

Cancer Control and Intervention Working Group

A Report from the Childhood Cancer Survivor Study

Claire Snyder, PhD, and Paul Nathan, MD, MSc, on behalf of the Working Group

CCSS

Childhood Cancer
Survivor Study



St. Jude Children's
Research Hospital

An NCI-funded Resource

Focused on reducing the long-term impact of cancer therapy on physical, psychological and social outcomes

- Health care utilization and late effects surveillance
- Health behaviors
- Health status
- Financial and social outcomes
- Interventions designed to promote early detection or reduce risk of late effects

Working Group Membership

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Member	Institution
Paul Nathan, MD, MSc (Co-Chair)	Hospital for Sick Children; University of Toronto
Claire Snyder, PhD (Co-Chair)	Johns Hopkins Schools of Medicine and Public Health
Jackie Casillas, MD, MSHS	University of California-Los Angeles
Elena Elkin, PhD, MPA	Columbia University
Jennifer Ford, PhD	Hunter College-CUNY
Tara Henderson, MD, MPH	University of Chicago-Medicine
I-Chan Huang, PhD	St. Jude Research Children's Research Hospital
Melissa Hudson, MD	St. Jude Research Children's Research Hospital
Xu Ji, PhD, MSPH	Emory University
Anne Kirchhoff, PhD, MPH	University of Utah
Wendy Leisenring, ScD	Fred Hutchinson Cancer Center
Kiri Ness, PhD	St. Jude Research Children's Research Hospital
Kevin Oeffinger, MD	Duke University
Lisa Schwartz, PhD	CHOP
Jennifer Yeh, PhD	Dana-Farber/Harvard Cancer Center

- 6 Published/In Press Manuscripts (since 1/1/2022)
- 1 Currently Submitted Manuscripts
- 8 Analysis/Manuscript in Process
- 5 New AOIs (total, since 1/1/2022)

Recently completed research and ongoing intervention studies

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- Financial hardship
- Medicaid
- Breast cancer screening
- EMPOWER II
- ASPIRES
- ENGAGE

Financial Hardship in Adult Survivors of Childhood Cancer in the Era After Implementation of the Affordable Care Act

Paul Nathan, I-Chan Huang, Yan Chen, Tara Henderson, Elyse Park, Anne Kirchhoff, Kevin Krull, Wendy Leisenring, Gregory Armstrong, Rena Conti, Yutaka Yasui, K. Robin Yabroff

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CCSS Financial Hardship Survey (2017-2019)

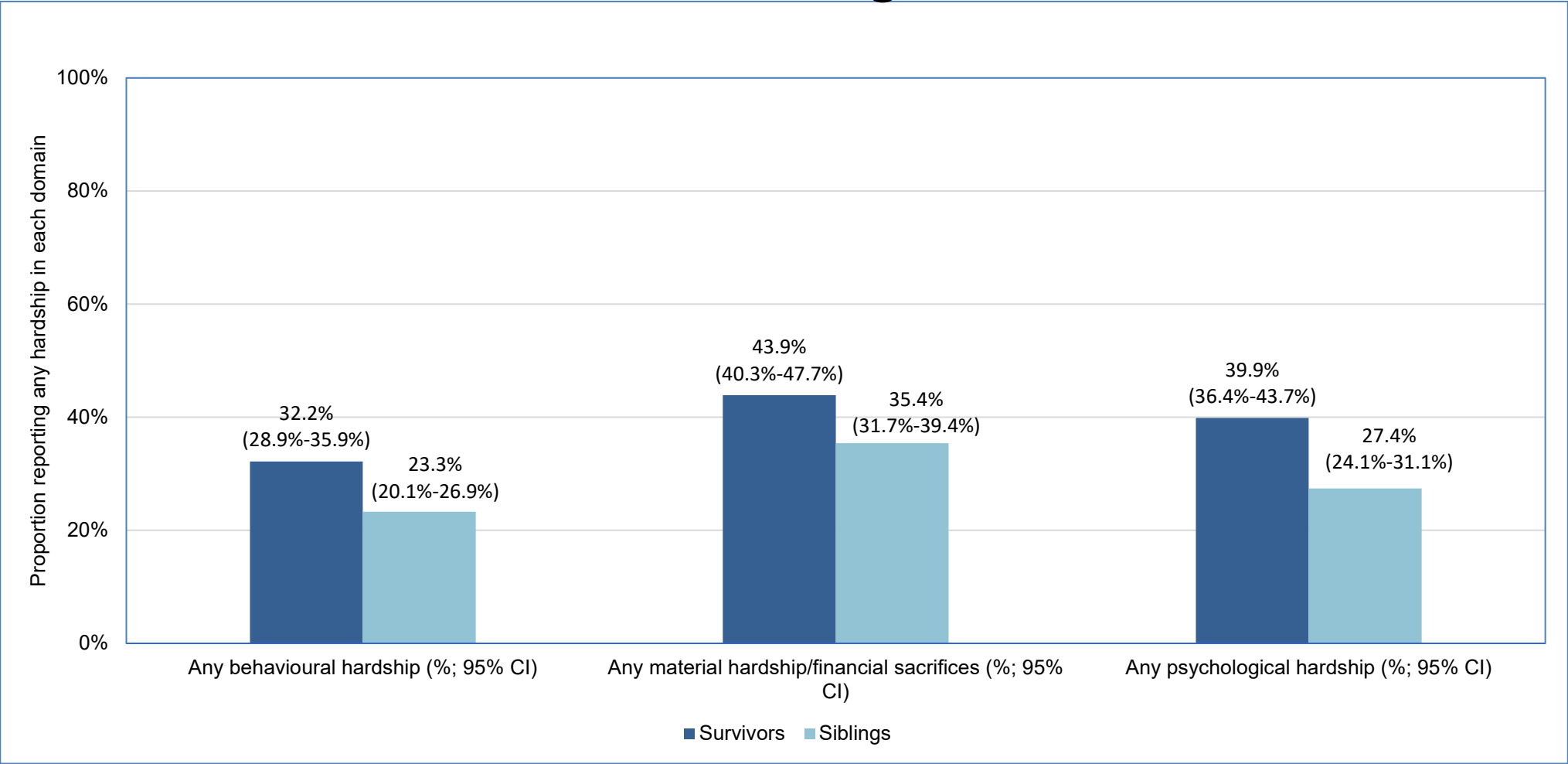
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- 21 items derived from US national surveys
 - Medical Expenditure Panel Survey Experiences
 - National Health Interview Survey
 - Behavioral Risk Factor Surveillance System
- Factor analysis used to define 3 domains
 - Material hardship/financial sacrifices (8 items)
 - Behavioral hardship (8 items)
 - Psychological hardship (3 items)
 - 2 separate items: debt collection, bankruptcy

Hardship domains	Survey question	Survivors (%)	Siblings (%)	P-value
Behavioral	Within the last 12 months, forgone...			
	...any needed medical care	14.1	7.8	<0.001
	...specialist	11.9	8.4	0.001
	...annual primary care visit	10.6	6.1	<0.001
	...prescription medicine	12.3	7.7	<0.001
	...dental care	22.0	16.2	<0.001
	...follow-up care*	8.0	NA	-
	...eyeglasses	13.2	11.0	0.08
	...mental health care/counselling	8.7	5.0	<0.001
	Summary			
	<i>Mean number of items with an affirmative response</i>	<i>1.0</i>	<i>0.62</i>	<i><0.001</i>
	<i>% of individuals having at one least item with an affirmative response</i>	<i>32.6</i>	<i>23.2</i>	<i><0.001</i>
Material hardship/financial sacrifices	Within the past 2 years,...			
	...reduced spending on vacation or leisure	23.8	19.2	<0.001
	...delayed or reduced spending on home improvement	17.4	14.2	0.004
	...reduced spending for large purchases	18.0	13.2	<0.001
	...used savings set aside for other purposes	16.4	14.0	0.04
	...reduced spending on basics	14.5	9.0	<0.001
	...made a change to living situation	6.3	3.3	<0.001
	Currently...			
	...has problems paying medical bills	20.7	12.8	<0.001
	...paying off medical bills over time	30.3	21.1	<0.001
	Summary			
	<i>Mean number of items with an affirmative response</i>	<i>1.47</i>	<i>1.07</i>	<i><0.001</i>
<i>% of individuals having at least one item with an affirmative response</i>	<i>43.9</i>	<i>35.2</i>	<i>0.001</i>	

Hardship domains	Survey question	Survivors (%)	Siblings (%)	P-value
Psychological hardship	Within the last 12 months, worry/stress about having enough money to...			
	...pay household utilities	28.6	17.1	<0.001
	...pay rent or mortgage	33.6	23.2	<0.001
	...buy nutritious meals	26.8	15.5	<0.001
	Summary			
	<i>Mean number of items with an affirmative response</i>	<i>0.89</i>	<i>0.56</i>	<i><0.001</i>
	<i>Percentage of individuals having at least one item with an affirmative response</i>	<i>40.3</i>	<i>27.3</i>	<i><0.001</i>
Individual questions*	Ever sent to debt collection	29.9	22.3	<0.001
	Ever filed for bankruptcy protection	7.9	7.7	0.53

Proportion reporting any financial hardship in each domain among survivors vs siblings



*P<0.001 for each survivor vs sibling comparison

**Comparisons adjusted for sex and age at questionnaire. GEE used to account for within-family correlation.

Factors	Levels	Behavioral hardship	Material hardship/ financial sacrifices	Psychological hardship
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Sex (ref: male)	Female	1.61	1.49	1.57
Race/ethnicity (ref: white, non-Hispanic)	Black, non-Hispanic	1.48	1.30	1.08
	Hispanic	1.05	1.19	1.03
	Other	0.68	0.49	1.19
Age at questionnaire (ref: >=45 years)	26-34 years	1.39	1.06	1.51
	35-39 years	1.21	1.09	1.41
	40-44 years	1.01	1.03	1.45
Education (ref: ≥College graduate)	<High school	2.48	1.37	2.99
	High school - <College graduate	1.71	1.77	2.10
Health insurance (ref: Private)	None	8.65	1.82	2.87
	Public	2.75	1.14	1.87
Marital status (ref: Married/living as married)	Single	1.03	0.78	1.10
	Divorced or separated	2.35	1.27	1.98
Anthracycline (ref: None)	>0-<250mg/m2	1.11	1.18	1.02
	≥250mg/m2	1.39	1.27	1.40
Alkylating agent (ref: None)	>0-<4000mg/m2	1.06	1.29	1.15
	4000-<8000mg/m2	1.03	1.17	0.88
	≥8000mg/m2	1.04	1.07	0.79
Radiation (ref: None)	TBI only	1.47	2.42	1.41
	Cranial RT, no TBI	1.07	1.36	1.22
	Chest RT without Cranial/TBI	1.35	1.09	1.01
	Other RT	1.06	1.18	0.90

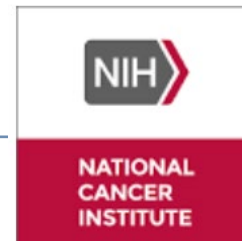
Understanding the impact of the Affordable Care Act on healthcare coverage, utilization, and outcomes for childhood cancer survivors (R03CA267456)

PI: Xu Ji, PhD

Co-I's: Ann C. Mertens, PhD; Sharon M. Castellino, MD, MSc; Anne C. Kirchhoff, PhD

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Aflac.
Cancer & Blood
Disorders Center
CHILDREN'S HEALTHCARE
OF ATLANTA



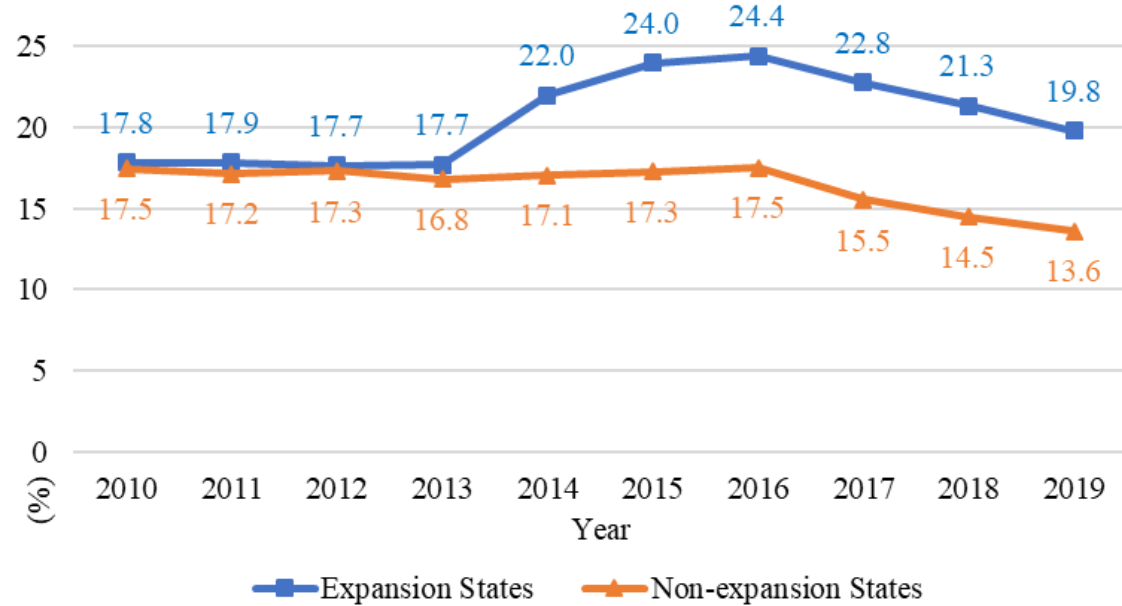
Study Aims:

- Among adult survivors of childhood cancer and siblings, investigate the effect of ACA Medicaid expansion on:
 - 1) Medicaid enrollment and coverage continuity
 - 2) Health service utilization (screening receipt, emergency department visits, hospitalizations)
 - 3) Mortality

Approach:

- Link the CCSS cohort to the 2010-2019 administrative Medicaid insurance data

Trend in % with Medicaid enrollment in CCSS survivors



Increases in Medicaid enrollment and Medicaid-covered days associated with ACA Medicaid expansion

Outcome	Expansion states			Non-expansion states			Adjusted DD	P
	Pre-ME	Post-ME	Absolute Difference	Pre-ME	Post-ME	Absolute Difference		
Any Medicaid enrollment (%)	17.8	22.7	4.9(4.4, 5.4)	17.2	15.9	-1.3(-2.0, -0.6)	7.3(6.2, 8.3)	<0.001
Medicaid-covered days (day)	57.2	73.8	16.6(14.8, 18.3)	54.5	52.6	-1.9(-4.3, 0.5)	19.3(15.5, 23.0)	<0.001

Breast Cancer Screening Among Childhood Cancer Survivors Treated Without Chest Radiation: Clinical Benefits and Cost-Effectiveness

Jennifer Yeh, PhD

Boston Children's Hospital & Harvard Medical School

Kathryn Lowry, Clyde Schechter, Lisa Diller, Grace O'Brien, Oguzhan Alagoz, Gregory Armstrong, John Hampton, Melissa Hudson, Wendy Leisenring, Qi Liu, Jeanne Mandelblatt, Diana Miglioretti, Chaya Moskowitz, Paul Nathan, Joseph Neglia, Kevin Oeffinger, Amy Trentham-Dietz, Natasha Stout

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Objective

To estimate the clinical benefits and cost-effectiveness of early breast cancer screening among leukemia and sarcoma survivors treated without chest radiation

Approach

Use CCSS data to adapt 2 Cancer Intervention and Surveillance Modeling Network (CISNET) models to reflect the elevated risks of breast cancer and competing mortality among leukemia and sarcoma survivors

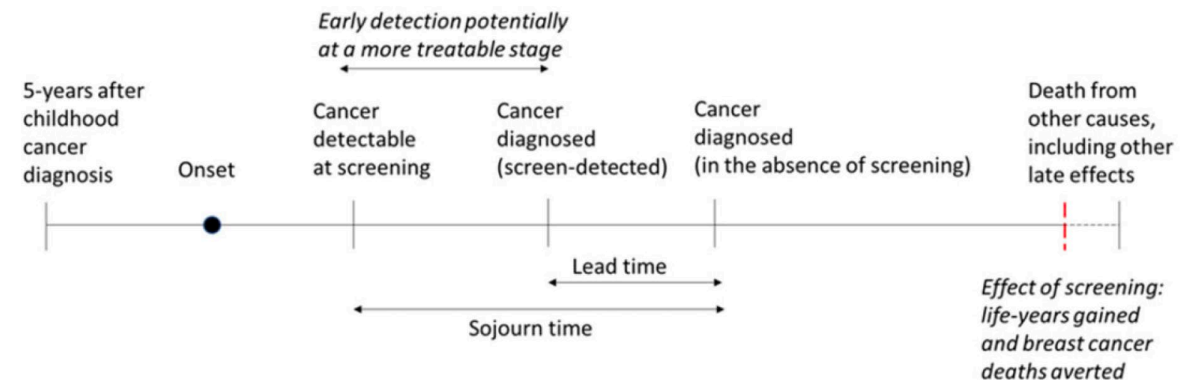
Strategies

- No screening
- Digital mammo + MRI screening starting at ages 25, 30, 35, or 40 years

Outcomes

- Breast cancer deaths averted
- False positive screening results
- Benign biopsies
- Incremental cost-effectiveness ratios

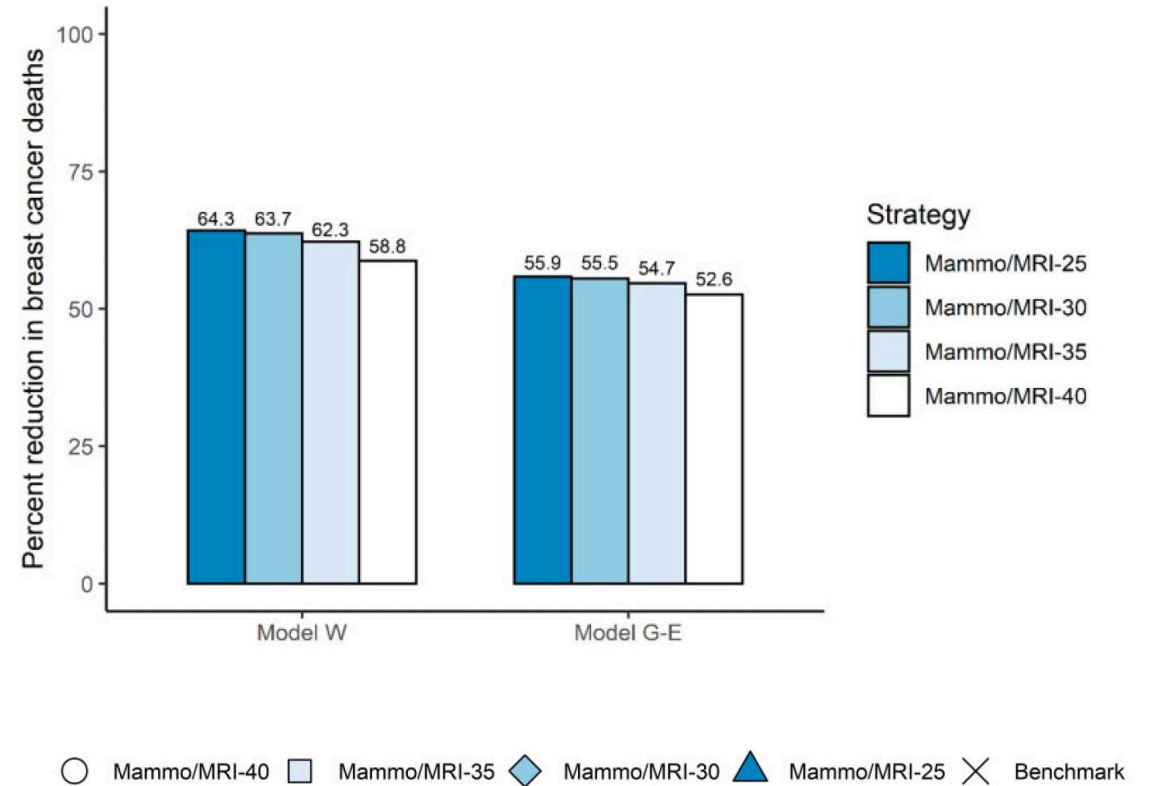
Life history with breast cancer and screening



Model-based findings

Reduction in breast cancer deaths

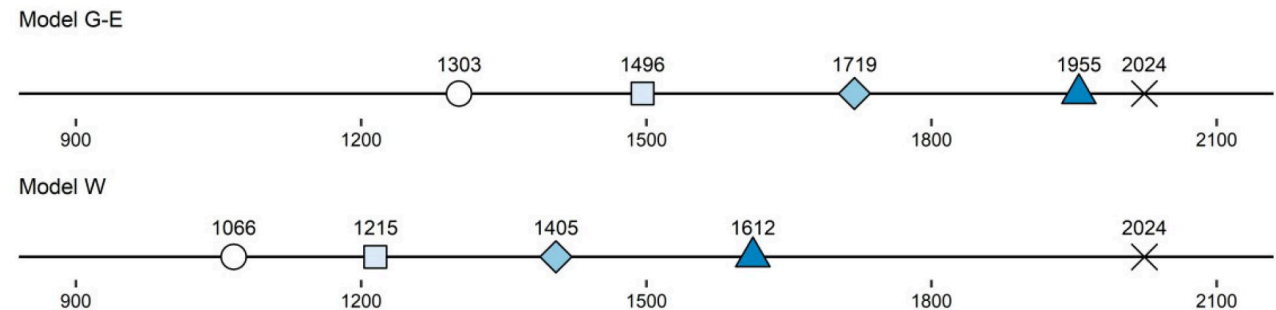
- In the absence of screening, 6.8%-7.0% of survivors would die from breast cancer in their lifetime
- Screening with mammography and MRI starting between ages 25 and 40 years would avert 53% to 64% of these breast cancer deaths



Harm-benefit tradeoffs

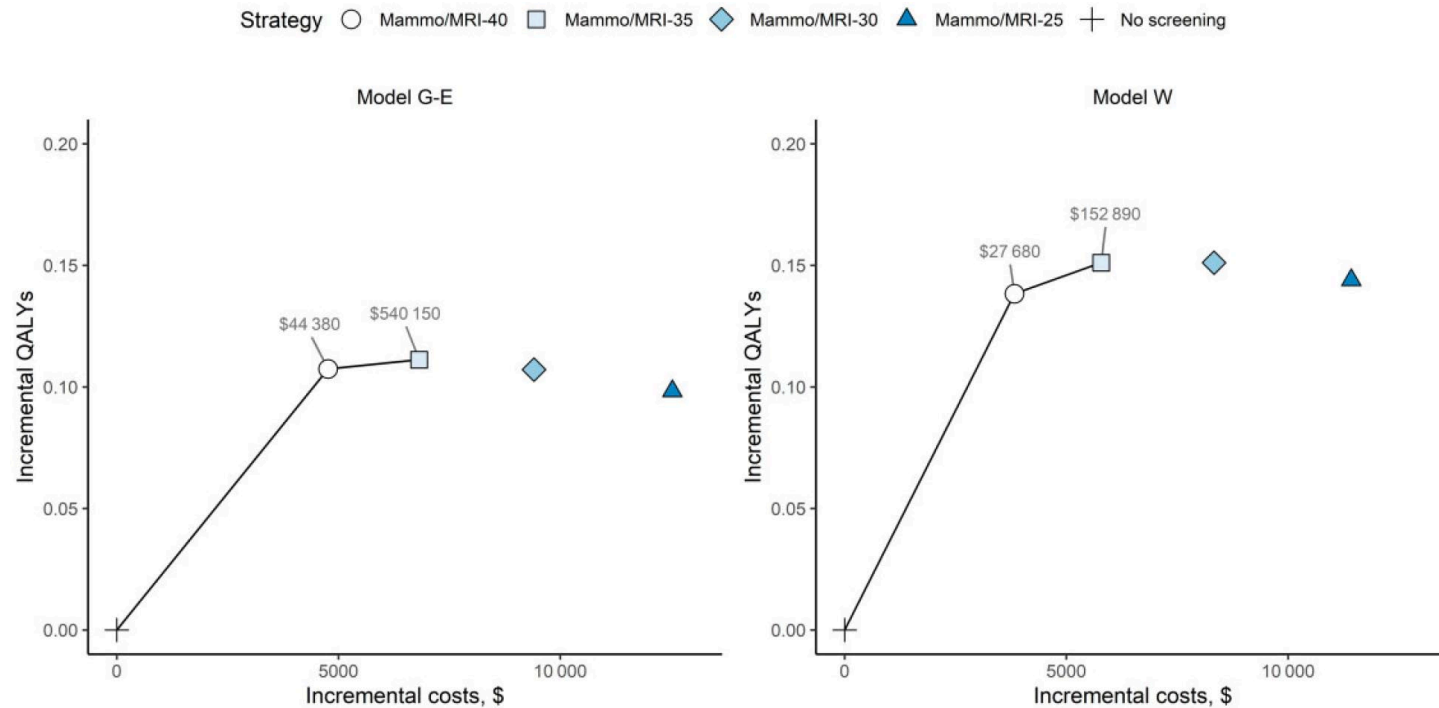
- For all screening strategies, the number of screening tests per death averted was more favorable in both models than accepted benchmarks

A Screen tests per breast cancer deaths averted



Cost-effectiveness

- When costs and quality-of-life were considered, compared with no screening, the incremental cost-effectiveness ratio (ICER) for screening starting at age 40 ranged between \$27,680 per QALY to \$44,380 per QALY gained across models
- ICERs for screening starting at age 35 were greater than the commonly cited \$100,000 per QALY gained threshold for “good value” in both models



Conclusion

- Among survivors of childhood leukemia or sarcoma, early initiation of breast cancer screening at age 40 years may reduce breast cancer deaths by half and is cost-effective

EMPOWER-II (Oeffinger, Ford, Barrett)

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- Boosting breast MRI screening rates

- Use of 2-way smartphone technology for patient activation
- Pri

PCP Advisory Board:

- Tell us what you want us to do in the first 7 seconds of reading
- Send (fax) information proximate to the visit
- Address clinical manager, not the PCP

291 women
• Age ≥ 25
• Previous
• No history
• Did not c
mammog

C
X

materials

R01CA134722-06

Start date: April 1, 2018

X

X

text messages,
video vignettes
CCSSapp / SCP

X

mail/fax information
and screening
recommendation



Christina Applegate Foundation



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Activating cancer Survivors and their Primary care providers (PCPs) to Increase coloREctal cancer Screening (ASPIRES) Study (Tara Henderson, Karen Kim)

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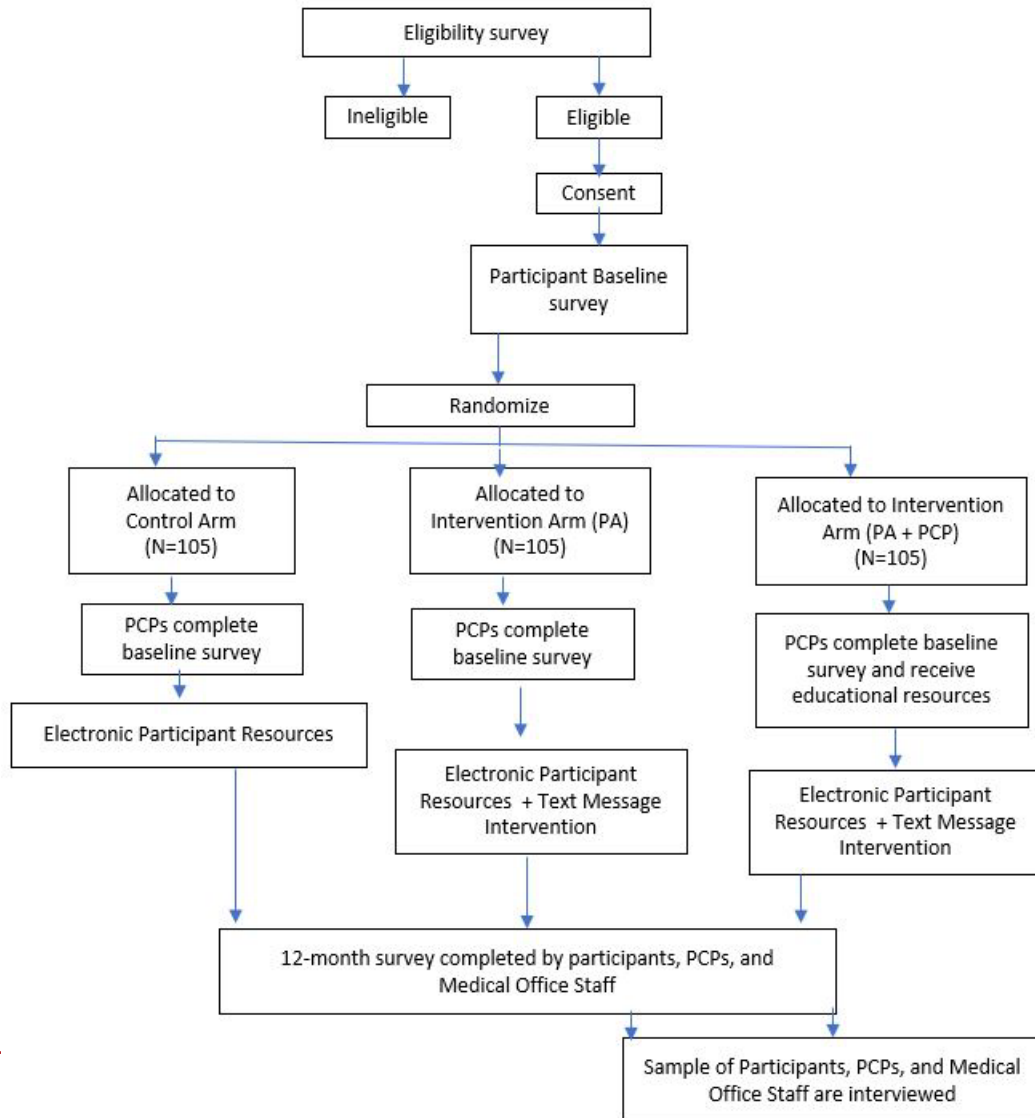
Primary Objective

- To compare the efficacy of a remote digital mHealth intervention aimed at either patient activation (PA), or patient plus PCP activation, as compared to controls on completing colonoscopy or a cologuard

Secondary Objectives

1. Evaluate the difference in the **proportion of patients who complete the colonoscopy or cologuard within 12 months** of enrolling on this study
2. Use the Consolidated Framework for Implementation Research (CFIR) to evaluate the **implementation process** and to identify **barriers and facilitators** to uptake
3. Identify the **moderators and mediators** of the uptake of colorectal cancer screening
4. Estimate the **costs** and incremental cost-effectiveness of the intervention

ASPIRES Study Schema and Key Details



- Launch Date: 02/14/2022
- Target Accrual: 315
- Actual accrual: 158
 - Arm 1: Control: 53
 - Arm 2: Intervention (PA): 52
 - Arm 3: Intervention (PA+PCP activation): 53

ENGaging and Activating cancer survivors in GENetic services (ENGAGE) Study

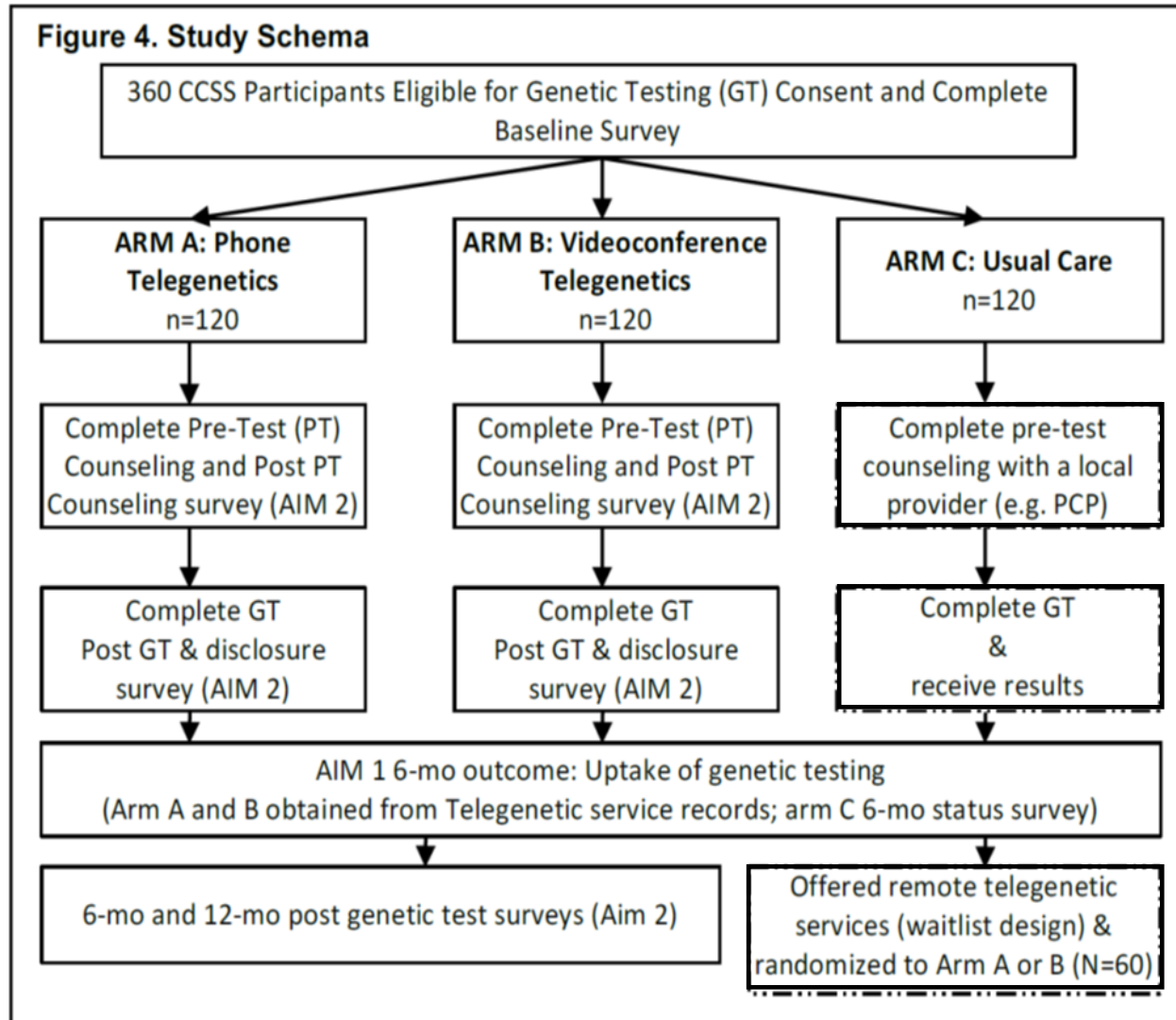
(Tara Henderson, Angela Bradbury)

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- Aim 1: To evaluate the effectiveness of our *in-home, collaborative PCP model* of remote telegenetic services to increase uptake of genetic testing at 6 months as compared to usual care among childhood cancer survivors who meet criteria for cancer genetic testing.
- Aim 2: To evaluate the effectiveness of remote videoconferencing to provide greater increase in knowledge and decrease in distress and depression as compared to remote phone services (Aim 2a), to examine the moderators of patient outcomes with remote telegenetic services (Aim 2b), and to estimate intervention costs and incremental cost-effectiveness of the three study arms (Aim 2c).
- Aim 3: To conduct a multi-stakeholder, mixed-methods process evaluation to understand patient, provider and system factors associated with uptake of counseling and testing in our adapted *in-home, collaborative PCP model* and facilitators and barriers to uptake to provide recommendations for future implementation.

ENGAGE Study Schema and Key Details

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- Launch Date: 08/16/2021
- Target Accrual: 360 who have completed baseline
- Actual Accrual: 346
 - Arm A: 109
 - Arm B: 121
 - Arm C: 116



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Approved Concept Proposals

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Analyses/Manuscripts in Process

1. Ohlsen. Medical financial hardship among long-term survivors of childhood cancer and their siblings in the Childhood Cancer Survivor Study (CCSS) in comparison to the general population
2. Fauer. Impact of Community Economic Characteristics on Financial Hardship among Adolescent and Young Adult Cancer Survivors
3. Shoag. Disparities in Adherence to Screening Guidelines in Hodgkin's Lymphoma Survivors
4. Ji. Understanding Health Service Utilization and Cost in Childhood Cancer Survivors Within the Medicaid System
5. Bhatt. Temporal Changes in Employment Outcomes of Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS)
6. Huang. Progression of Late Medical Effects and Impact on Financial Hardship Among Adult Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study.
7. Onerup. Association between voluntary increase in physical activity and future morbidity in the Childhood Cancer Survivor Study
8. Snyder. Managing Comorbid Conditions in Childhood Cancer Survivors: Communication, Coordination, and Continuity

Open

- Activating cancer Survivors and their Primary care providers to Increase coloREctal cancer Screening (ASPIRES) Study (Henderson, Kim)
- Improving delivery of genetic services to high-risk CCS (Henderson, Bradbury)
- Health Insurance Navigator Program (Park)
- Impact of eHealth intervention for insomnia on late effects of childhood cancer (SLEEPWELL Intervention Trial) (Brinkman)
- Study of LifeStyle Activation (SALSA) (Chow)

Data under analysis

- EMPOWER-II (Oeffinger)
- CHIIP (Chow)

- Enhance the CCSS resource *by facilitating the conduct of health services research* through collection of data to evaluate patient, provider, and health care system factors and their associations with access, quality, and cost of care
- Provide the research community with a resource that will identify *how survivors' health care influences their outcomes* in order to inform strategies to provide life-long, risk-adapted care to this vulnerable population

Follow-Up 8 Enhancements

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- Add assessment of survivors' perspectives of their unmet needs in next survey
 - Build on *CCSS Needs Assessment Questionnaire* (Cox et al)
 - 135-item instrument comprising 9 unidimensional domains
- 58 items addressing:
 - Access (e.g., ability to see specialists)
 - Quality (e.g., knowing surveillance recommendations)
 - Costs (e.g., affordability of medical treatments)
- Plus, questions regarding health care utilization previously featured in CCSS surveys
- To enable exploration of the associations between unmet needs and poor outcomes (e.g., hospitalizations), as well as health care disparities related to race/ethnicity
- Gaps in care identified by these surveys will inform subsequent research, including intervention studies

Ancillary studies

ANCILLARY STUDY	BACKGROUND & RATIONALE	SIGNIFICANCE
Leveraging the CCSS myLTFU patient portal and mobile app to collect real time data about health care use	<ul style="list-style-type: none"> Limited detail regarding health service use can be collected based on retrospective questions asked every 2-3 years Innovation: real-time reporting of health service use through the portal 	<ul style="list-style-type: none"> Allows for a deeper, broader and more accurate understanding of health care use in real time Platform can be leveraged for future intervention studies
Linkage to administrative claims datasets (e.g. Medicaid, private insurance databases, etc.).	<ul style="list-style-type: none"> Another approach to obtaining more detailed health service use data is to link with administrative claims databases A current pilot is linking CCSS participants with Medicaid claims 	<ul style="list-style-type: none"> Captures granular information about health care use that cannot be obtained by patient report Allows for more precise assessment of quality of care Gives critical insight into disparities in care between different provider models
Use of geocoding to assess structural measures of health care quality by linking to area resource files	<ul style="list-style-type: none"> Another approach to enhance the health service research opportunities in the CCSS is to obtain data on available resources (e.g., cancer centers, physicians) in geographic areas 	<ul style="list-style-type: none"> Identifies structural targets for interventions that can enhance survivor care
Obtain perspectives of primary care and specialist physicians regarding care of childhood cancer survivors	<ul style="list-style-type: none"> Only limited information on primary care providers' perspectives regarding the care of childhood cancer survivors is available Because of the many comorbidities experienced by survivors, the perspectives of specialist physicians are also highly relevant 	<ul style="list-style-type: none"> Will inform development of interventions to improve survivor care that target providers
Estimate the costs of caring for survivors, with an aim towards estimating the cost-effectiveness of different models of survivorship care	<ul style="list-style-type: none"> There are many models of childhood cancer survivorship care Robust data regarding the costs and resource requirements associated with these care models are needed to enable cost-effectiveness analyses 	<ul style="list-style-type: none"> Will inform decisions around the "best" models of survivor care
Intervention studies	<ul style="list-style-type: none"> Possible interventions for exploration include patient navigators, web-based resources, and remote counseling 	<ul style="list-style-type: none"> Completes the translation of CCSS findings from discovery to having a direct impact on survivor outcomes Goal is for these to be scalable to the broader population of childhood cancer survivors across North America

Social Determinants of Health and Health Disparity Research for CCSS

I-Chan Huang, PhD

Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA

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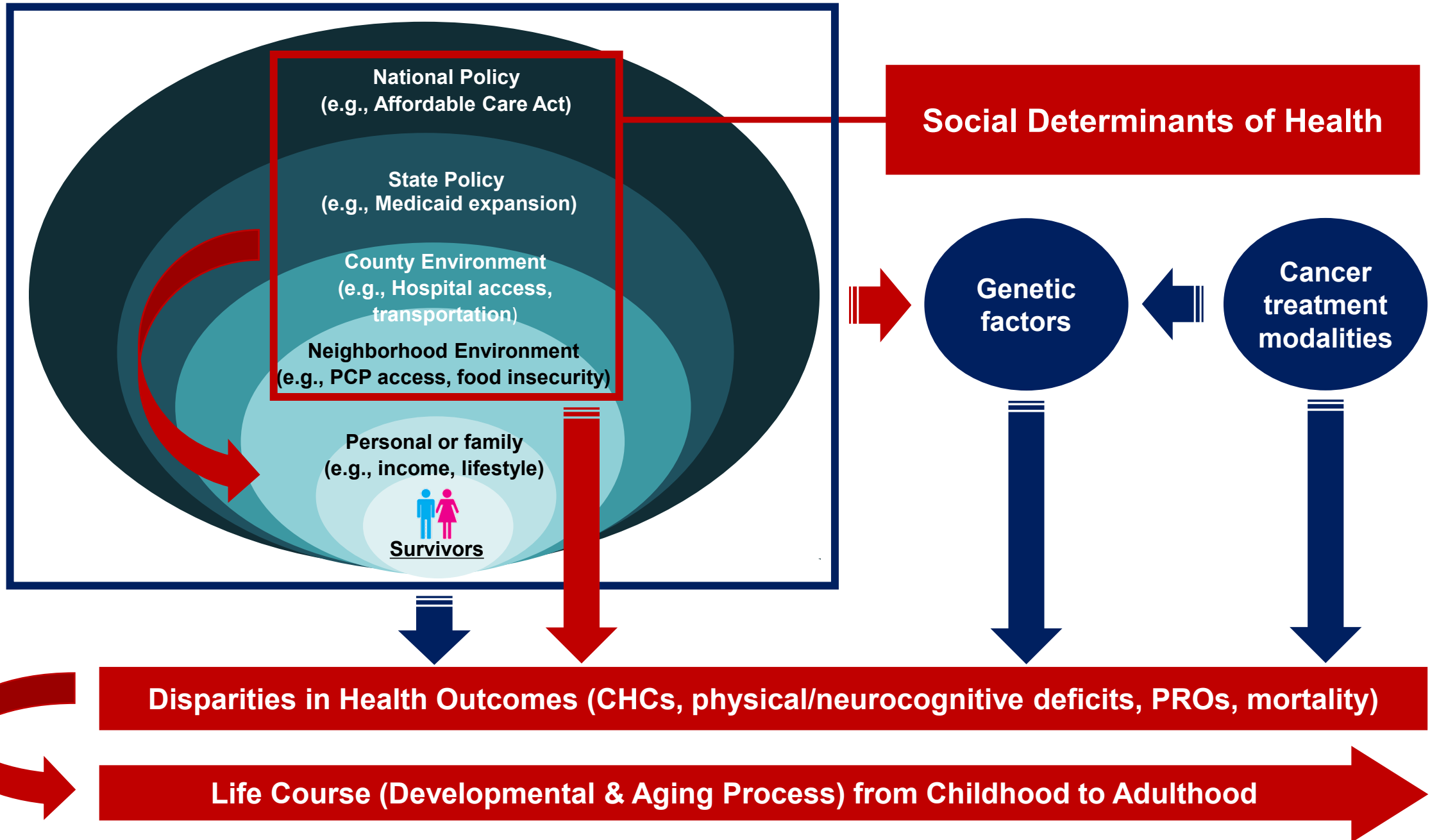


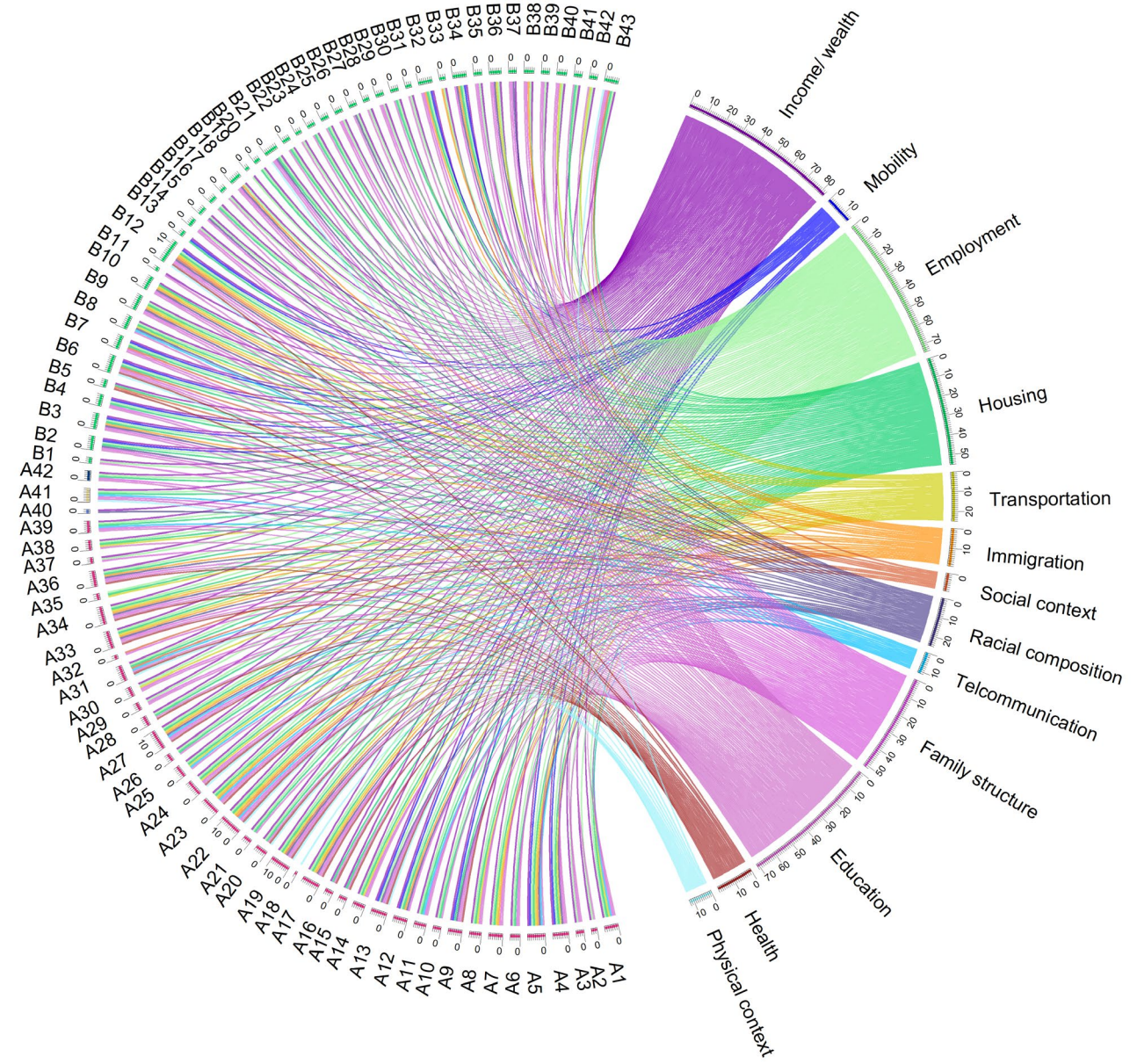
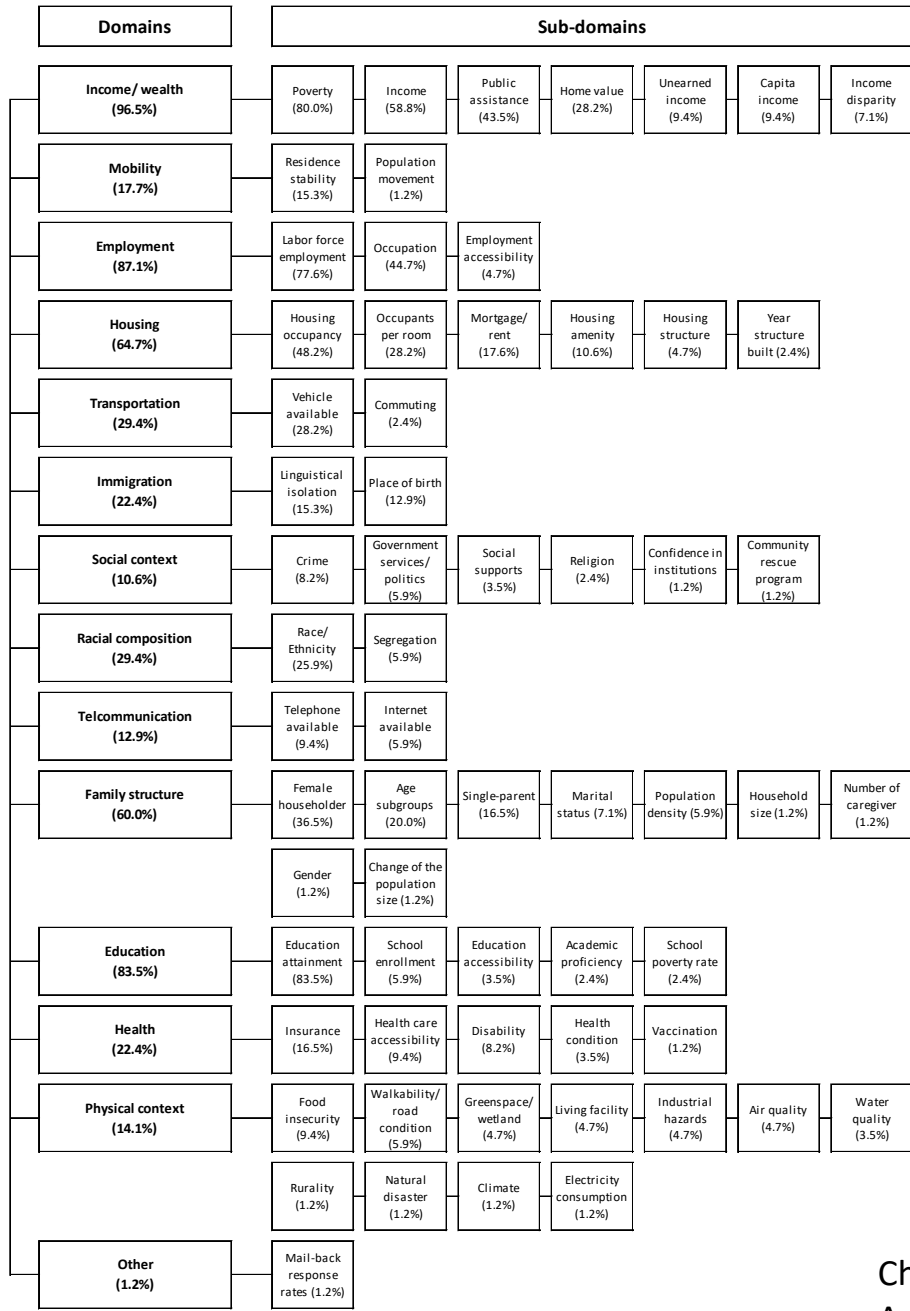
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- Definition
 - “... the conditions in the **environments** where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks.”

Social Determinants of Health







Choi/Huang. A Comparison of Neighborhood-Level Deprivation Measures: A Scoping Review. A Poster Presentation (P-80) at ISLCCC, 2023, Atlanta, Georgia, USA.

Neighborhood Adversity Measures for CCSS

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Measure	Geographical unit	Specific domain
Area Deprivation Index (ADI)	Census block groups	None
Neighborhood Deprivation Index (NDI)	Census tract	None
Social Vulnerability Index (SVI)	Census tract, and County	Socioeconomic, Household Composition, Minority Status/Language, and Housing/ Transportation
Minority Health Social Vulnerability Index (MH-SVI)	County	Socioeconomic, Household Composition, Minority Status/Language, Housing/ Transportation, Health Care Infrastructure, and Medical Vulnerability
Baseline Resilience Indicators for Communities (BRIC)	County	Social Resilience, Economic Resilience, Infrastructural Resilience, Community Capital Resilience, Infrastructural Resilience, and Environmental Resilience
Child Opportunity Index (COI) 2.0	Census tract	Education domain, Health and environment, and Social and economic
County Health Rankings (CHR)	County	Length of Life, Quality of Life, Health Behaviors, Clinical Care, Social Economic Factors, and Physical environment

Potential SDOH/HD Topics for CCSS

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Neighborhood SDOH:

- Area SES deprivation (by domains)
- Redlining/persistent poverty
- Food insecurity
- Local healthcare resources
- Rurality (RUCA)

Health Outcomes:

- CHC burden
- Healthcare utilization (PCP, ER, hospitalization)
- PROs (emotional distress, functional status, QOL)
- Lifestyle
- Mortality

Example Topics:

- Impact of residential segregation/structural racism on cumulative CHC burden and mortality
- Associations of food insecurity and cardiovascular/metabolic disorders
- Area deprivation, community resilience, and PROs
- The compound effect of personal SES and community adversity on adverse outcomes

- Continue work using Financial Hardship Data (follow-up 6)
- Leverage recently frozen follow-up 7 data:
 - Geocoding data: Area Deprivation Index & other measures of Social Determinants of Health
 - Gender identity
 - Health care costs (more granular health care use data)
 - Medicaid data
 - Impact of COVID on data, specific outcomes (e.g., health care use)

Questions

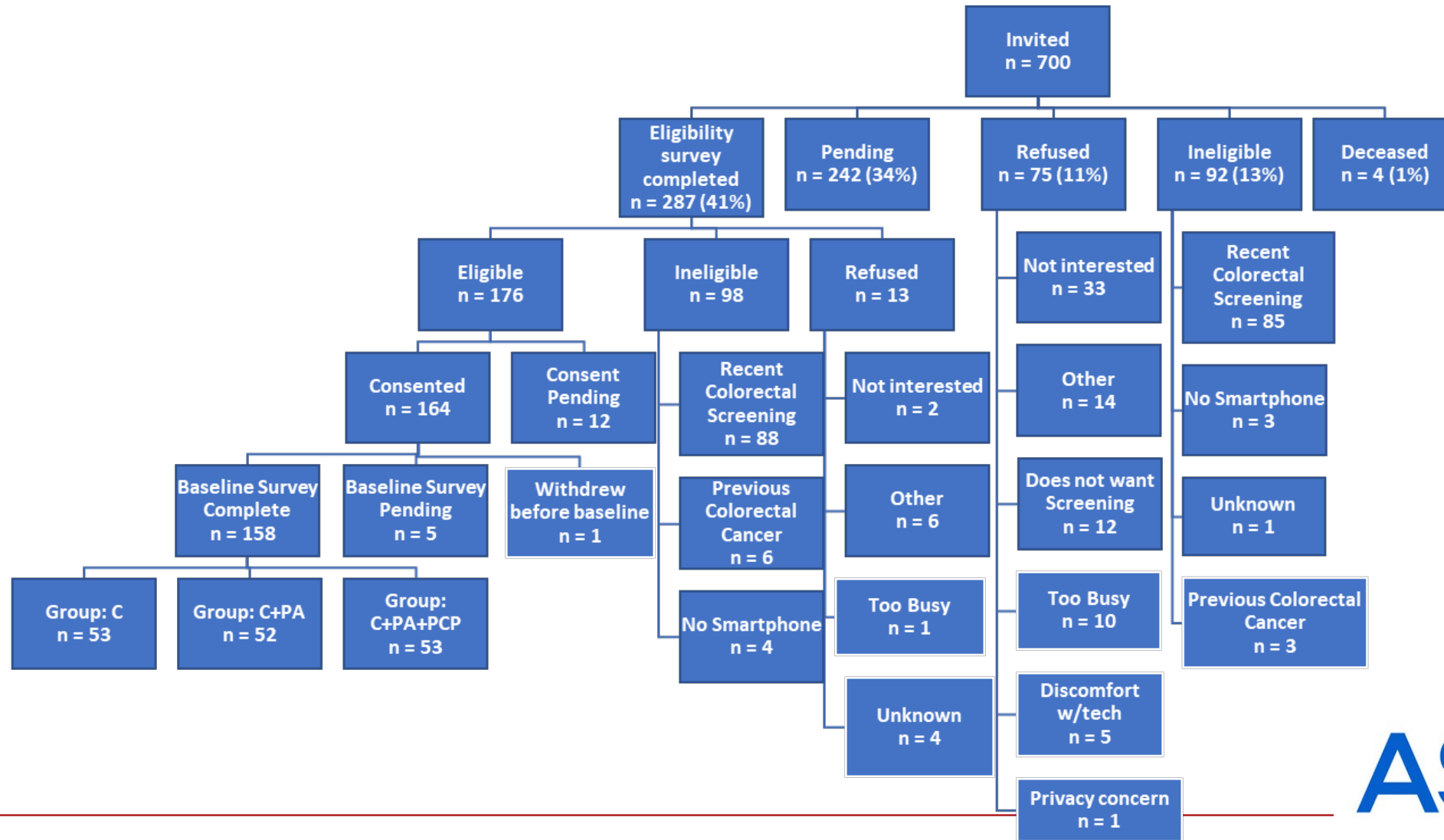
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- Genetics: Dogwood
- Chronic Disease: Emory Amphitheater
- Subsequent Neoplasm: Mountain Laurel
- Cancer Control and Intervention: Hickory
- Psychology: Azalea
- Biostatistics/Epidemiology: Basswood

Appendix: ASPIRES Consort Diagram

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Appendix: ENGAGE Consort Diagram

