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Post-Acute Outcomes after Hodgkin Lymphoma: An Epidemiologic Perspective

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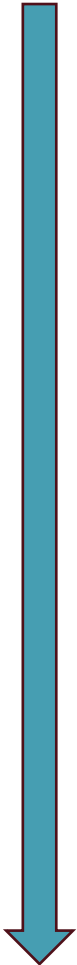


Disclosures

- No relevant financial relationships to disclose.

Evolution of Hodgkin Lymphoma Treatment

1970 Chemotherapy Radiotherapy Survival



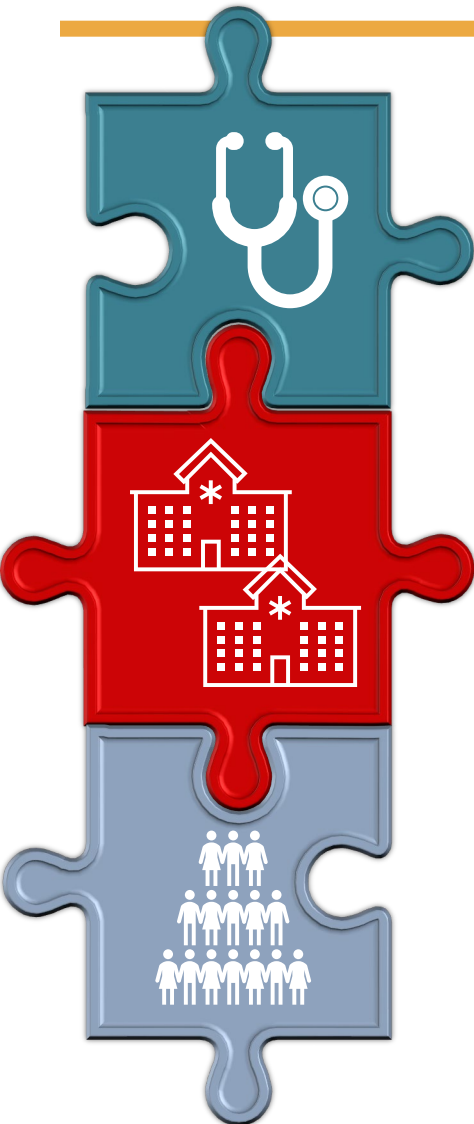
Clinical Approach to Hodgkin Lymphoma

- Survival



- Relapse
- Acute toxicity
- Late toxicity

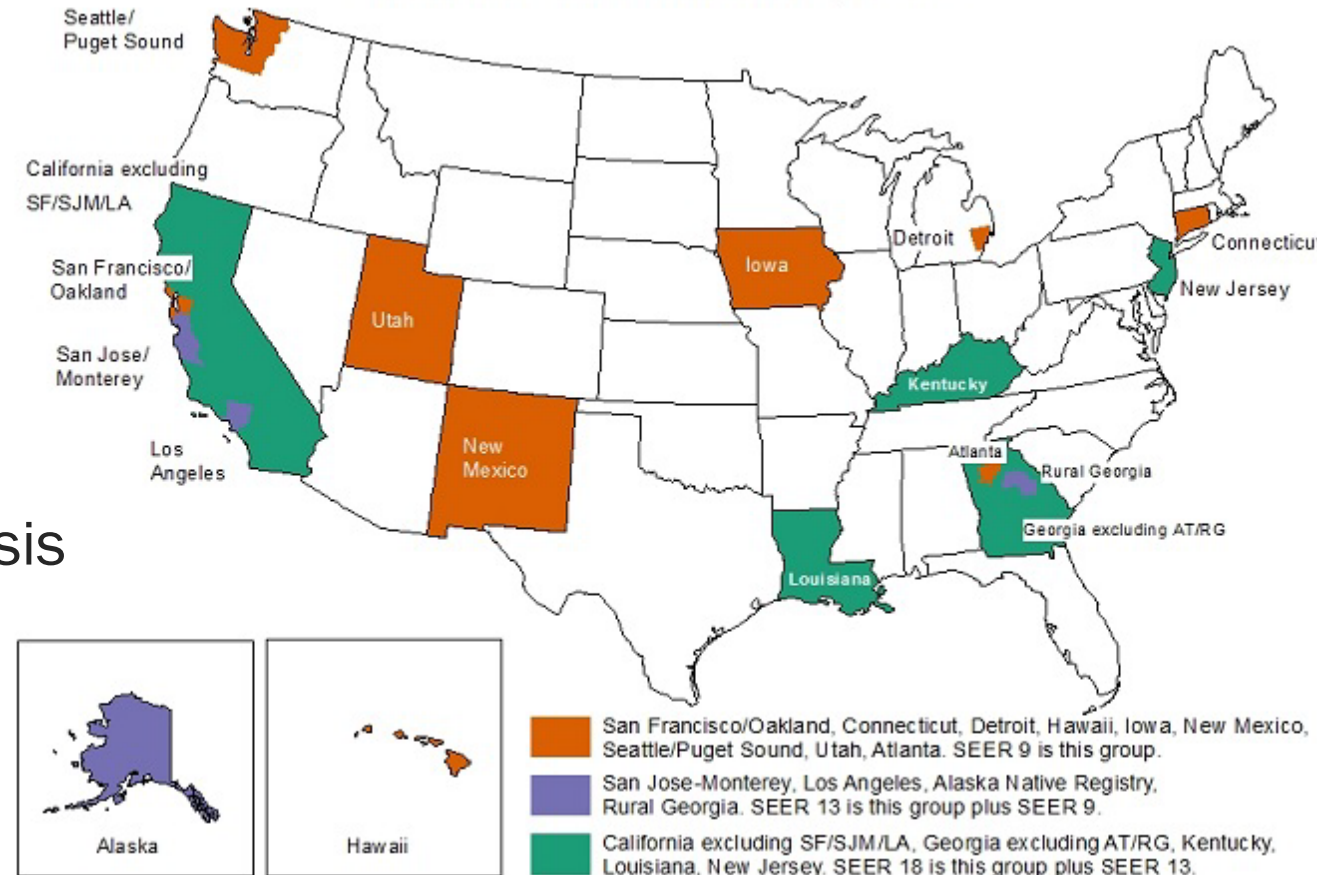
Approaches to Adverse Effects Research



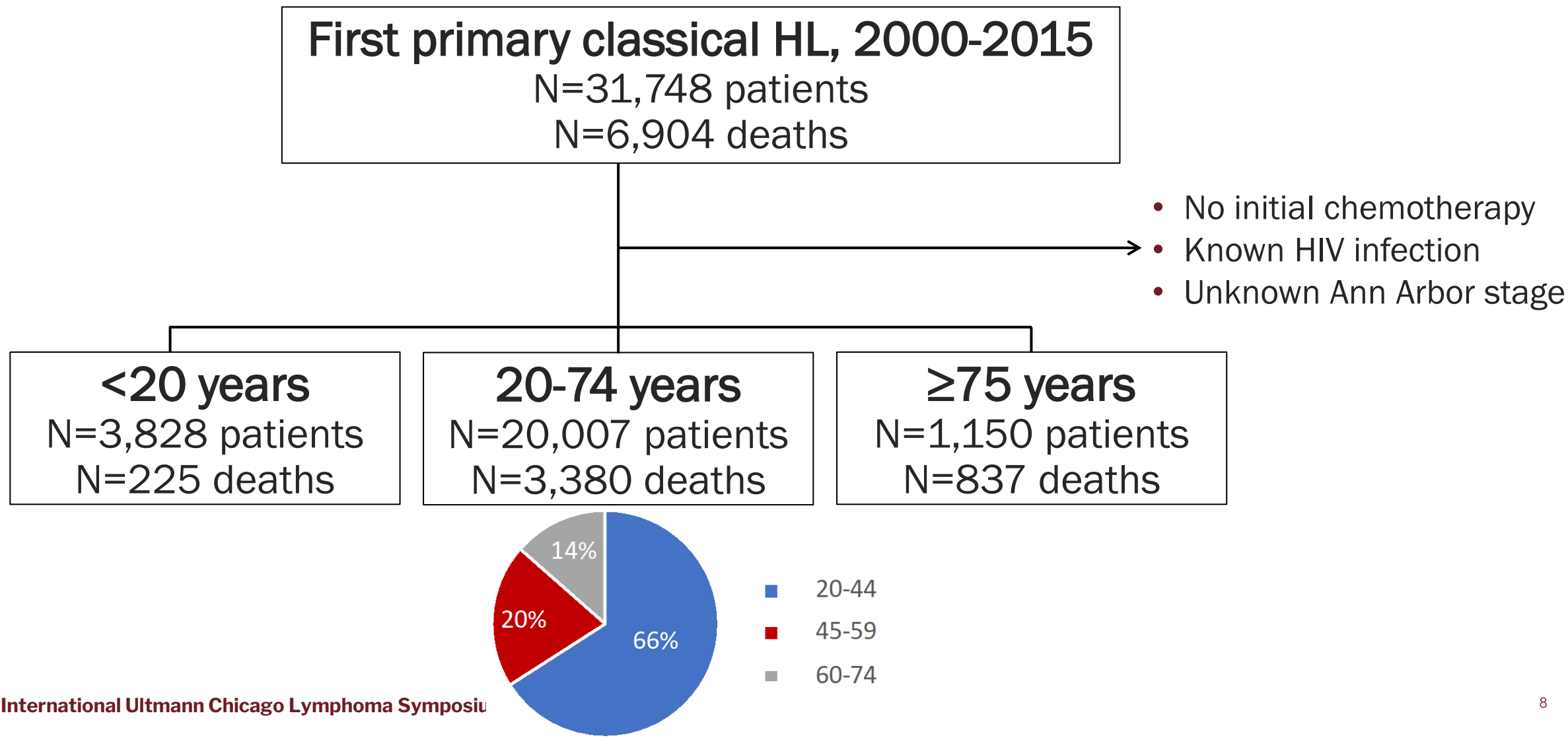
	Treatment Data	Clinical Data	Sample Size	Follow-Up
Clinical Trials				
Institution-Based Cohorts				
Population-Based Cancer Registries				

SEER Population-Based Cancer Registry Data

- 17 registries
 - ~25% US population
 - >95% of cancer diagnoses
- Limited clinical data
 - Ann Arbor stage
 - Initial chemotherapy (yes/no), radiotherapy (yes/no)
 - HIV infection at the time of HL diagnosis
- Systematic, long-term follow-up
 - Vital status (even if emigrate)
 - Cause of Death (ICD-10, National Center for Health Statistics)

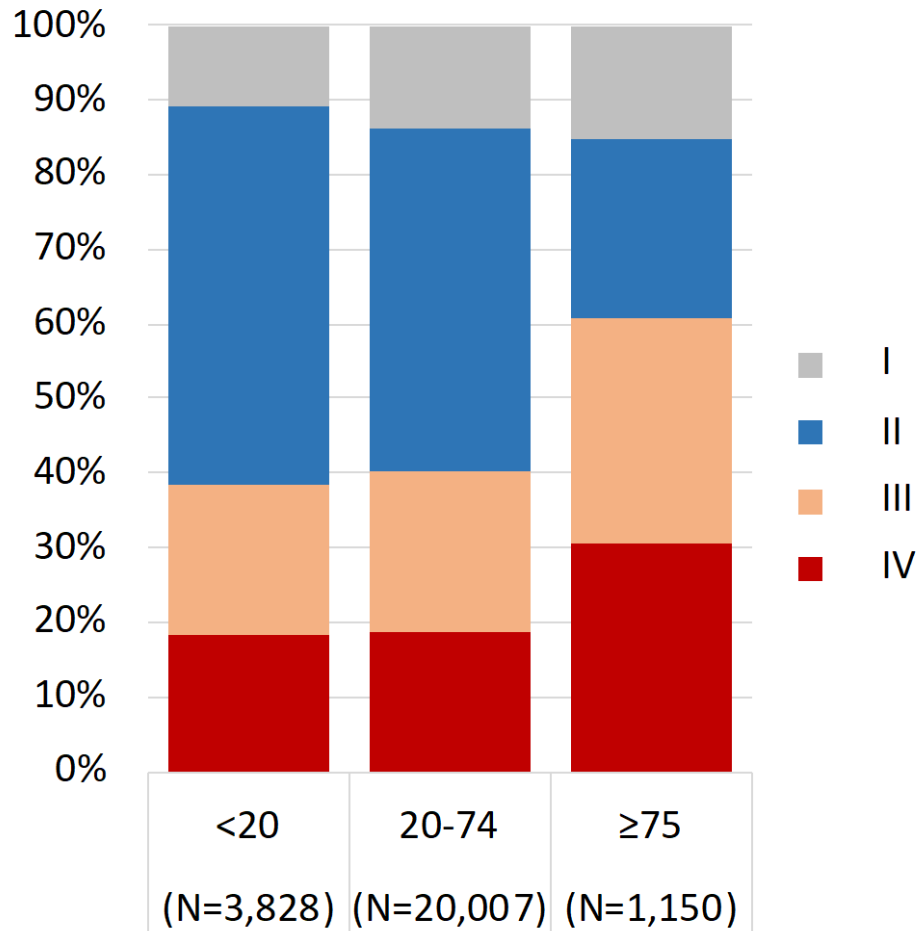


Mortality in Pop'n-Based cHL Cohort, 2000-2016

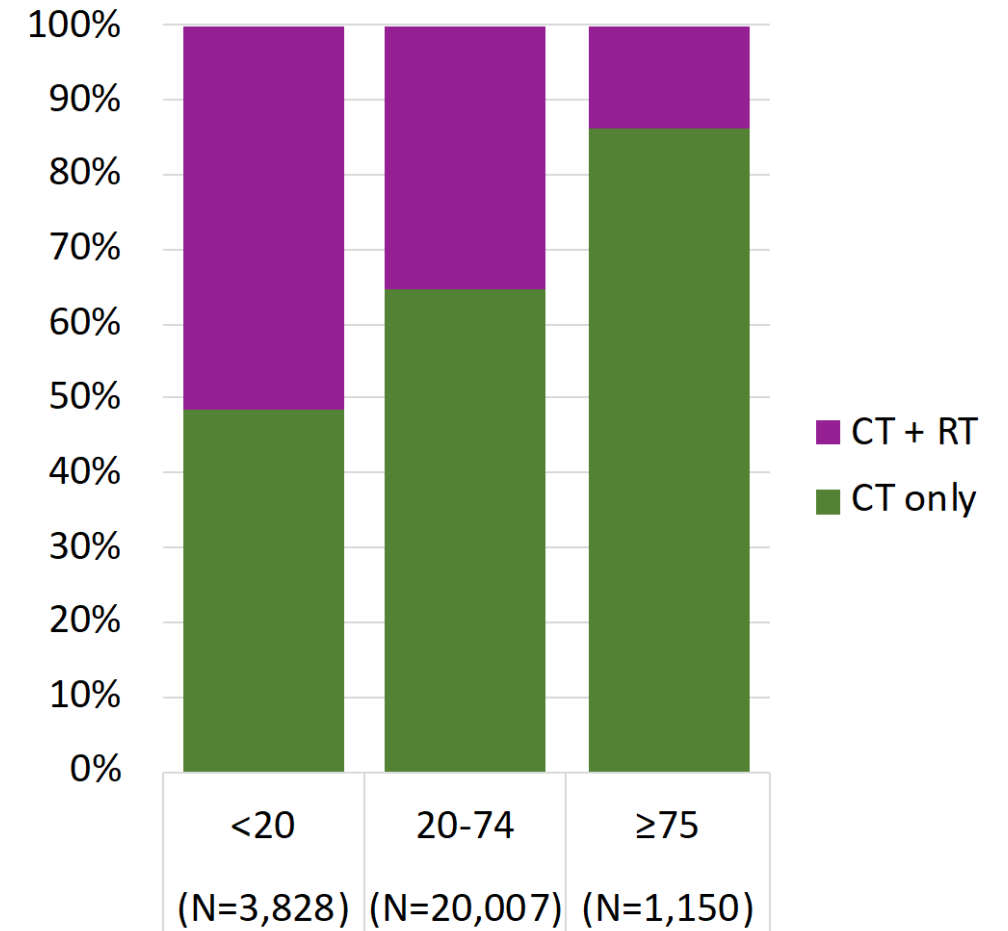


Study Population

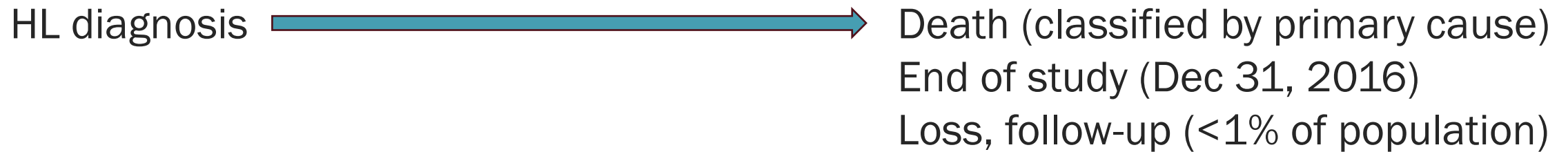
cHL Stage



Initial Treatment



Mortality in Pop'n-Based cHL Cohort, 2000-2016

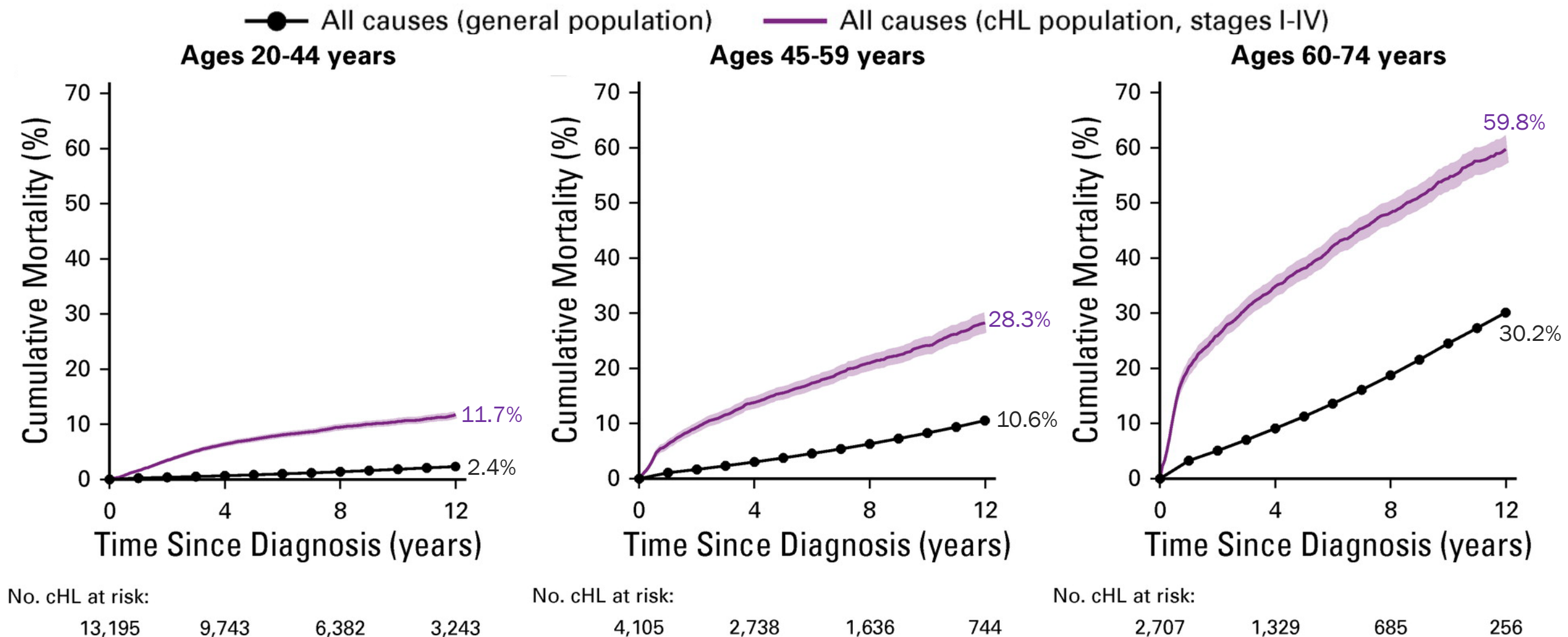


cHL Stage	Mean age at cHL	Mean person-years at risk
I/II	38	8.0
III/IV	43	6.6

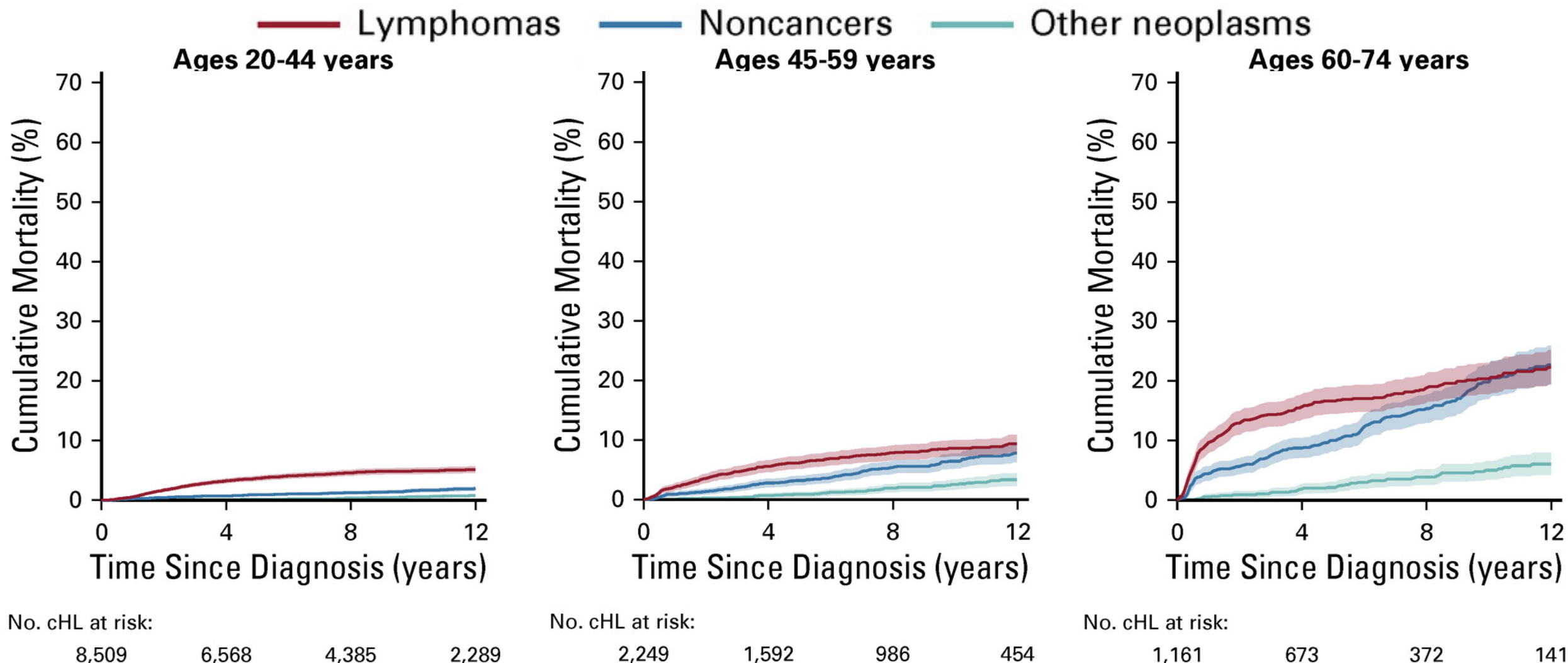
Statistical Analyses

- Absolute risk of death: Cumulative mortality, absolute excess risk
 - Relative risk of death: Standardized mortality ratio → multivariable Poisson regression
- ** Comparisons with the general population (accounting for age, sex, race, calendar year, and follow-up time)

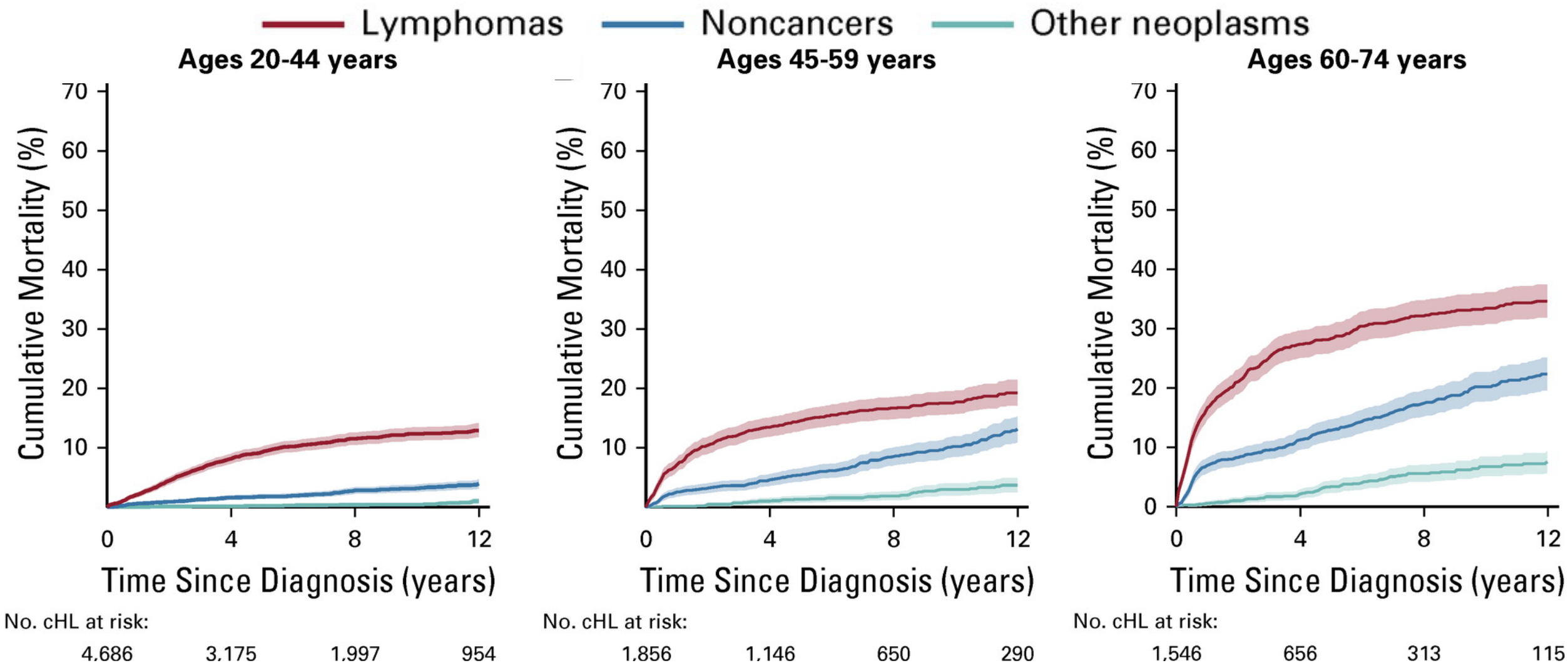
Overall Cumulative Mortality, All Stages



Cause-Specific Cumulative Mortality, Stage I/II



Cause-Specific Cumulative Mortality, Stage III/IV



SMRs: cHL, ages 20-74

	Stage I/II		Stage III/IV	
	Obs.	SMR(95% CI)	Obs.	SMR(95% CI)
All causes	1,400	3.3(3.2, 3.5)	1,980	6.0(5.8, 6.3)
All causes, excl. lymphoma	618	1.5(1.4, 1.6)	703	2.2(2.0, 2.4)

SMRs: cHL, ages 20-74

	Stage I/II		Stage III/IV	
	Obs.	SMR(95% CI)	Obs.	SMR(95% CI)
Infections	54	2.2(1.6, 2.8)	76	3.9(3.1, 4.9)
Septicemia	17	2.9(1.7, 4.7)	18	3.8(2.3, 6.1)
Respiratory infections	17	2.0(1.2, 3.2)	29	4.3(2.9, 6.2)
Gastrointestinal infections	9	2.3(1.0, 4.3)	11	3.6(1.8, 6.5)

SMRs: cHL, ages 20-74

	Stage I/II		Stage III/IV	
	Obs.	SMR(95% CI)	Obs.	SMR(95% CI)
Cardiovascular diseases	154	1.6(1.4, 1.9)	166	2.1(1.8, 2.5)

SMRs: cHL, ages 20-74

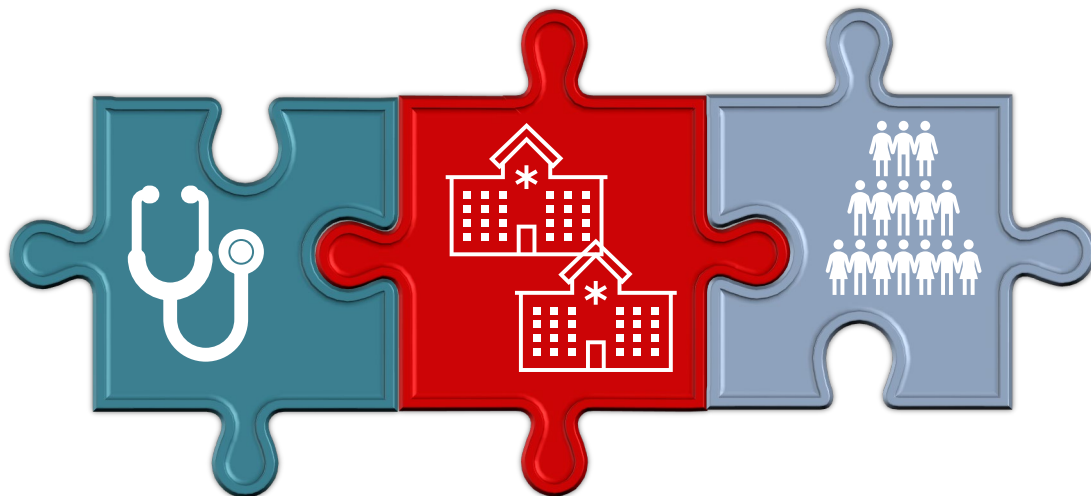
Cause of Death Yrs since cHL diagnosis	Stage I/II		Stage III/IV	
	Obs.	SMR(95% CI)	Obs.	SMR(95% CI)
Interstitial lung diseases				
<1.0	23	91.4(58.0, 137.2)	34	122.6(84.9, 171.4)
≥1.0	15	5.6(3.2, 9.3)	20	9.2(5.6, 14.3)
P _{diff} (latency)		<0.001		<0.001

SMRs: cHL, ages 20-74

Cause of Death Yrs since cHL diagnosis	Stage I/II		Stage III/IV	
	Obs.	SMR(95% CI)	Obs.	SMR(95% CI)
Heart disease				
<1.0	20	2.5(1.5, 3.8)	31	3.6(2.4, 5.1)
1.0-4.9	48	1.6(1.2, 2.2)	47	1.7(1.3, 2.3)
≥5.0	80	1.7(1.3, 2.1)	73	2.1(1.6, 2.6)
P _{diff (latency)}		0.291		0.008
Chronic obstructive pulmonary diseases				
<1.0	4	2.3(0.6, 5.9)	6	3.0(1.1, 6.5)
≥1.0	27	1.5(1.0, 2.1)	29	1.9(1.3, 2.7)
P _{diff (latency)}		0.435		0.247

Conclusions

- Patients treated in the ABVD era have increased mortality compared with the general population
 - Interstitial lung disease
 - Adverse events
 - Infections
 - Heart disease
- Stage III/IV cHL, <1 year after diagnosis
- Lower SMRs, but large fraction of excess deaths



- Roadmap for targeted efforts to further reduce mortality burden after cHL
- Diverse approaches needed to understand adverse effects as cHL treatments continue to evolve

Acknowledgements

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Supplementary Data

SMRs: cHL, ages <20

	Stage I/II		Stage III/IV	
	Obs.	SMR(95% CI)	Obs.	SMR(95% CI)
All causes	115	8.2(6.8, 9.8)	110	13.1(10.8, 15.8)
All causes, excl. lymphoma	32	2.3(1.6, 3.3)	28	3.4(2.3, 4.9)

SMRs: cHL, ages ≥ 75

	Stage I/II		Stage III/IV	
	Obs.	SMR(95% CI)	Obs.	SMR(95% CI)
All causes	325	2.2(1.9, 2.4)	512	3.4(3.1, 3.7)
All causes, excl. lymphoma	166	1.1(1.0, 1.3)	174	1.2(1.0, 1.4)

SMRs: cHL, ages ≥ 75

	Stage I/II		Stage III/IV	
	Obs.	SMR(95% CI)	Obs.	SMR(95% CI)
Infections	20	1.9(1.1, 2.9)	9	0.8(0.4, 1.6)
Respiratory infections	13	2.1(1.1, 3.7)	5	0.8(0.3, 2.0)
Digestive diseases	<3	~ ~	12	3.0(1.6, 5.3)
Neurologic diseases	22	0.7(0.4, 1.0)	23	0.7(0.4, 1.0)
Dementia	10	0.5(0.3, 1.0)	5	0.3(0.1, 0.6)
Cerebrovascular disease	11	1.1(0.5, 1.9)	16	1.6(0.9, 2.6)
Cardiovascular diseases	55	1.2(0.9, 1.5)	63	1.3(1.0, 1.7)
Heart disease	51	1.2(0.9, 1.5)	59	1.4(1.0, 1.8)
Respiratory diseases	25	2.2(1.4, 3.3)	21	1.8(1.1, 2.8)
COPD	8	0.9(0.4, 1.7)	6	0.6(0.2, 1.4)
Interstitial lung diseases	15	12.3(6.9, 20.4)	15	11.8(6.6, 19.5)
Accidents, falls, adverse events	4	1.1(0.3, 2.8)	10	2.7(1.3, 5.0)
All adverse events	3	3.5(0.7, 10.3)	7	8.3(3.3, 17.0)