21ST INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM™

Sociopolitical determinants of Hodgkin lymphoma outcomes

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Disclosures

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Brief agenda for today's talk

1. Racial/ethnic and socioeconomic disparities in Hodgkin lymphoma
   - Clinical trial data
   - Registry data
2. Ongoing efforts to understand mechanisms driving observed disparities

My goals today are to convince this audience that:

a) Outcome disparities remain an urgent issue even in our most treatable cancers

b) The only way to address disparities is to incorporate *social determinants of health* into the way we evaluate risk and provide care

Social determinants of health (SDOH)

SDOH: The conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes.

- Economic stability
- Education access and quality
- Healthcare access and quality
- Neighborhood and built environment
- Social and community context

Racism

A complex array of **social structures**, **interpersonal interactions**, and **shared beliefs** by which groups in power categorize people into socially constructed “races” to create a hierarchy in which minority groups are

1. **Disempowered**
2. **Devalued**, and
3. **Denied equal access to resources**

Structural racism

Operates through **laws** and **policies** that allocate resources away from members of racial and ethnic minority groups

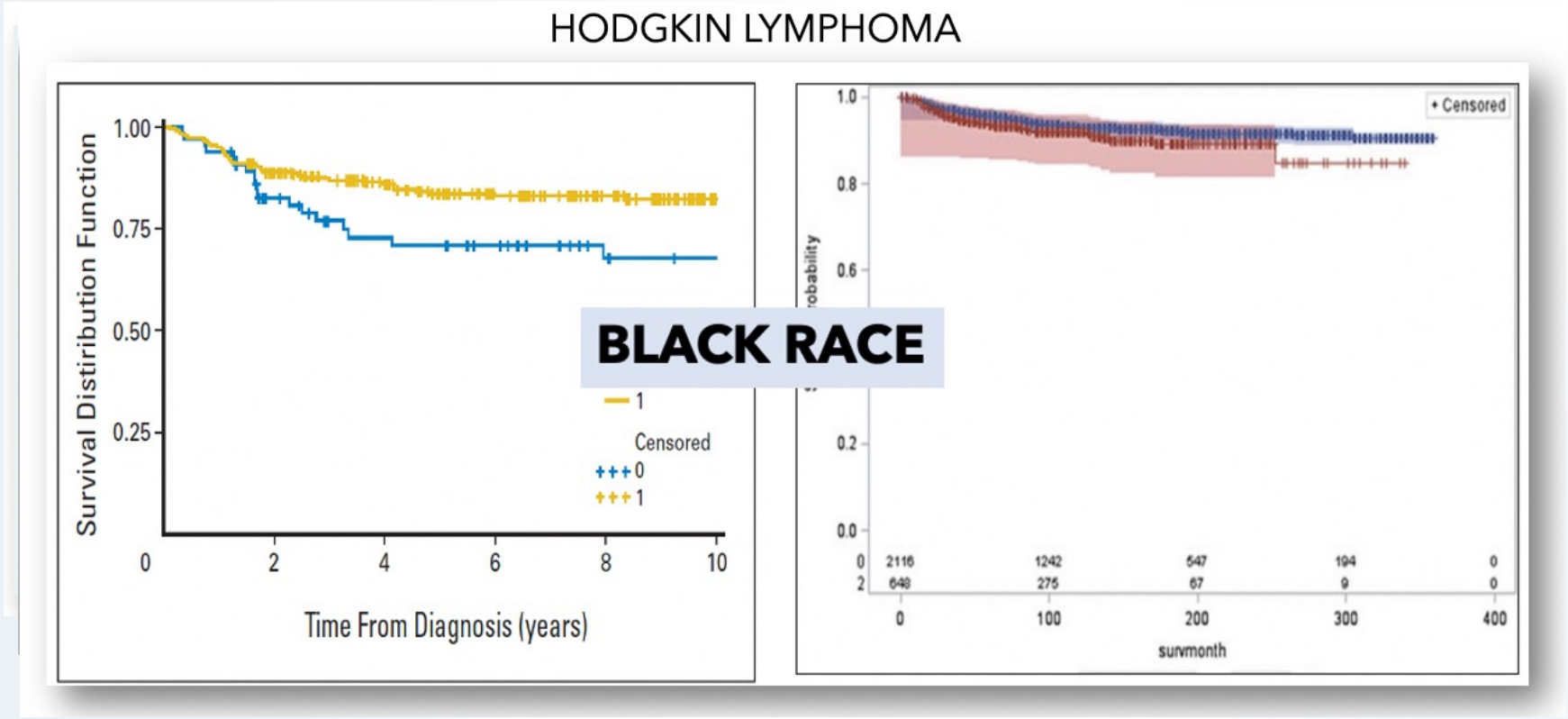
Encompasses macro-level social systems — housing, education, employment, criminal justice, healthcare — that interact to reinforce inequities across populations






Why disparities research?

Advances in childhood and adolescent cancer outcomes over the past 40 years are some of the most dramatic and successful in modern medicine



Hunger et al, NEJM, 2005; 2008; Bona et al, PBC, 2016; Bona et al JNCI 2020; Kahn et al, PBC, 2018

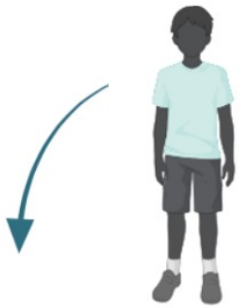
HEALTHCARE ↔ ECONOMICS ↔ EDUCATION ↔ ENVIRONMENT ↔ COMMUNITY

Discriminatory policies, historic and contemporary racism

COMMUNITY SOCIAL STRUCTURE
- INCOME INEQUALITY
- RACIAL RESIDENTIAL SEGREGATION
- AREA DEPRIVATION

GEOGRAPHIC LOCATION
- PROXIMITY TO CARE
- TRANSPORTATION
- TRAVEL TIME

Race
Ethnicity
Gender
Disability
Ancestry



Language
Literacy
Family history

Diagnosis and presentation

- Insurance
- Household material hardship
- Presenting location
- Referrals
- Delay in diagnosis
- Health beliefs
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- Mistrust
- Discrimination

Up-front therapy

- Stage
- Acuity
- Location of care
- Clinical trial
- Chemotherapy
- Radiation
- Immunotherapy
- Toxicities
- Supportive care
- Psychosocial support

Post-therapy follow-up

- Salvage
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- Transplantation
- Survivorship
- Palliative care
- Late effects

SURVIVAL

Hodgkin lymphoma (HL): Highly treatable cancer

~10,000 new cases annually

- Most common cancer in adolescent/young adult (AYA; 15 – 39 years)
- 5-year event-free survival (EFS) ~ 85%; overall survival (OS) > 95%

Improvements in HL outcomes in recent decades attributed to:

1. Research to identify disease-related predictors of poor outcome
2. Personalized use of risk-directed, response-adapted, combined-modality therapy (chemotherapy, immunotherapy, radiation)
3. Sequential therapeutic trials to inform and advance the standard-of-care

Despite excellent outcomes, disparities persist

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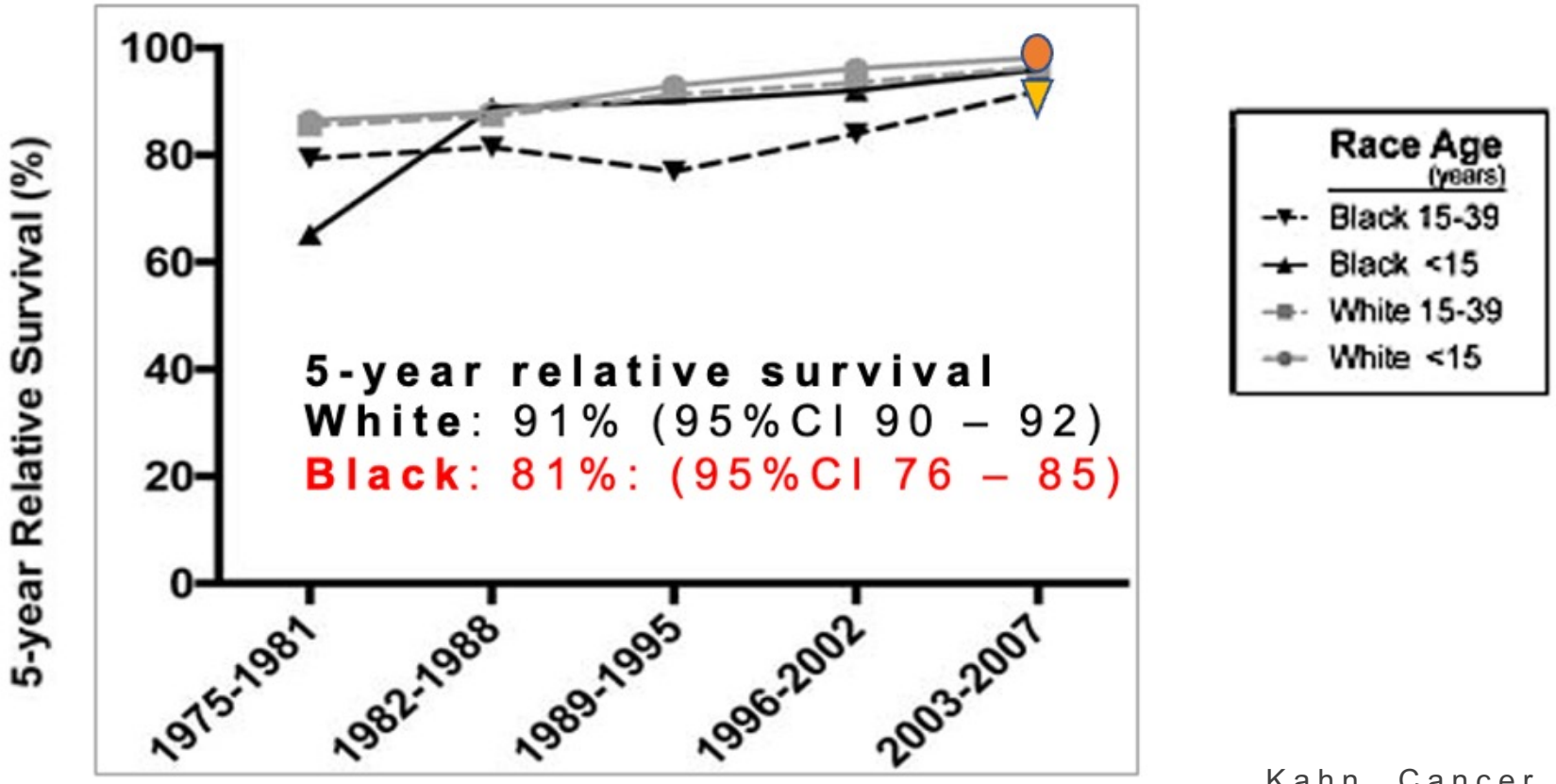
SEER analysis:
HL survival from 1975 – 2017 (N= 15,107)



Kahn, Cancer, 2016

Clinical trials data can address some limitations

Study #1: Are disparities observed among children and adolescents treated for HL on cooperative group clinical trials?

Hypothesis: In the absence of different biology, equal access to clinical trials may mitigate racial/ethnic differences reported at population level.

Cohort and approach

Pooled analysis of patient-level data from three phase 3 Children's Oncology Group (COG) trials (2002 – 2012)

Patients 1 – 21 years with *de novo* HL (N = 1,605)

- Low, intermediate, high-risk

Race/Ethnicity: As reported to COG by study sites

- Non-Hispanic White (NHW)
- Non-Hispanic Black (NHB)
- Hispanic

Categorized *a priori* to reflect groups impacted by structural racism in the U.S.

Outcomes:

- Event-free survival: Relapse, second cancer, death from any cause
- Overall survival

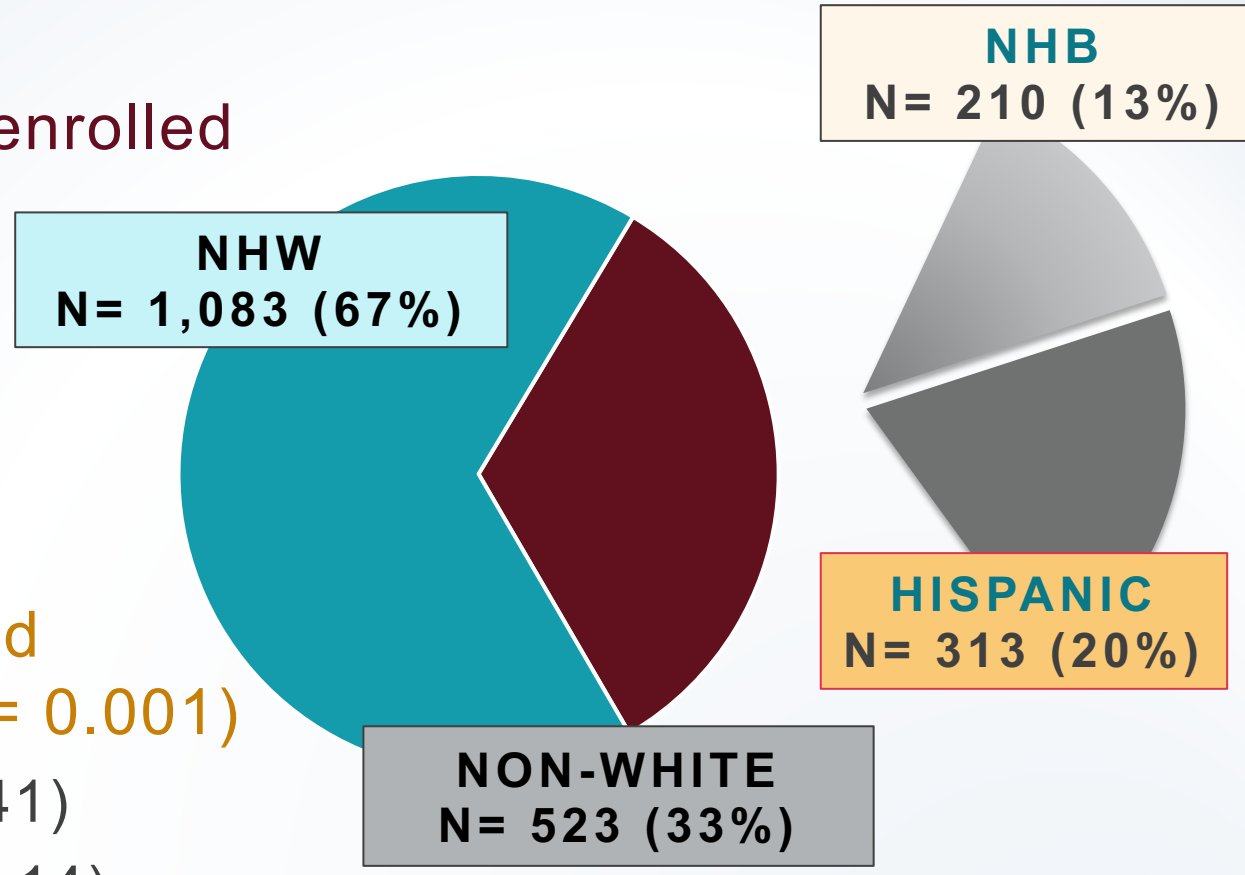
Results: Baseline characteristics

Between 2002 and 2012: N= 2,155 enrolled

N= 1,606 (75%) included

Sex: N= 825 male (53%)

Mean Age: 14.6 (± 3.5) years



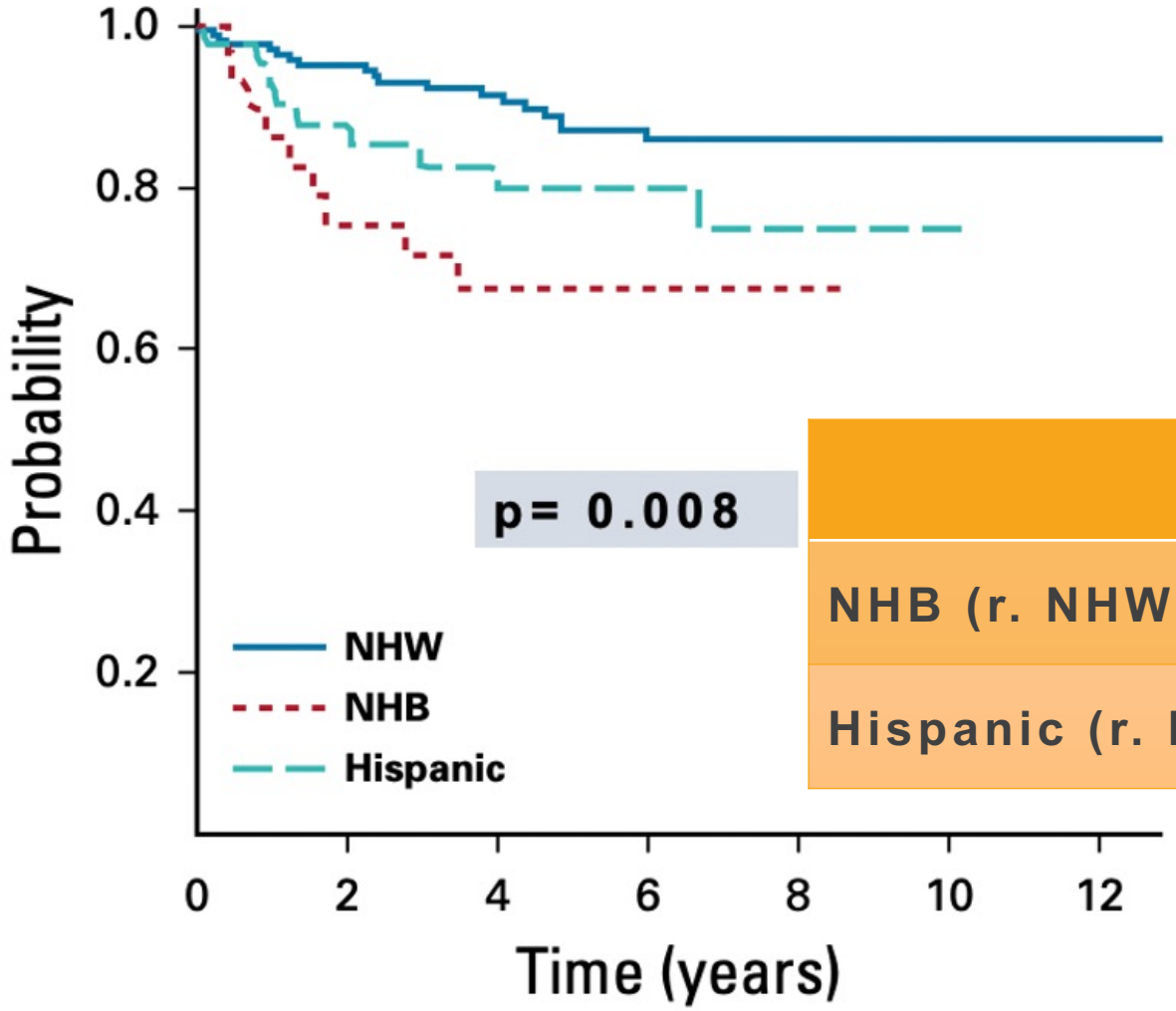
Stage: Higher proportion of Black and Hispanic patients with stage III/IV (p= 0.001)

- No difference in **B-symptoms** (p= 0.41)
- No difference in **bulky disease** (p= 0.14)
- No difference in **receipt of radiation** (p= 0.32)

5-year EFS and OS (Median f/u = 6.9 years)

	HR	(95% CI)	p-value
Non-White (r. NHW)	**1.9**	**1.1 – 3.3**	**0.031**
MC Histology (r. NS)	1.1	0.3 – 3.8	0.980
Stage I/II (r. Stage IV)	0.8	0.4 – 1.9	0.800
Stage III (r. Stage IV)	0.7	0.3 – 1.9	
No B-Symptoms (r. Yes)	0.4	0.2 – 0.7	0.004
No Bulk Disease	0.5	0.3 – 1.1	0.180
No Radiation	0.9	0.5 – 1.8	0.760

Post-relapse survival (N = 262; f/u 4.5 years)



87% (NHW)

80% (Hispanic)

67% (NHB)

	HR	(95% CI)	p-value
NHB (r. NHW)	3.5	1.5 – 8.2	0.005
Hispanic (r. NHW)	2.7	1.2 – 6.2	0.018

Kahn et al, JCO, 2019

Summary and limitations

Among patients enrolled on phase 3 clinical trials for newly diagnosed HL, relapse/EFS does not differ by race/ethnicity.

- *However:* In the subgroup with relapsed disease, Black and Hispanic patients were up to 3.5 times more likely to die than White patients.

Limitations of these data

- Classification of race/ethnicity not exclusively self-report
- Minimal individual-level data on socioeconomic position (income, wealth, education)
- Unable to examine details of therapy beyond up-front setting
- No addresses → No neighborhood data or SDOH

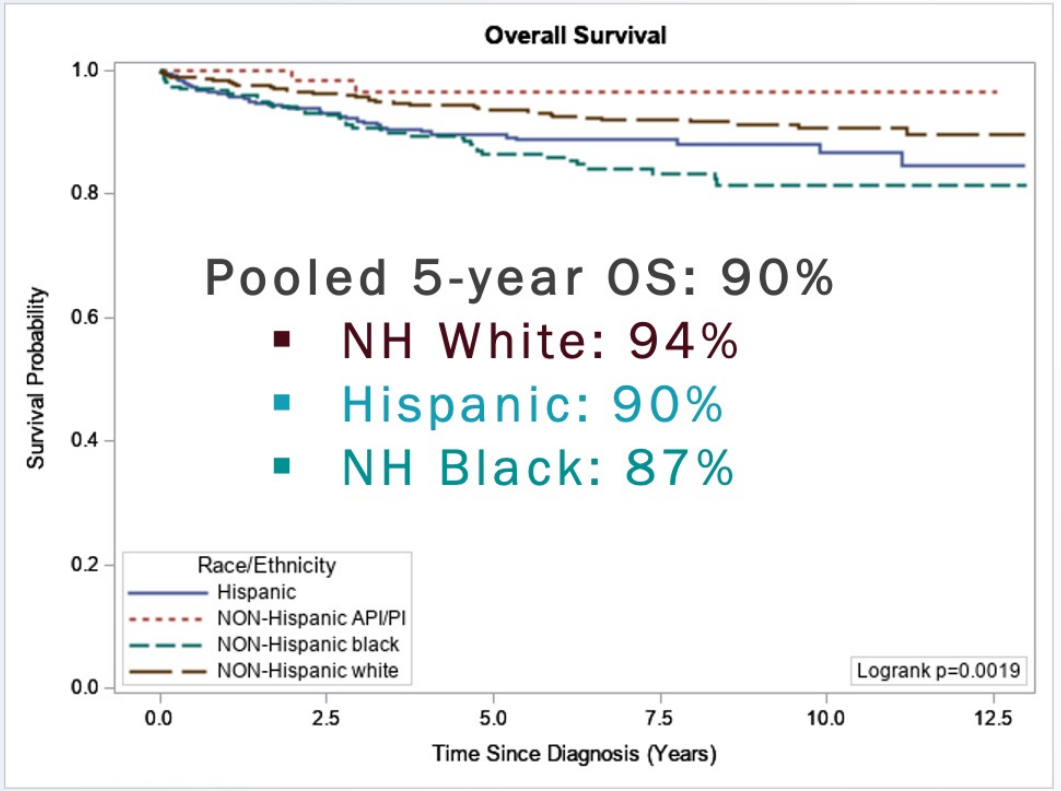
Clinical trials cohorts are subject to selection bias → What is happening in the ”real world?”

Knowledge gap: Real-world care and outcomes?

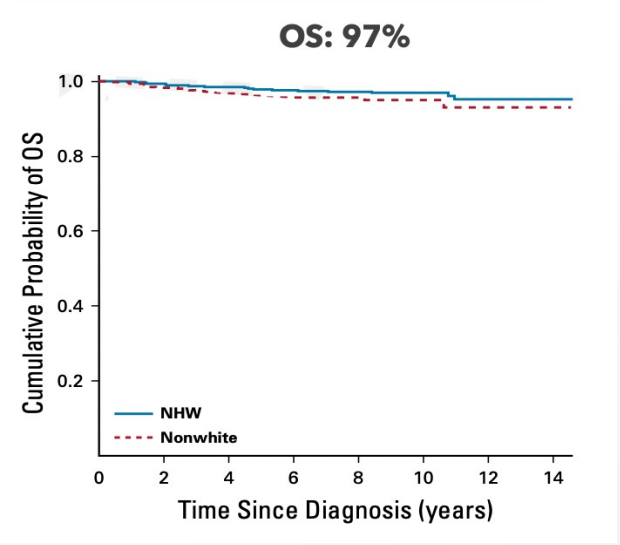
Study #2: **Registry data**
Racial Disparities in Children, Adolescents, and Young Adults with Hodgkin Lymphoma Enrolled in the New York State Medicaid Program

Kahn et al, JAYAO, 2021

N=1,231 Medicaid, <1 – 39y, median f/u 6.6 years



Reminder!
OS in COG = 97%



No. at risk		3 year	5 year	7 year	10 year
NHW	571	476	376	283	132
NH Black	276	224	171	117	45
Hispanic	323	273	204	140	64
NH A/PI	61	50	37	26	11

Multivariable models for survival

Overall survival		HR	95% CI		p-value
Race/ethnicity (v. NH White)					
	NH Black	1.58	1.02	2.46	0.042
Stage (vs. I/II)					
	Stage III/IV	1.86	1.25	2.78	0.002

HL-specific survival		HR	95% CI		p-value
Location of care (R: NCI-affiliate)					
	Non-NCI or COG affiliate	2.71	1.47	4.98	0.001

Adjusted for: Age, sex, race/ethnicity, disease characteristics, Medicaid enrollment status, neighborhood SES, **chemotherapy regimens based on NCCN guidelines,** RT

Kahn et al, JAYAO, 2021

Adjusted models for advanced stage and location of care

AYA age → higher odds of **treatment at non-NCI cancer center**

Odds of treatment at NCI or COG-affiliate				
	OR	95% CI		p-value
Age, y (R: <1 – 14 y)				
15 – 19 y	0.4	0.2	0.8	0.006
20 – 29 y	0.2	0.1	0.3	<0.001
30 – 39 y	0.1	0.1	0.3	<0.001

Black or Hispanic race/ethnicity → higher odds of **advanced stage**

Odds of stage III/IV disease				
Race/ethnicity (R: NH White)	OR	95% CI		p-value
NH Black	1.6	1.2	2.2	0.002
Hispanic	1.5	1.1	1.9	0.013

Kahn et al, JAYAO, 2021

NYSCR + Medicaid summary

Within cohort of Medicaid-insured children and AYAs with HL:

1. Overall survival ~ 6 – 7 percentage-points lower than national average
2. Black patients → 60% more likely than White patients to die
3. Non-NCI location-of-care → worse HL-specific survival
4. Black and Hispanic race/ethnicity → higher odds of late stage
5. AYA age → lower odds of treatment at NCI cancer center

Factors beyond insurance are contributing to disparate outcomes in socially vulnerable children and AYAs with lymphoma.

Question #1:

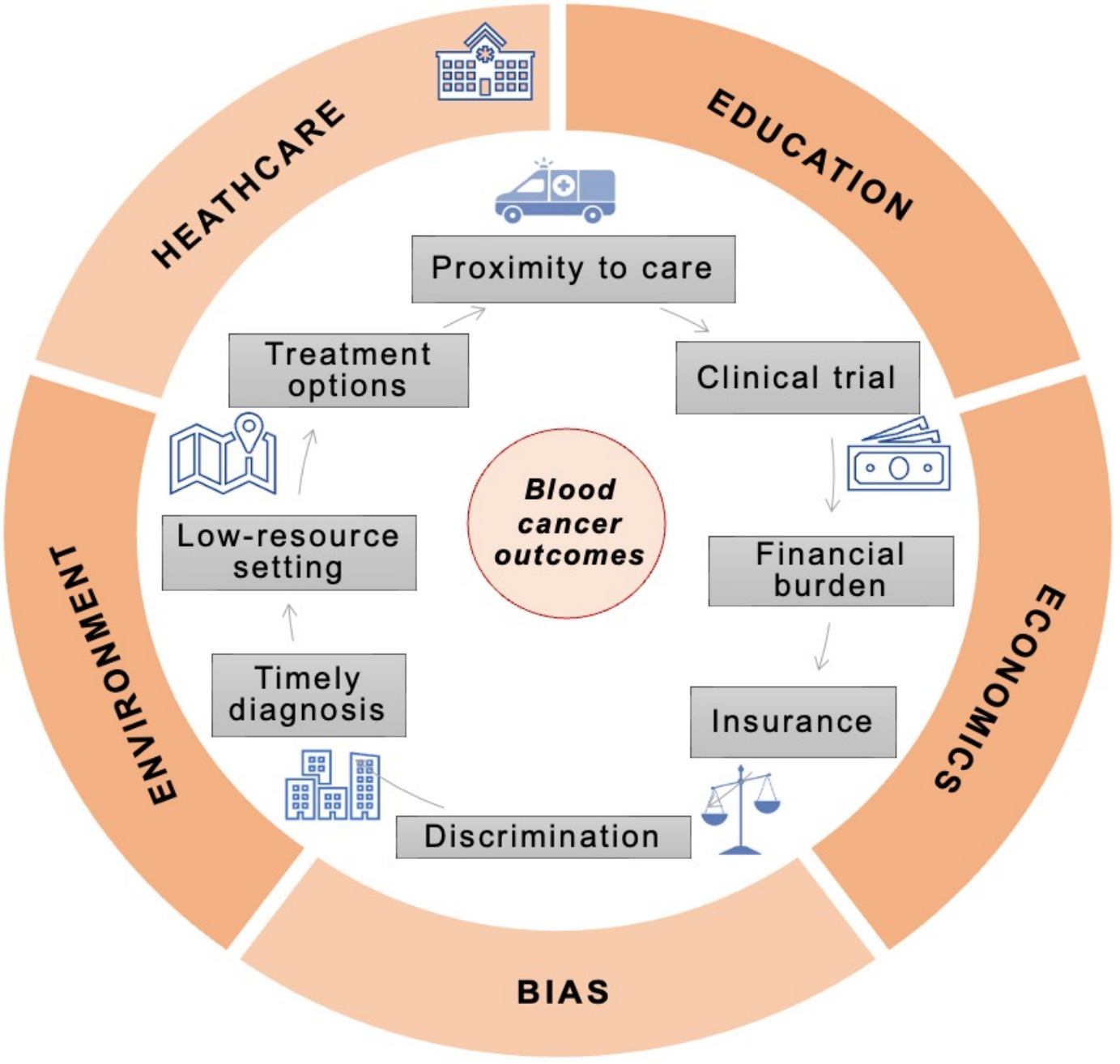
What factors are driving the relationships between race/ethnicity and survival?

Proposed mechanism #1:

Unmeasured exposures (SDOH) and patient-level factors impacting access-to-care

Concept map

Potential mechanisms through which ***access to care*** may mediate the effects of SDOH on lymphoma outcomes.



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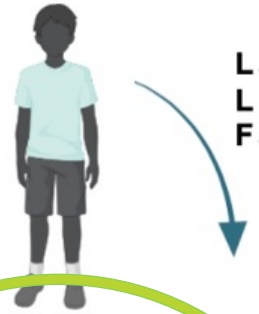

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SURVIVAL

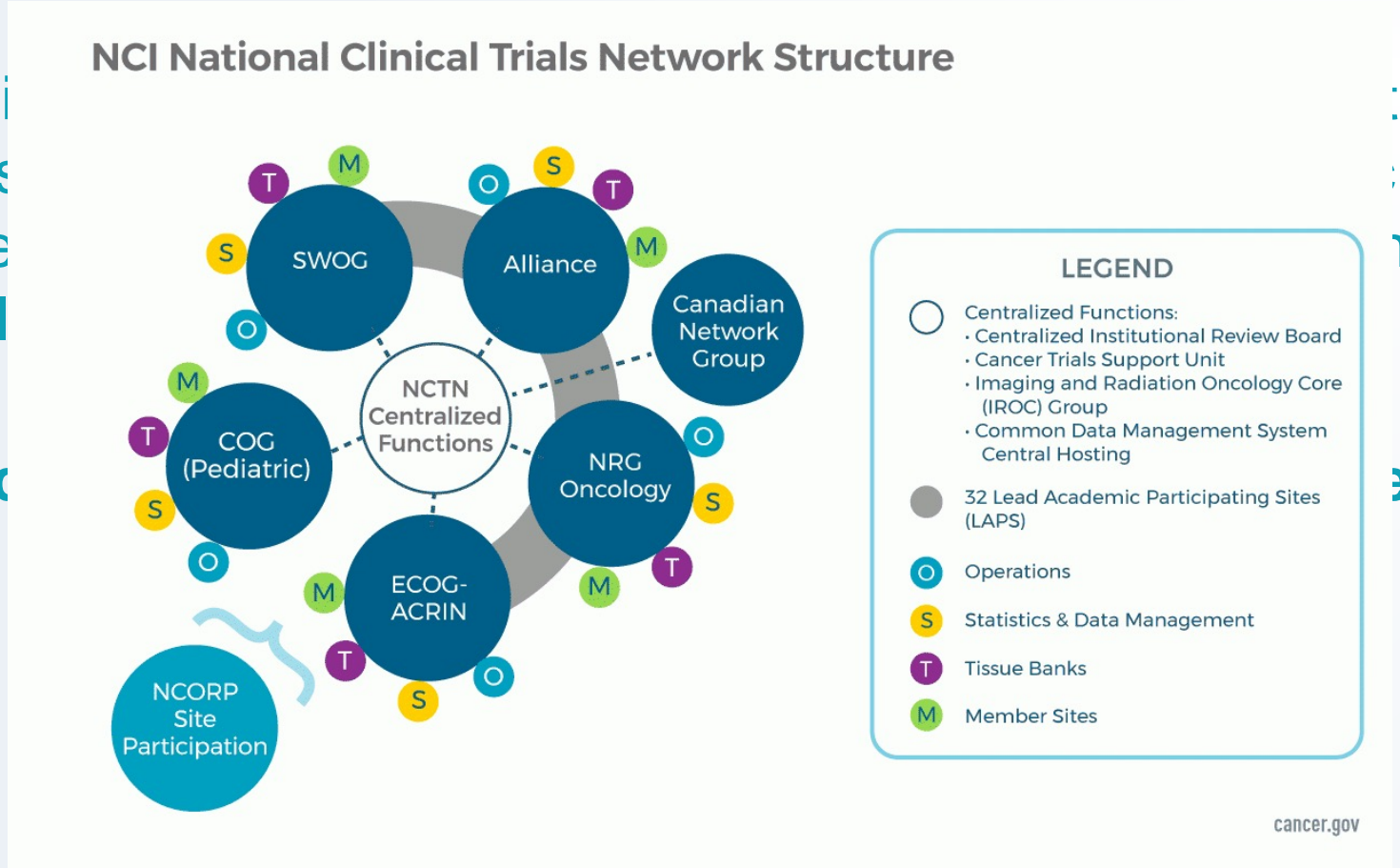
Big picture questions

1. **What are the potential mechanisms linking race/ethnicity to outcomes?**
    1. Variations in disease or host biology?
    2. Non-biologic factors impacting care?
    3. Combination of the two?
2. **What data do we need to answer these questions?**
    1. Ancestry, treatment tolerability, chemo-immunotherapy sensitivity
    2. Some measures of access, multilevel SDOH, language, literacy
    3. Systematically collected long-term follow-up data
    4. Treatment data for patients with relapsed/refractory disease

Definitions: The NCTN

The NCI-Nati ion of
organizations ancer clinical
trials at more nada, and
internationall

NCTN provic ent and clinical trials.



This infrastructure is **built** for the sole purpose of collecting and analyzing longitudinal, patient-level data and outcomes

*RHETORICAL!

An opportunity….

The question*: Can we leverage the cooperative group infrastructure to change how we study and address disparities?

The proposal: Integrate disparities questions into efficacy questions prospectively; collect the data necessary to understand mechanisms

The plan:

1. **Collect the pre-diagnosis data:** Standardize (*and normalize)* collection of demographic and social determinants data
   - Bank these data and use them to annotate clinical outcomes
2. **Evaluate biomarkers** associated with outcome in systematically under-studied populations
3. **In populations of interest, measure survival <u>prospectively</u>**
4. **Build capacity for long-term follow-up in hard-to-reach populations**

Laying foundation for disparities research across NCTN

In COG we are pushing to include hypothesis-driven correlative science questions in NCI-sponsored clinical trials

Below studies include baseline collection of demographic and SDOH data either with or without associated study objectives

- AHOD2131: Outcomes by race/ethnicity adjusting for SDOH
- ANBL1531: Impact of *Household Material Hardship (HMH)* on outcomes
- AALL1731: Trajectory of HMH over time
- ASCT2031: Baseline collection for banking

We still have a ways to go…more to come next year

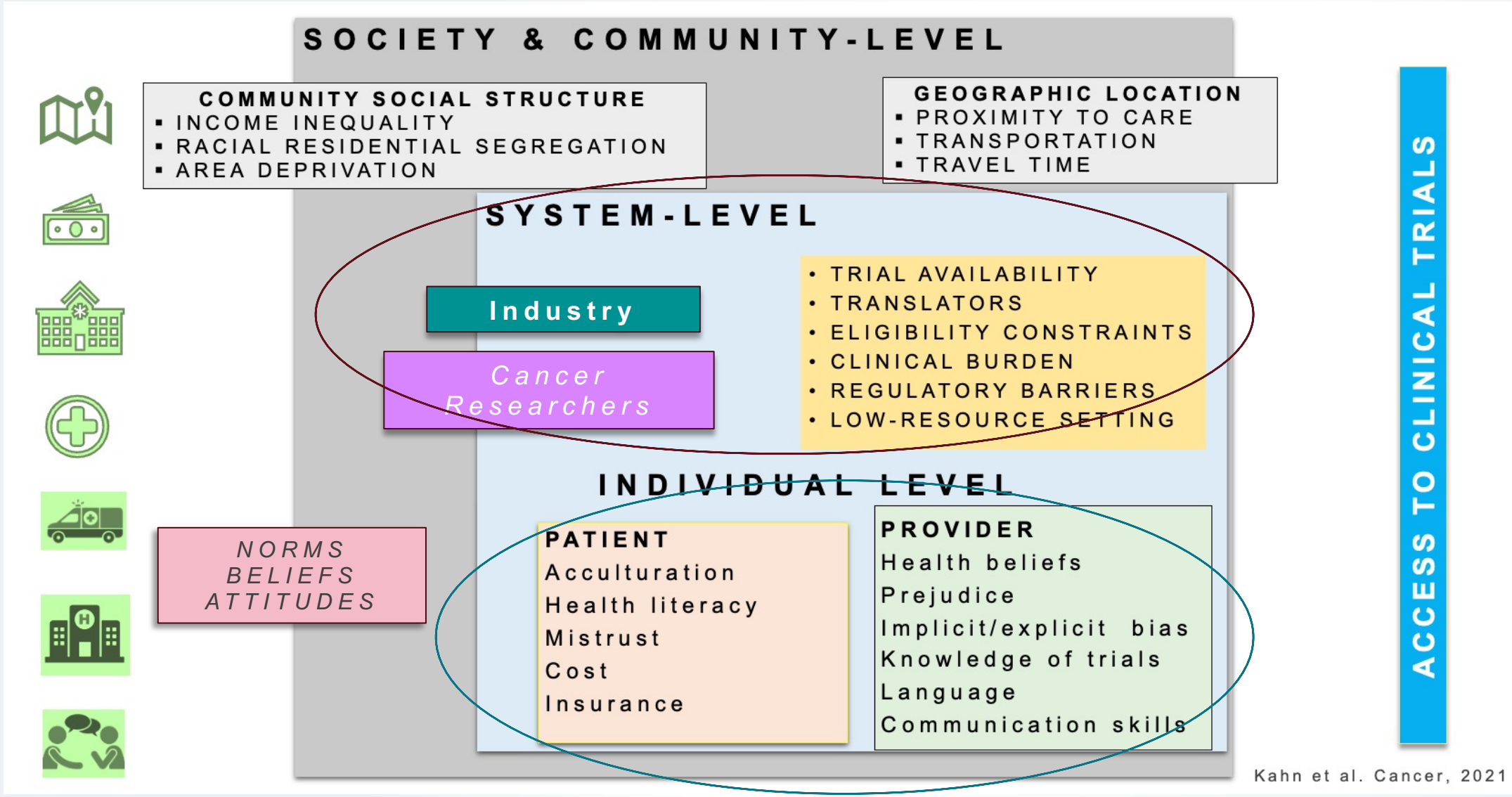
Question #2:

What is driving observed differences in overall survival?

Proposed mechanism #2:

System-level barriers to salvage trials and novel agents

What influences clinical trial participation?



Embedding inequity into racialized policies over time

Inequitable systems of care result from historic and contemporary racism operating at multiple levels

RACISM

1930s: State-sponsored segregation

- ***Redlining:*** *Denial of mortgages based on "neighborhood" (systemic)*
- ***Lending bias:*** *Denial of loans based on race (individual)*

STRUCTURAL → Under-resourced neighborhoods

1946: Federal Hospital Survey & Construction Act: Mandates access for "all," but **funds construction of segregated facilities**

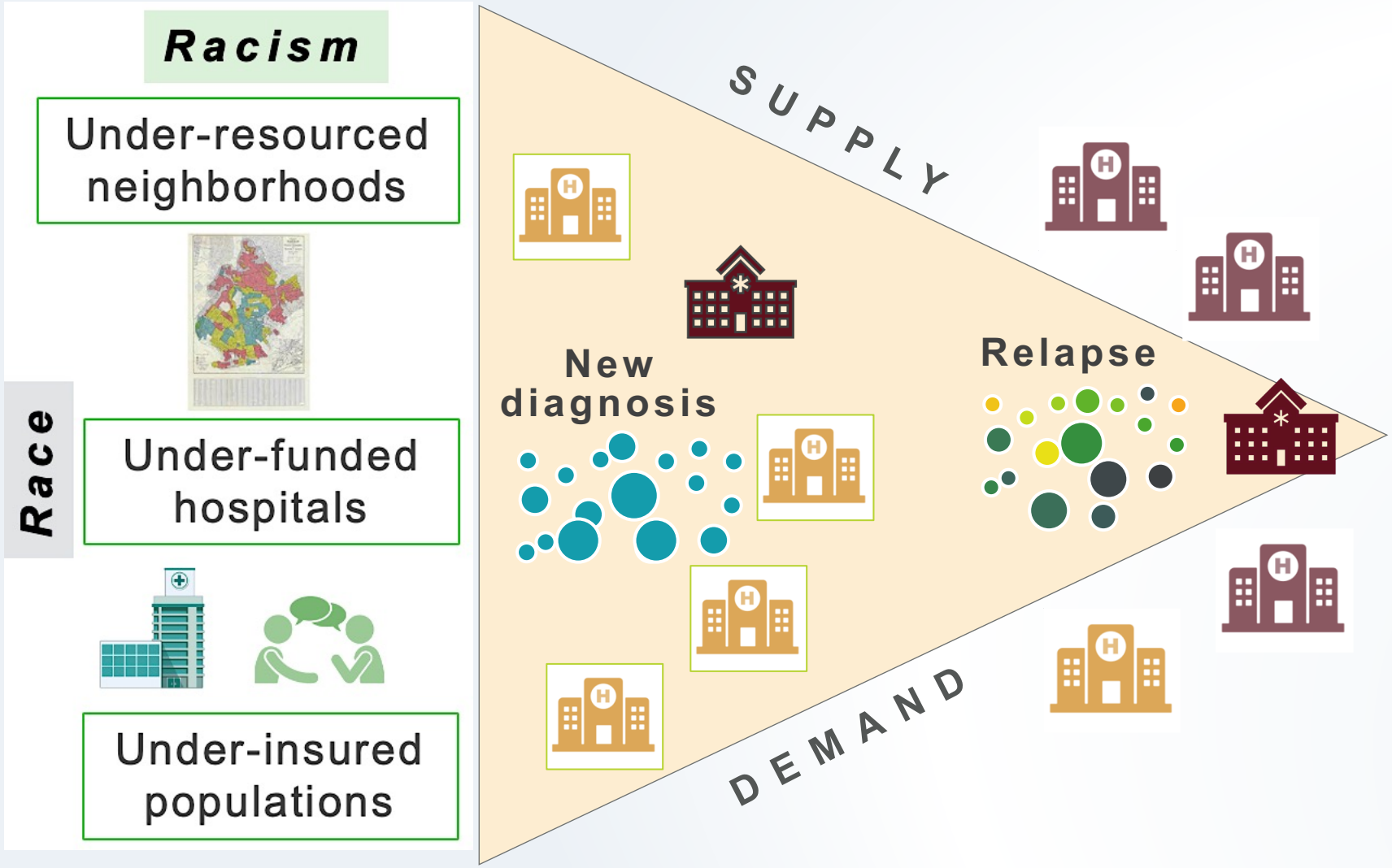
SYSTEMIC → Under-funded hospitals

1935: National Labor Relations Act: Expands union benefits **(insurance)**, but **excludes service, domestic, agricultural industries**

INDIVIDUAL → Under-insured populations

Kahn, in press, 2024

How does this impact access to salvage trials



In under-resourced settings, the capacity to run early phase trials is limited by:

1. Fewer research staff
2. Sparse regulatory support
3. Lab capabilities
4. IRB, language and translation services
5. And so on…

Kahn, *In press*, 2022

Improving access to clinical trials and novel agents

Trial planning from concept → to rollout → to follow-up

1. **Simplify**. **Consider trial complexity during design and development**
   - Include patient representatives from the start
   - Understand research team capacity at smaller sites
2. **Partner. Join forces with the communities that we serve.**
   - Listen to advocates
   - Establish peer navigator programs
   - Collaborate with community health workers
   - Connect with oncology teams from small and rural centers
3. **Build**. **Assist in building the infrastructure for collaborative trials.**
4. **Advocate**. **Push for federal and local mandates to support access**

Putting it all together

Health care disparities exist in the context of historic and contemporary racism and serve as evidence of persistent inequities rooted in many aspects of American life.

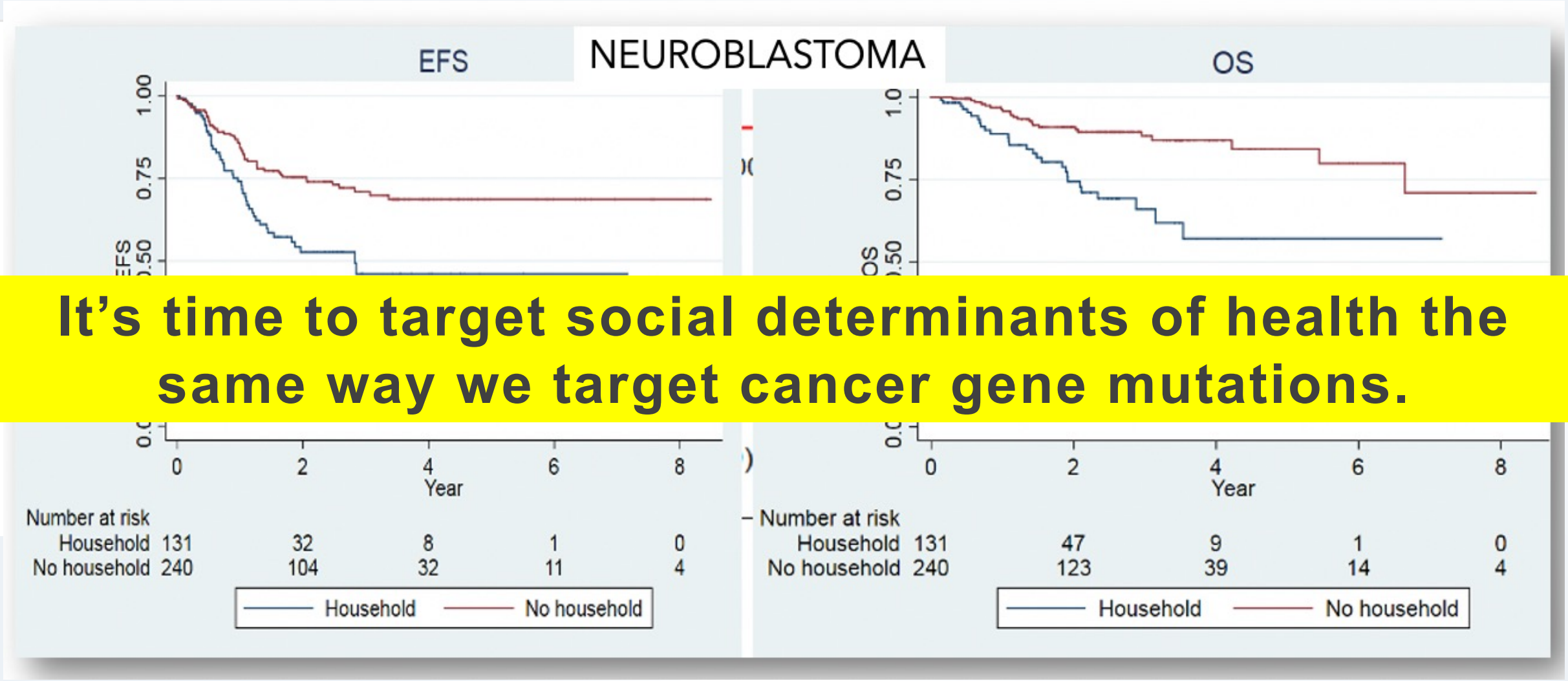
These disparities are often framed as an issue of “race,” yet, **race is a sociopolitical construct reflecting systemic inequities experienced by a person across the life course**

Research is needed to understand the socio-contextual factors drive cancer disparities by place and race.

- **To conduct meaningful studies, we must collect better data.**

Then, structural and policy changes that can be implemented to support a broader range of interventions beyond the individual.

The model of discovery in cancer medicine



It's time to target social determinants of health the same way we target cancer gene mutations.

Credit for this concept: Kira Bona

Finally

Practically speaking, eliminating disparities among patients with lymphoma means reducing mortality and improving survival among the disadvantaged. **This is the goal.**

Myriad opportunities:

- Identify and address barriers to clinical trial enrollment
- Leverage and improve clinical trials infrastructure toward collecting SDOH, self-reported demographic data
- Develop translational collaborations to identify biomarkers associated with outcomes in children and AYAs with lymphoma
- Conduct targeted intervention testing across continuum of care

Gratitude

Thank you IUCLS for this invite!

Mentors and Advisors:

- Kara Kelly (Roswell Park)
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Boyu Hu (Utah)

Adam DuVall (U Chicago)