know
- Give out fact sheets, info-cards, or other tools as “conversation starters” and to remind people of the information they discussed

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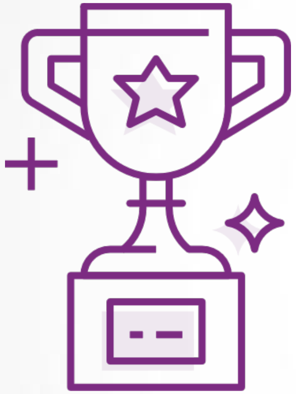
How is a POL’s Success Measured?



- The POL model is often used in partnership with academic centers
- POL participation in studies is just as valued as professional input
- POLs record who they’ve spoken with and observations about meetings
- POL success if measured by the number of people they are able to engage and persuade with the intended message
- POLs demonstrate their influence by changing health seeking norms, in this case increasing the understanding of lupus clinical trials in their communities.

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RAY®: Research Accelerated by You

Safoah Agyemang, MS
Manager, Research and Health Outcomes
Lupus Foundation of America

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What is a Patient Registry?

- A place to stored detailed information about individuals with a specific disease.
- LFA has built a **patient-powered** registry, meaning all of the information generated in RAY® comes directly from people living with lupus and their families.

Registry History

2016

21st Century Cures Act

2017

Launch of Research.forME Registry

Launch of Lupus Research Registry 2.0/ Data Platform – Research Accelerated By You (RAY®)

2020

21st Century Cures Act (2016)

- **Accelerate** medical product development.
- **Invest** in medical research.
- **Advance** mental health and substance disorder treatment.
- **Enhance** Information technology.

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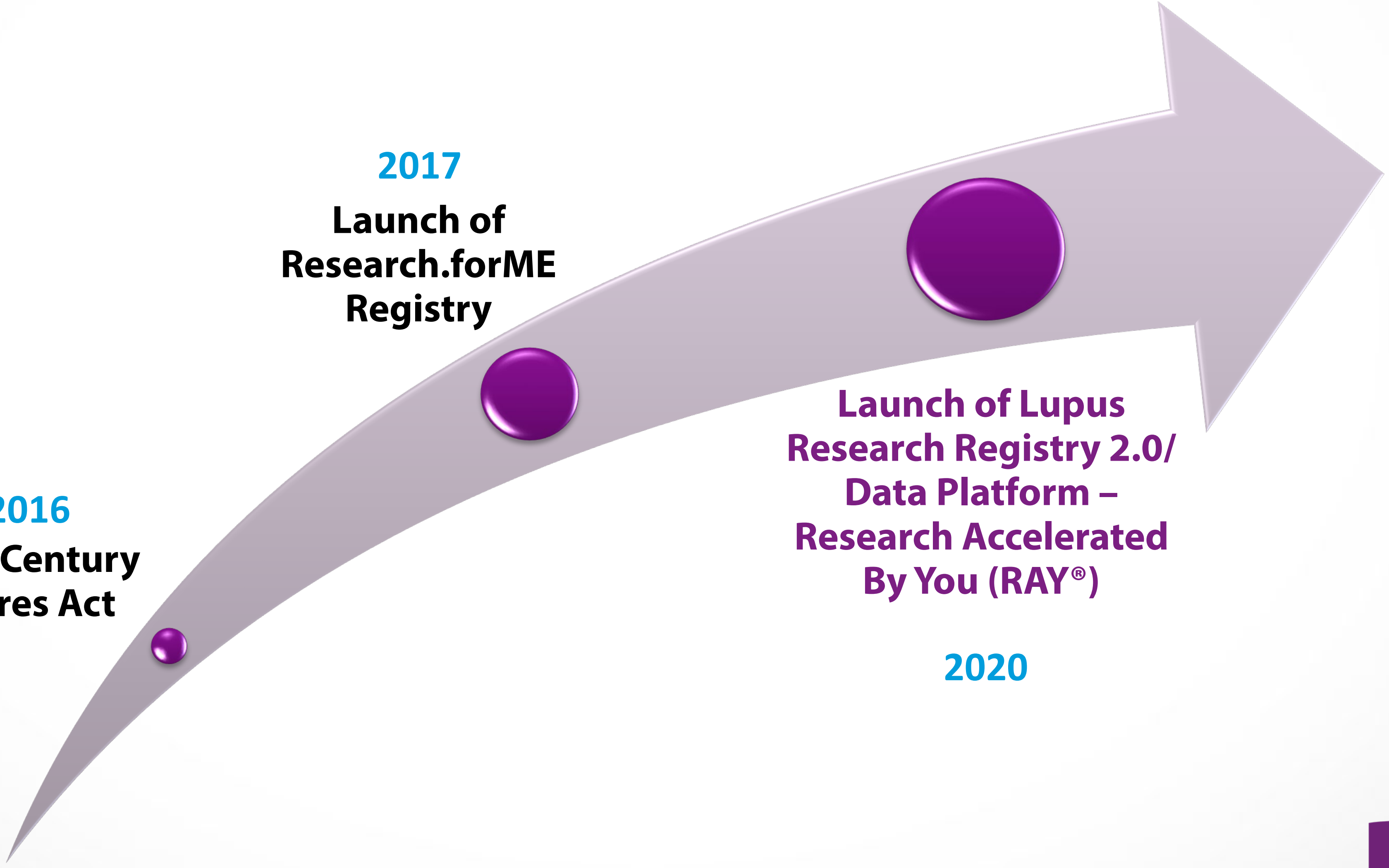
Registry History



2016

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2020

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Purpose of the RAY® Registry

- **Improve** our understanding of lupus.
- Use data to **advocate** for treatments and clinical trials that will improve health outcomes.
- **Engage** you in research opportunities that matter to you!

What is RAY®?

- 1st step to increasing participation in lupus clinical trials!
- An online set of questions about your health, medical history, demographics, and lupus experience.
  - **Can be completed from the comfort of your own home!**
- The data you provide from the survey is securely collected, stored, and combined with other participants data to help us learn more.

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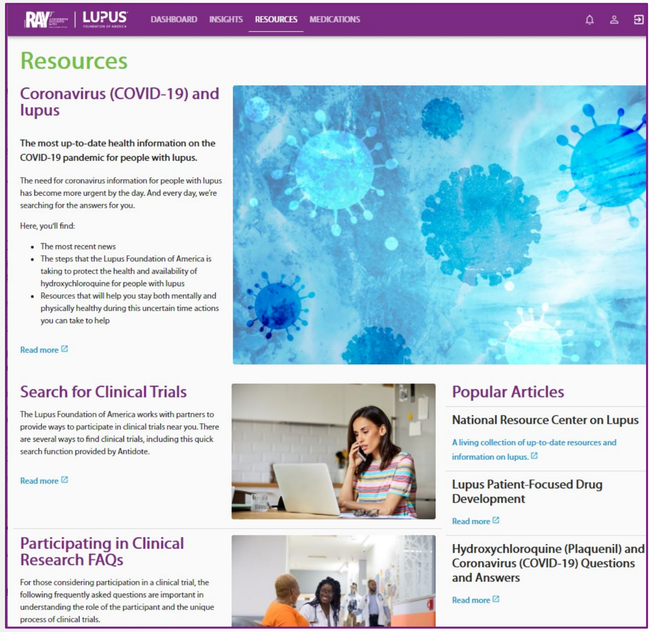
What is RAY®?



Resources

Coronavirus (COVID-19) and lupus

The most up-to-date health information on the COVID-19 pandemic for people with lupus.

The need for coronavirus information for people with lupus has become more urgent by the day. And every day, we're searching for the answers for you.

Here, you'll find:

- The most recent news
- The steps that the Lupus Foundation of America is taking to protect the health and availability of hydroxychloroquine for people with lupus
- Resources that will help you stay both mentally and physically healthy during this uncertain time actions you can take to help

Read more

Search for Clinical Trials

The Lupus Foundation of America works with partners to provide ways to participate in clinical trials near you. There are several ways to find clinical trials, including this quick search function provided by Antidote.

Read more

Participating in Clinical Research FAQs

For those considering participation in a clinical trial, the following frequently asked questions are important in understanding the role of the participant and the unique process of clinical trials.

Popular Articles

National Resource Center on Lupus

A living collection of up-to-date resources and information on lupus.

Lupus Patient-Focused Drug Development

Read more

Hydroxychloroquine (Plaquenil) and Coronavirus (COVID-19) Questions and Answers

Read more

- A place where you can learn more about research and engagement opportunities that will help advance lupus drug development.
- Once you join, it allows us to provide you with personalized, up-to-date information about research that may interest you.
  - **Helps researchers incorporate the patient perspective every step of the way!**

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Who Can Participate

- Adult Participants
  - 18 years of age or older
  - Have a lupus diagnosis
  - Be willing to provide informed consent
  - Be able to read and understand the Registry in English
- Participants under 18 (or <19 in AL & NE) must have an adult complete the Registry.
  - Adult must be parent/legal guardian/legally authorized representative of the participant who has a lupus diagnosis

Type of Information Collected

- Demographics
- Diagnosis
- Symptoms
- Treatments
- Quality of Life (SF-20)
- Treatment preferences (PFDD)
- Clinical trial participation
- Fatigue (FACIT-F)
- Work productivity (WPAI)

How Is Your Privacy Protected

- Your personal information will be associated with a **unique registry code** that is specific to you.
- Only authorized individuals from LFA and approved individuals from IQVIA will be able to link that registry code with your contact information.
- This registry has to follow applicable laws to protect your privacy.

How can RAY® data be used to advance research?

Addressing Unmet Need

Outcomes Research

- Comparative effectiveness
- Healthcare utilization
- Quality of life
- Cost-effectiveness

Clinical Development

- Clinical trial support, stratifying patients and site selection
- Protocol refinement and development
- Study feasibility
- PFDD efforts

Surveillance

- Post-marketing, including identifying serious adverse event reporting
- Value assessment
- Adherence
- Real-world evidence

Using RAY® to Advance Research

- FDA Listening Sessions
- Ad Panels

Data Overview

Enrollment to Date

Launch of RAY®: October 2020

	Enrollment Total*	Completion of Main Survey	Completion Rate
Research.forME Legacy Registry	3,178	1,736	55%
RAY®	**2,003**	**1,475**	**74%**
Total Reach	**5,181**		

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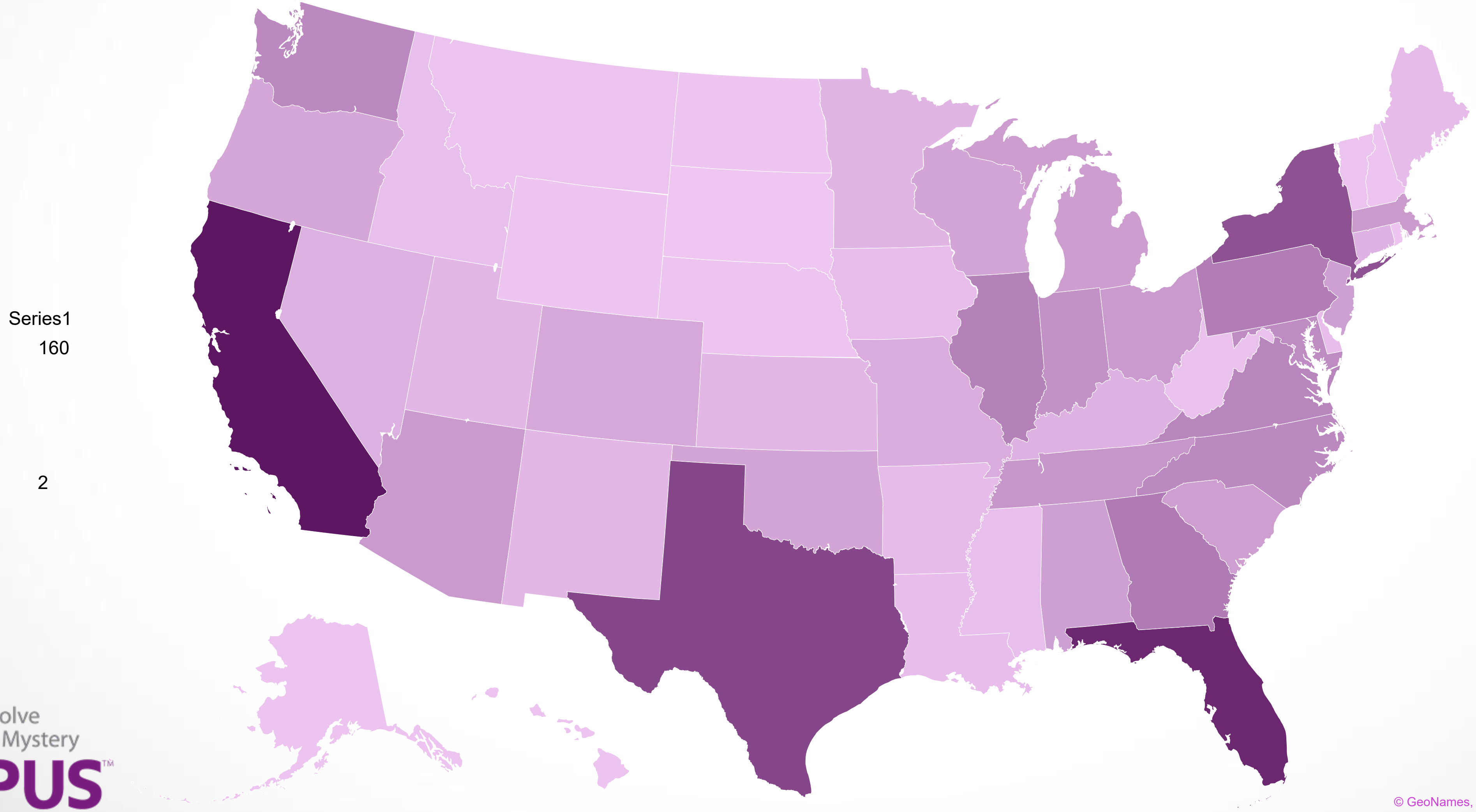
Participants in the United States



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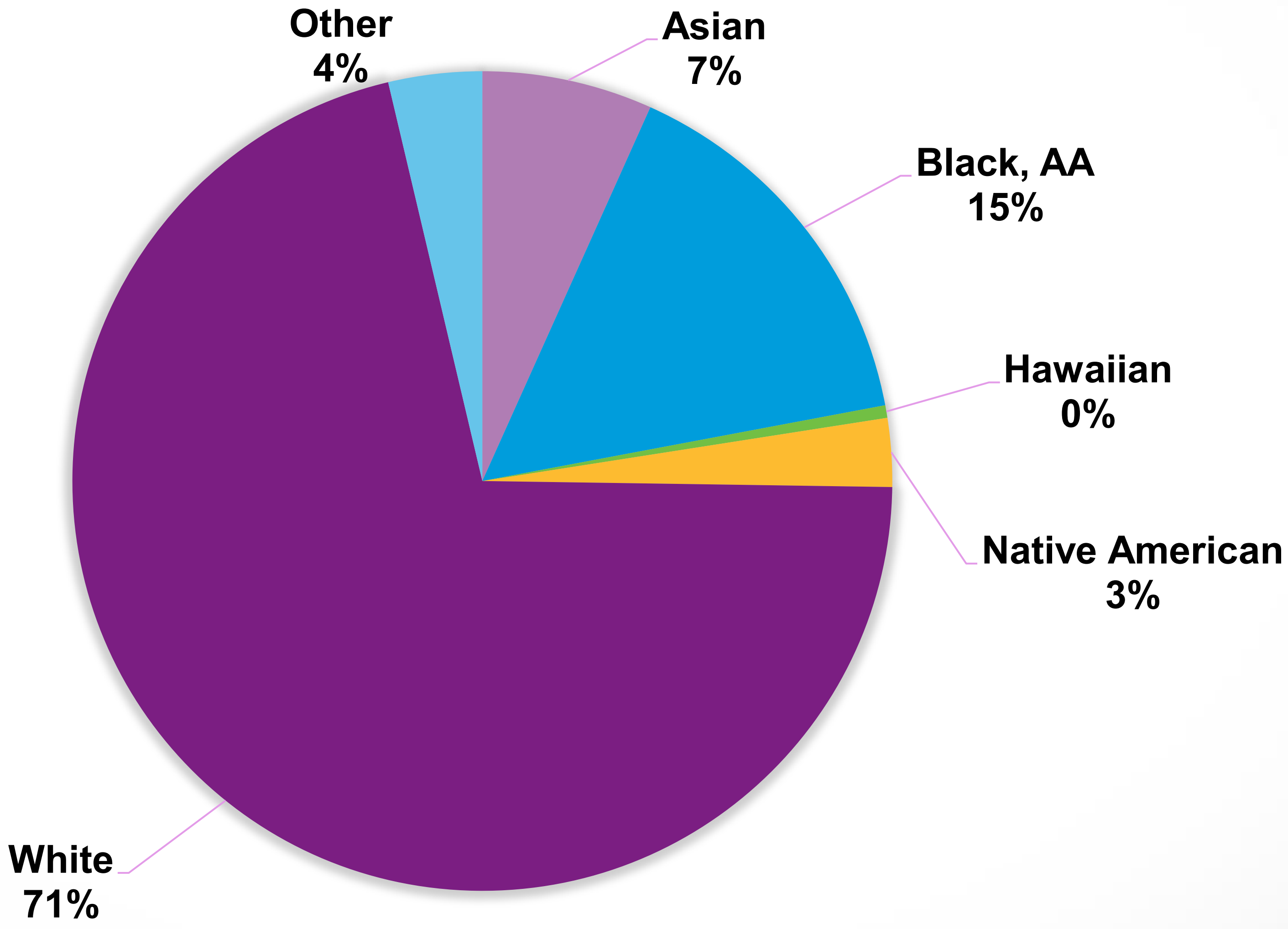
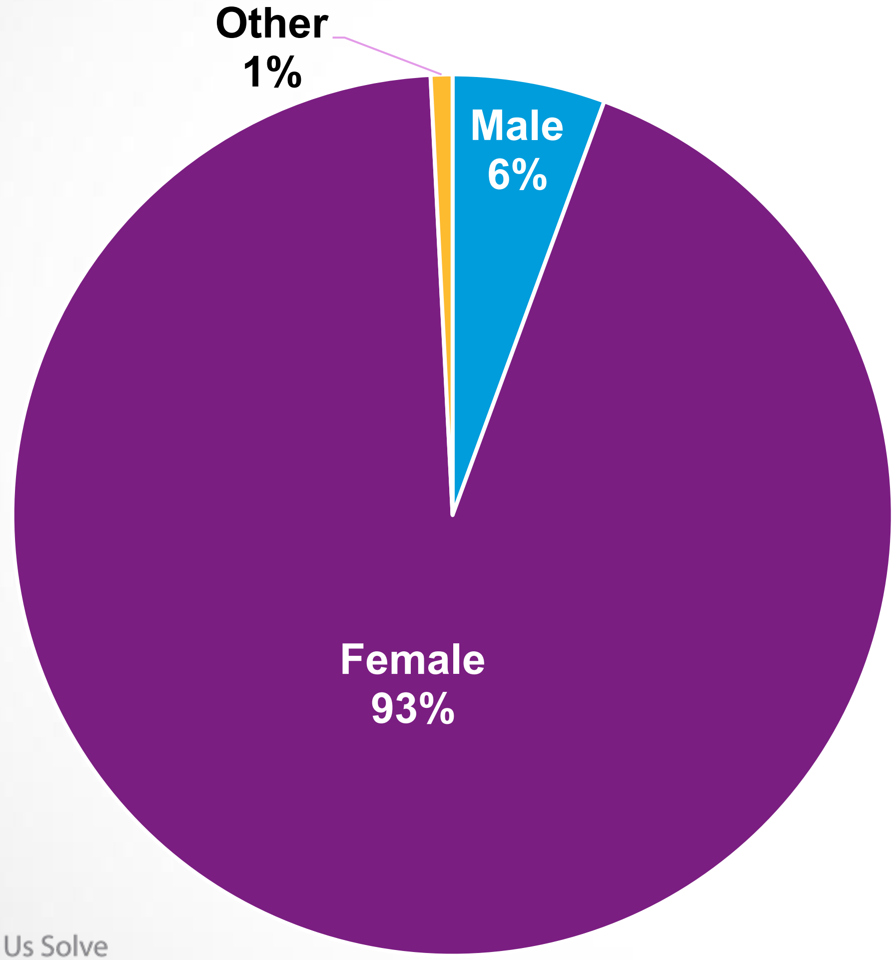
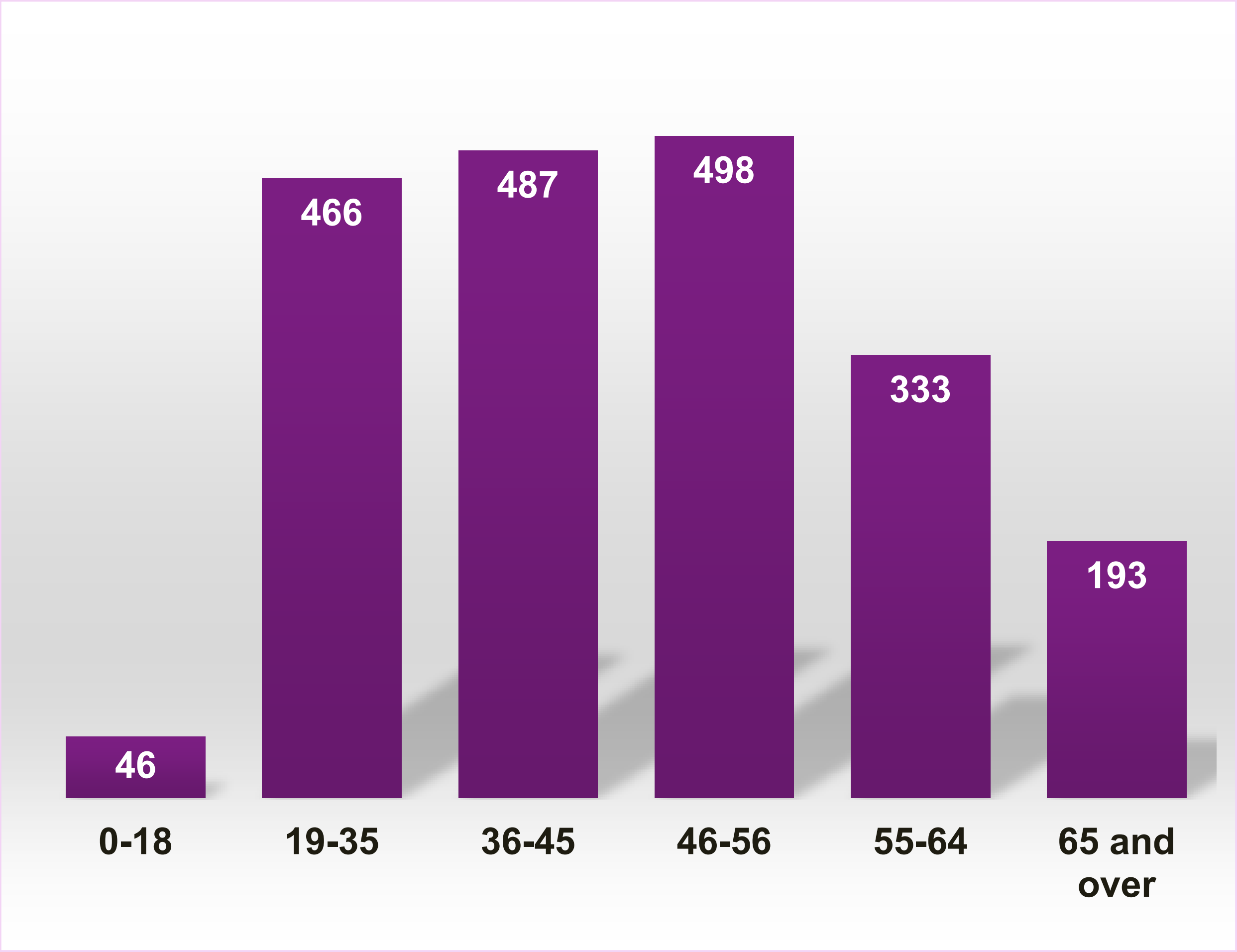
Race/Ethnicity



Gender/Age





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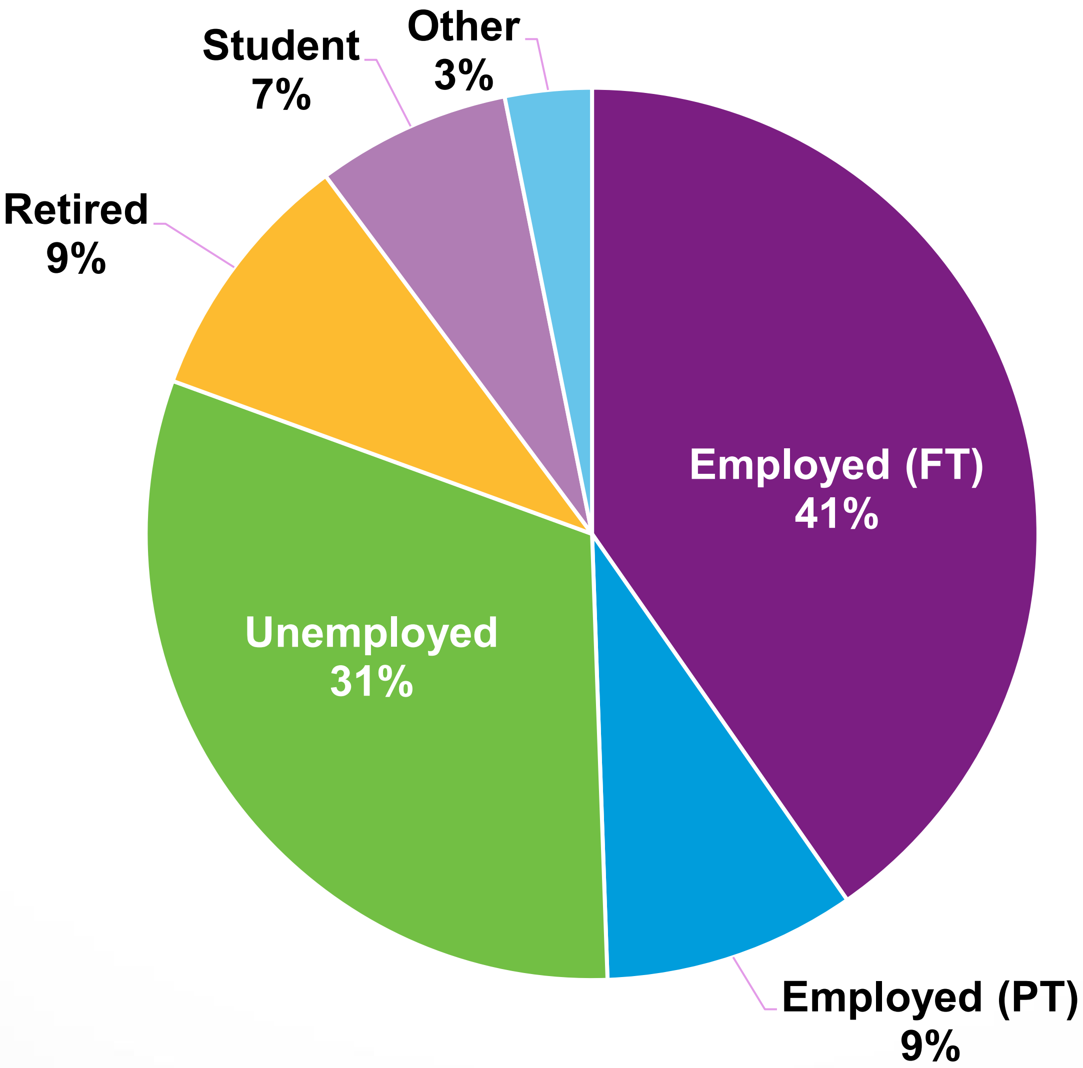
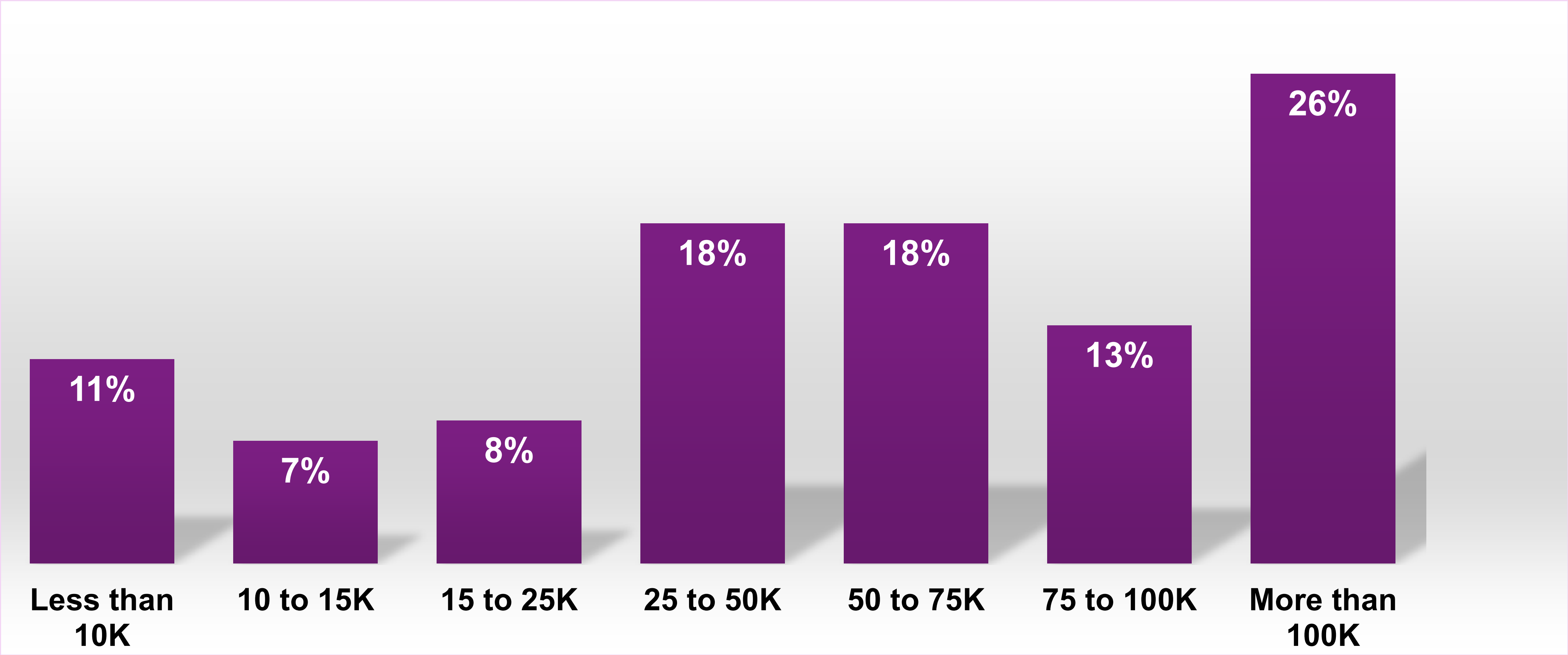
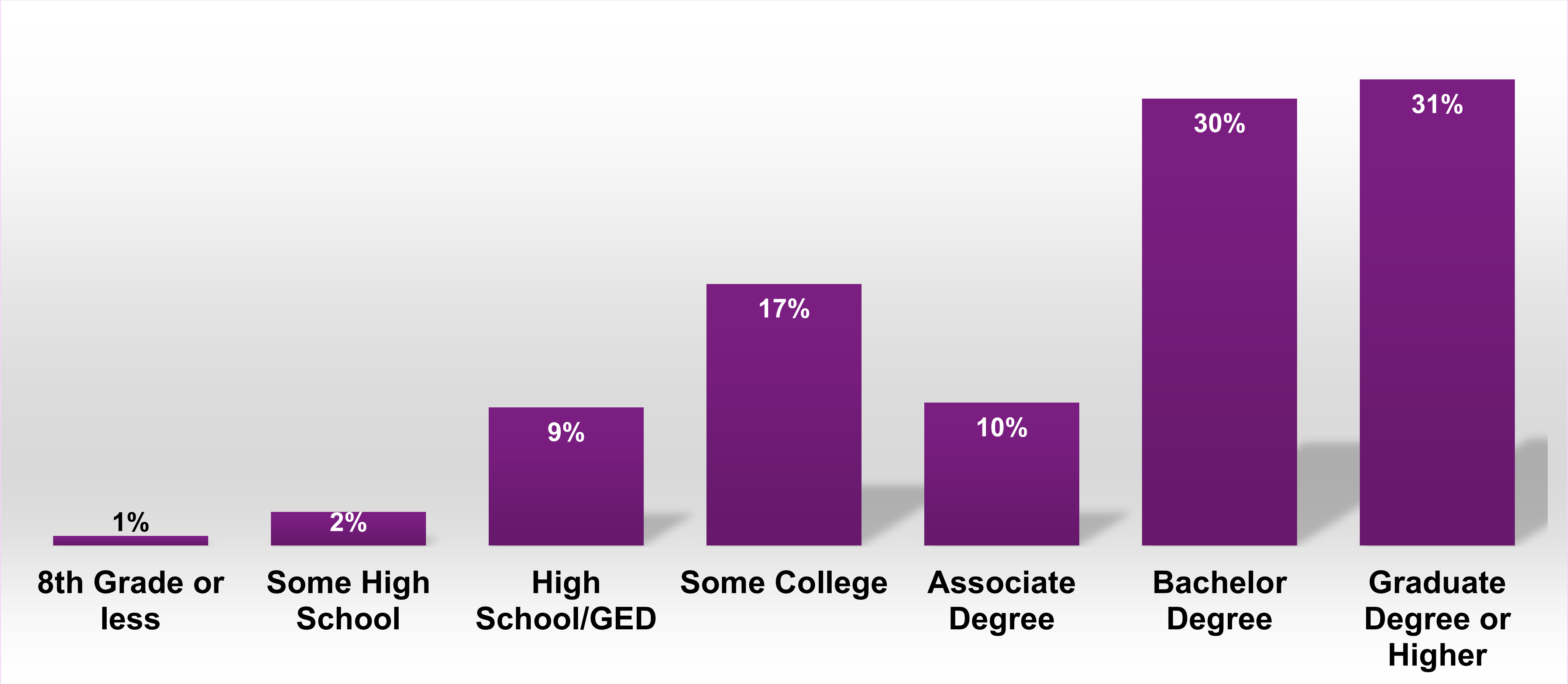
Employment


Other
3%
Student
7%
Retired
9%
Employed (FT)
41%
Unemployed
31%
Employed (PT)
9%

Household Income



Education Level



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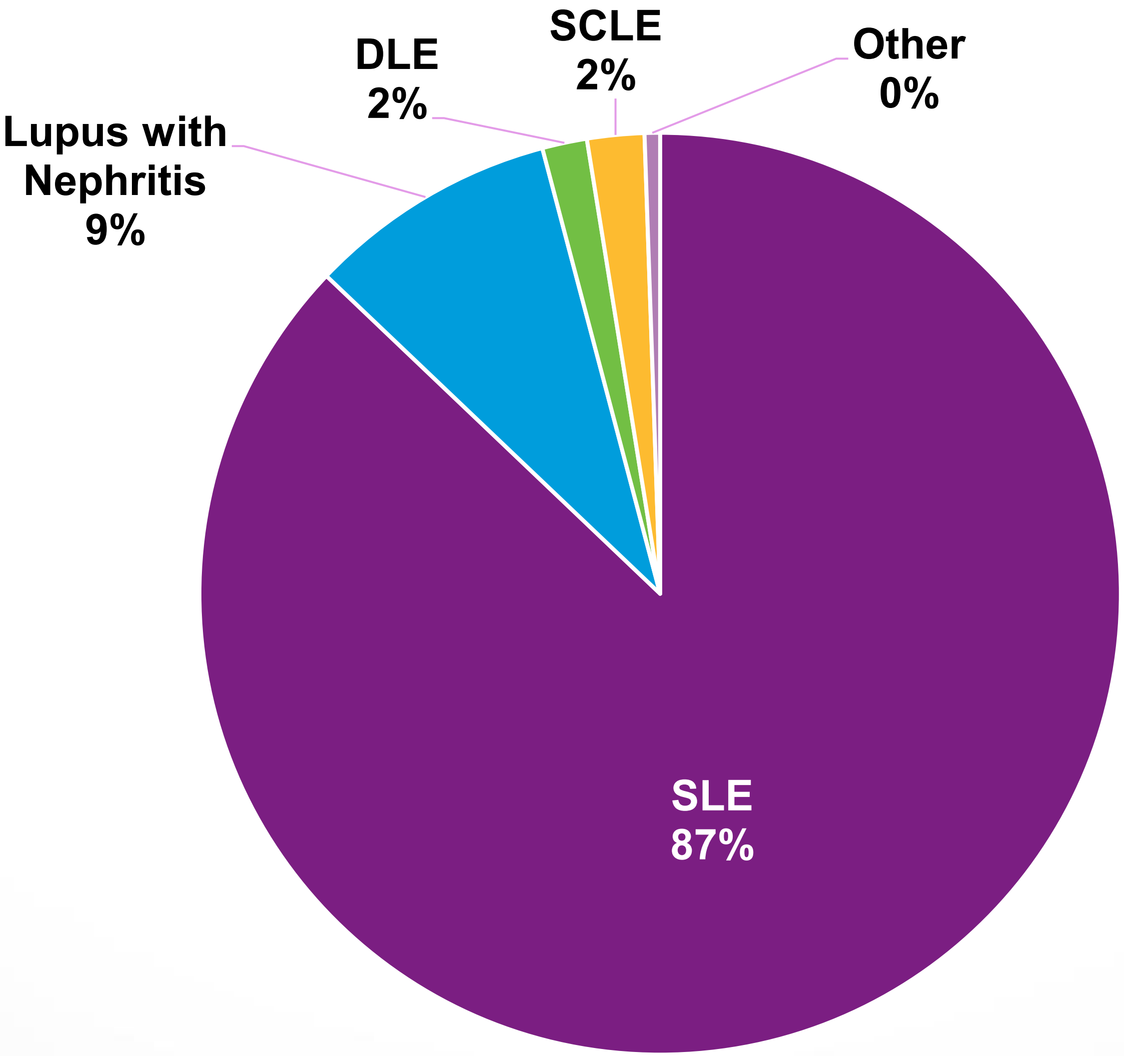
Diagnosis Type



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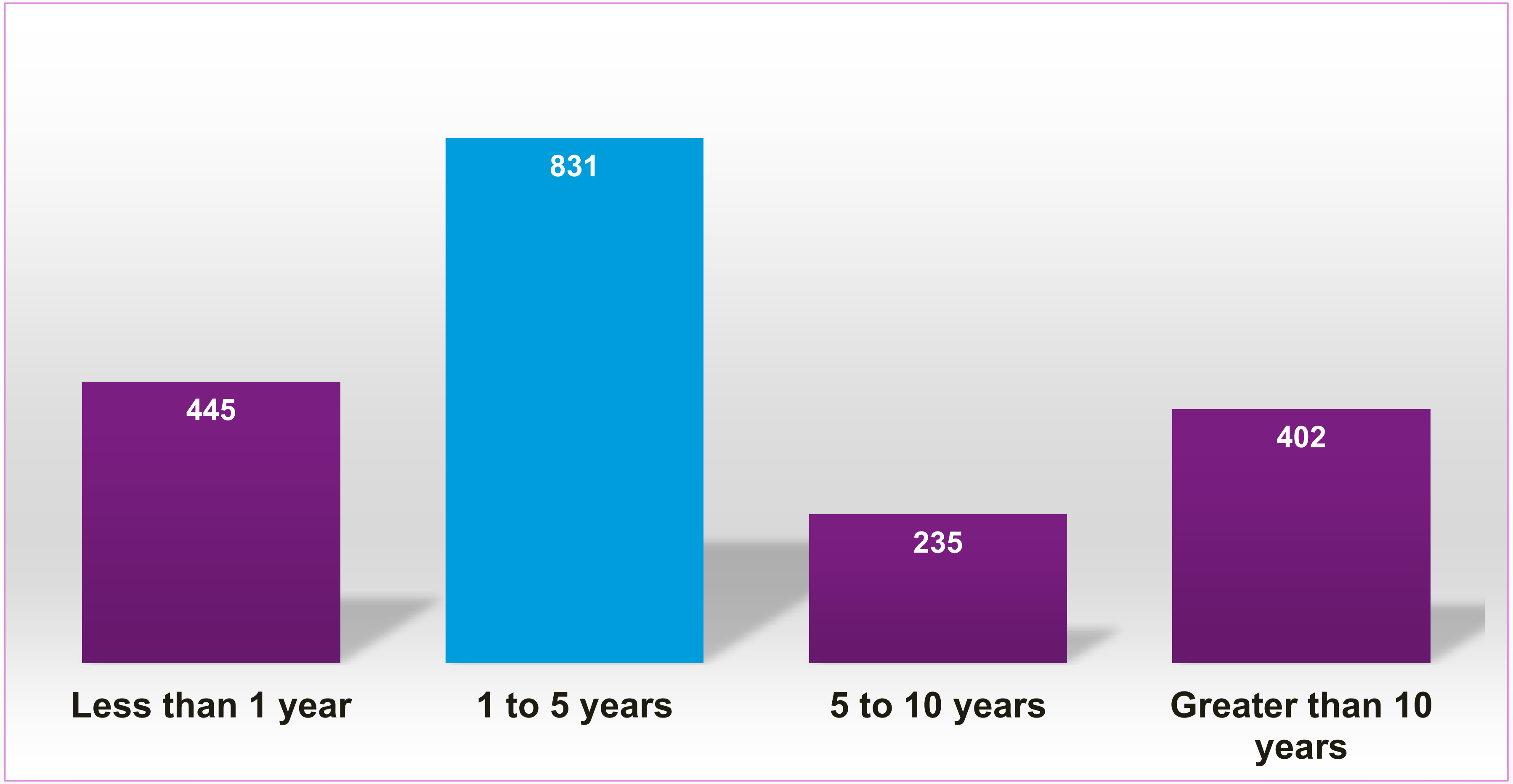
Time to Diagnosis



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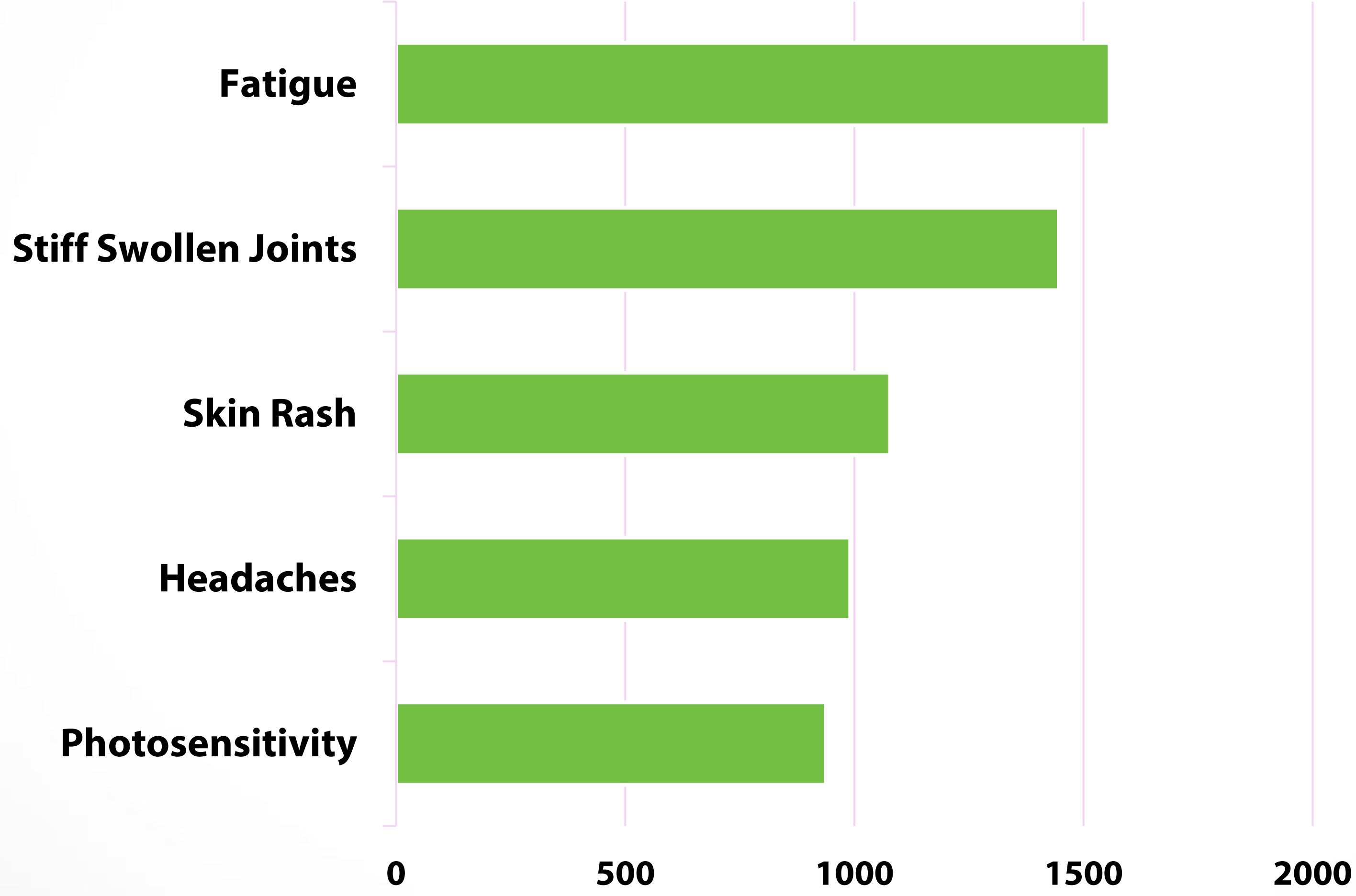
Top 5 Most Reported Symptoms



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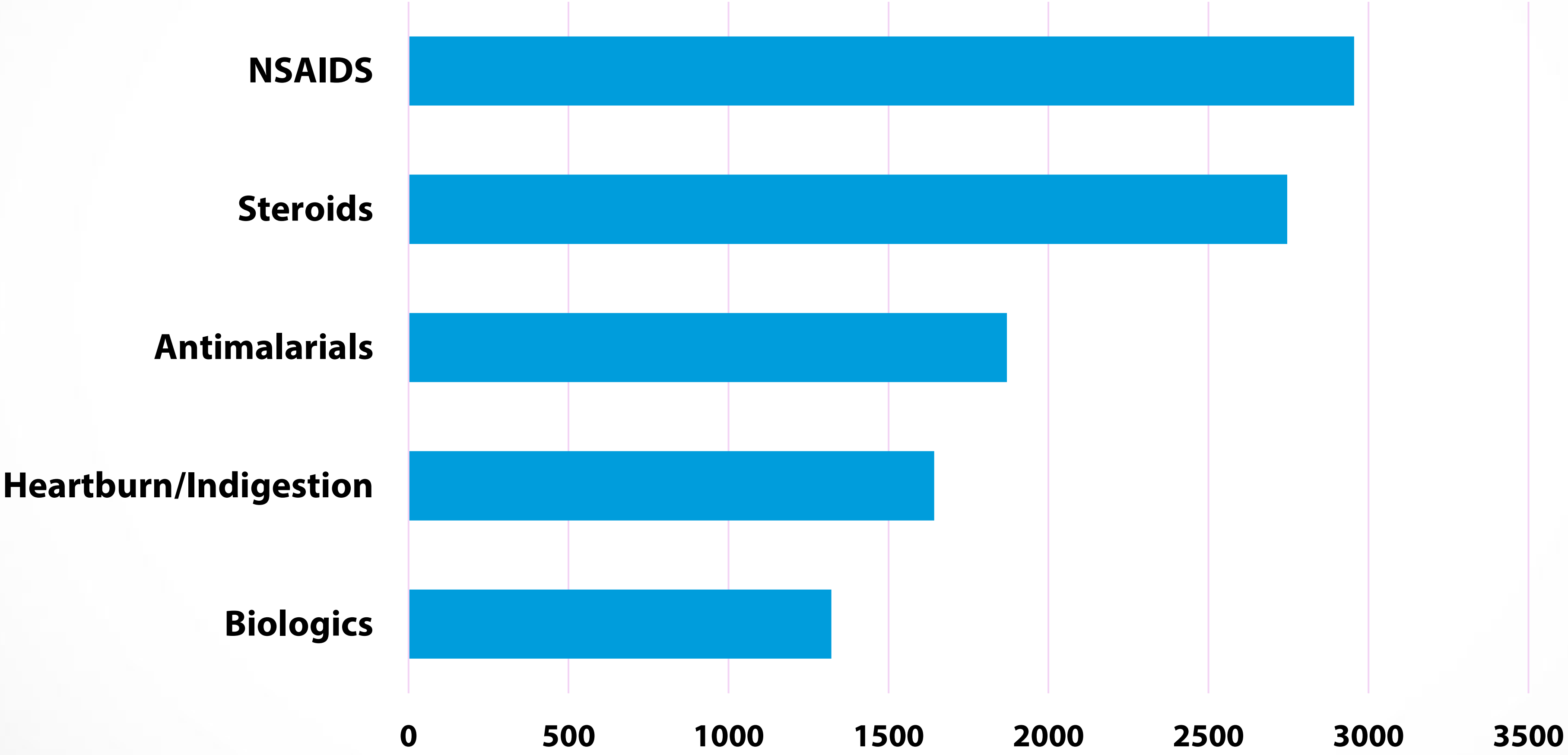
Top 5 Most Reported Medications



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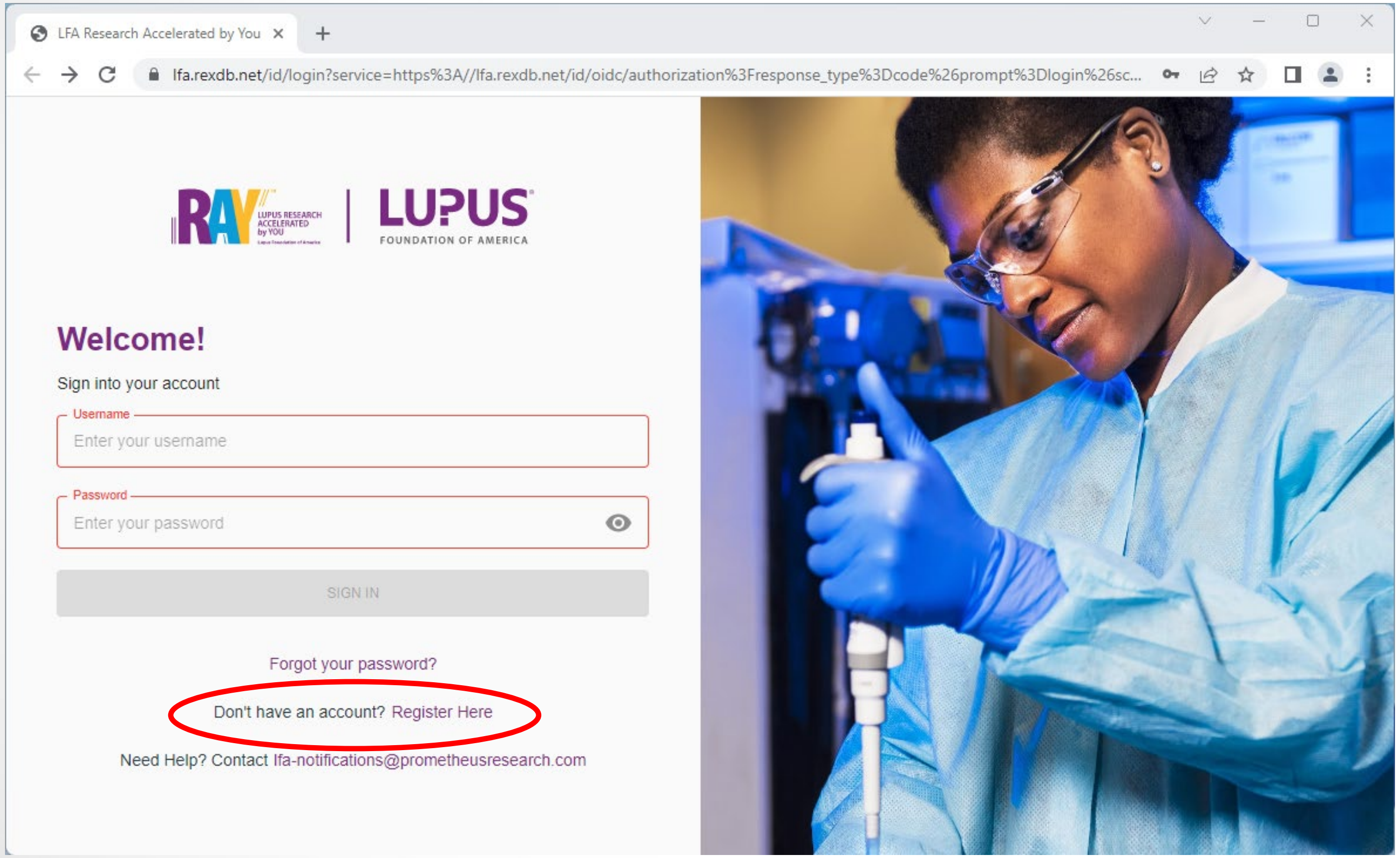
How to sign up for RAY®

To Register:



Welcome!

Sign into your account

Username: Enter your username

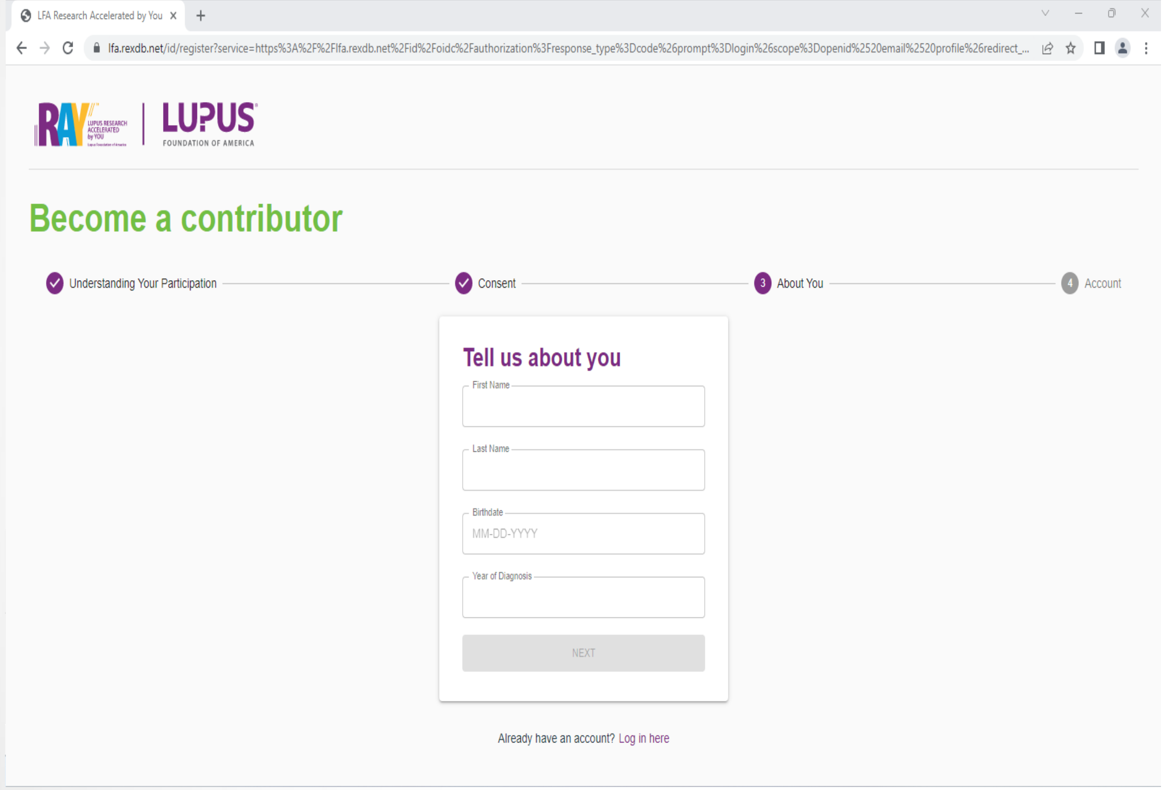
Password: Enter your password

Forgot your password?

Don't have an account? Register Here

Need Help? Contact lfa-notifications@prometheusresearch.com

- Visit https://www.lupus.org/research/enroll-in-a-lupus-registry
- Scroll to the bottom of the page and click "Join RAY"
- Click "Register Here"



Become a contributor

✓ Understanding Your Participation — ✓ Consent — 3 About You — 4 Account

Tell us about you

First Name

Last Name

Birthdate MM-DD-YYYY

Year of Diagnosis

NEXT

Already have an account? Log in here

- Read through the consent form and click "Continue" in the bottom right corner.
- Click "consent" to continue.
- Complete the "Tell Us About You" to create your account!

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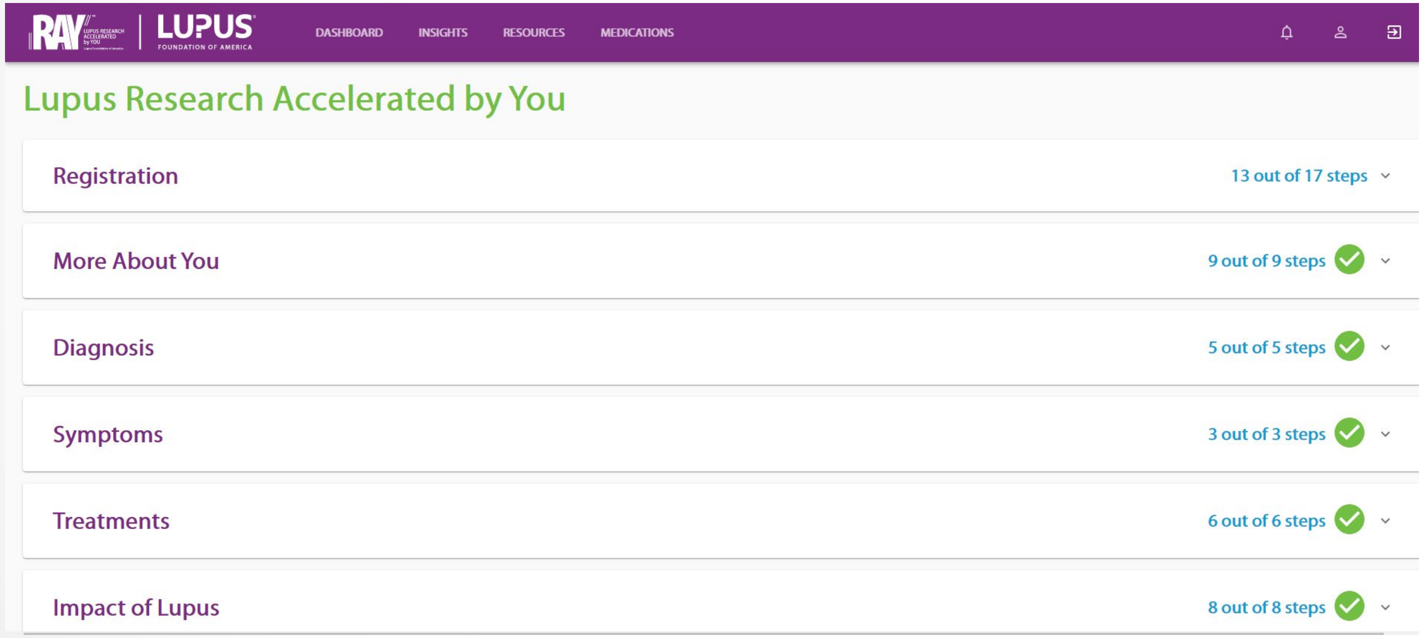

Lupus Research Accelerated by You

Registration	13 out of 17 steps
More About You	9 out of 9 steps ✓
Diagnosis	5 out of 5 steps ✓
Symptoms	3 out of 3 steps ✓
Treatments	6 out of 6 steps ✓
Impact of Lupus	8 out of 8 steps ✓

- Once your account has been created, you can begin to fill out the survey questions and submit your responses!

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RAY®
LUPUS RESEARCH
ACCELERATED
by YOU
Lupus Foundation of America

Questions?

Visit RAY® table in the lobby to register!

Compensation is available for those who complete the initial survey!

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How to Talk about Trials: What, where, when

Pat Wildman
Senior VP, Advocacy and Governmental Relations
Lupus Foundation of America

You ARE the Popular Opinion Leader

- What you do can make a difference
  - Trusted source, community leaders
  - Raise awareness and understanding within your community and networks
  - Share resources and information
  - Connect to opportunities
  - Expand reach
  - Elevate the patient voice in lupus research

You ARE the Popular Opinion Leader

- What to communicate and how
  - Context Matters
    - Group setting – Lupus & You, Support Groups
    - Personal networks and one-on-one conversations – friends and family, social networks, church or communities you're involved with
    - Social Media
- Opportunities
- Resources to help!

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How to Talk about Trials

Elements of the Conversation

- Introduction/Start the conversation (note the context):
  - Ask questions to engage the audience and introduce the topic:
    - Have you heard about RAY?
    - Are you looking for new treatment options?
    - Did you know that you can help researchers find new treatments for lupus?
    - Are you interested in learning more about what you can do to advance lupus research?
- Share your story
  - Share your experience…with lupus, quality of life, with treatments, with clinical trials.
    - Identify with the audience and communicate trust.

How to Talk about Trials

Elements of the Conversation

- Why it’s important…to you…to all people with lupus:
  - Why are you participating in LRAN, why is lupus research important to you, share your experience, if applicable
  - Share key points – clinical trials are the only way to develop new treatments, participations of PWL is essential, ethnic and racial minority groups are underrepresented in clinical trials
- How to learn more… the “Ask”:
  - Share opportunities (don’t tell them what to do):
    - LFA website/Antidote
    - RAY
    - Ask your doctor

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Tips and Suggestions

- Keep conversation focused:
  - Interactions with you and the person living with lupus or your audience, if in a group setting, are about them, not you
- Keep your own story brief:
  - Stories should be short and have a purpose (you want them to learn more about opportunities to participate in RAY and lupus research and clinical trials)
  - Use your story to relate to your audience or the person you are speaking with, relate why research and trials are important to you, your experiences and how/why you decided to get more involved. Communicate trust. You are a Lupus Warrior too.
  - Your story should only be 3-4 bullets/key points

The Why: Key Points

- Clinical trials offer high quality care
  - Lupus specialists, expert medical care
  - Access to new treatments before they are widely available
  - Potential for compensation for participating
- Lupus trials need more participation and diversity
  - Black/African Americans make up 43% of lupus cases nationally, yet only 14% of participants in lupus clinical trials
  - Hundreds of research studies and trials are available and need patients to participate

The Why: Key Points

- Clinical trials are the only way to get new treatments
  - There are seven FDA approved treatments (three developed specifically for lupus)
  - Lupus affects each person differently, a diverse group of people living with lupus participating in research helps to ensure treatments have the greatest effect on the largest number of patients
- Participation is always voluntary and safety is a priority
  - Your decision to participate is not permanent, you may choose to leave the study at any time
  - Researchers follow detailed protocols and safety requirements to make each trials as safe as possible

How to Learn More: The Asks

- Research Accelerated by You (RAY)
  - Enrollment allows access to information on clinical trial opportunities. Share what is most important to PWL and what it is like to live with lupus.
- Ask you Doctor for more information
  - Your doctor may be able to tell you about trials available for which you may qualify. They can help explain the benefits and risks and whether a trial may be right for you.
- LFA Resources
  - National Resource Center on Lupus
    - https://www.lupus.org/resources (search clinical trials)
  - Antidote: clinical trial search tool
    - https://www.antidote.me/conditions/lupus

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Where to Talk about Trials

We will share opportunities with you!

- Lupus Walk
- Lupus and You Meetings
- Support Group Meetings
- Advocacy Summit
- At the doctor's office
- Social and community gatherings, such as church or other community organizations you're involved with
- Engaging with other Lupus Warriors
- Social Media

How to Talk About Trials

- YOUR Ideas!
  - Start the conversation/Introduction
  - About you
  - Why? Why important to you… and all people living with lupus
  - How to learn more… the Ask - what they can do
- Breakout Rooms (4 Groups)
  - Group One Facilitator: Amy Yalden
  - Group Two Facilitator: Sue Gloor
  - Group Three Facilitator: Cindy Messerle
  - Group Four Facilitator: Stephanie Slan

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Your Action Plan: Next Steps and Resources

Pat Wildman
Senior VP, Advocacy and Governmental Relations
Lupus Foundation of America

Now What?

Next Steps and Resources

- Its time to use the information you have learned today
- We have created some tools to help you as you share your knowledge with other people living with lupus
- We will be here to support you as you speak in your communities.

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Lupus Clinical Trial Resources

- Variety of resources about clinical trials and value of volunteer participants
  - Specific resources available tied to minority participation in research
- Learn about clinical trials
  - What is a clinical trial?
  - Why should I volunteer?
  - What lupus trials are enrolling?
  - How do I find a trial near me?
- Find lupus clinical trials
- Explore ways to get involved in research
  - lupus.org/advancing-research/get-involved-in-research

Lupus Clinical Trial Resources

- Online HUB available exclusively for LRAN members
  - Information about RAY and links to enroll
  - Fact sheets and links to information about clinical trials
  - Antidote search tool to identify trials near you and for which you may be eligible to participate
  - Talking points, handouts, sample presentations to guide you in speaking at events
  - Information and public links you can share to learn more about clinical trials
  - LRAN training presentations
  - Continuously updated with additional content, including based on your feedback

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LRAN Engagement

- Forum for LRAN participants to share experiences and engage with each other
- Sharing your activities
  - Regional Directors, Chapter Leaders, LFA national staff
  - Details: date, locations, audience
  - Best Practices: what works, what can be improved
  - Your ideas and needs: how can we help you?