

# Prognostic value of tumor bulk in modern management of common lymphoma subtypes: an Australasian Lymphoma and Related Diseases Registry study

Eliza Chung,<sup>1</sup> Luke Wang,<sup>1,2</sup> Cameron Wellard,<sup>1</sup> Allison Barraclough,<sup>3</sup> Belinda A. Campbell,<sup>4-6</sup> Geoffrey Chong,<sup>7</sup> Pietro Di Ciaccio,<sup>8,9</sup> Gareth P. Gregory,<sup>3,10</sup> Greg Hapgood,<sup>11,12</sup> Anna M. Johnston,<sup>13,14</sup> Constantine S. Tam,<sup>15,16</sup> Stephen Opat,<sup>1,10</sup> Erica M. Wood,<sup>1</sup> Zoe K. McQuilten<sup>1,15#</sup> and Eliza A. Hawkes<sup>1,17#</sup>

<sup>1</sup>School of Public Health and Preventive Medicine, Monash University, Melbourne; <sup>2</sup>Eastern Health, Box Hill; <sup>3</sup>Fiona Stanley Hospital, Murdoch; <sup>4</sup>Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne; <sup>5</sup>The Sir Peter MacCallum Department of Oncology, The University of Melbourne, Parkville; <sup>6</sup>Department of Clinical Pathology, The University of Melbourne, Parkville; <sup>7</sup>Ballarat Regional Integrated Cancer Centre, Ballarat; <sup>8</sup>Department of Haematology, The Canberra Hospital, Canberra; <sup>9</sup>College of Health and Medicine, Australian National University, Canberra; <sup>10</sup>School of Clinical Sciences at Monash Health, Monash University, Melbourne; <sup>11</sup>Princess Alexandra Hospital, Brisbane; <sup>12</sup>School of Medicine, University of Queensland, Brisbane; <sup>13</sup>Royal Hobart Hospital, Hobart; <sup>14</sup>University of Tasmania, Hobart; <sup>15</sup>Alfred Health, Melbourne; <sup>16</sup>Central Clinical School, Monash University, Melbourne and <sup>17</sup>Olivia Newton-John Cancer Research Institute at Austin Health, Heidelberg, Australia

*#ZKM and EAH contributed equally as senior authors.*

**Correspondence:** E.A. Hawkes  
[Eliza.Hawkes@onjcri.org.au](mailto:Eliza.Hawkes@onjcri.org.au)

**Received:** March 28, 2025.

**Accepted:** September 15, 2025.

**Early view:** September 25, 2025.

<https://doi.org/10.3324/haematol.2025.287919>

©2026 Ferrata Storti Foundation

Published under a CC BY-NC license



## Supplementary Appendix

**Supplementary Table S1. Lymphoma treatment regimens from the LaRDR according to intensity.**

<b>Low intensity</b>
(R) Gemcitabine and vinORELBine
Brentuximab Vedotin
Chlorambucil and Rituximab
ChIVPP (Chlorambucil vinBLASTine Procarbazine Prednisolone)
Ibrutinib
PVAG (Prednisolone vinBLASTine DOXOrubicin Gemcitabine)
Rituximab monotherapy
VinCRISTine
<b>Standard intensity</b>
(R) ICE (Fractionated or infused IFOSFamide cARBOplatin Etoposide +/-rituximab)
(R) GDP (Gemcitabine Dexamethasone cISplatin)
(R)-CHOP21
ABVD (DOXOrubicin Bleomycin VinBLASTine Dacarbazine)-like
Bendamustine and RITUximab
R-CEOP (Rituximab, Cyclophosphamide, Etoposide Phosphate, Vincristine, Prednisolone)
R-CHEP (Rituximab / Cyclophosphamide / Doxorubicin / Etoposide Phosphate / Prednisolone)
R-CVP (RITUximab CYCLOPHOSPHamide vinCRISTine Prednisolone)
R-DHAP (RITUximab Dexamethasone Cytarabine cISplatin)
R-GCVP (Rituximab Gemcitabine Cyclophosphamide Vincristine and Prednisolone)
R-GemOX (RITUximab Gemcitabine Oxaliplatin)
R-miniCHOP (rituximab combined with low-dose CHOP)
R-MPV (RITUximab, Methotrexate, Procarbazine, and Vincristine)
<b>High intensity</b>
(R) CHOEP21 (rituximab, CYCLOPHOSPHamide DOXOrubicin vinCRISTine Etoposide Prednisolone)
(R)-CHOP14 (CYCLOPHOSPHamide DOXOrubicin vinCRISTine Prednisolone)
BEACOPP Escalated (Bleomycin Etoposide DOXOrubicin CYCLOPHOSPHamide VinCRISTine Procarbazine Prednisolone)
DA-R-EPOCH (Dose Adjusted RITUximab Etoposide Prednisolone vinCRISTine CYCLOPHOSPHamide DOXOrubicin)
ESHAP (Etoposide Methylprednisolone Cytarabine cISplatin)
Hyper CVAD Part A and B
IVAC (iFOSFamide etoposide cytarabine) followed by Cy-TBI

R-CHOEP14
R-CODOX-M +/-IVAC (Rituximab, CYCLOPHOSPHamide vinCRISTine DOXOrubicin Methotrexate, IFOSFamide Etoposide Cytarabine)
R-maxi-CHOP and R-HiDAC Treatment
SMARTE-R-CHOP14 (RITUximab CYCLOPHOSPHamide DOXOrubicin VinCRISTine Prednisolone)
SMILE (Dexamethasone Methotrexate IFOSFamide L-asparaginase Etoposide)

**Supplementary Table S2. Frontline treatment selection according to presence of bulk as defined by survey in each disease subtype.**

	Aggressive lymphoma								Indolent lymphoma									
	DLBCL (7.5cm)		TCL (7.5cm)		HL (10cm)		BL (7.5cm)		FL (7cm)		MZL (7.5cm)		SMZL*	MALT	NMZL			
	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y						
N evaluable in exploratory analysis	584		34		202		21		232		38		-	-	13	22		
Bulk	208	376	14	26	137	65	13	9	67	165	15	23	-	-	8	5	6	16
Treatment categories																		
Systemic chemotherapy only	177 (85)	307 (82)	14 (100)	23 (88)	118 (87)	52 (80)	13 (100)	9 (100)	<b>52</b> <b>(78)</b>	<b>151</b> <b>(92)</b>	<b>8</b> <b>(53)</b>	<b>21</b> <b>(91)</b>	-	-	3 (38)	4 (80)	4 (67)	15 (94)
Chemotherapy with consolidative radiotherapy	28 (14)	64 (17)	0 (0)	3 (12)	18 (13)	13 (20)	0 (0)	0 (0)	<b>2</b> <b>(3)</b>	<b>7</b> <b>(4)</b>	<b>0</b> <b>(0)</b>	<b>0</b> <b>(0)</b>	-	-	0 (0)	0 (0)	0 (0)	0 (0)
Localized treatment <sup>†</sup>	3 (<1)	3 (1)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	<b>13</b> <b>(19)</b>	<b>7</b> <b>(4)</b>	<b>7</b> <b>(47)</b>	<b>2</b> <b>(9)</b>	-	-	5 (62)	1 (20)	2 (33)	1 (6)

DLBCL: diffuse large B-cell lymphoma; TCL: T-cell lymphoma; HL: Hodgkin lymphoma; BL: Burkitt lymphoma; FL: follicular lymphoma; MZL: marginal zone lymphoma; SMZL: splenic marginal zone lymphoma; MALT: extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue; NMZL: nodal marginal zone lymphoma.

Bold font denotes statistically significant difference ( $p \leq 0.05$ ).

\* Further details of the subtypes of marginal zone lymphoma (SMZL, MALT, and NMZL) were provided in the table. No data was available in the SMZL group by using bulk cut-off of 7.5 cm for analysis due to a small sample size.

<sup>†</sup>Local treatment includes surgical excision and/or localized radiotherapy and/or helicobacter pylori eradication therapy for gastric MZL patients.

**Supplementary Table S3. Hazard ratios of PFS and OS according to bulk as defined by survey in each disease subtype.**

	Aggressive lymphoma				Indolent lymphoma	
	DLBCL (>7.5cm)	TCL (>7.5cm)	HL (>10cm)	BL (>7.5cm)	FL (>7cm)	MZL (>7.5cm)
<b>Bulk</b>						
PFS (95% CI)	<b>1.23</b> <b>(1.01 – 1.51)</b>	0.90 (0.55 – 1.47)	0.50 (0.20 – 1.22)	3.06 (0.93 – 10.06)	0.96 (0.65 – 1.40)	0.78 (0.27 – 2.19)
OS (95% CI)	1.17 (0.95 – 1.45)	0.91 (0.53 – 1.56)	Not evaluable†	<b>3.80</b> <b>(1.14 – 12.63)</b>	0.85 (0.51 – 1.43)	1.68 (0.60 – 4.72)
<b>Bulk adjusted for prognostic scores*</b>						
PFS (95%CI)	1.11 (0.91 – 1.36)	-	0.54 (0.22 – 1.35)	-	0.89 (0.61 – 1.30)	-
OS (95%CI)	1.04 (0.84 – 1.28)	-	Not evaluable†	-	0.70 (0.41 – 1.17)	-

PFS: progression-free survival; OS: overall survival; CI: confidence interval; DLBCL: diffuse large B-cell lymphoma; TCL: T-cell lymphoma; HL: Hodgkin lymphoma; BL: Burkitt lymphoma; FL: follicular lymphoma; MZL: marginal zone lymphoma.

Bold font denotes statistically significant difference (p≤0.05).

\*Prognostic scores used in estimating hazard ratios: DLBCL, RIPI; FL, FLIPI; HL, Hasenclever international prognostic score.

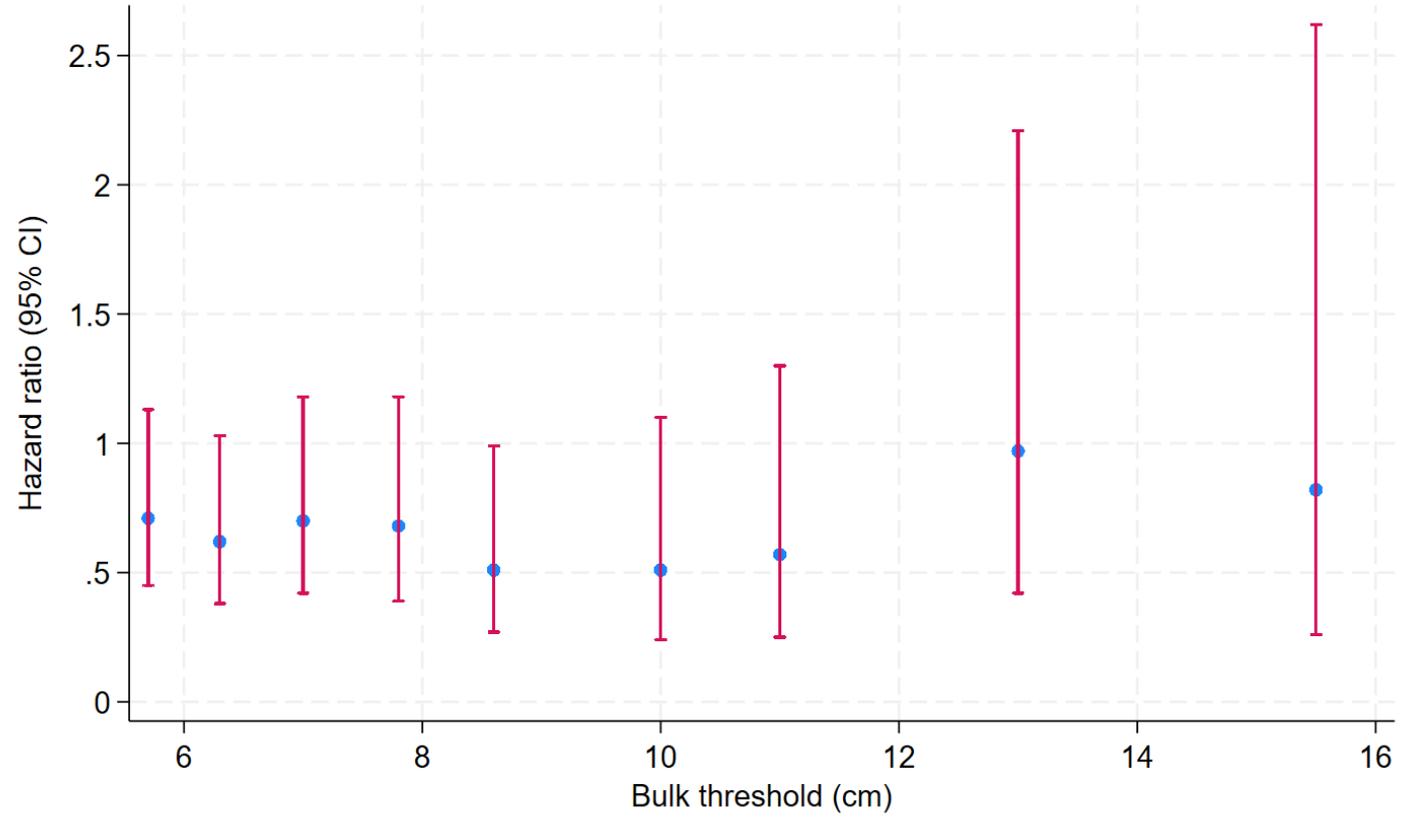
† Overall survival of HL patients was not evaluable due to small sample size.

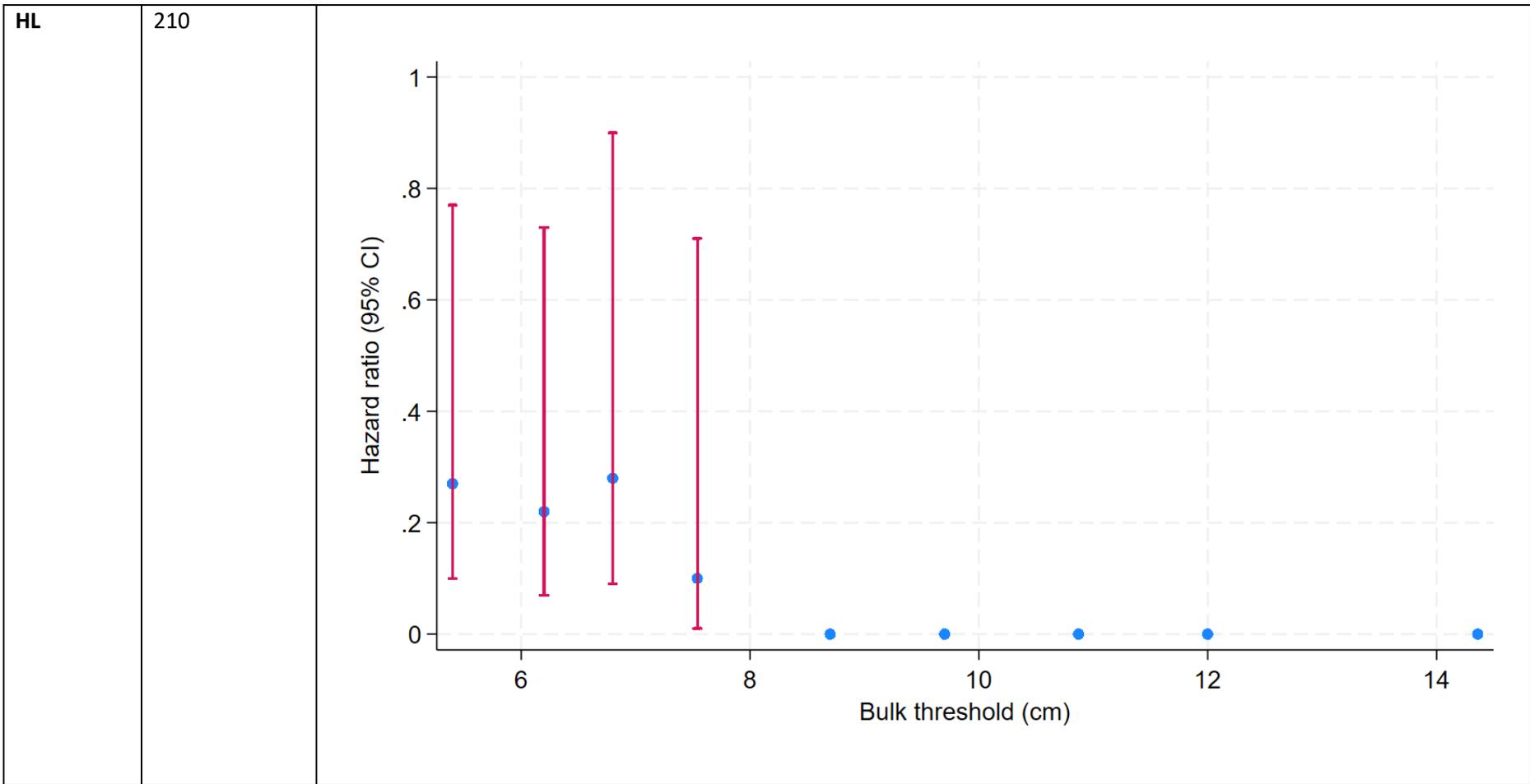
Supplementary Table S4. Hazard ratios of overall survival using different definitions of bulk in DLBCL, FL and HL.

Lymphoma subtypes	Number of patients with reported measurement	Hazard ratios for overall survival using different definitions of bulk																		
DLBCL	611	<table border="1"> <caption>Data extracted from the forest plot</caption> <thead> <tr> <th>Bulk threshold (cm)</th> <th>Hazard ratio (95% CI)</th> </tr> </thead> <tbody> <tr> <td>6</td> <td>1.0 (0.85, 1.25)</td> </tr> <tr> <td>7</td> <td>1.0 (0.85, 1.25)</td> </tr> <tr> <td>8</td> <td>1.0 (0.85, 1.25)</td> </tr> <tr> <td>9</td> <td>1.1 (0.85, 1.35)</td> </tr> <tr> <td>10</td> <td>1.2 (0.95, 1.55)</td> </tr> <tr> <td>11</td> <td>1.2 (0.95, 1.55)</td> </tr> <tr> <td>13</td> <td>1.2 (0.95, 1.55)</td> </tr> <tr> <td>16</td> <td>1.3 (0.85, 2.15)</td> </tr> </tbody> </table>	Bulk threshold (cm)	Hazard ratio (95% CI)	6	1.0 (0.85, 1.25)	7	1.0 (0.85, 1.25)	8	1.0 (0.85, 1.25)	9	1.1 (0.85, 1.35)	10	1.2 (0.95, 1.55)	11	1.2 (0.95, 1.55)	13	1.2 (0.95, 1.55)	16	1.3 (0.85, 2.15)
Bulk threshold (cm)	Hazard ratio (95% CI)																			
6	1.0 (0.85, 1.25)																			
7	1.0 (0.85, 1.25)																			
8	1.0 (0.85, 1.25)																			
9	1.1 (0.85, 1.35)																			
10	1.2 (0.95, 1.55)																			
11	1.2 (0.95, 1.55)																			
13	1.2 (0.95, 1.55)																			
16	1.3 (0.85, 2.15)																			

FL

260

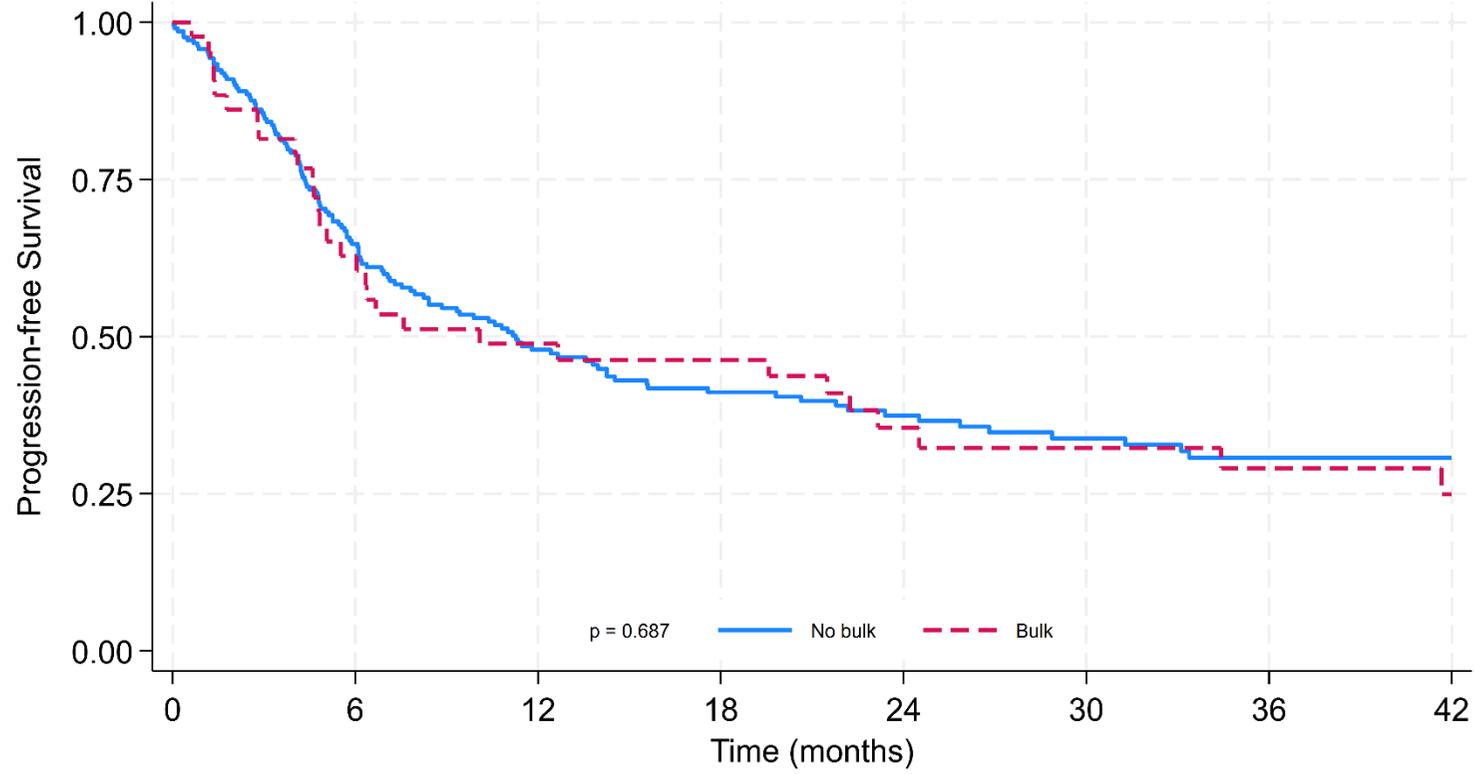




DLBCL: diffuse large B-cell lymphoma; FL: follicular lymphoma; HL: Hodgkin lymphoma.

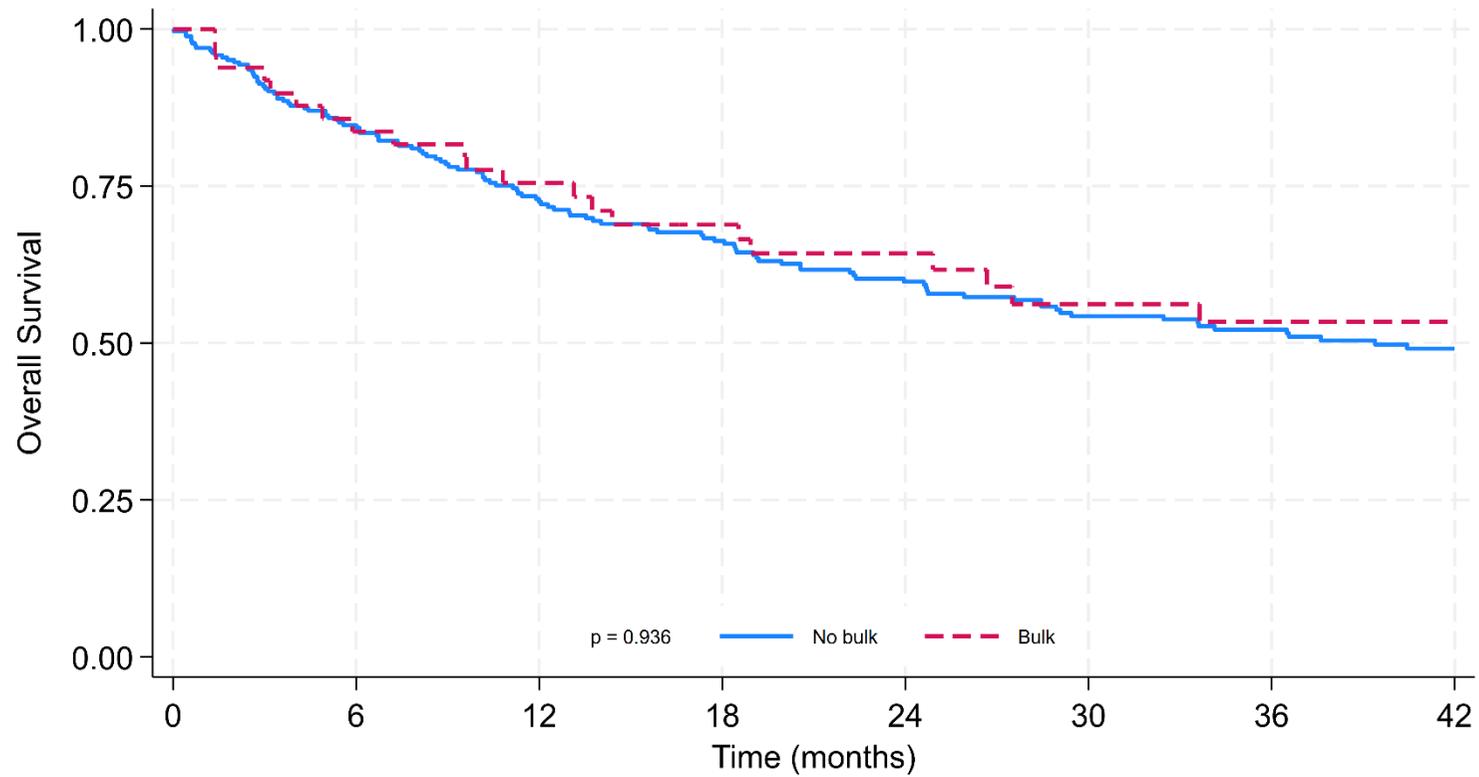
**Supplementary Figure S1. Survival outcomes of the patients according to the presence of bulky disease. (A) PFS of TCL. (B) OS of TCL. (C) PFS of BL. (D) OS of BL. (E) PFS of MZL. (F) OS of MZL. PFS: progression-free survival; OS: overall survival; TCL: T-cell lymphoma; BL: Burkitt lymphoma; FL: follicular lymphoma; MZL: marginal zone lymphoma.**

(A)



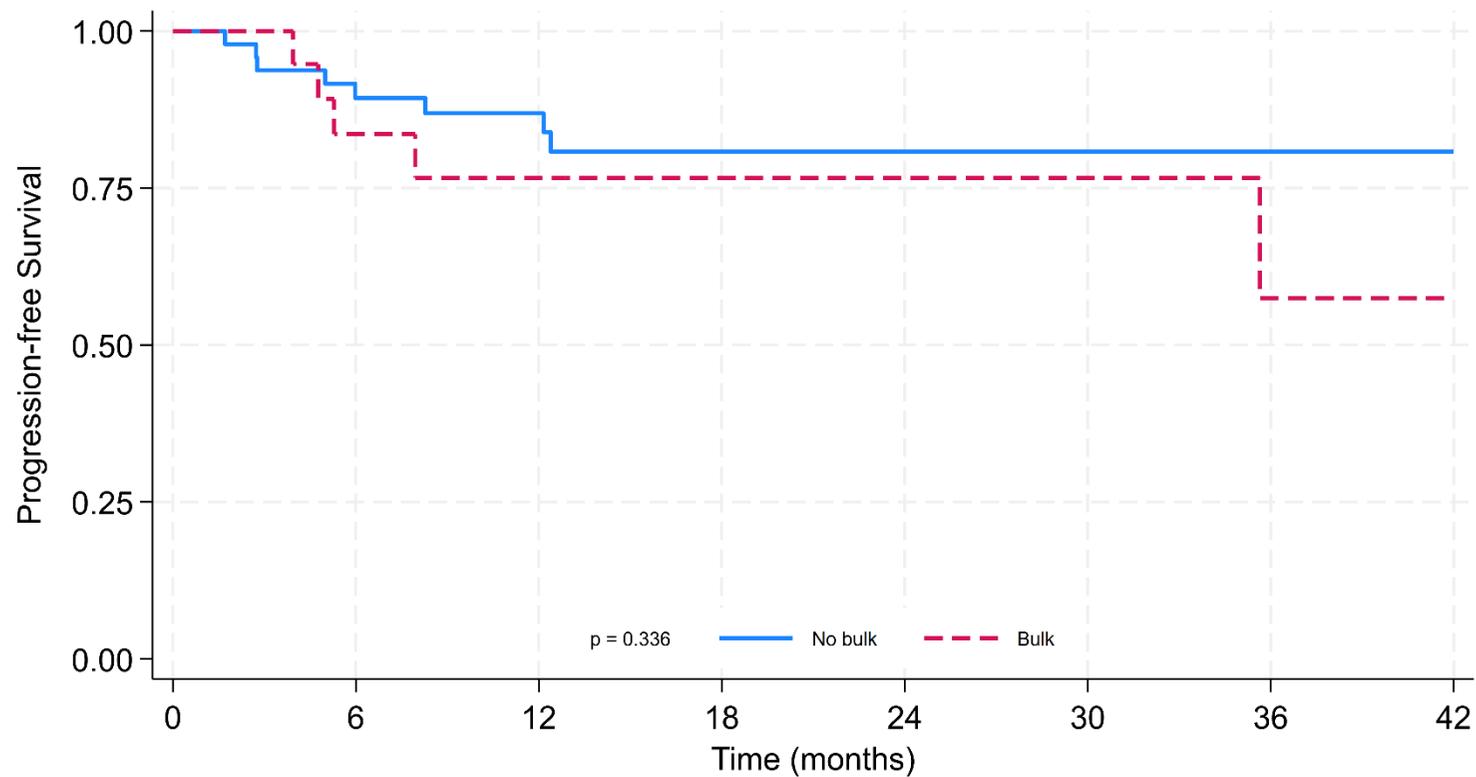
At risk	0	6	12	18	24	30	36	42
No bulk	211	122	83	63	46	33	28	21
Bulk	44	27	19	18	11	10	9	6

(B)



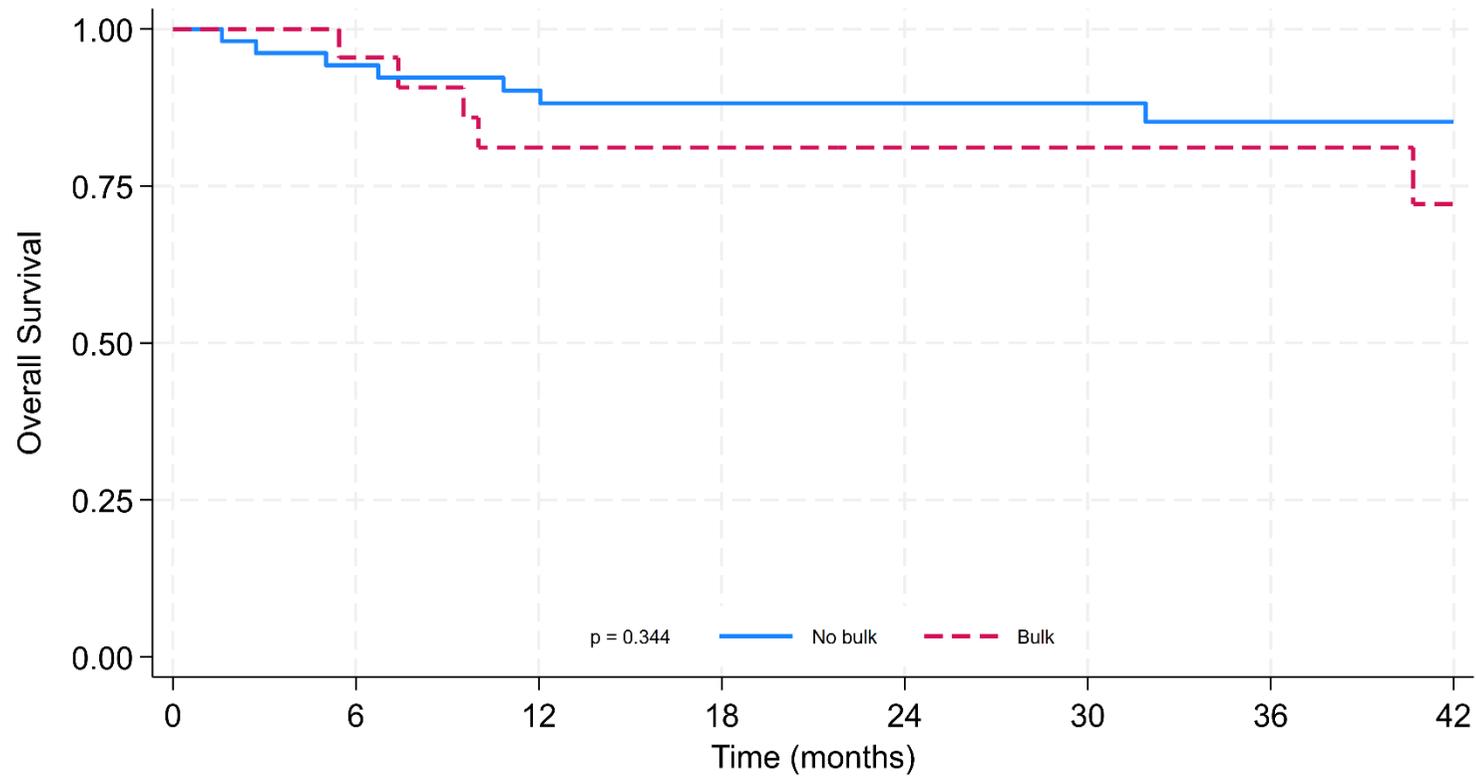
At risk	0	6	12	18	24	30	36	42
No bulk	269	213	168	146	123	104	93	74
Bulk	49	41	35	30	26	20	18	16

(C)



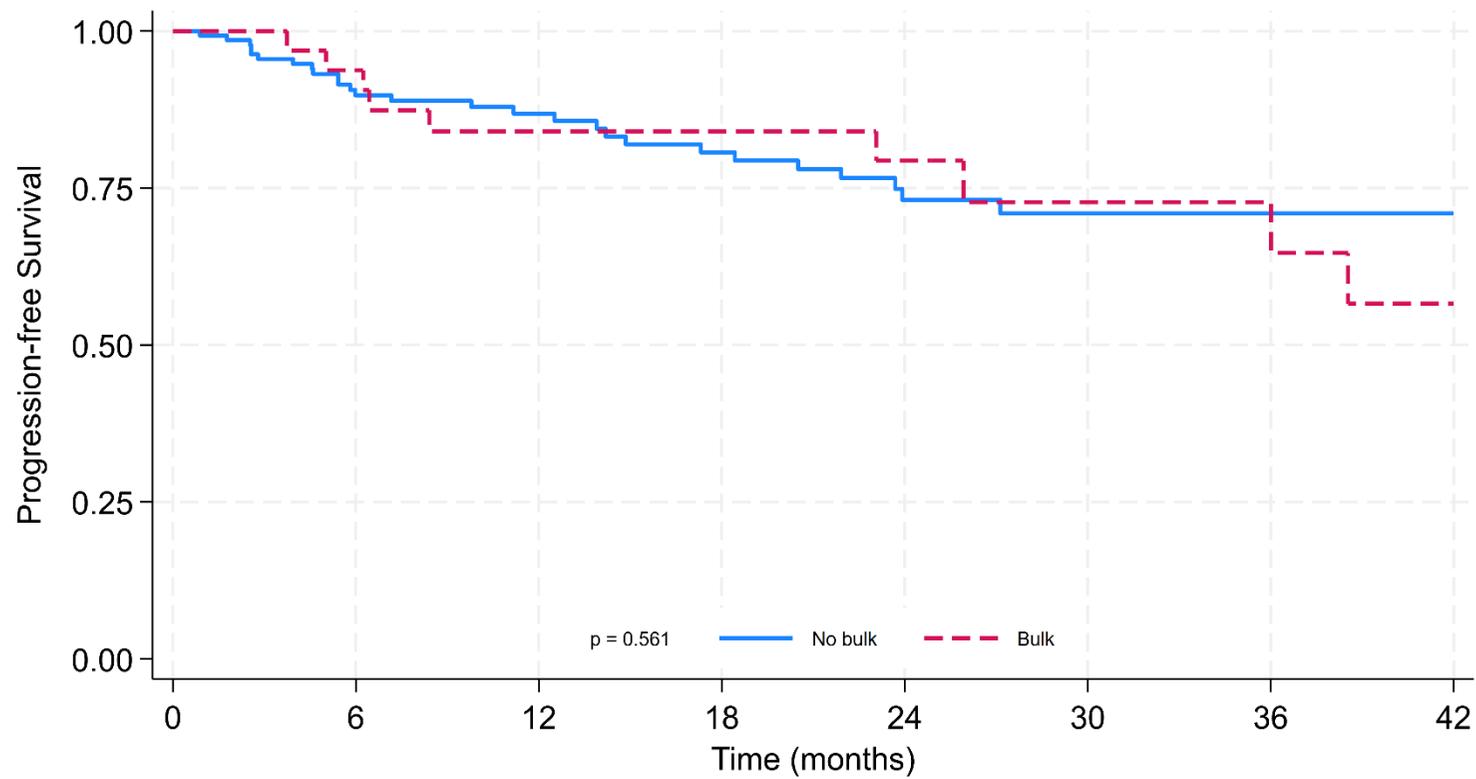
At risk	0	6	12	18	24	30	36	42
No bulk	48	39	30	18	13	8	7	4
Bulk	21	13	8	6	5	4	3	1

(D)



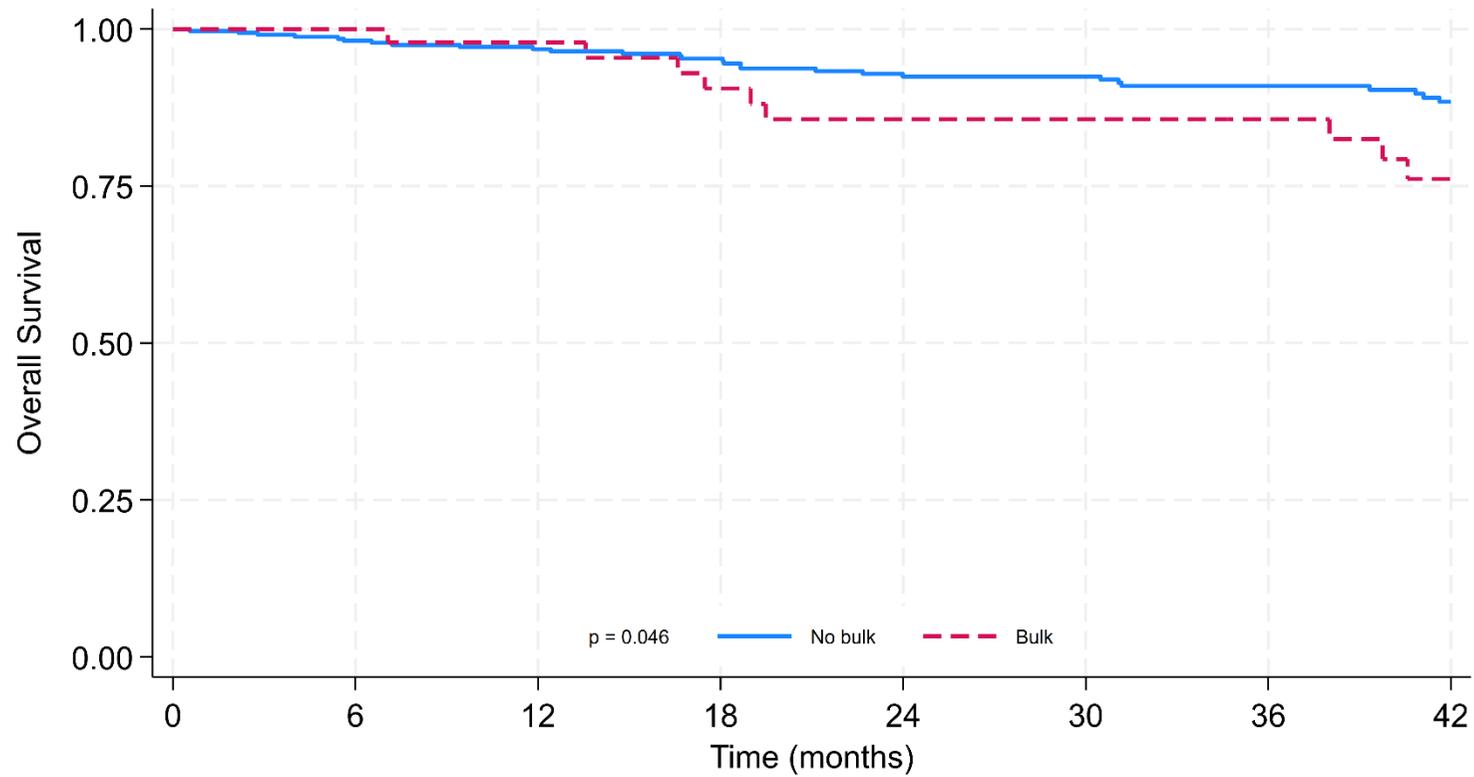
At risk		0	6	12	18	24	30	36	42
No bulk		54	48	44	38	35	30	28	25
Bulk		25	20	17	15	13	13	12	7

(E)



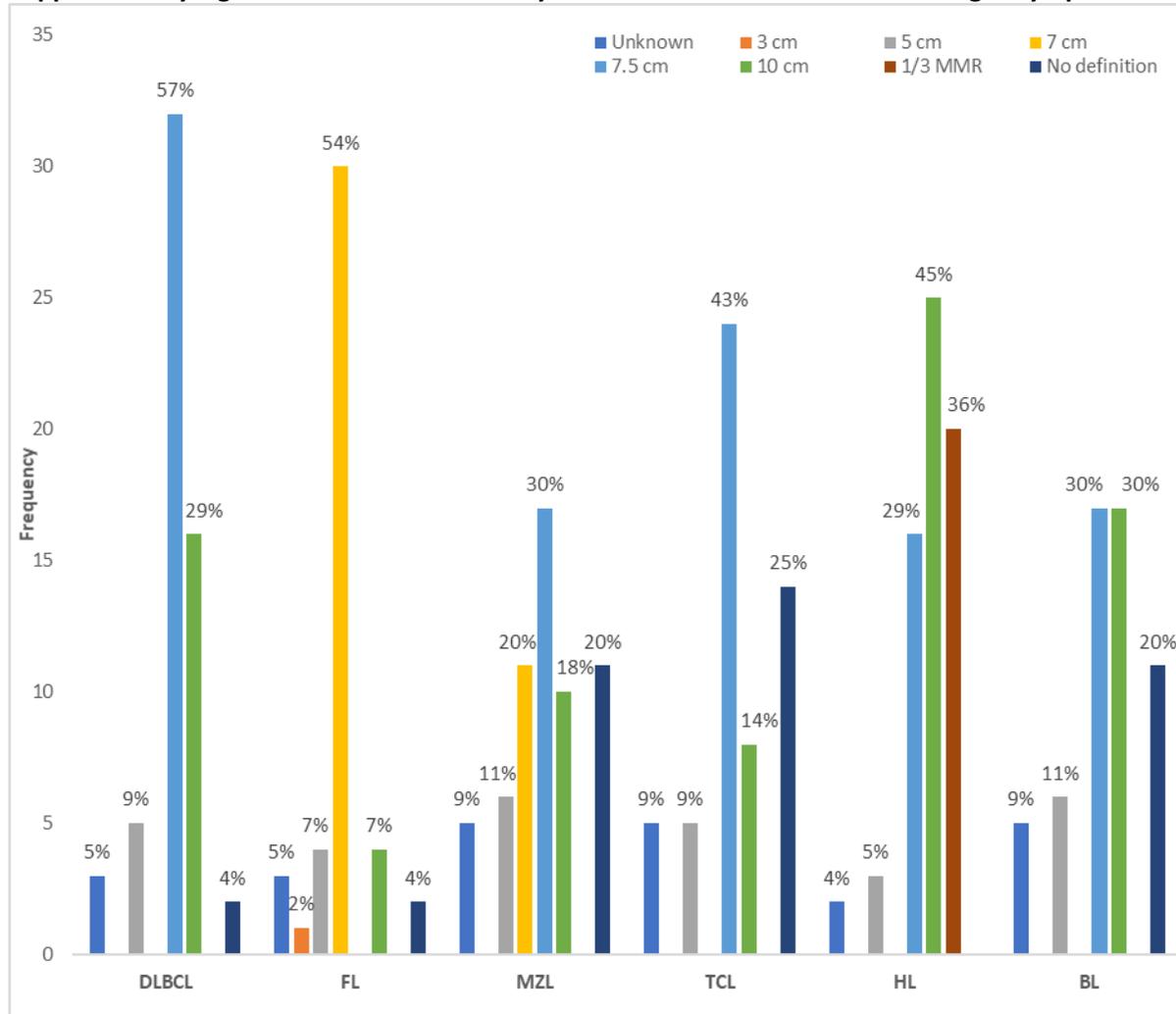
At risk	0	6	12	18	24	30	36	42
No bulk	140	106	78	62	42	28	22	20
Bulk	32	30	23	21	14	11	9	7

(F)



At risk	0	6	12	18	24	30	36	42
No bulk	334	306	277	243	209	190	162	138
Bulk	53	49	40	37	34	32	29	23

Supplementary Figure S2. Definitions used by LaRDR affiliated clinicians according to lymphoma subtype. MMR: mediastinal mass ratio.



## **Appendix: Participating sites and principal investigators at LaRDR**

Dr Susan Morgan, Alfred Hospital; Dr Leanne Berkahn, Auckland City Hospital; Dr Tamara Marconi, Box Hill Hospital; A/Prof Melita Kenealy, Cabrini Health; Dr Emma-Jane McDonald, Christchurch Hospital; Dr Kyle Crassini, Coffs Harbour Health Campus; Prof Judith Trotman, Concord Hospital; Prof Miles Prince, Epworth Hospital; Dr Kate Manos, Flinders Medical Centre; A/Prof Tara Cochrane, Gold Coast University Hospital; Dr Tasman Armytage, Gosford Hospital; A/Prof Geoffrey Chong, Grampians Health; Dr Nicholas Viiala, Liverpool Hospital; Dr Rory Bennett, North Shore Hospital; Dr Teresa Leung, Northern Health; Prof Michael Dickinson, Peter MacCallum Cancer Centre; Dr Jock Simpson, Port Macquarie Base Hospital; Dr Annmarie Bosco, Prince of Wales Hospital; A/Prof Colm Keane, Princess Alexandra Hospital; Dr Hun Chuah, Rockingham General Hospital; Dr Pratyush Giri, Royal Adelaide Hospital; Dr May Chiu, Royal Darwin Hospital; Dr Luke Coyle, Royal North Shore Hospital; Dr John Balendra, Royal Perth Hospital; Prof Chan Cheah, Sir Charles Gairdner Hospital; A/Prof Matthew Ku, St Vincent's Hospital Melbourne; Prof Nada Hamad, St Vincent's Hospital Sydney; Dr Manjunath Narayana, Sunshine Coast University Hospital; Prof Dipti Talaulikar, The Canberra Hospital; Dr Howard Mutsando, Toowoomba Hospital; Dr Joel Wight, Townsville Hospital; Dr Sumita Ratnasingam, University Hospital Geelong; Dr Hayden Jina, Wellington Regional Hospital; Dr Ming Ong, Western Health.