The relationship between comorbidities and enrollment in cancer clinical trials by age at diagnosis

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Cancer Clinical Trial (CCT) Enrollment Criteria

- To be eligible, patients are screened based on inclusion and exclusion criteria.
  - Keep criteria broad to increase number of participants and generalize results to other populations.
  - Narrow criteria for patient safety as well as accurate measurements and efficacy of treatment.

Need to Re-evaluate Criteria

- Only 3% enrollment of adult cancer patients
  - Potential barriers: stringent criteria (molecular targets), age, comorbidities, prior treatment
- American Society of Clinical Oncology (ASCO), Friends of Cancer Research, and US Food and Drug Administration (FDA) are re-examining CCT criteria for inclusiveness.
  - Recruit more patients
  - Have participants who are more reflective of the general population
  - Have more treatments for patients

Barriers for Enrollment

- Age:
  - Patients > 65 years make up > 60% cancer cases, but are underrepresented in CCT.
- Comorbidities:
  - Multiple chronic conditions in 1 in 4 U.S. adults
  - Encompass 60% of eligibility criteria
- Prior malignancy:
  - Effects of prior cancer treatment
  - May alter interpretation of CCT
- Drug toxicity:
  - 33% physicians do not offer CCT

Objective

- What is the prevalence of comorbidities in CCTs at Sidney Kimmel Comprehensive Cancer Center (SKCCC)?

- Do certain comorbidities limit enrollment based on age groupings?

Methods - Design

- Johns Hopkins Hospital cancer registry (SKCCC)
  - Date of first contact: 2014 and 2016
  - Date of diagnosis: on or after 2013
  - United States resident
  - Older than 18 years
- Total: 17,959 patients included

Methods - Variables

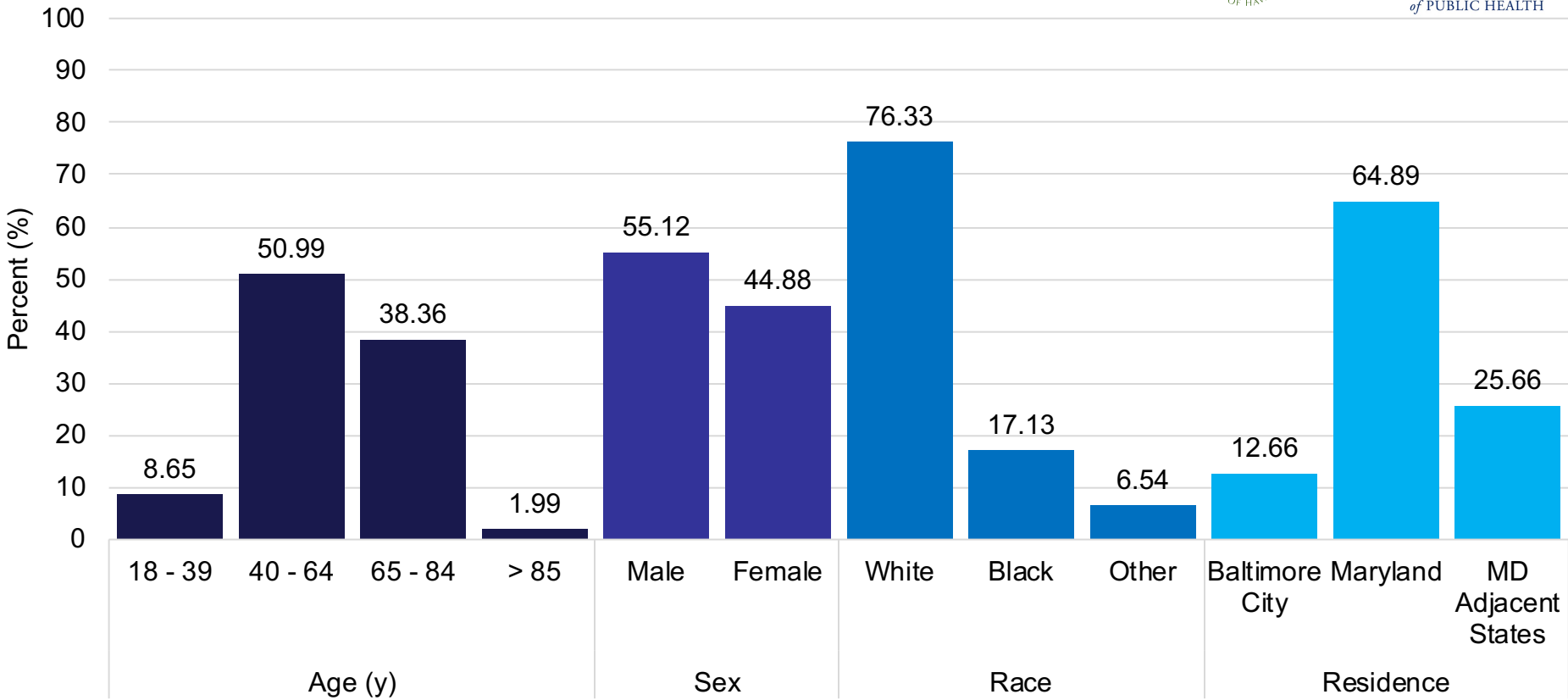
- Comorbidities grouped based on ICD-9 and ICD-10
  - Heart disease/hypertension (HTN)
  - Cerebrovascular disease
  - Respiratory disease
  - Hepatic disease
  - Renal disease
  - Diabetes
  - HIV
  - Prior cancer
  - Tobacco use
  - Other (excluding smoking/prior cancer)
- Outcome: enrollment in CCTs

Methods - Analysis

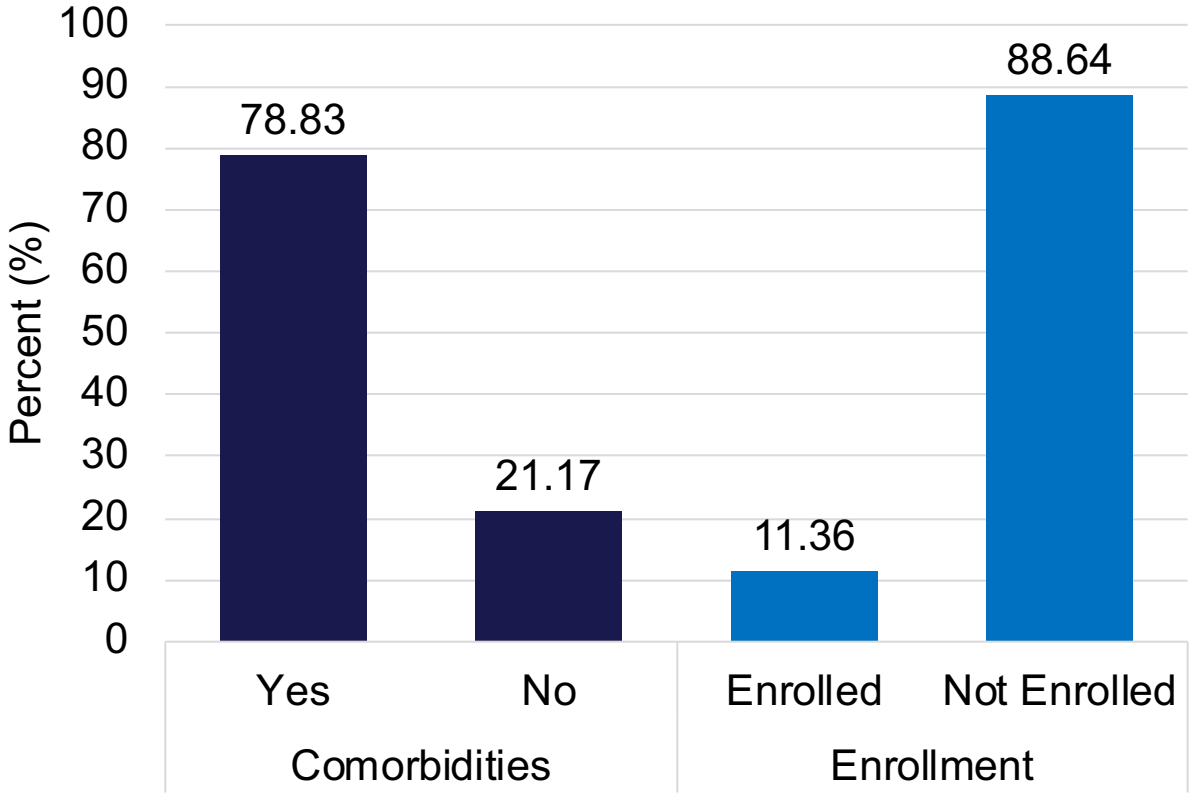
- Prevalence of age groupings, comorbidities, demographics, residence, and other factors.
- Chi-square and univariate logistic regressions: relationships among age, comorbidities, and CCT enrollment.
- Multinomial logistic regression: CCT enrollment by age (adjusted by demographics and residence).

RESULTS

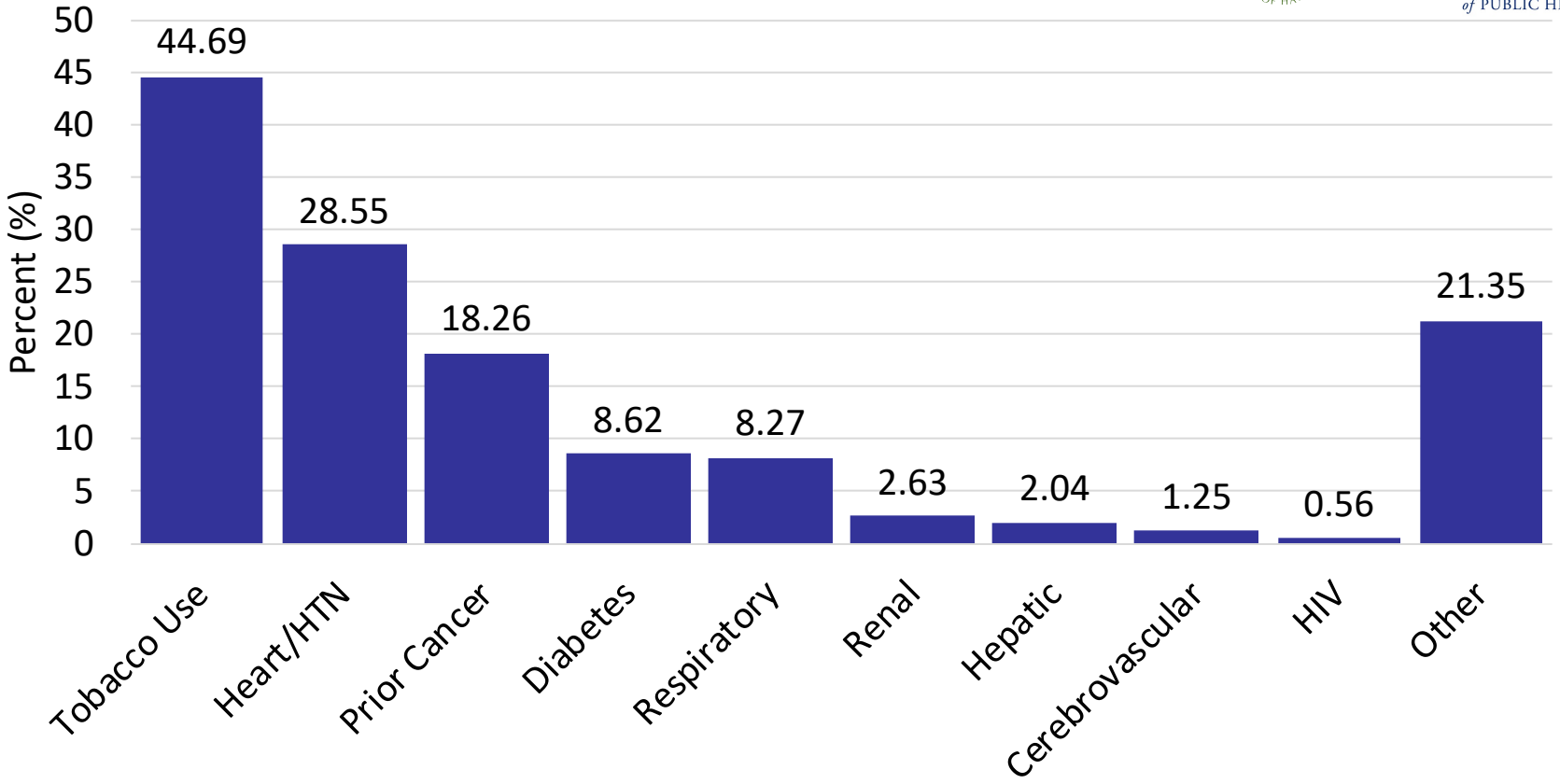
Patient Population



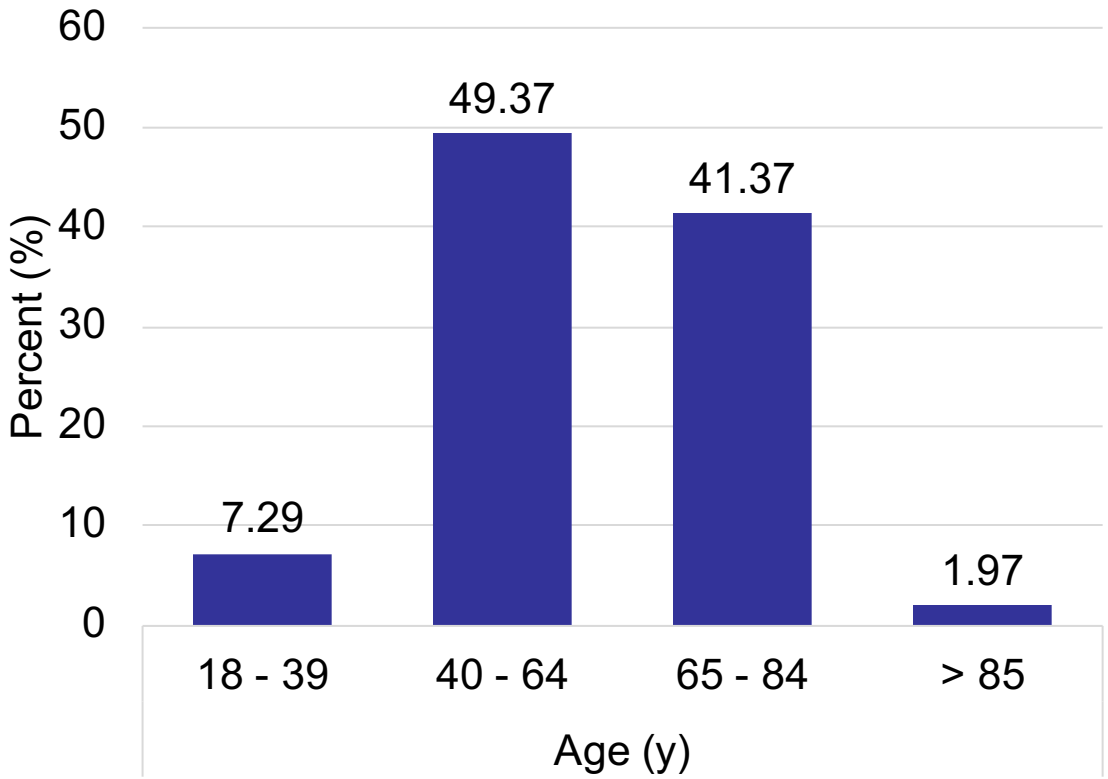
Patient Population



Comorbidities in Population



Distribution of Comorbidities



CCT Enrollment

Univariate Logistic Regression

Characteristic		Enrolled	Not Enrolled	P-value
Age (y)	18 - 39	7.99%	8.74%	ref
	40 - 64	51.47%	50.93%	0.26
	65 - 84	39.56%	38.21%	0.17
	> 85	0.98%	2.12%	0.01
Sex	Male	64.75%	53.89%	ref
	Female	35.25%	46.11%	<0.001
Race	White	78.87%	76.00%	ref
	Black	15.49%	17.34%	0.02
	Other	5.64%	6.65%	0.05
Residence*	Baltimore City	10.39%	12.95%	0.001
	Maryland	59.95%	65.52%	<0.001
	MD Adjacent States	28.77%	25.27%	0.001

CCT Enrollment

Univariate Logistic Regression

Characteristic		Enrolled	Not Enrolled	P-value
Comorbidity*	Heart/HTN	21.37%	29.47%	<0.001
	Cerebrovascular	0.93%	1.29%	0.17
	Respiratory	5.54%	8.62%	<0.001
	Diabetes	7.84%	8.72%	0.19
	Hepatic	1.47%	2.11%	0.06
	Renal	1.96%	2.71%	0.05
	HIV	0.39%	0.58%	0.28
	Other	21.57%	21.33%	0.80
	Prior Cancer	15.49%	18.62%	0.001
	Tobacco Use	43.04%	44.90%	0.11

CCT Enrollment by Age at Diagnosis

Multinomial Logistic Regression

Age (y)		18 - 39		40 - 64		65 - 84		> 85	
		OR	P-value	OR	P-value	OR	P-value	OR	P-value
Comorbidities	Heart/HTN			0.63	<0.001	0.57	<0.001		
	Respiratory			0.67	<0.001				
	Prior Cancer	0.45	0.09			0.65	<0.001		
	Prior Tobacco Use					0.73	0.04		
	Other			0.84	0.04	0.84	0.08		
Demographics	Sex			0.63	<0.001	0.59	<0.001		
	Race: Black	1.43	0.10					4.18	0.02
	Race: Other					0.71	0.07		
Residence	Baltimore City			1.01	0.05	0.75	0.04		

Comorbidity Effects After Adjustment by Age

- Independent of comorbidities:
  - Females enrolled less often amongst ages 40 - 64 and 65 - 84.
  - Baltimore City residence had a mixed effect, increasing enrollment in ages 40 - 64 while decreasing enrollment among ages 65 - 84.
- Comorbidities uniformly dampened participation in clinical trials, but only in the age span of 40 - 84.
  - Heart disease/HTN diminishes enrollment in both age groups.
  - Lower enrollment due to respiratory disease and other comorbidities in ages 40 - 64 and to prior cancer and tobacco use in ages 65 - 84.

Conclusions

- Majority of patients had comorbidities, mainly tobacco use and heart disease/HTN, and did not enroll in CCTs.
- Comorbidities were most prevalent in ages 40 to 84 years.
- Heart disease/HTN, respiratory disease, prior cancer, and prior tobacco use were the main comorbidities associated with CCT enrollment.

Strengths and Limitations

Strengths

- One of the first studies evaluating the effect of age and specific comorbidities on CCT enrollment.
- Large patient population

Limitations

- Only patients of Johns Hopkins Hospital cancer registry
- Only patients who have solid tumors

Future Directions

- Various sites should evaluate CCT eligibility criteria with their population of patients.
- Cancer centers should re-examine whether patients 40 to 84-years-old with heart disease/HTN, respiratory disease, tobacco use or prior cancer can safely be included in CCTs to have more representativeness in enrollees.

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Thank you!

Questions?

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