

6TH ANNUAL VALUE IN CANCER CARE SUMMIT 2019



Afternoon Plenary: Disparities in Cancer Survival



Christopher Flowers MD, MS, FASCO

- Professor of Hematology and Oncology, Winship Cancer Institute at Emory University School of Medicine
- Clinical Director for Oncology Informatics Program
- Director of the lymphoma program at Emory University



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the National Cancer Institute



Disparities in Cancer Survival HICOR Value in Cancer Care Summit

Christopher Flowers, MD, MSc, FASCO
Professor, Hematology and Medical Oncology
Director, Lymphoma Program
Scientific Director, Winship Research Informatics
Emory School of Medicine

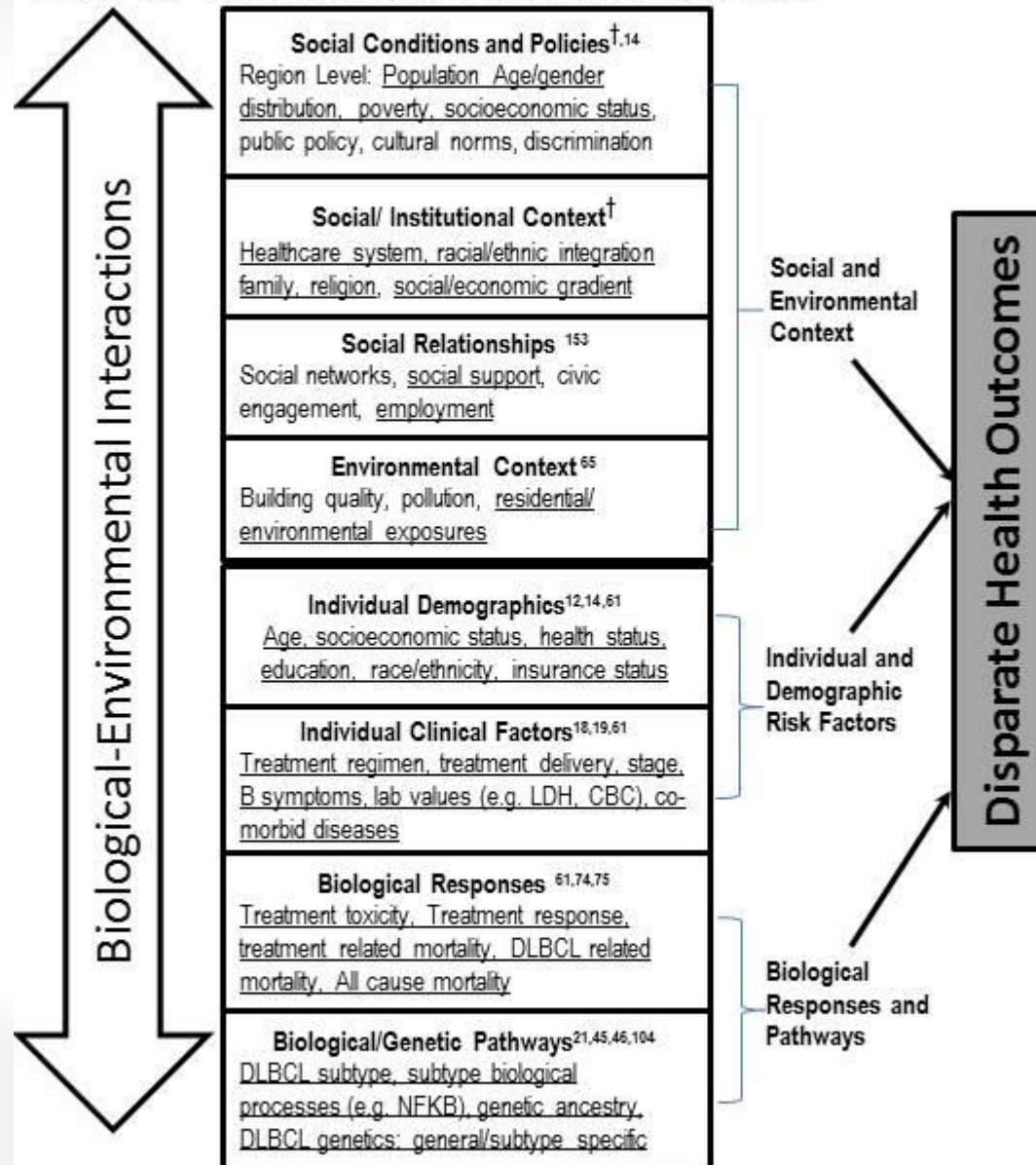
May 13, 2019

Disclosures

Consultant: Consultant: Abbvie, Astra Zeneca, Bayer, Celgene (unpaid), Denovo Biopharma, Genentech/Roche (unpaid), Gilead, OptumRx, Karyopharm, Pharmacyclics/Janssen, Spectrum

Research Funding: Abbvie, Acerta, Celgene, Gilead, Genentech/Roche, Janssen Pharmaceutical, Millennium/Takeda, Pharmacyclics, TG Therapeutics, Burroughs Wellcome Fund, Eastern Cooperative Oncology Group, National Cancer Institute, V Foundation

(a) Adapted from: Warnecke et al. *Am J Public Health* 2008; 98:1608–1615 and Northridge et al. *J Urban Health*, 2003; 80:556–68.



[†] Undergoing pilot evaluation in collaboration with CPIC Similar to their prior work described in Warner & Gomez *J Community Health* 2010.
 Numbered references refer to our prior publications examining racial disparities in lymphoma at each of these levels.

Charting the Future of Cancer Health Disparities Research: A Position Statement From the American Association for Cancer Research, the American Cancer Society, the American Society of Clinical Oncology, and the National Cancer Institute

Blase N. Polite, MD, MPP¹; Lucile L. Adams-Campbell, PhD²; Otis W. Brawley, MD³; Nina Bickell, MD⁴; John M. Carethers, MD⁵; Christopher R. Flowers, MD⁶; Margaret Foti, PhD, MD (hc)⁷; Scarlett Lin Gomez, PhD, MPH⁸; Jennifer J. Griggs, MD, MPH⁹; Christopher S. Lathan, MD, MS, MPH¹⁰; Christopher I. Li, MD, PhD¹¹; J. Leonard Lichtenfeld, MD¹²; Wortia McCaskill-Stevens, MD, MS¹³; Electra D. Paskett, PhD¹⁴

Special Report

Cancer Research

Charting the Future of Cancer Health Disparities Research: A Position Statement from the American Association for Cancer Research, the American Cancer Society, the American Society of Clinical Oncology, and the National Cancer Institute



Blase N. Polite¹, Lucile L. Adams-Campbell², Otis W. Brawley³, Nina Bickell⁴, John M. Carethers⁵, Christopher R. Flowers⁶, Margaret Foti⁷, Scarlett Lin Gomez⁸, Jennifer J. Griggs⁹, Christopher S. Lathan⁹, Christopher I. Li¹⁰, J. Leonard Lichtenfeld³, Wortia McCaskill-Stevens¹¹, and Electra D. Paskett¹²

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ASCO SPECIAL ARTICLE

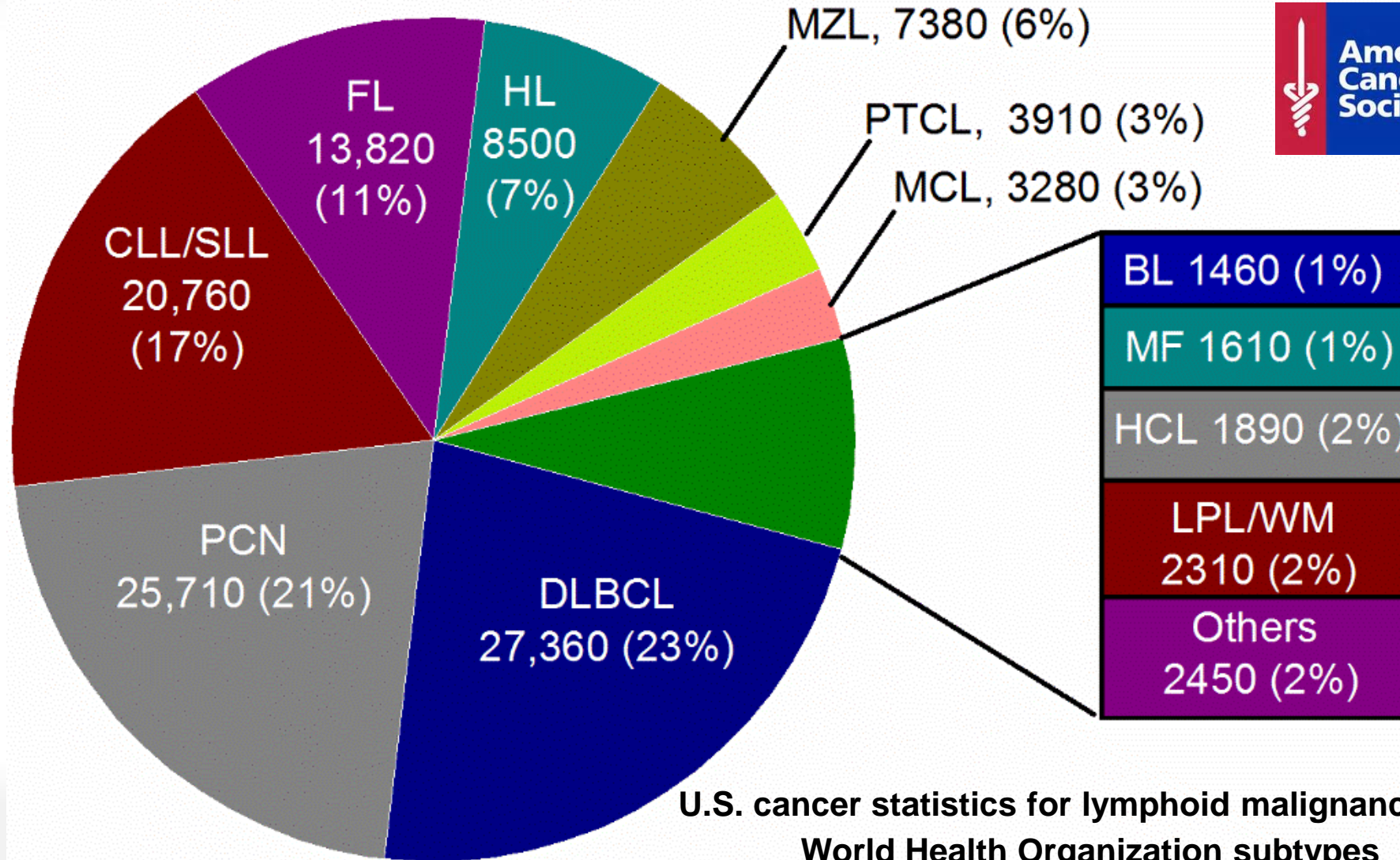
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Non-Hodgkin Lymphomas

- Non-Hodgkin lymphomas (NHLs)
 - heterogeneous group of B-cell and T-cell neoplasms
 - differing patterns of growth and response to treatment
- Prognosis depends on histologic type, stage, and treatment

Annual Lymphoid Cancers in the US

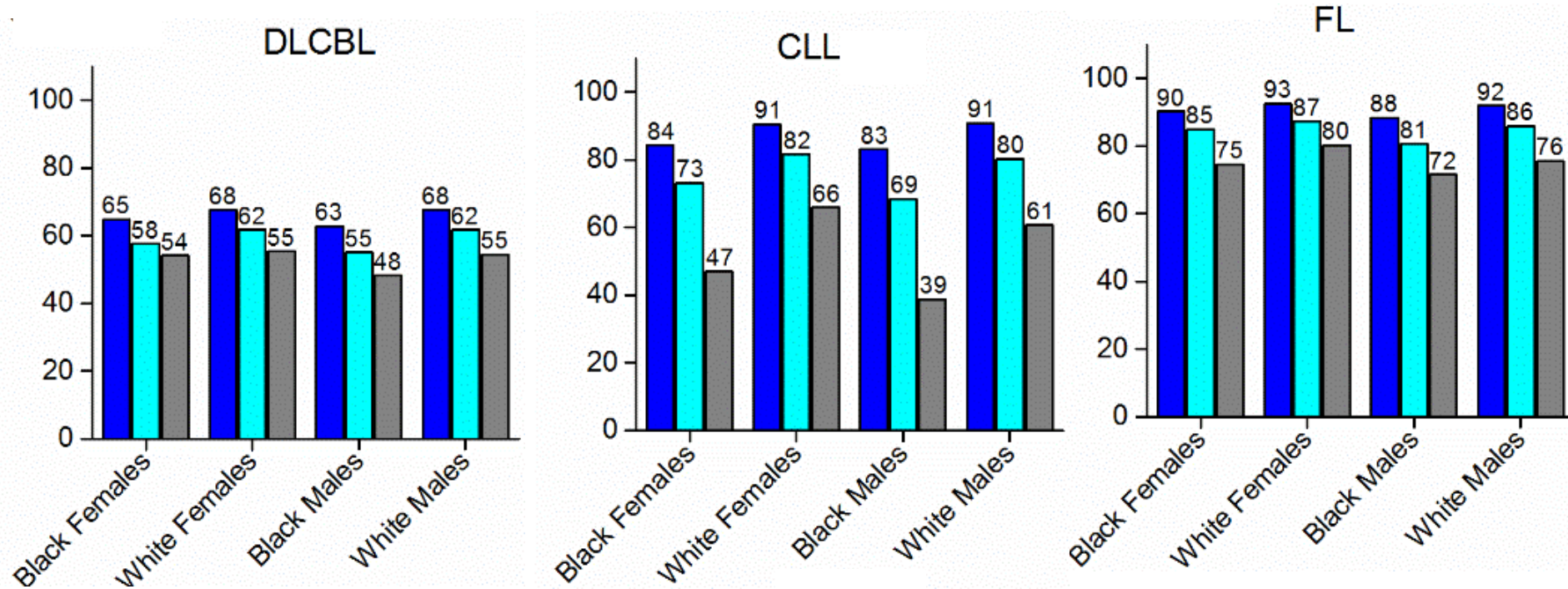


U.S. cancer statistics for lymphoid malignancies by World Health Organization subtypes

Teras LR, DeSantis CE, Morton LM, Cerhan JR, Jemal A, Flowers CR

Survival by Gender and Race for NHL Subtypes

■ 2-year
 ■ 5-year
 ■ 10-year

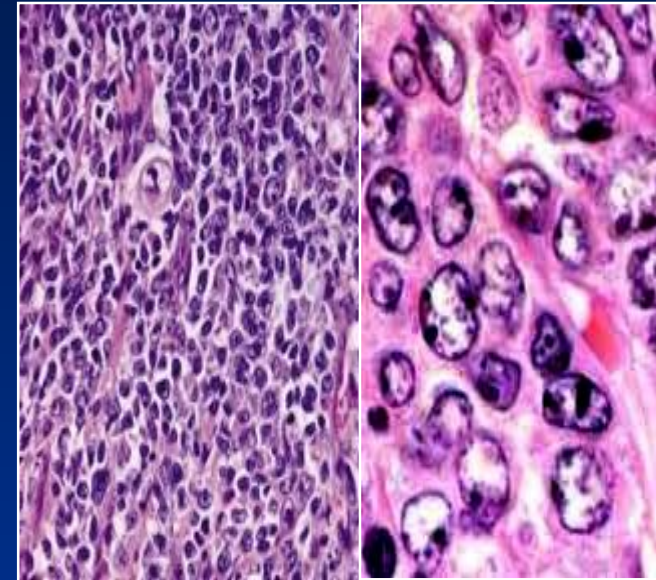


**U.S. cancer statistics for lymphoid malignancies by
 World Health Organization subtypes**

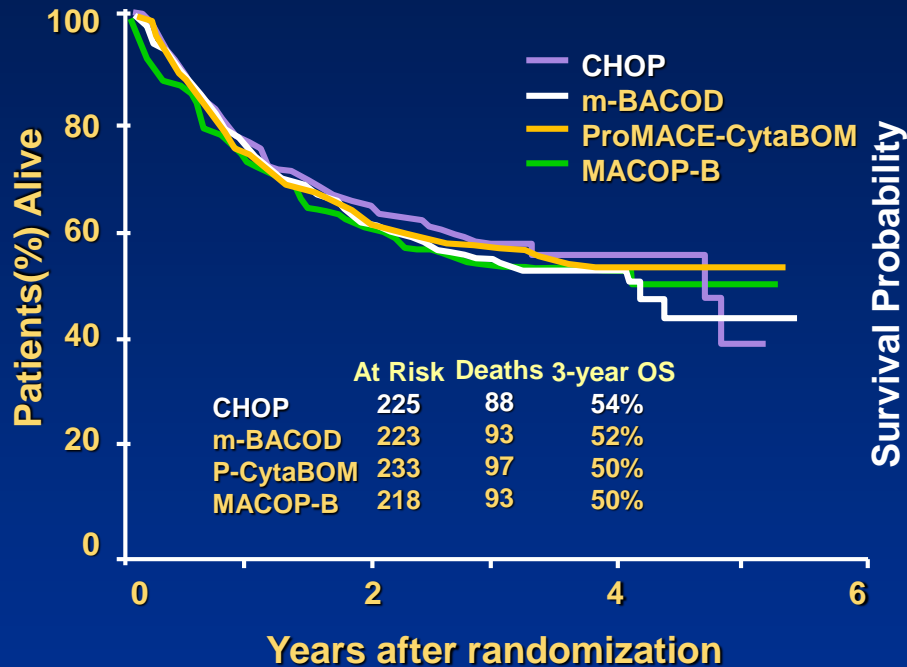
Teras LR, DeSantis CE, Morton LM, Cerhan JR, Jemal A, Flowers CR
 CA Cancer J Clin. 2016

Diffuse Large B-Cell Lymphoma

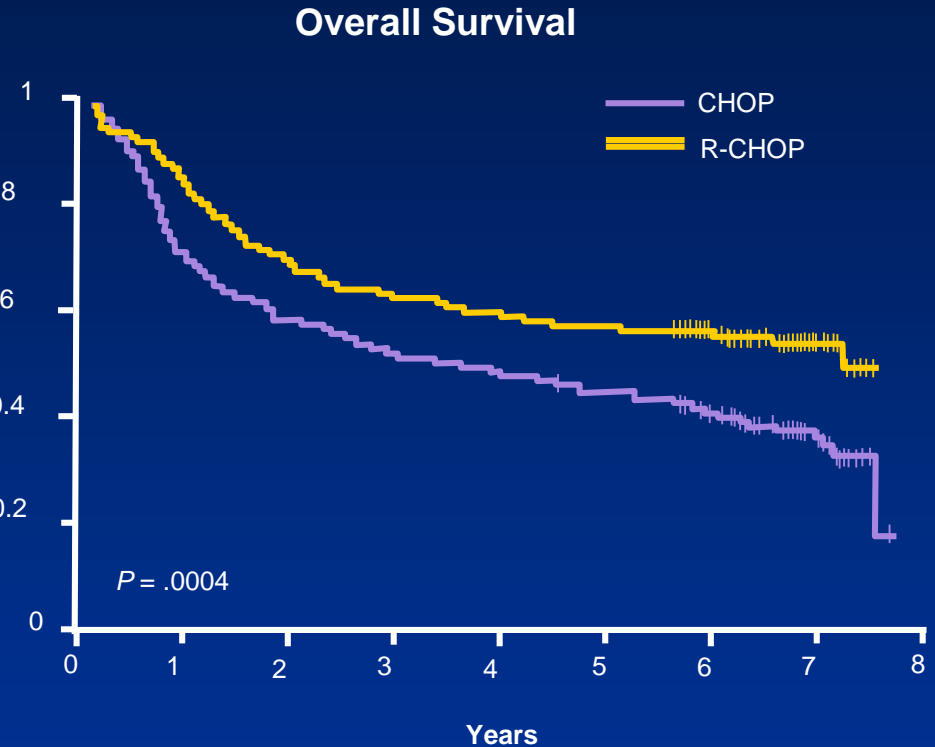
- Most common lymphoid malignancy
 - 31% of adult NHL
- Aggressive: rapid growth and limited survival in the absence/inadequate tx
- Curable in 50% or more of cases
- **Clinical outcomes highly variable**



Advances in Treatment Improve Survival for Patients with Lymphoma



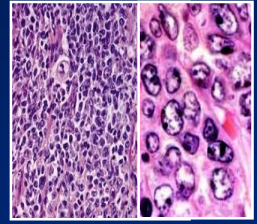
Fisher RI, et al. *N Engl J Med.* 1993



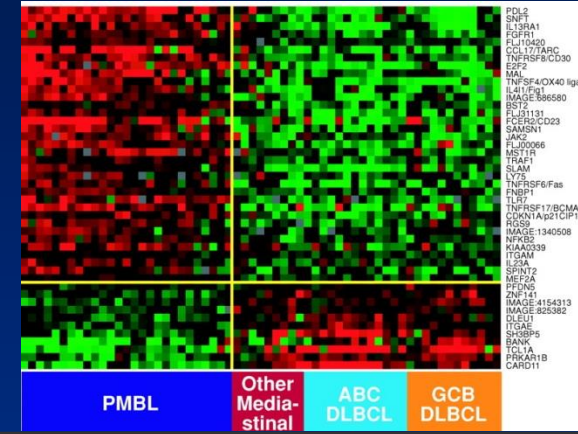
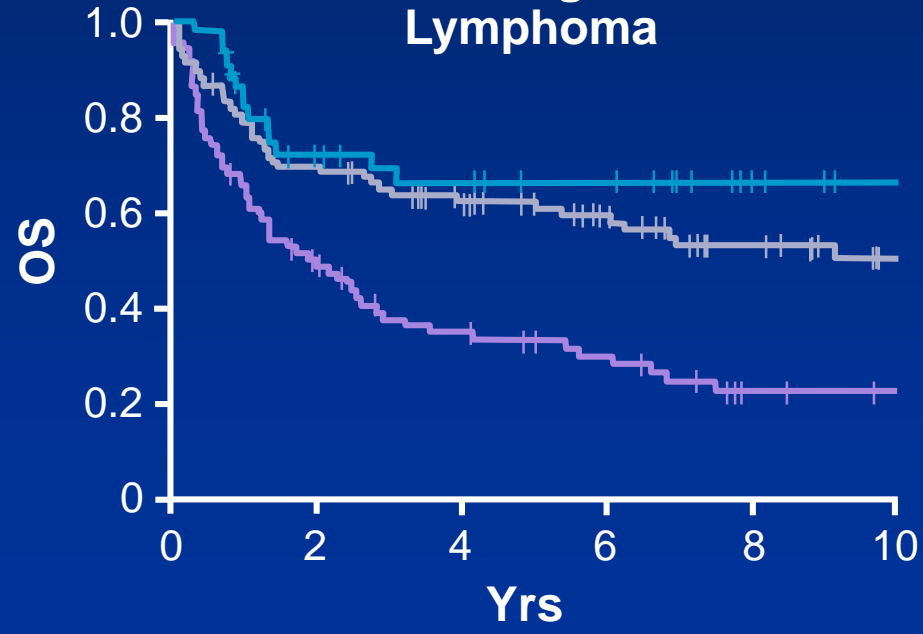
Coiffier B, et al. *N Engl J Med.* 2002.

Coiffier B, et al. ASCO 2007. Abstract 8009.

Gene Expression Defines Molecularly and Clinically Distinct Subgroups in DLBCL



Diffuse Large B-cell Lymphoma

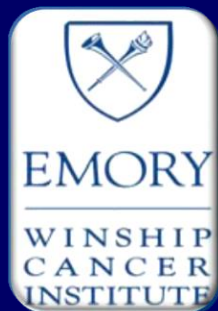


DLBCL Subgroup	5-Yr OS, %
PMBL	64
GCB DLBCL	59
ABC DLBCL	30

Racial Differences in the Presentation and Outcomes of Diffuse Large B-Cell Lymphoma in the United States

Neha Malik, Pareen J. Shenoy, MBBS, MPH, Kevin Bumpers, MPA, Rajni Sinha, MD, MRCP and Christopher R. Flowers, MD

Winship Cancer Institute
Emory University



Advancing the possibilities...

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Data Source: SEER

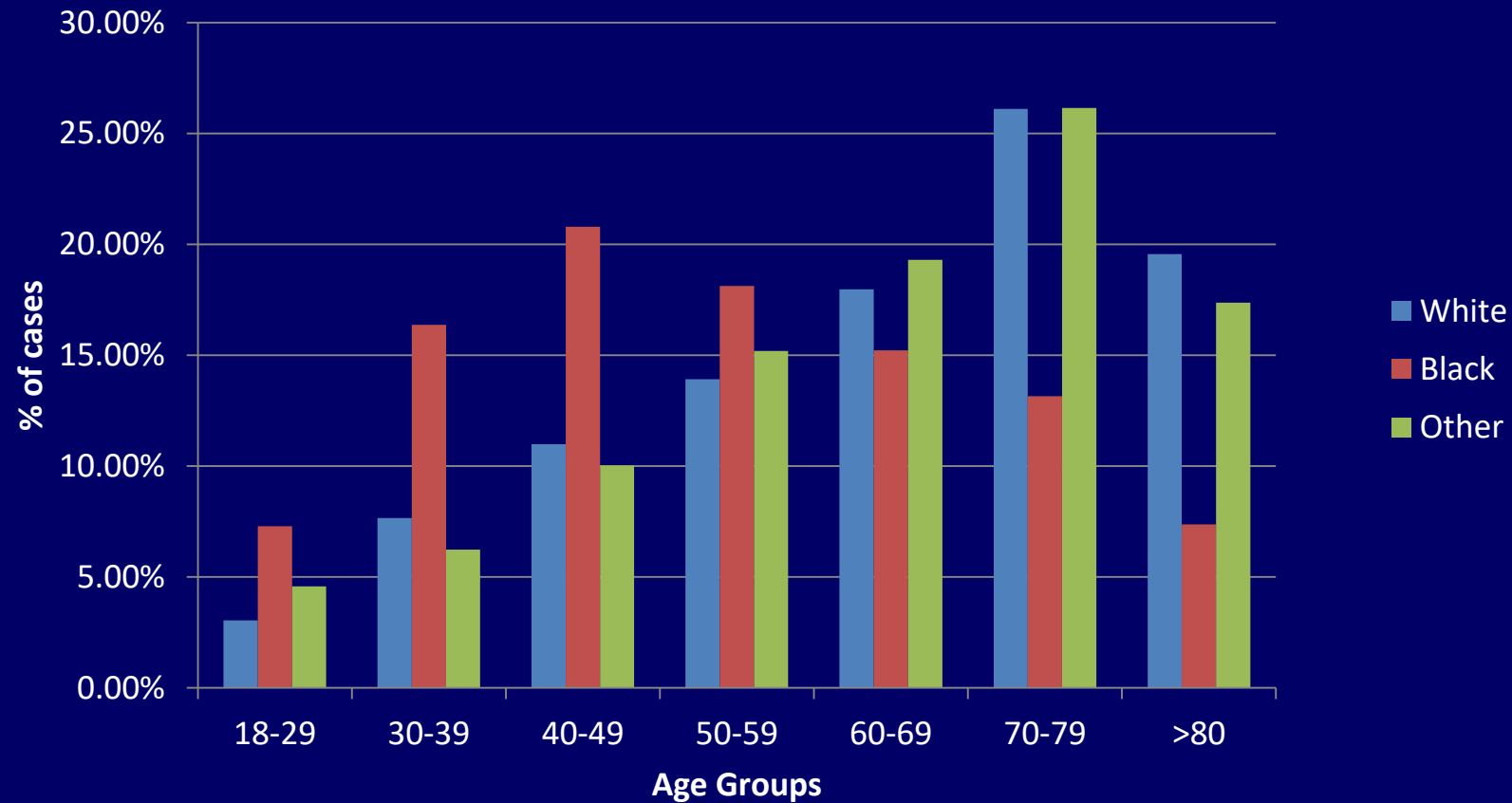
Surveillance, Epidemiology and End Results (SEER)

- ▶ **Population-based cancer registry**
 - collect information on new cancers and survival from specific geographic areas
 - Represents 26% of the US population
- ▶ **Contains standardized data elements**
 - tumor characteristics (including stage and histopathology)
 - patient demographics, baseline characteristics
 - survival data

Study Population

- ▶ **Diagnosed with DLBCL 1992 to 2005**

Age Distribution of DLBCL by Race



DLBCL Demographics by HIV Status: SEER

	White			Black		
	N	%	Med Age	N	%	Med Age
HIV+	353	4%	46	126	17%	44
HIV-	3295	39%	68	309	42%	56
Unknown	4852	57%	71	295	41%	56
Total	8500		69	730		53

InterLymph Clustering of Other WHO Classified Lymphoid Malignancies

NHL Subtype	ICD-O-3	White median Age	Black median Age	Other median age
B-CELL NEOPLASM				
B-cell prolymphocytic leukemia	9833	75.5	57	46.5
Lymphoplasmacytic lymphoma	9671	71	60	69
Follicular lymphoma, NOS	9690	66	56	65
Follicular lymphoma Grade 1	9695	63	58	59
Follicular lymphoma Grade 2	9691	64	60	62
Follicular lymphoma Grade 3	9698	65	55	67
Diffuse large B-cell lymphoma	9680	68	52	66
Immunoblastic diffuse large B-cell lymphoma	9684	60	48	67
Primary effusion lymphoma	9678	58	50.5	
Mediastinal (thymic) large cell lymphoma	9679	35	21.5	39
Burkitt lymphoma	9687	41	39.5	49
T-CELL AND NK-CELL NEOPLASM				
Precursor T-cell neoplasm				
Peripheral T-cell lymphoma, unspecified	9702	65	54	65.5
HODGKIN LYMPHOMA				
Classical Hodgkin lymphoma	9650	50	39	41
Lymphocyte-depleted classical Hodgkin lymphoma	9653	58.5	43	69

Clinical Features at Presentation by Race

	White (n=31,285)	Black (n=2,511)	Other (n=3,213)	p-value W v. B
Characteristic	Percentage			
Stage				
I/II	52%	44%	58%	<.0001
III/IV	48%	56%	42%	

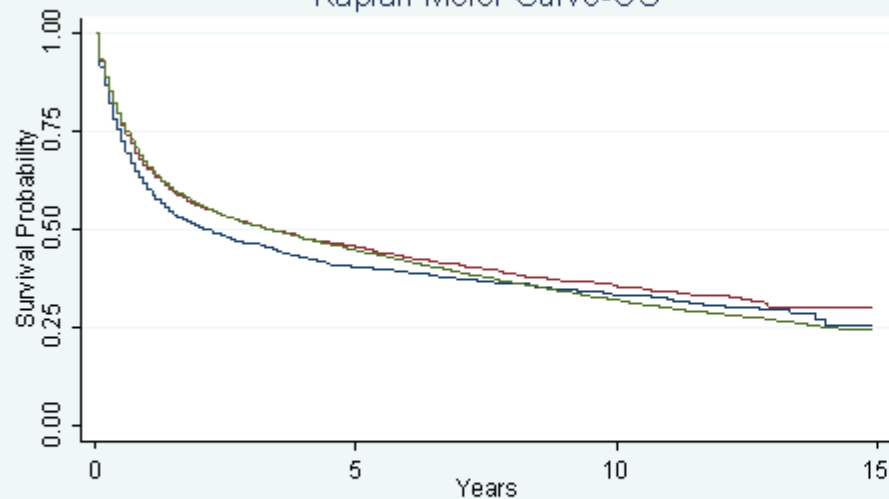
Pts with complete staging (n=7,835)

	White	Black	Other	p-value
B Symptoms				
Yes	5.6%	8.5%	5.9%	<.0001
No	10.6%	11.4%	13.8%	
Unknown	83.8%	80.1%	80.3%	

Clinical Features at Presentation by Race

- Black patients with DLBCL
 - **Younger Age**
 - **More Advanced Stage**
 - **Shorter Survival**

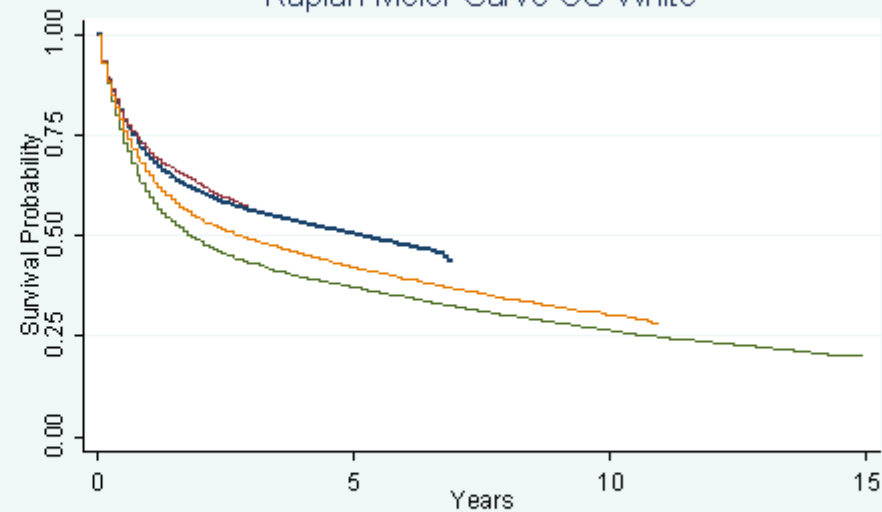
Kaplan Meier Curve-OS



W vs B p 0.0007
W vs O p 0.2433

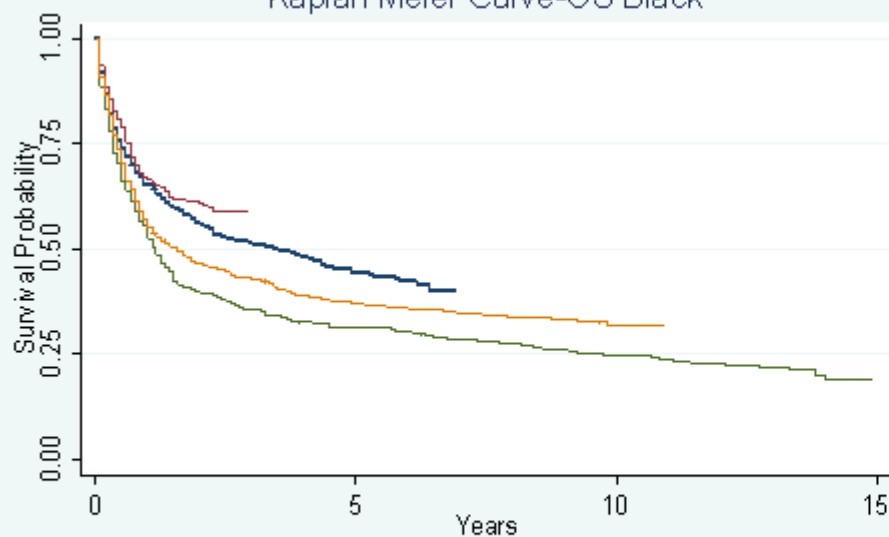
— Black — Other
— White

Kaplan Meier Curve-OS White



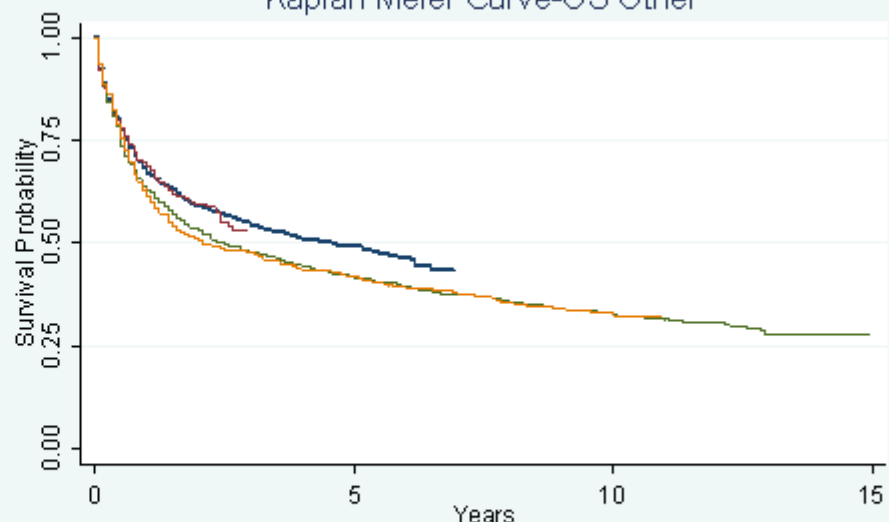
— 00-03 — 04-06
— 92-95 — 96-99

Kaplan Meier Curve-OS Black



— 00-03 — 04-06
— 92-95 — 96-99

Kaplan Meier Curve-OS Other



— 00-03 — 04-06
— 92-95 — 96-99

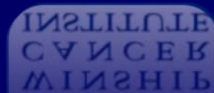
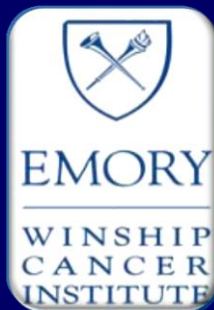
Challenges

- Do all patients with DLBCL in the US receive standard chemo-immunotherapy?
- How does modern treatment of DLBCL impact survival in the US?
- Are there clinically differences in DLBCL that may reflect underlying biological variants (ABC vs GCB)?

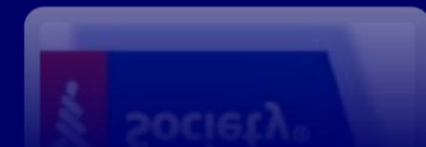
Disparities in the Use of Chemo- Immunotherapy for Diffuse Large B-Cell Lymphoma in the United States

Christopher Flowers, MD, MSc¹, Stacey Fedewa, MPH², Amy Chen, MD, MPH², Joseph Lipscomb, PhD¹, Otis Brawley, MD², Elizabeth Ward, PhD²

¹Winship Cancer Institute
Emory University



²American Cancer Society



Data Source: NCDB

National Cancer Database

- ▶ **Hospital-based cancer registry jointly sponsored by American Cancer Society & American College of Surgeons**
- ▶ **Contains standardized data elements**
 - tumor characteristics (including stage and histopathology), and first course of treatment
 - patient demographics, patient insurance status, county of residence, facility type in which patients were treated

Study Population

- ▶ **diagnosed with DLBCL (ICD-O codes 9679 & 9680)
Jan 1, 2001- Dec 31, 2004**
- ▶ **received all or part of their first course of treatment at the reporting facility**

Black Pts with DLBCL Present at Younger Age: NCDB

Characteristics	White (n=31,671)	Black (n=3,001)	p-value
Median Age years (IQR)	70 (57-79)	53 (42-68)	
Age > 60 years	70%	38%	<.0001
Sex, female	48%	46%	0.0341
Stage			<.0001
I/II	46	40	
III/IV	41	45	
Unknown	13	15	

Features at Presentation by Race

- Black patients with DLBCL
 - **Younger Age**
 - **More Advanced Stage**
- Black patients with DLBCL
 - **More likely Uninsured**
 - **More likely Medicaid insured**
 - **Less likely to receive Chemoimmunotherapy**

Study Limitations

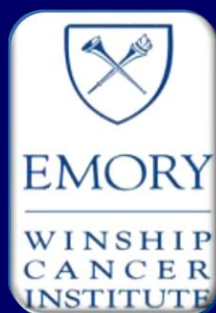
- ▶ No direct pharmacy data for rituximab or chemotherapy
 - Comparison to SEER:Medicare
- ▶ Pt-level SES is not available in the NCDB
- ▶ Additional clinical data influence prognosis and treatment decisions
- ▶ Insufficient follow-up to describe impact on outcomes
 - Shenoy ASH 2009 (n=348 W and 107 B)
 - No racial differences in R-CHOP use, but differences in OS

Black/White Differences in the Treatment and Outcomes of Diffuse Large B Cell Lymphoma: A Matched Cohort Analysis

Pareen Shenoy, Kevin Bumpers, Nassoma King, Taoying Huang, Neha Malik, Rajni Sinha, Christopher Flowers

To examine Black/White differences in pts with DLBCL across:

- Baseline characteristics at diagnosis
- Use of CHOP vs. R-CHOP
- Treatment outcomes

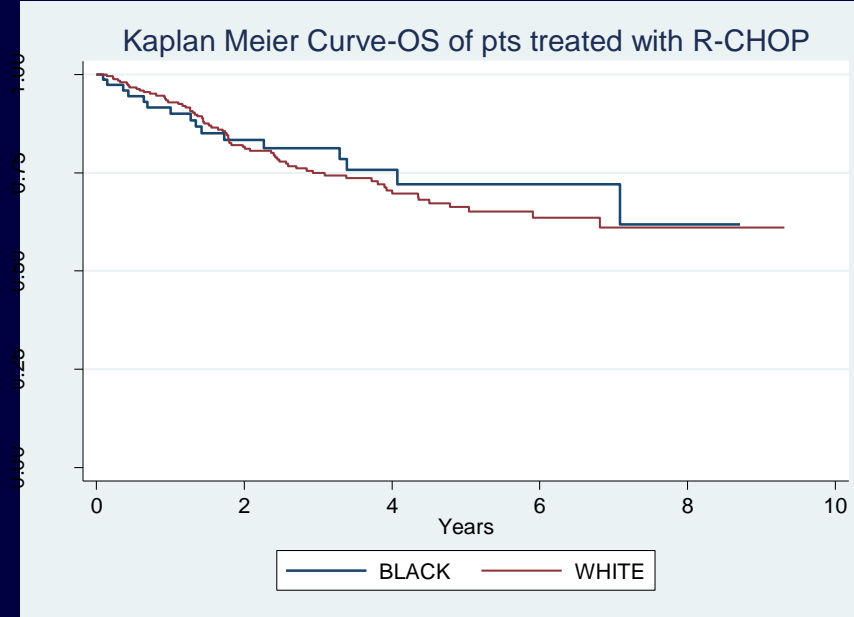
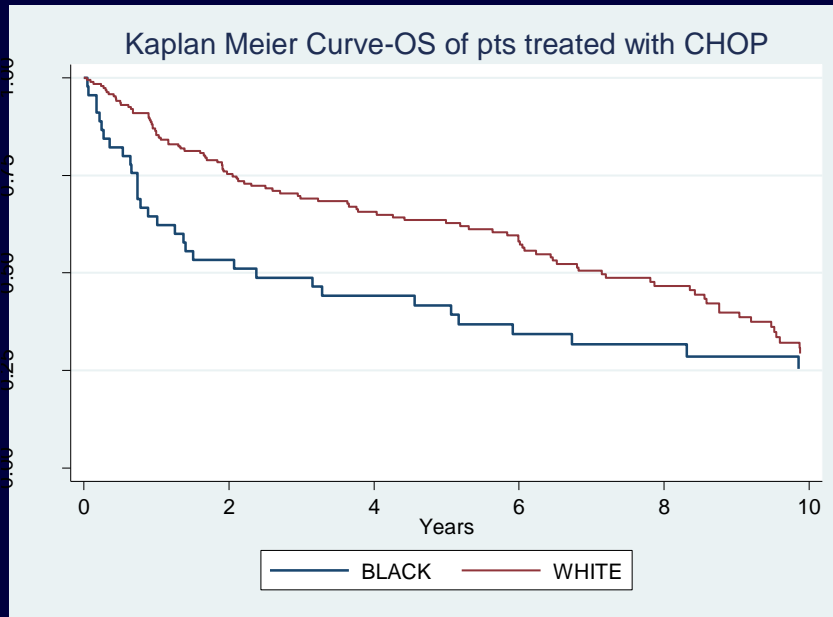


Advancing the possibilities...

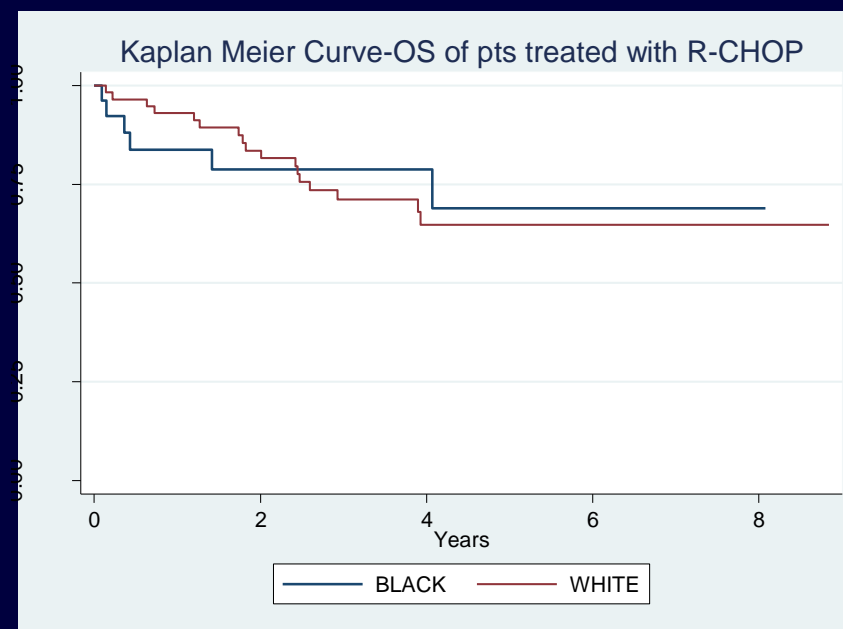
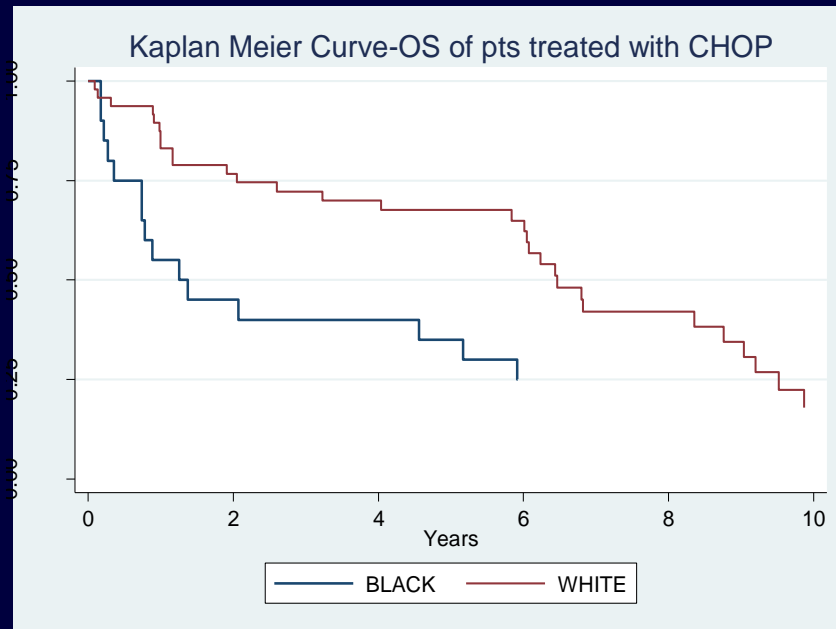
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All patients



TMA patients

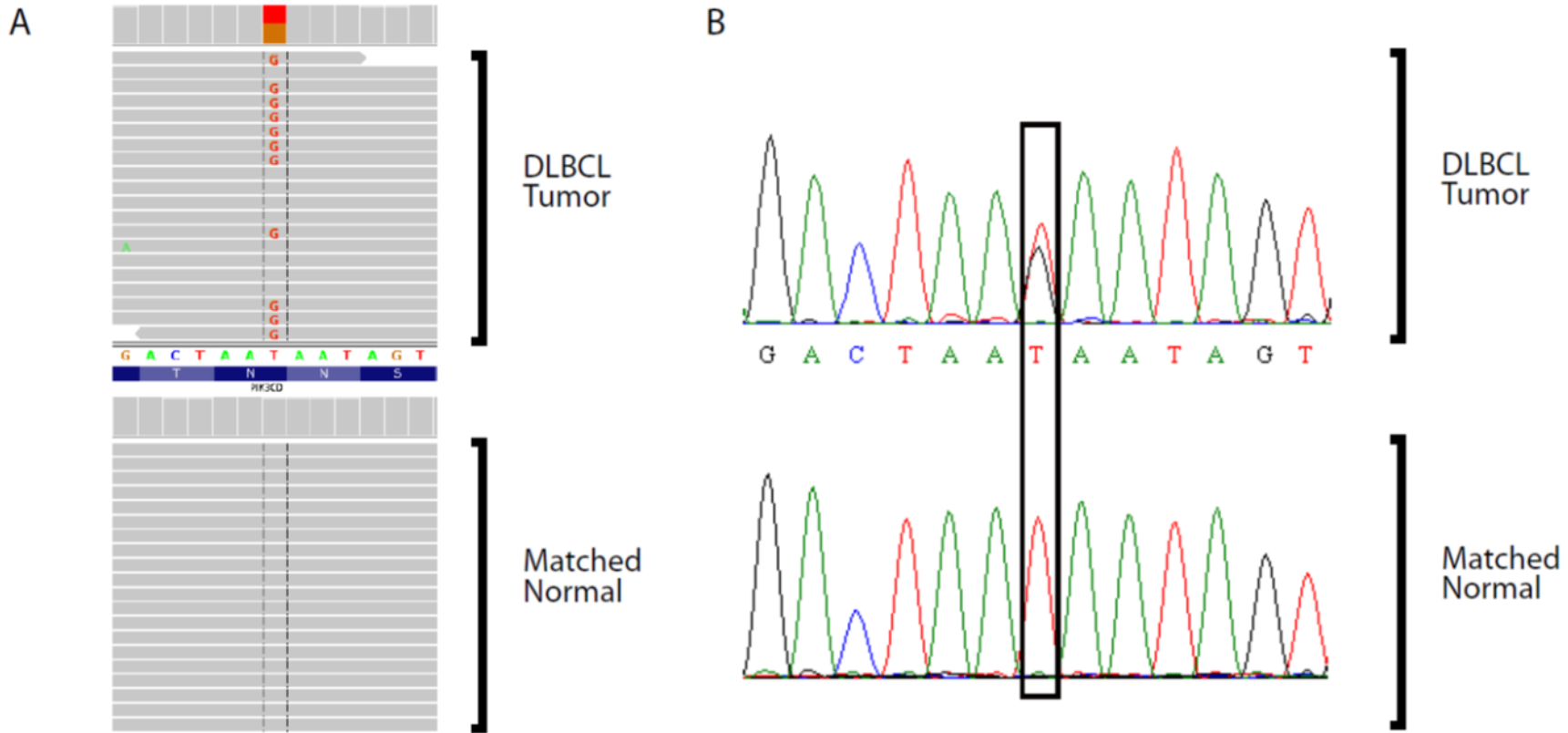


Conclusions and Future Directions

- ▶ Racial differences in the presentation of DLBCL
 - **Younger Age, More Advanced Stage, Shorter Survival**
- ▶ Racial differences present in other lymphomas
 - ▶ CLL/SLL, PTCL, FL, HL
- ▶ Additional studies are needed to explore etiology and prognostic significance

Whole Exome Sequence Analysis

Figure 4



Whole Exome Sequence Analysis

PNAS

Genetic heterogeneity of diffuse large B-cell lymphoma

Jenny Zhang^{a,b,1}, Vladimir Grubor^{a,1}, Cassandra L. Love^a, Anjishnu Banerjee^c, Kristy L. Richards^d, Piotr A. Mieczkowski^d, Cherie Dunphy^d, William Choi^e, Wing Yan Au^e, Gopesh Srivastava^e, Patricia L. Lugar^f, David A. Rizzieri^f, Anand S. Lagoo^f, Leon Bernal-Mizrachi^g, Karen P. Mann^g, Christopher Flowers^g, Kikkeri Naresh^h, Andrew Evensⁱ, Leo I. Gordon^j, Magdalena Czader^k, Javed I. Gill^l, Eric D. Hsi^m, Qingquan Liu^a, Alice Fan^a, Katherine Walsh^a, Dereje Jima^a, Lisa L. Smithⁿ, Amy J. Johnsonⁿ, John C. Byrdⁿ, Micah A. Luftig^f, Ting Ni^o, Jun Zhu^o, Amy Chadburn^l, Shawn Levy^p, David Dunson^c, and Sandeep S. Dave^{a,b,f,2}

^aDuke Institute for Genome Sciences and Policy, ^bDuke Cancer Institute and Department of Medicine, and ^cDepartment of Statistical Science, Duke University, Durham, NC 27710; ^dUniversity of North Carolina at Chapel Hill, Chapel Hill, NC 27599; ^eThe University of Hong Kong, Queen Mary Hospital, Hong Kong, China; ^fDuke University Medical Center, Durham NC 27710; ^gEmory University, Atlanta GA 30322; ^hImperial College, London, United Kingdom; ⁱUniversity of Massachusetts, Worcester, MA 01655; ^jNorthwestern University, Chicago IL 60208; ^kIndiana University, Indianapolis IN 46202; ^lBaylor University Medical Center, Dallas TX 75246; ^mCleveland Clinic, Cleveland, OH 44195; ⁿDivision of Hematology and Comprehensive Cancer Center, Ohio State University, Columbus, OH 43210; ^oGenetics and Development Biology Center, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD 20892; and ^pHudson Alpha Institute for Biotechnology, Huntsville, AL 35806

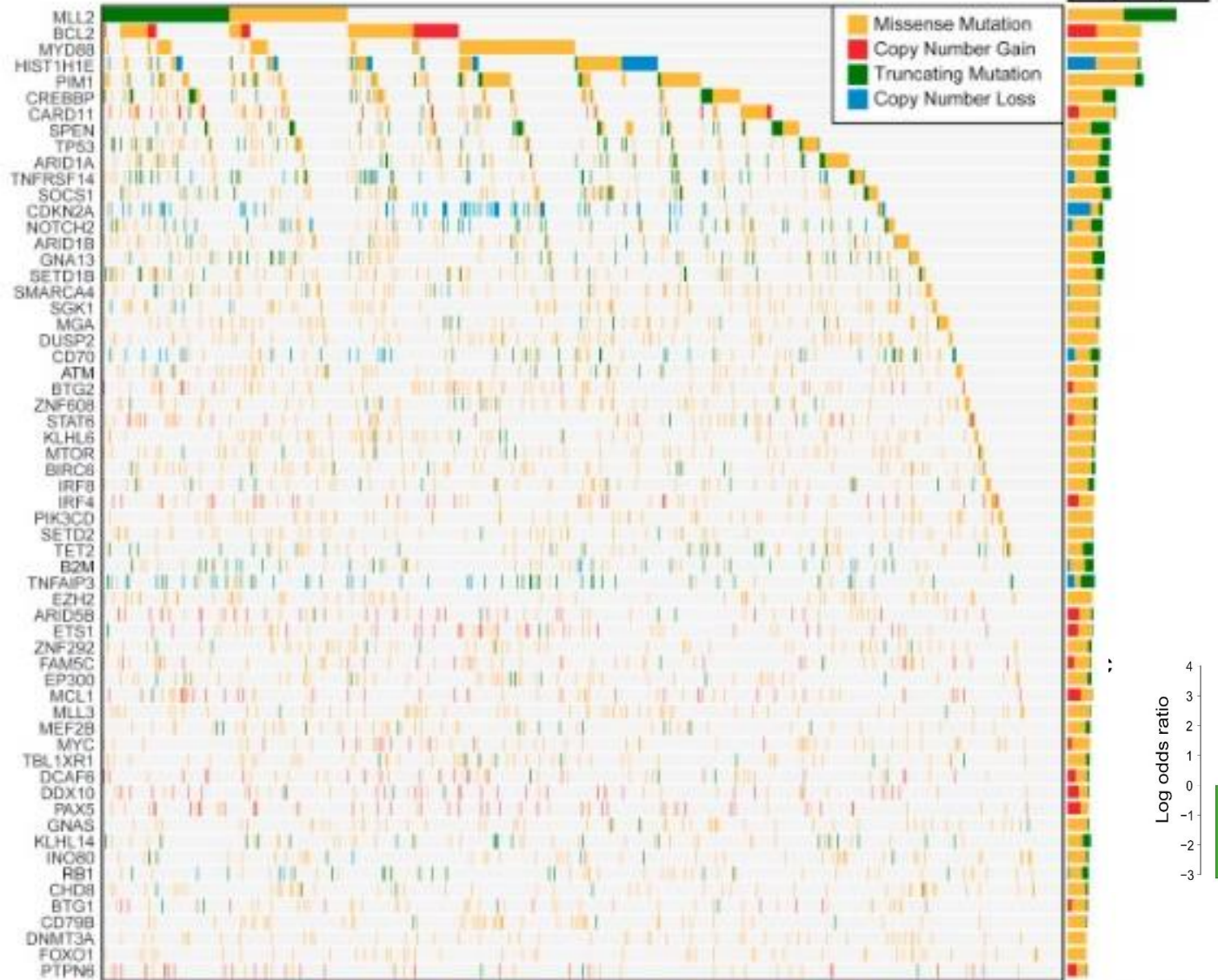
Edited* by Elliott Kieff, Harvard Medical School and Brigham and Women's Hospital, Boston, MA, and approved November 27, 2012 (received for review April 2, 2012)

Genetic and Functional Drivers of Diffuse Large B Cell Lymphoma

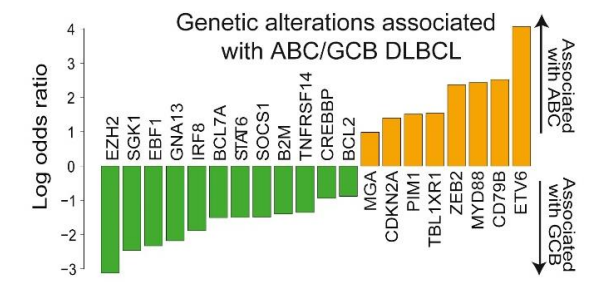
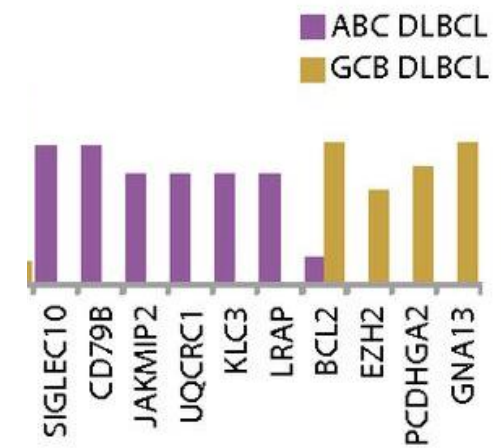


Anupama Reddy,^{1,2,22} Jenny Zhang,^{1,2,22} Nicholas S. Davis,^{1,22} Andrea B. Moffitt,^{1,22} Cassandra L. Love,¹ Alexander Waldrop,¹ Sirpa Leppa,³ Annika Pasanen,³ Leo Meriranta,³ Marja-Liisa Karjalainen-Lindsberg,³ Peter Nørgaard,⁴ Mette Pedersen,⁴ Anne O. Gang,⁴ Estrid Høgdal,⁴ Tayla B. Heavican,⁵ Waseem Lone,⁵ Javeed Iqbal,⁵ Qiu Qin,¹ Guojie Li,¹ So Young Kim,¹ Jane Healy,¹ Kristy L. Richards,⁶ Yuri Fedoriw,⁶ Leon Bernal-Mizrachi,⁷ Jean L. Koff,⁷ Ashley D. Staton,⁷ Christopher R. Flowers,⁷ Ora Paltiel,⁸ Neta Goldschmidt,⁸ Maria Calaminici,⁹ Andrew Clear,⁹ John Gribben,⁹ Evelyn Nguyen,¹⁰ Magdalena B. Czader,¹⁰ Sarah L. Ondrejka,¹¹ Angela Collie,¹¹ Eric D. Hsi,¹¹ Eric Tse,¹² Rex K.H. Au-Yeung,¹² Yok-Lam Kwong,¹² Gopesh Srivastava,¹² William W.L. Choi,¹² Andrew M. Evens,¹³ Monika Pilichowska,¹³ Manju Sengar,¹⁴ Nishitha Reddy,¹⁵ Shaoying Li,¹⁶ Amy Chadburn,¹⁷ Leo I. Gordon,¹⁸ Elaine S. Jaffe,¹⁹ Shawn Levy,²⁰ Rachel Rempel,¹ Tiffany Tzeng,¹ Lanie E. Happ,¹ Tushar Dave,¹ Deepthi Rajagopalan,¹ Jyotishka Datta,¹ David B. Dunson,²¹ and Sandeep S. Dave^{1,2,23,*}

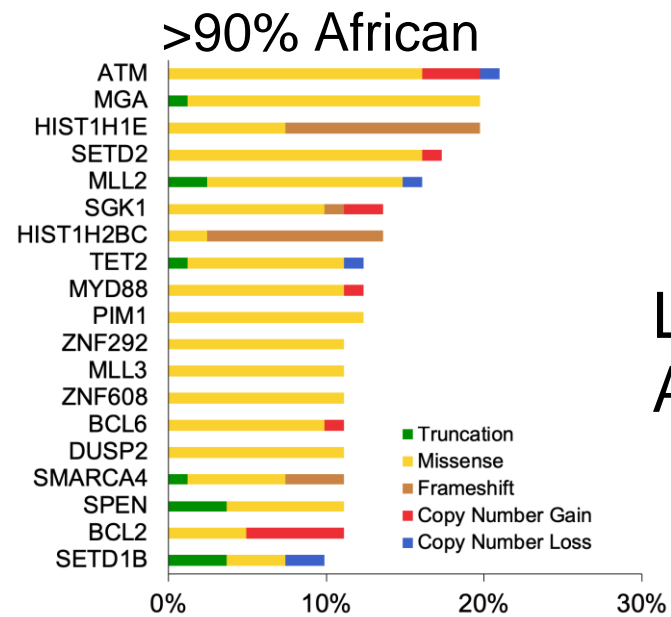
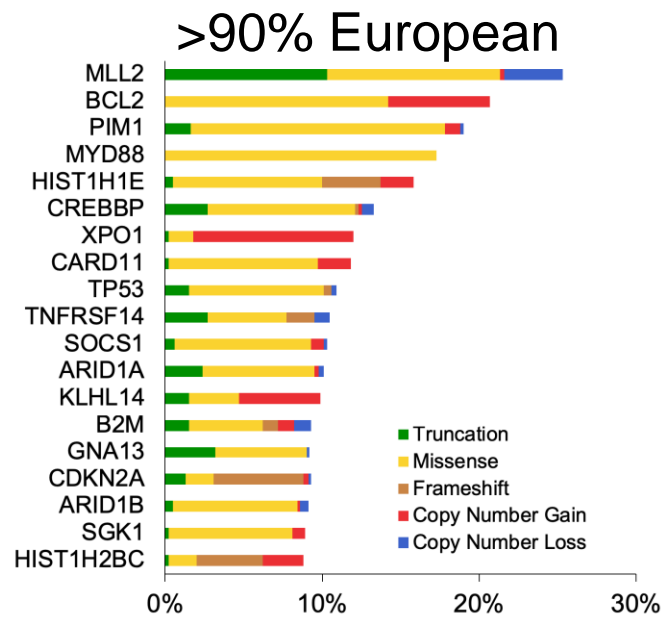
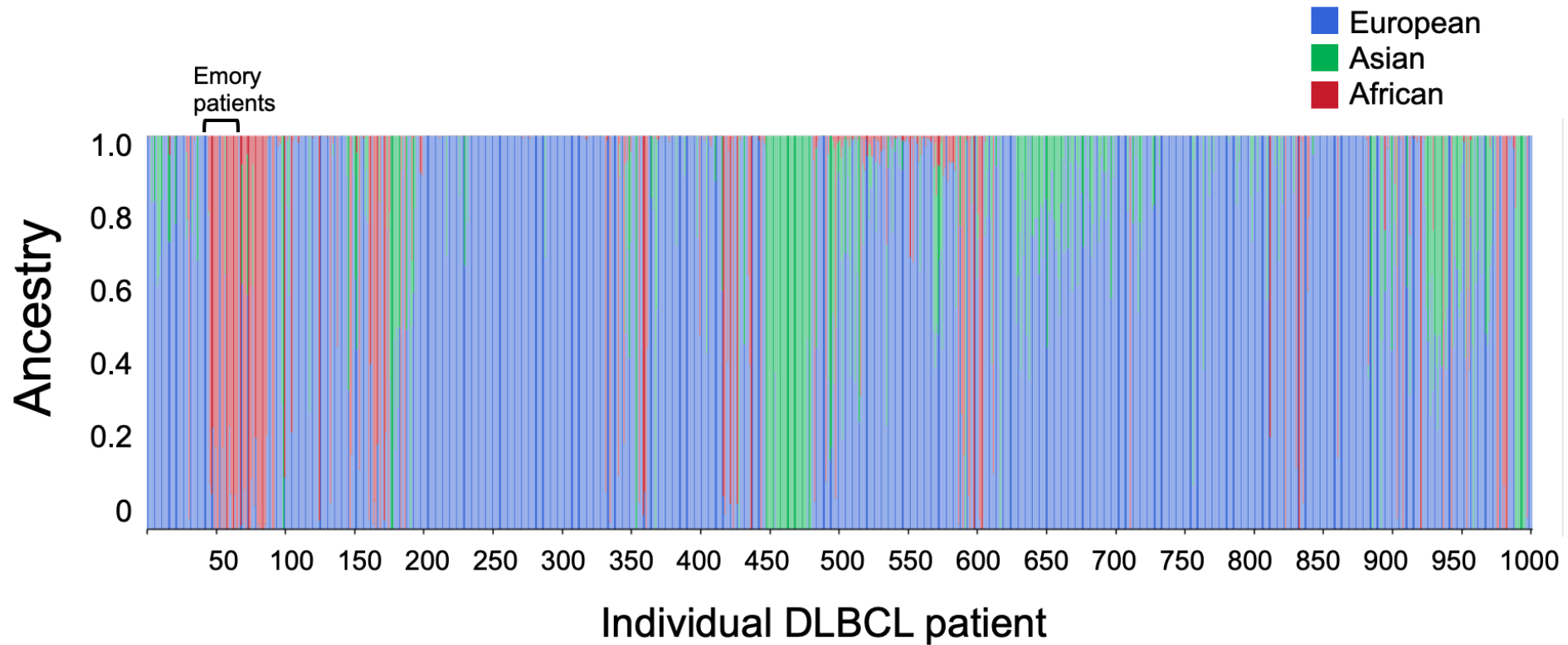
DLBCL Cases (N=1001)



DLBCL Genomics

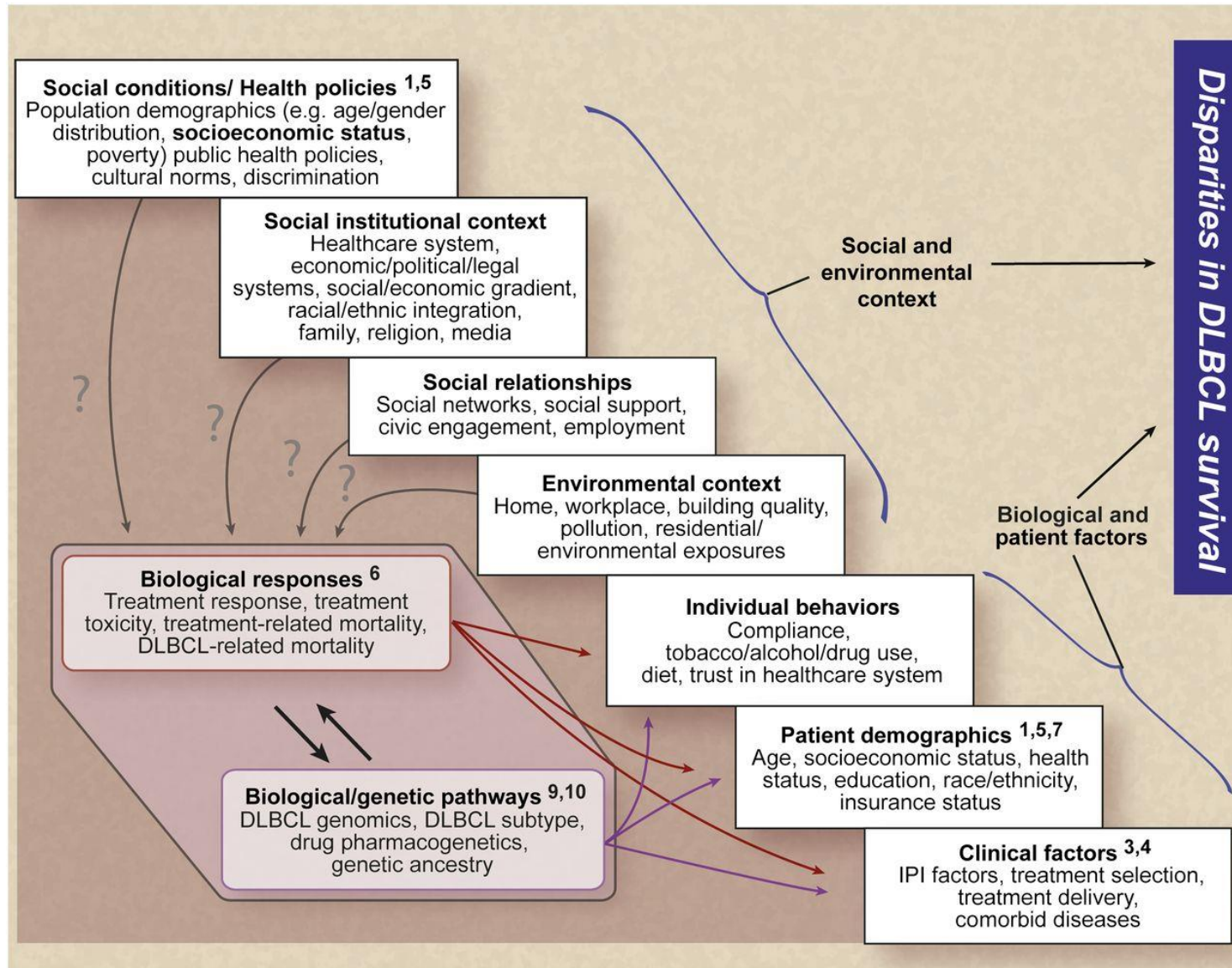


Reddy Cell 2017
Zhang PNAS. 2013



Lee *et al.*
AACR 2019

A framework for understanding the relationships between social, environmental, biological, and patient-related factors and disparities in DLBCL survival (numbers indicate example publications from the references that address specific factors).



Flowers CR , and Nastoupil LJ Blood 2014;123:3530-3531

Conclusions and Future Directions

- ▶ Racial differences in the presentation of DLBCL
 - **Younger Age, More Advanced Stage, Shorter Survival**
- ▶ Racial differences present in other lymphomas
 - ▶ CLL/SLL, PTCL, FL, HL
- ▶ Additional studies are needed to explore etiology and prognostic significance

- ▶ Georgia State Registry

- ▶ LEO Cohort Study

(U01 CA195568) **The Lymphoma Epidemiology of Outcomes Cohort Study**



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Chris Flowers MD, MS

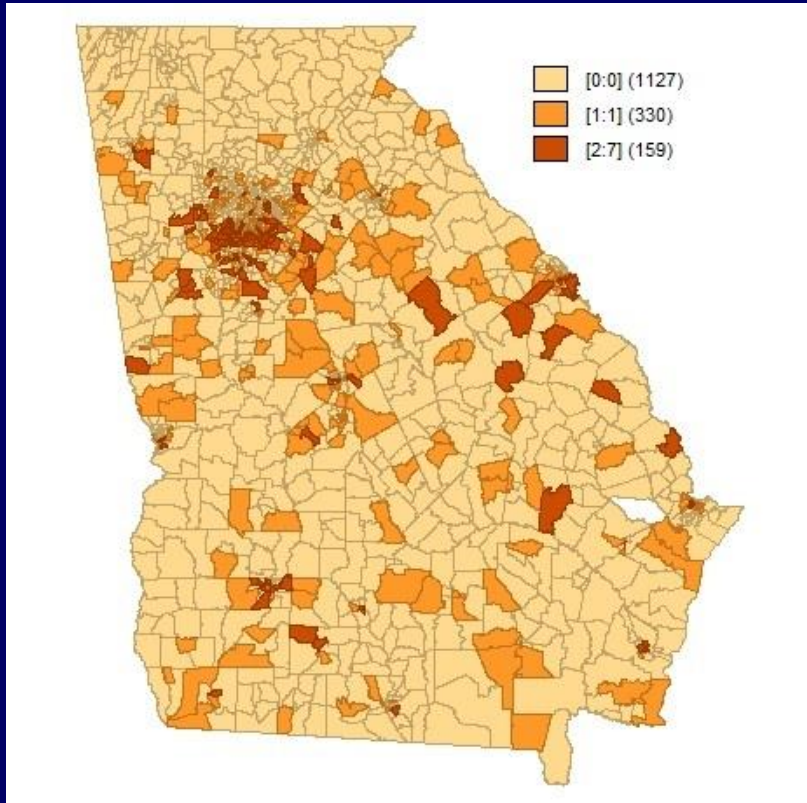
Jim Cerhan MD, PhD



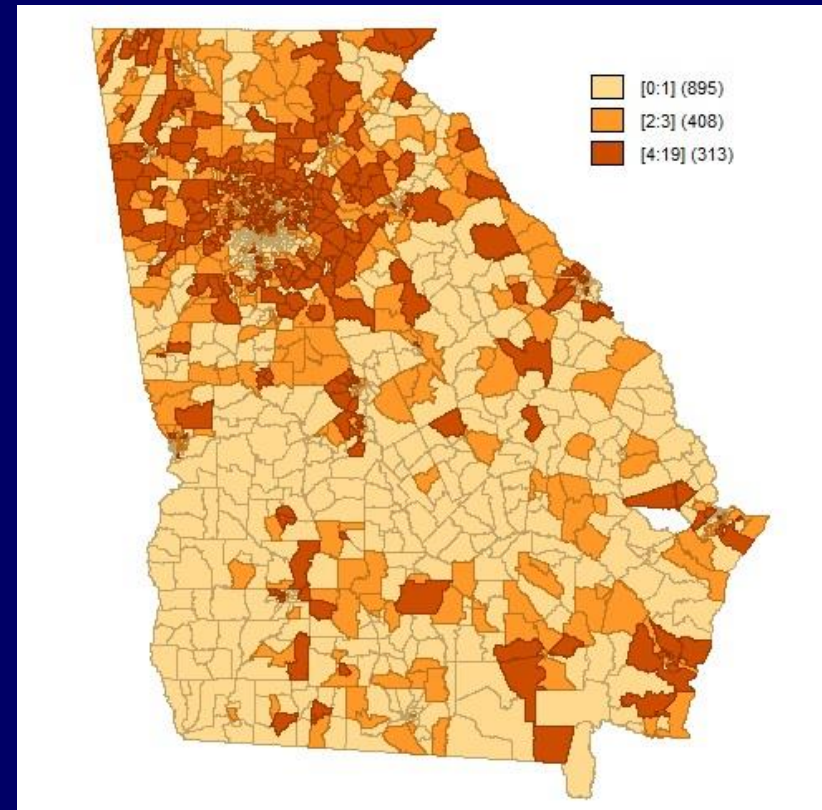
GOAL:
TO FACILITATE
RESEARCH
THAT USES
LEO
INFRASTRUCTURE AND
SUPPORTS
INTERACTION
WITH
LYMPHOMA
NCTN

- AIMS:**
- 1) Recruit 12,900 newly diagnosed NHL pts
 - including 3,600 DLBCL and 3,100 FL
 - 2) Build a NHL tumor bank w/ TMA, tumor DNA and RNA
 - 3) Central biorepository: PB, serum, plasma, DNA
 - 4) Collect clinical, epidemiologic, pathology and treatment data
 - 5) Prospectively follow patients for clinical and patient-reported outcomes

Racial Differences in DLBCL: Georgia



Black

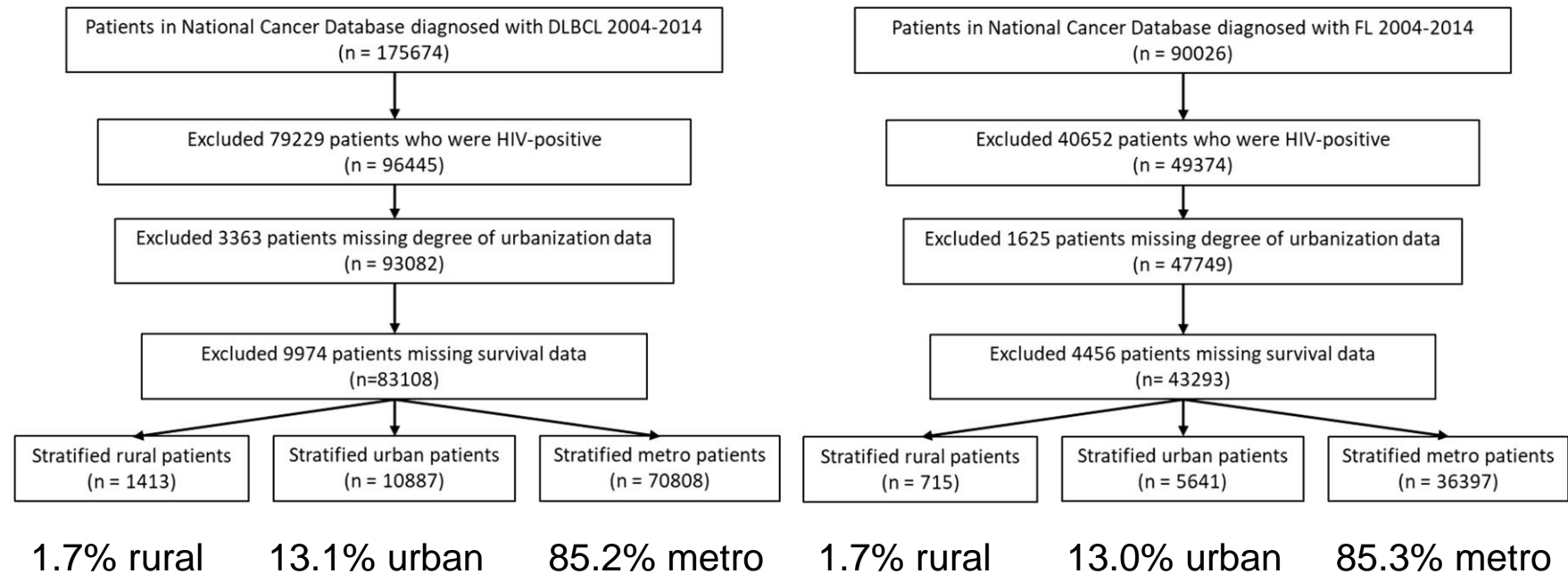


White

Rural and urban patients with DLBCL and follicular lymphoma have reduced overall survival: a National Cancer DataBase study.

Ritter AJ, Goldstein JS, Ayers AA, Flowers CR. Leuk Lymphoma. 2019 Jan 11:1-12

- National Cancer Data Base (NCDB)
 - National registry: American College of Surgeons and the American Cancer Society
 - >70% of all new cancer diagnoses in the US from >1,500 CoC-accredited hospitals
- Received treatment 2004-2014
 - **Rural:** counties with <2,500 people
 - **Urban:** 2,500+ people but NO metro areas of at least 50,000 urbanized people
 - **Metro:** urbanized population of at least 50,000 in county

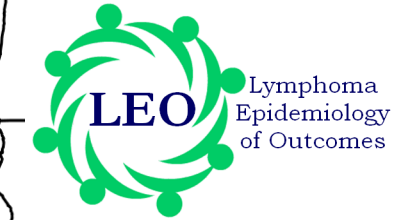
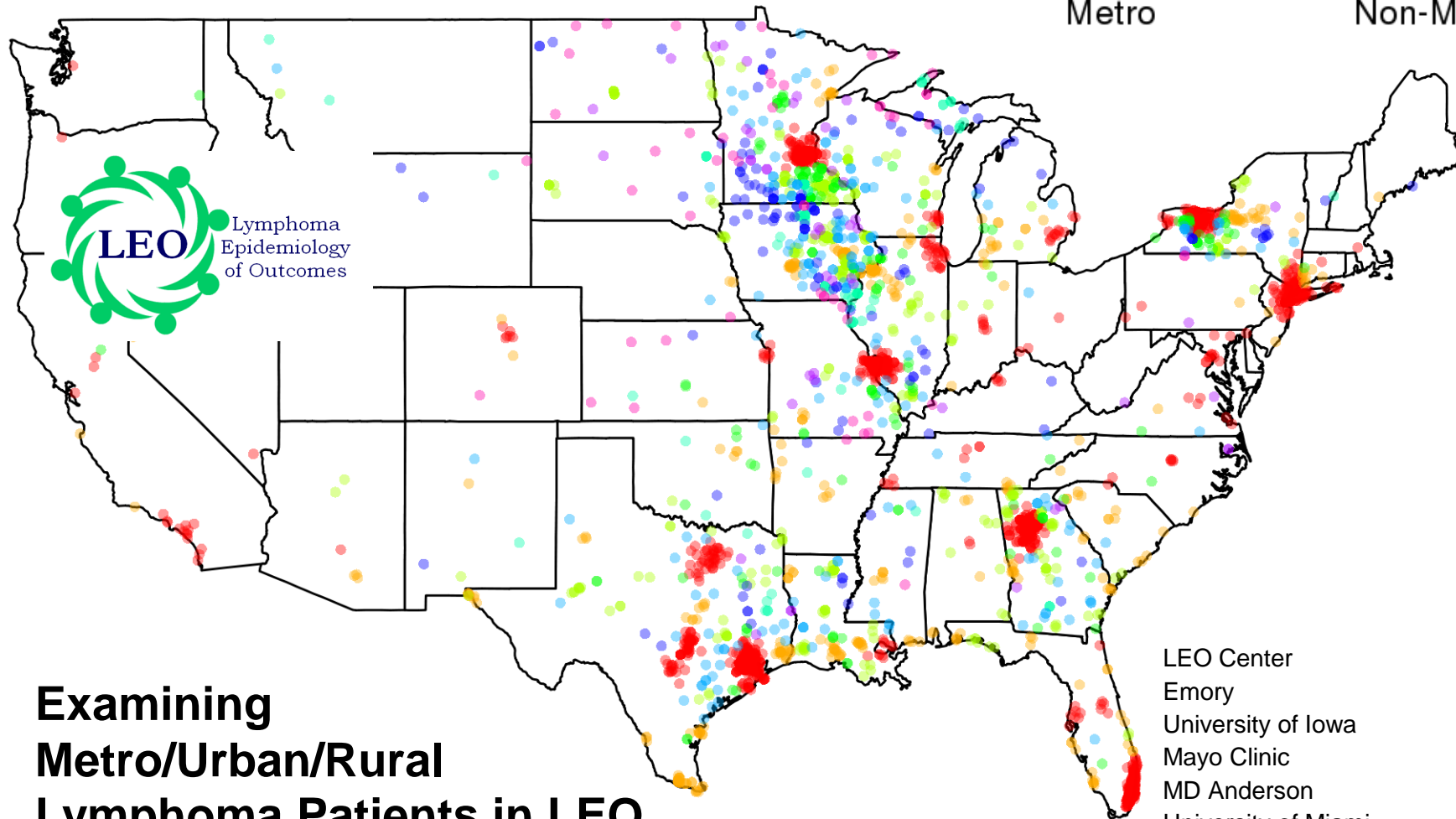


RUCC 2013



Metro

Non-Metro



Examining Metro/Urban/Rural Lymphoma Patients in LEO

LEO Center	n
Emory	330
University of Iowa	222
Mayo Clinic	736
MD Anderson	887
University of Miami	262
University of Rochester	310
Cornell University	272
Washington University	218



Emory Lymphoma Program

Program Goals:

To eliminate death and suffering from lymphoma

Physician Team:

- Chris Flowers



- Mary Jo Lechowicz



- Jonathon Cohen



- Leon Bernal-Mizrachi



- Jean Koff



- Pamela Allen

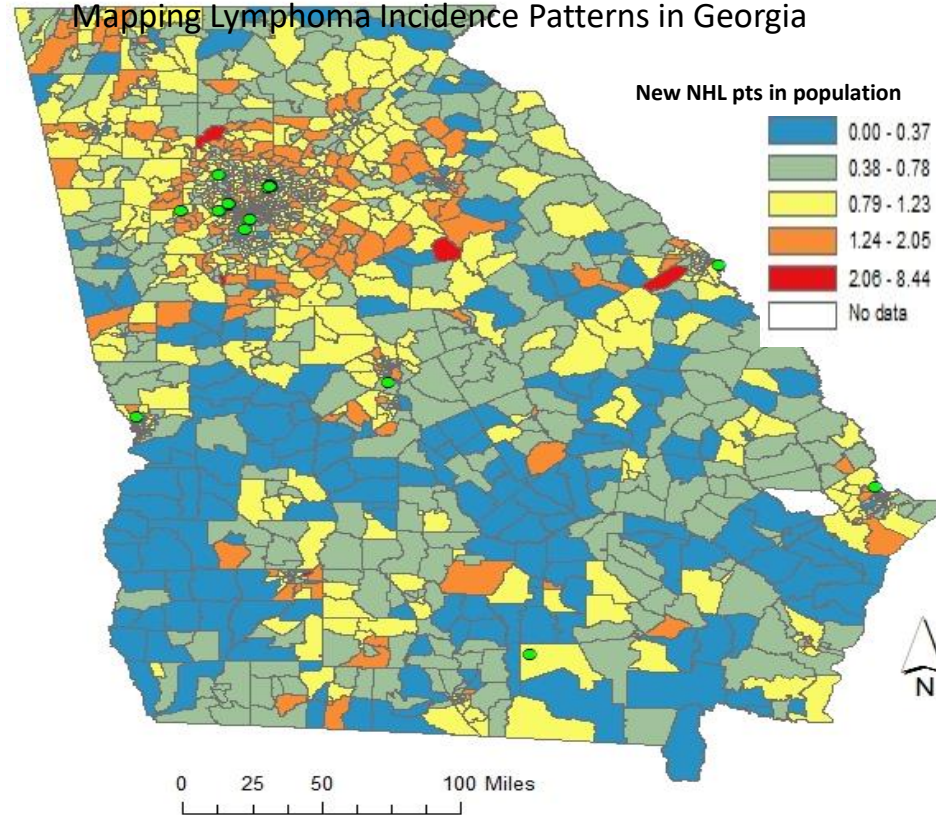


- Kristie Blum



**Winship CPC Pilot Grant
ACTSI Healthcare Innovation Grant**

Mapping Lymphoma Incidence Patterns in Georgia



U01 CA220401

K24 CA208132

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