

Lymphomas and other haematological cancers in the elderly

Henrik Frederiksen, professor

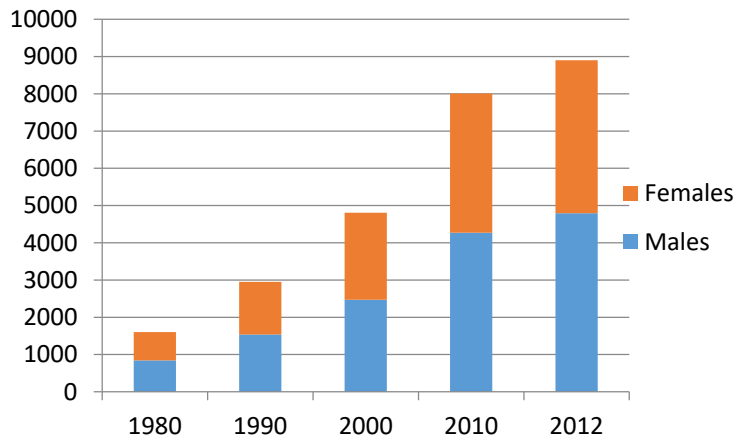
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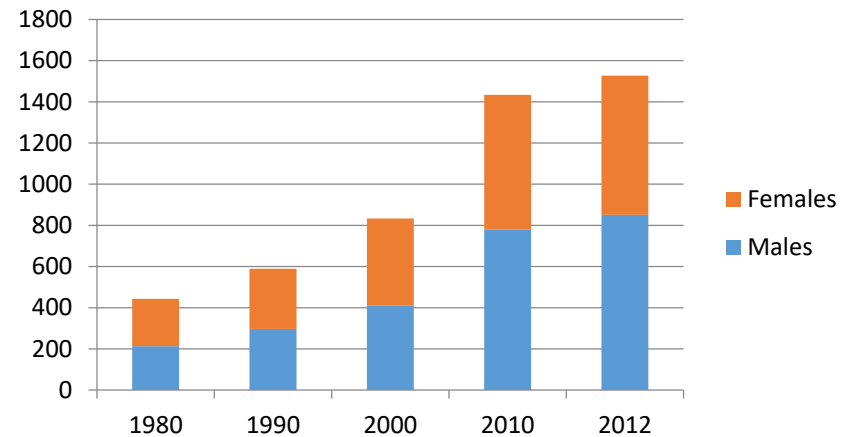
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Prevalence in Denmark

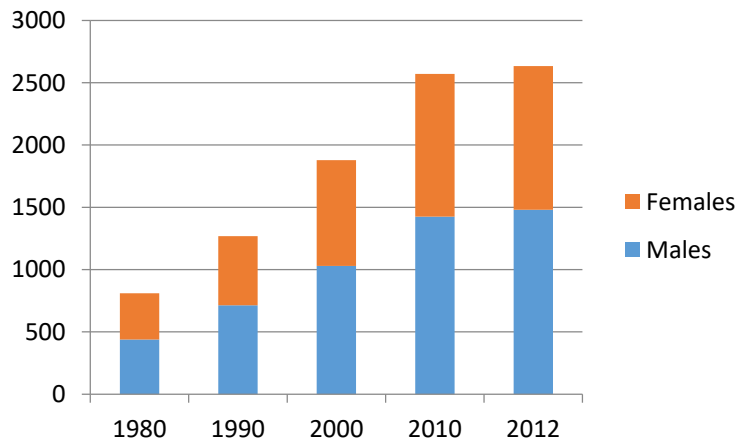
Non-hodgkin lymphoma (NHL)



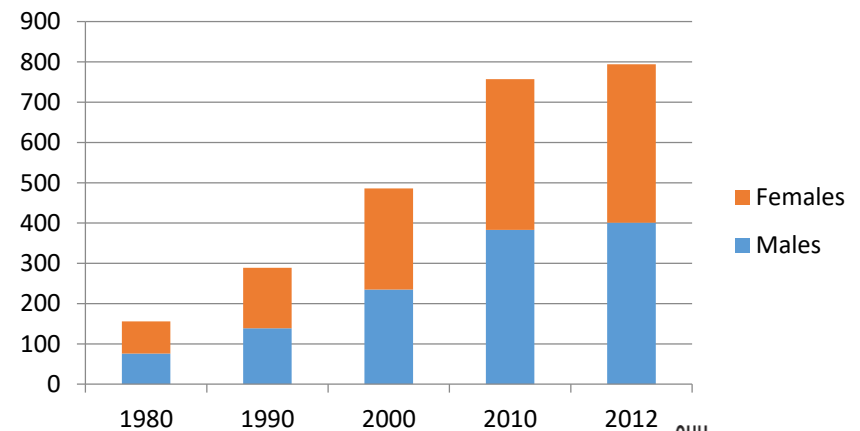
Multiple myeloma

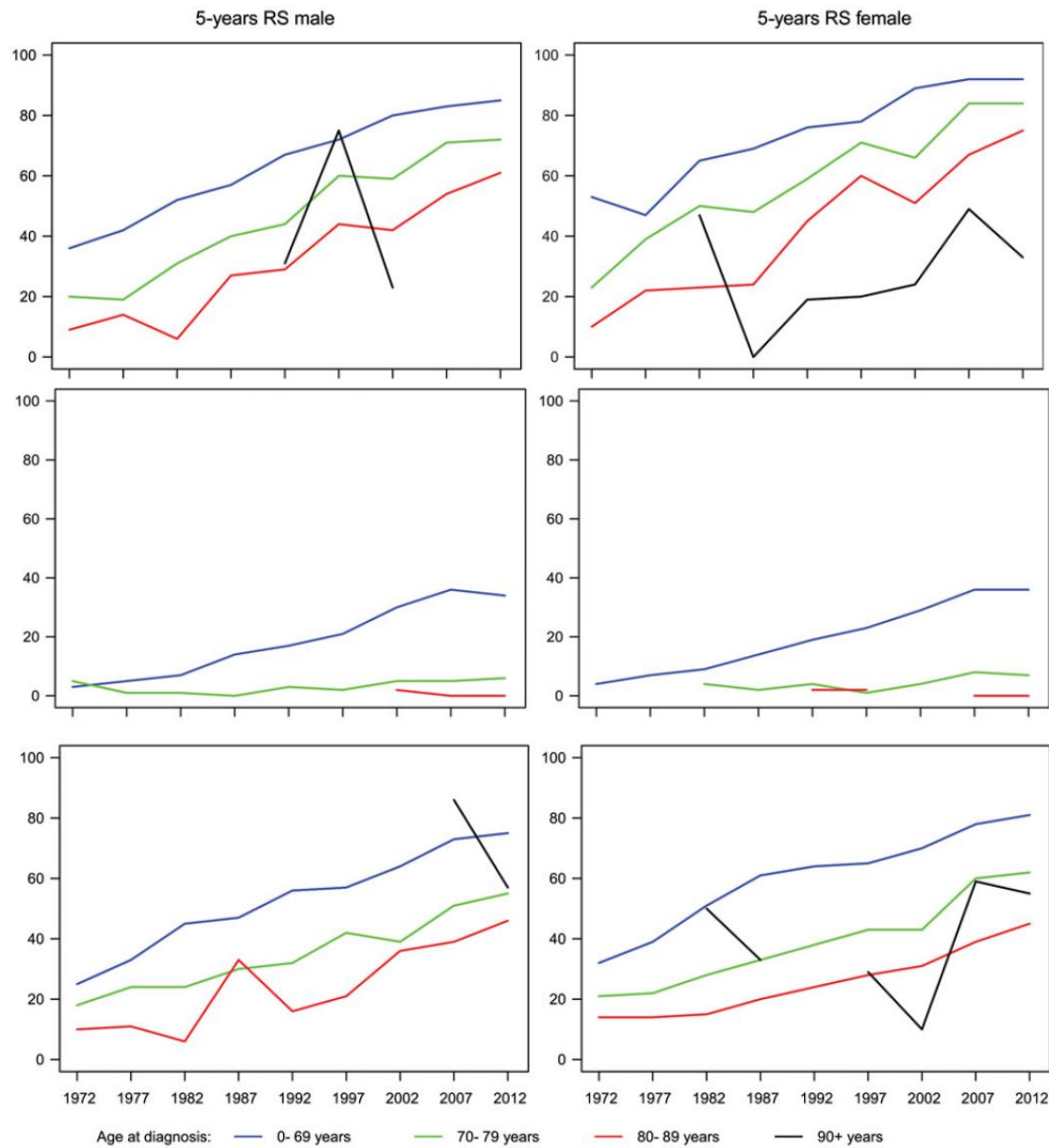


CLL



AML



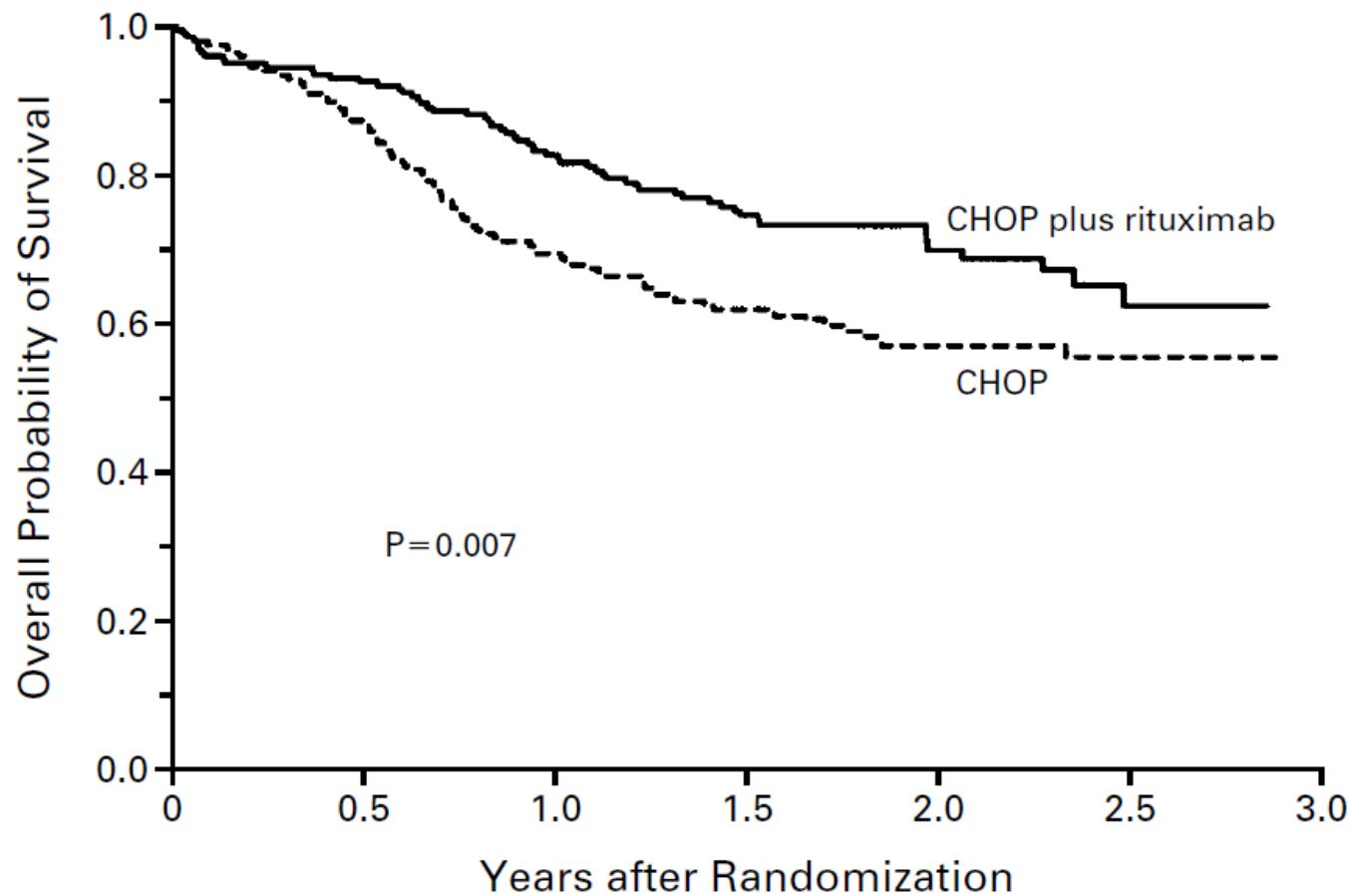


CLL

AML

NHL

Ocias et al, Acta Oncol, 2015



No. AT Risk

CHOP plus rituximab	202	187	167	118	64	21
CHOP	197	171	136	96	58	16

DLBCL - background

- DLBCL is a disease of the elderly - median age at diagnosis is 70 years¹
- Age specific incidence rate increases from <10/100.000 at the age of 50 years to >40/100.000 at the age of 80 years¹
- In clinical trials:
 - 3 year OS > 70% among patients above 60 years treated with R-CHOP²
 - 2 year OS 59% with R-miniCHOP for patients > 80 years³
- Frailty and comorbidities often preclude elderly from clinical trials
- Limited knowledge on the optimal treatment strategy among the oldest DLBCL patients

1 Haematological Malignancy Research Network (HMRN) 2004–2012

2 Pfreundschuh M et al, Lancet Oncol 2008

3 Peyrade F et al, Lancet Oncol 2011



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Original Research

Treatment strategies and outcomes in diffuse large B-cell lymphoma among 1011 patients aged 75 years or older: A Danish population-based cohort study[☆]



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Aim

- In old DLBCL patients to investigate
 - Comorbidity
 - Treatment strategies
 - Hospitalization
 - Survival (PFS/OS)
 - Using a population-based cohort

Patients and methods

- Patients ≥ 75 yr newly diagnosed DLBCL between 2003-2012 were identified using Danish National Lymphoma Registry-LYFO
 - Exclusion: Primary CNS involvement or low-grade lymphoma
- From LYFO
 - Patients, stage, IPI, Performance status, date of diagnosis, baseline pathological features
- From medical records
 - Details on treatment and relapse
- From Danish National health registries
 - Charlson comorbidity index (CCI)
 - Survival

Treatment

- Standard treatment (R-CHOP)
- Less intensive regimens (e.g. R-CEOP, R-CVP)
- Palliative treatment (e.g. prednisolone, R-mono, oral chemo, radiotherapy)

Outcomes

- Hospital admission
- Progression / relapse when proven by -
 - Biopsy, or
 - Imaging, or
 - Clinical findings strongly suggestive of relapse
- Mortality

	75-79 years	80-84 years	>85 years	All
Number (%)	403 (100)	367 (100)	241 (100)	1011 (100)
Time trend				
2003-2007	187 (46)	184 (50)	110 (46)	481 (48)
2008-2012	216 (54)	183 (50)	131 (54)	530 (52)
Sex				
Male	192 (48)	188 (51)	136 (56)	516 (51)
Female	211 (52)	179 (49)	105 (44)	495 (49)
Ann Arbor Stage				
1 - Stage I-II	150 (37)	162 (44)	97 (40)	409 (40)
2 - Stage III-IV	244 (61)	186 (51)	119 (49)	549 (54)
Unknown	9 (2)	19 (5)	25 (10)	53 (5)
ECOG Performance Status				
0-1	281 (70)	251 (68)	150 (62)	682 (67)
2-4	117 (29)	112 (31)	87 (36)	316 (31)
Unknown	5 (1)	4 (1)	4 (2)	13 (1)
IPI				
1	82 (20)	84 (23)	49 (20)	215 (21)
2-3	192 (48)	161 (44)	94 (39)	447 (44)
4-5	100 (25)	81 (22)	56 (23)	237 (23)
Unknown	29 (7)	41 (11)	42 (17)	112 (11)
Co-morbidity (CCI)				
None (0)	160 (40)	158 (43)	100 (41)	418 (41)
Moderate (1-2)	154 (38)	143 (39)	94 (39)	391 (39)
High (3-)	89 (22)	66 (18)	47 (20)	202 (20)
Treatment				
1-Standard	336 (83)	239 (65)	76 (32)	651 (64)
2-Less intensive	36 (9)	62 (17)	45 (19)	143 (14)
3-Palliative	31 (8)	66 (18)	120 (50)	217 (21)

Full dosage ~ R-CHOP $\geq 80\%$

- Intended full dosage
 - 84% 75-79 yr
 - 52% 80-84 yr
 - 45% 85+ yr
- Completion of full dosage of those with intended
 - 69% 75-79 yr
 - 56% 80-84 yr
 - 51% 85+

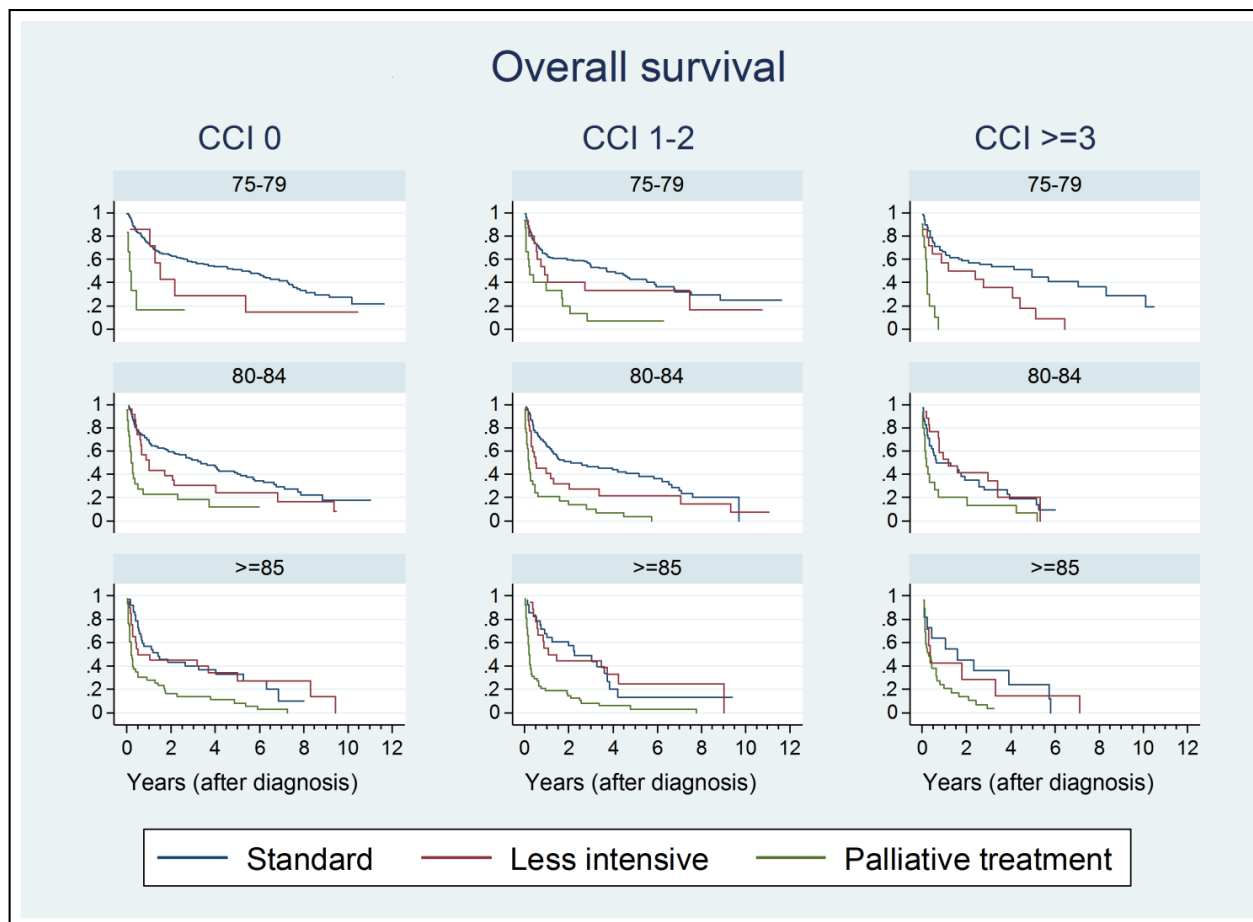
Reasons for reduced treatment

- Less intensive
 - cardiac comorbidity
- Palliative
 - Patients decision
 - Dementia
 - Neurological comorbidity
- Rituximab included for:
 - 74% 2003-07
 - 93% 2008-12

Results

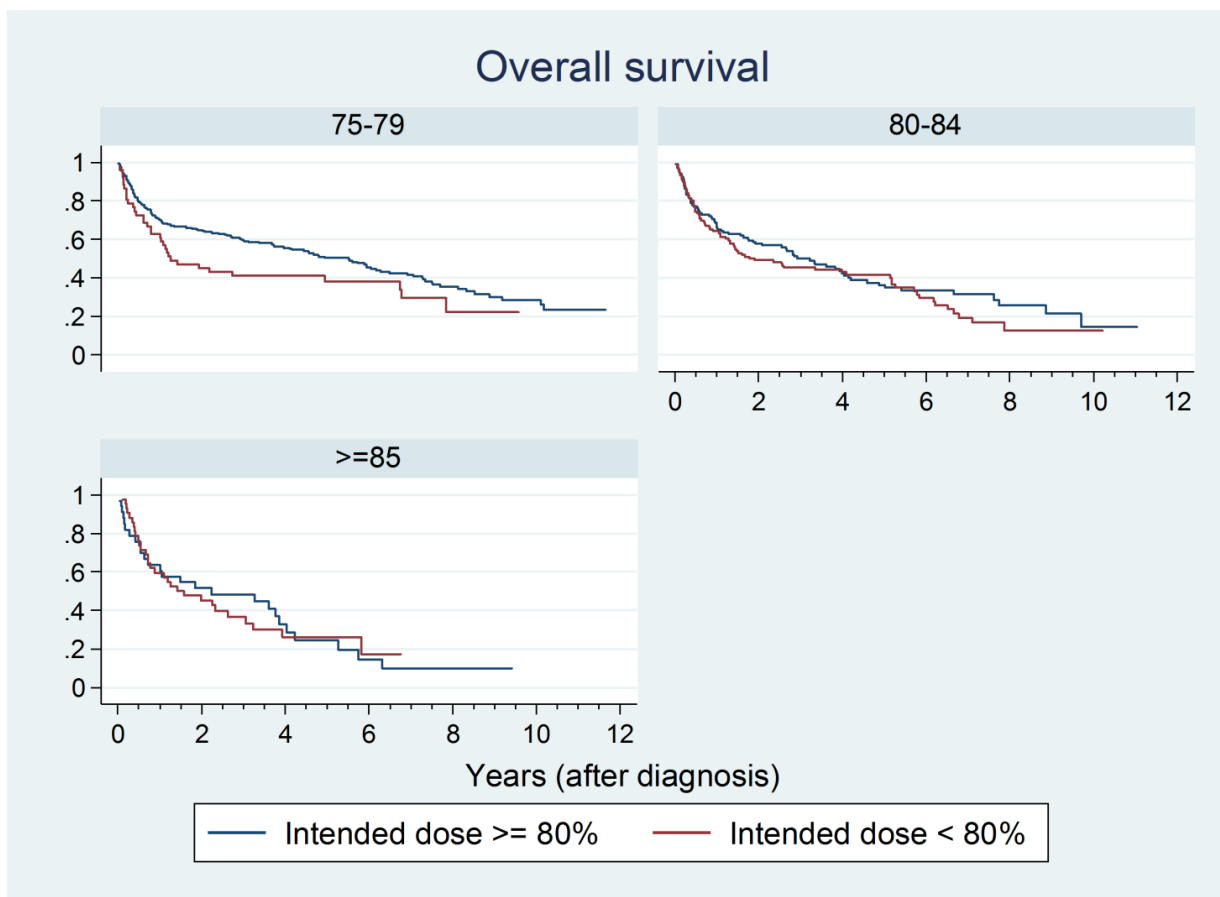
3 year OS	75-79	80-84	85+
Standard	56% (50-61)	46% (40-53)	43% (31-54)
Less intensive	32% (18-46)	29% (18-40)	40% (26-53)
Palliative	5% (0-19)	15% (7-24)	9% (5-16)
5 year OS			
Standard	47% (41-53)	38% (31-44)	26% (16-37)
Less intensive	25% (13-40)	21% (12-32)	23% (11-36)
Palliative	5% (0-19)	7% (2-15)	5% (2-10)

3- and 5 years OS estimates (95% CI)



	75–79 years	80–84 years	85+ years
	Adjusted HR	Adjusted HR	Adjusted HR
Time period			
2003–2007	1 (Ref)	1 (Ref)	1 (Ref)
2008–2012	0.93 (0.72–1.21)	0.70 (0.55–0.89)	1.00 (0.75–1.35)
Age			
Hazard per year	1.05 (0.96–1.15)	1.01 (0.93–1.10)	1.01 (0.96–1.06)
Sex			
Female	0.82 (0.64–1.05)	0.94 (0.74–1.18)	1.30 (0.98–1.72)
IPI			
1	1 (Ref)	1 (Ref)	1 (Ref)
2–3	1.69 (1.20–2.40)	1.84 (1.34–2.53)	1.62 (1.09–2.42)
4–5	2.83 (1.92–4.16)	4.24 (2.96–6.08)	3.18 (2.09–4.83)
Unknown	2.60 (1.58–4.29)	2.43 (1.57–3.76)	2.31 (1.47–3.61)
Comorbidity (CCI score)			
None (0) ^a	1 (Ref)	1 (Ref)	1 (Ref)
Moderate (1–2)	1.25 (0.94–1.66)	1.35 (1.04–1.75)	1.03 (0.76–1.39)
High (3–)	1.14 (0.82–1.57)	1.86 (1.34–2.58)	1.19 (0.83–1.72)
Treatment			
Standard	1 (Ref)	1 (Ref)	1 (Ref)
Less intensive	1.54 (1.04–2.30)	1.39 (1.01–1.91)	1.04 (0.69–1.58)
Palliative	4.15 (2.73–6.31)	3.16 (2.32–4.29)	2.70 (1.89–3.85)

R-CHOP treatment



OS stratified by intended (R-)CHOP dose

Conclusions – THIS IS NOT A CLINICAL TRIAL, however.....

- (R-)CHOP provides durable remissions among elderly DLBCL-patients – outside clinical trials
- No survival benefit with (R-)CHOP at age above 85 years or age above 80 years with comorbidities
- No adverse impact on OS with planned dose reduction in patients above 80 years
- No excess hospitalization with (R-)CHOP
- In patients above 80 years, candidates for anthracycline containing treatment must be carefully selected

Acknowledgements

PROCRIN

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PROGRAM FOR CLINICAL RESEARCH INFRASTRUCTURE

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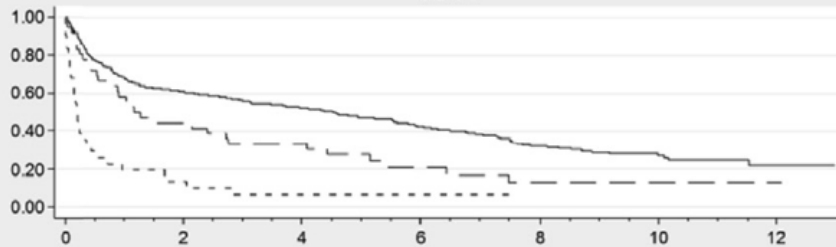
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Plans for the future

- Study toxicity
 - Immediate and late effects
 - Cardiovascular
 - Neurological
 - Psychiatric
 - Malignancies
 - Hospitalization up to 5-years following diagnosis
 - Compared to age-sex matched general population

OS

75-79

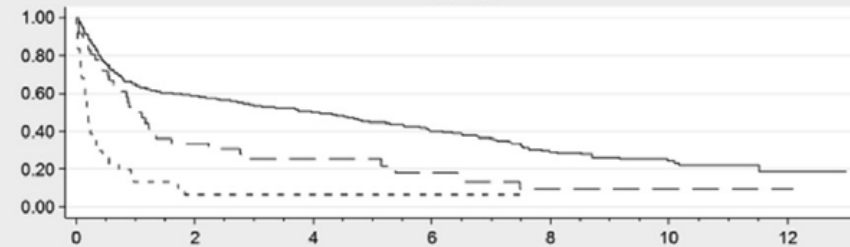


Number at risk							
ST	336	205	163	93	52	24	5
LI	36	16	12	5	3	2	1
PT	31	4	1	1	0	0	0

Logrank p-value for the difference between ST and LI: 0.008.

PFS

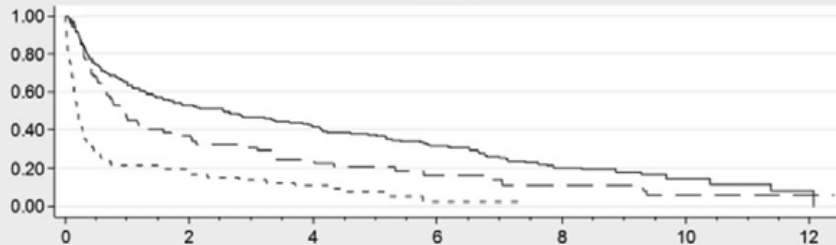
75-79



Number at risk							
ST	335	196	155	88	45	22	4
LI	36	12	9	4	2	1	1
PT	31	2	1	1	0	0	0

Logrank p-value for the difference between ST and LI: 0.003.

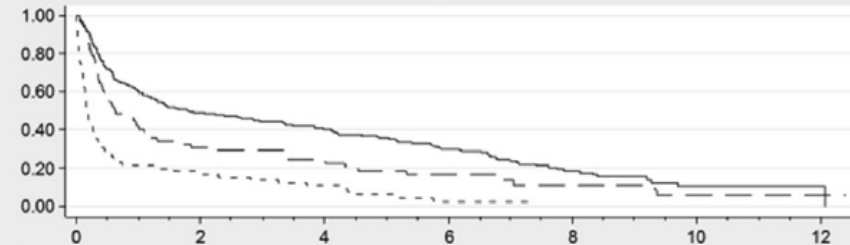
80-84



Number at risk							
ST	239	126	92	50	21	7	2
LI	62	23	13	7	4	2	1
PT	66	12	7	1	0	0	0

Logrank p-value for the difference between ST and LI: 0.011.

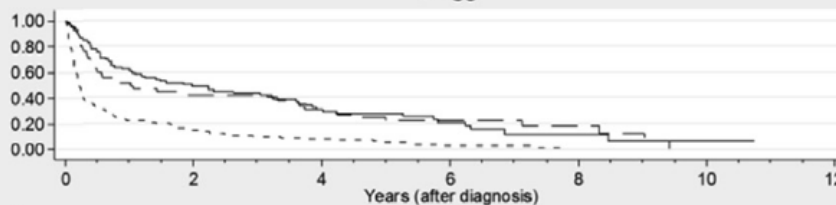
80-84



Number at risk							
ST	238	117	88	47	19	4	2
LI	62	19	13	7	4	2	1
PT	66	12	7	1	0	0	0

Logrank p-value for the difference between ST and LI: 0.010.

>=85

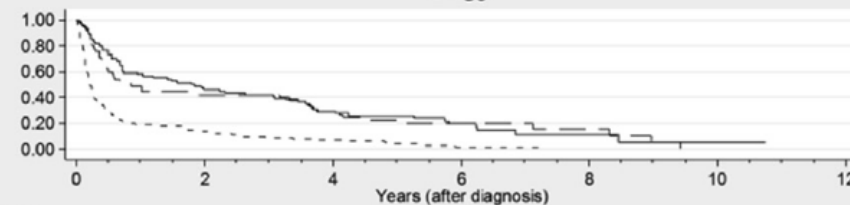


Number at risk							
ST	76	37	19	8	3	1	0
LI	45	19	14	9	3	0	0
PT	120	18	9	2	0	0	0

— Standard — Less intensive - - - Palliative treatment

Logrank p-value for the difference between ST and LI: 0.736.

>=85



Number at risk							
ST	76	35	18	8	3	1	0
LI	45	19	13	8	3	0	0
PT	120	17	8	1	0	0	0

— Standard — Less intensive - - - Palliative treatment

Logrank p-value for the difference between ST and LI: 0.710.

Causes of death

