

**13-15 Aprile 2016**

**Reggio Children c/o Centro Internazionale Loris Malaguzzi – REGGIO EMILIA**



# **Incidenza di NHL, leucemie linfatiche e tumori plasmacellulari in Puglia. Confronto con tassi Haemacare e di RT Modena**

**Grazia Antonella Cannone**

**Registro Tumori Puglia (RTP)-Istituto Tumori Giovanni Paolo II I.R.C.C.S. Bari**

**Francesco Cuccaro, Danila Bruno, Simona Carone, Maria Giovanna Burgio Lo Monaco, Anna Melcarne,  
Antonino Ardizzone, Enzo Coviello, Gruppo di lavoro Registro Tumori Puglia**

# INTRODUZIONE



Stimare l'incidenza di Linfomi non Hodgkin (NHL), leucemie linfatiche (LL), tumori plasmacellulari (PT) per istotipo in Puglia ed effettuare un confronto con i dati dello studio Haemacare e dello studio di Luminari et al. per la provincia di Modena.

## Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project

Milena Sant,<sup>1</sup> Claudia Allemani,<sup>1</sup> Carmen Tereanu,<sup>1</sup> Roberta De Angelis,<sup>2</sup> Riccardo Capocaccia,<sup>2</sup> Otto Visser,<sup>3</sup> Rafael Marcos-Gragera,<sup>4</sup> Marc Maynadié,<sup>5</sup> Arianna Simonetti,<sup>2</sup> Jean-Michel Lutz,<sup>6</sup> Franco Berrino,<sup>7</sup> and the HAEMACARE Working Group

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## Research Article

### Incidence, clinical characteristics and survival of malignant lymphomas: a population-based study from a cancer registry in northern Italy

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# GRUPPI MORFOLOGICI HAEMACARE (neoplasie linfoidi escluso LH- Tabella 2 )

## Mature B-cell neoplasms

SBL/CLL	9670	Malignant lymphoma, small B-cell lymphocytic, NOS
	9823	B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma
Immunoproliferative diseases	9671	Malignant lymphoma, lymphoplasmacytic
	9760	Immunoproliferative disease, NOS
	9761	Waldenström macroglobulinemia
	9762	Heavy chain disease, NOS
Mantle cell/centrocytic lymphoma	9673	Mantle cell lymphoma
Follicular B-cell lymphoma	9690	Follicular lymphoma, NOS
	9691	Follicular lymphoma, grade 2
	9695	Follicular lymphoma, grade 1
	9698	Follicular lymphoma, grade 3
Diffuse B-cell lymphoma	9675	Malignant lymphoma, mixed small and large cell, diffuse (obsolete)
	9678	Primary effusion lymphoma
	9679	Mediastinal large B-cell lymphoma
	9680	Malignant lymphoma, large B-cell, diffuse, NOS
	9684	Malignant lymphoma, large B-cell, diffuse, immunoblastic, NOS
Burkitt lymphoma/leukemia	9687	Burkitt lymphoma, NOS
	9826	Burkitt cell leukemia
Marginal zone lymphoma	9689	Splenic marginal zone B-cell lymphoma
	9699	Marginal zone B-cell lymphoma, NOS/mucosa-associated lymphoid tissue lymphoma
	9764	Immunoproliferative small intestinal disease (Mediterranean lymphoma)
Mature B-cell leukemia	9833	Prolymphocytic leukemia, B-cell type
	9940	Hairy cell leukemia
Plasma cell neoplasms	9732	Multiple myeloma
	9733	Plasma cell leukemia
	9731	Plasmacytoma, NOS
	9734	Plasmacytoma, extramedullary
<b>Mature T-cell and NK-cell neoplasms</b>		
Cutaneous T-cell lymphoma	9700	Mycosis fungoides
	9701	Sézary syndrome
	9708	Subcutaneous T panniculitis-like T-cell lymphoma
	9709	Cutaneous T-cell lymphoma, NOS
	9718	Primary cutaneous CD30 <sup>+</sup> T-cell lymphoproliferative disorder

Other T-cell lymphomas	9702	Mature T-cell lymphoma, NOS
	9705	Angioimmunoblastic T-cell lymphoma
	9714	Anaplastic large cell lymphoma, T-cell and null cell type
	9716	Hepatosplenic $\gamma\delta$ cell lymphoma
	9717	Intestinal T-cell lymphoma
	9948	Aggressive NK-cell leukemia
	9719	NK/T-cell lymphoma, nasal and nasal-type
	9827	Adult T-cell leukemia/lymphoma (HTLV-1 positive)
	9831	T-cell large granular lymphocytic leukemia
	9834	Prolymphocytic leukemia, T-cell type
<b>Lymphoblastic lymphoma/acute (precursor cell) lymphatic leukemia</b>		
B-cell	9728	Precursor B-cell lymphoblastic lymphoma
	9836	Precursor B-cell lymphoblastic leukemia
T-cell	9729	Precursor T-cell lymphoblastic lymphoma
	9837	Precursor T-cell lymphoblastic leukemia
NOS	9727	Precursor cell lymphoblastic lymphoma, NOS
	9835	Precursor cell lymphoblastic leukemia, NOS
<b>Unknown lymphoid neoplasms</b>		
Lymphoma, NOS	9590	Malignant lymphoma, NOS
NHL, NOS	9591	Malignant lymphoma, NHL, NOS
Lymphatic leukemia, NOS	9820	Lymphoid leukemia, NOS
	9832	Prolymphocytic leukemia, NOS

# GRUPPI MORFOLOGICI STUDIO LUMINARI ET AL. PROVINCIA DI MODENA

PL subtype	ICD-O-3 codes
<b>B-cell lymphoma, all cases</b>	9670–9699, 9761, 9823, 9940
CLL/SLL	9670, 9823
LPC/WM	9671, 9761
HCL	9940
FL	9690–9698
MZL	9689, 9699
MCL	9673
DLBCL and BL	9675–9687
<b>T/NK-cell lymphoma, all cases</b>	9700–9719
MF/SS	9700, 9701
PTCL	9702–9708, 9716–9719
ALCL	9714
<b>Hodgkin lymphoma, all cases</b>	9650–9667
<b>PL, NOS</b>	9590–9596, 9709, 9760, 9827–9834, 9970
<b>All cases</b>	

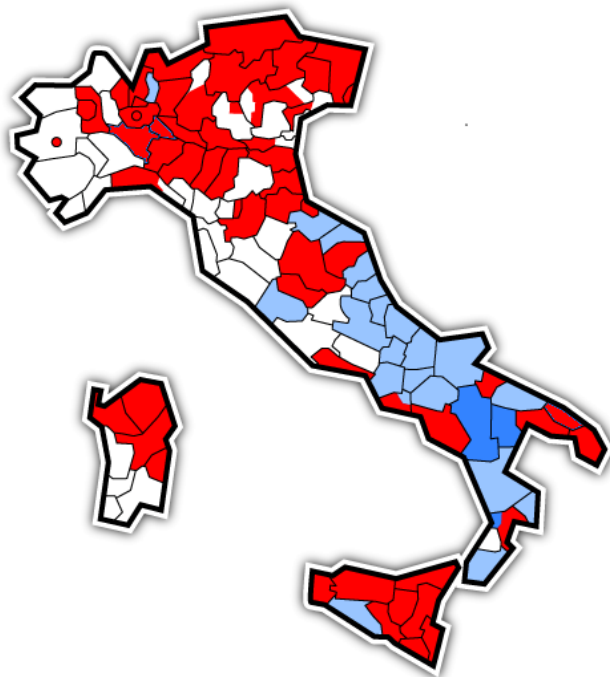
ASR; age-standardized rates; M, male; F, female; CLL/SLL, chronic lymphocytic leukaemia/small lymphocytic lymphoma; LPC/WM, lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia; HCL, hairy cell leukaemia; FL, follicular lymphoma; MZL, marginal zone lymphoma; MCL, mantle cell lymphoma; DLBCL, diffuse large b-cell lymphoma; BL, Burkitt lymphoma; MF/SS, mycosis fungoides/Sezary syndrome; PTCL, peripheral T-cell lymphoma; ALCL, anaplastic large cell lymphoma; NOS, not otherwise specified. Freq., frequency.

# GRUPPI MORFOLOGICI IN QUESTO STUDIO



Gruppi	ICD-O-3
Mature B cell neoplasms	
SPLL/CLL	9670, 9823
Immunoproliferative diseases	9671, 9760, 9761, 9762
Mantle cell/centrocytic	9673
Follicular B-cell lymphoma	9690, 9691, 9695, 9698
Diffuse B-cell lymphoma	9675, 9678, 9679, 9680, 9684
Burkitt lymphoma/leukemia	9687, 9826
Marginal zone lymphoma	9689, 9699, 9764
Mature B Leukemia	9833, 9940
Plasma cell neoplasms	9731-9734
Mature T e NK cell neoplasms	9700- 9702, 9705, 9708, 9709, 9714, 9716-9719, 9827, 9831, 9834, 9948
Lymphoblastic lymphoma/acute (precursor cell) lymphatic leukemia	9727-9729, 9835-9837
Lymphoma NOS	9590
NHL NOS	9591

# MATERIALI E METODI



Anni	Registro			
	RTBR	RTBT	RTLE	RTTA
2004			207	
2005			235	
2006	147	112	226	141
2007	128	134	243	180
2008	133	121		165
2009		112		169
2010		110		160
Totale	408	589	911	815



2165162 ab (54% popolazione pugliese)

# MATERIALI E METODI

- Tassi di incidenza standardizzati diretti (popolazione standard europea e mondiale)
- Tassi età specifici
- SIR (tassi di riferimento Haemacare)



# INDICATORI DI QUALITA'

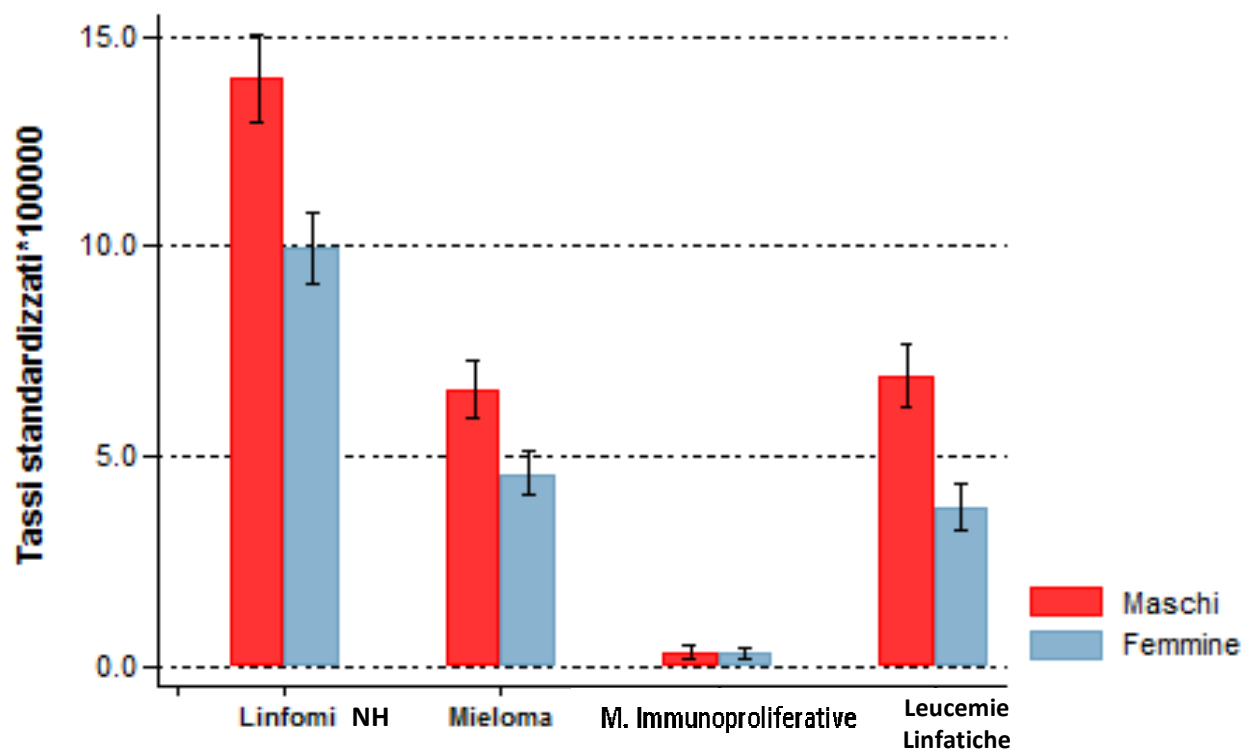
Base diagnosi	RTBR		RTBT		RTLE		RTTA		Totale	
	N.	%	N.	%	N.	%	N.	%	N.	%
DCO	5	1.23	5	0.85	9	0.99	10	1.23	29	1.07
CLINICA	8	1.96	6	1.02	16	1.76	23	2.82	53	1.95
STRUMENTALE	3	0.74	3	0.51	14	1.54	36	4.42	56	2.06
MARKER	4	0.98	10	1.7	2	0.22	7	0.86	23	0.84
CITOLOGICA	39	9.55	27	4.58	64	7.03	100	12.27	230	8.45
ISTOLOGICA	349	85.54	538	91.34	806	88.46	639	78.4	2332	85.63
<b>Totale</b>	<b>408</b>		<b>589</b>		<b>911</b>		<b>815</b>		<b>2723</b>	

Registro	Linfomi NOS		Linfomi Non Hodgkin NOS		Totale NOS		Totale
	N.	%	N.	%	N.	%	
RTBR	5	2.4	4	2.0	9	4.4	205
RTBT	8	2.9	14	5.0	22	7.9	279
RTLE	18	3.7	61	12.6	79	16.3	486
RTTA	23	5.8	42	10.6	65	16.5	395
<b>Totale</b>	<b>54</b>	<b>4.0</b>	<b>121</b>	<b>8.9</b>	<b>175</b>	<b>12.8</b>	<b>1365</b>



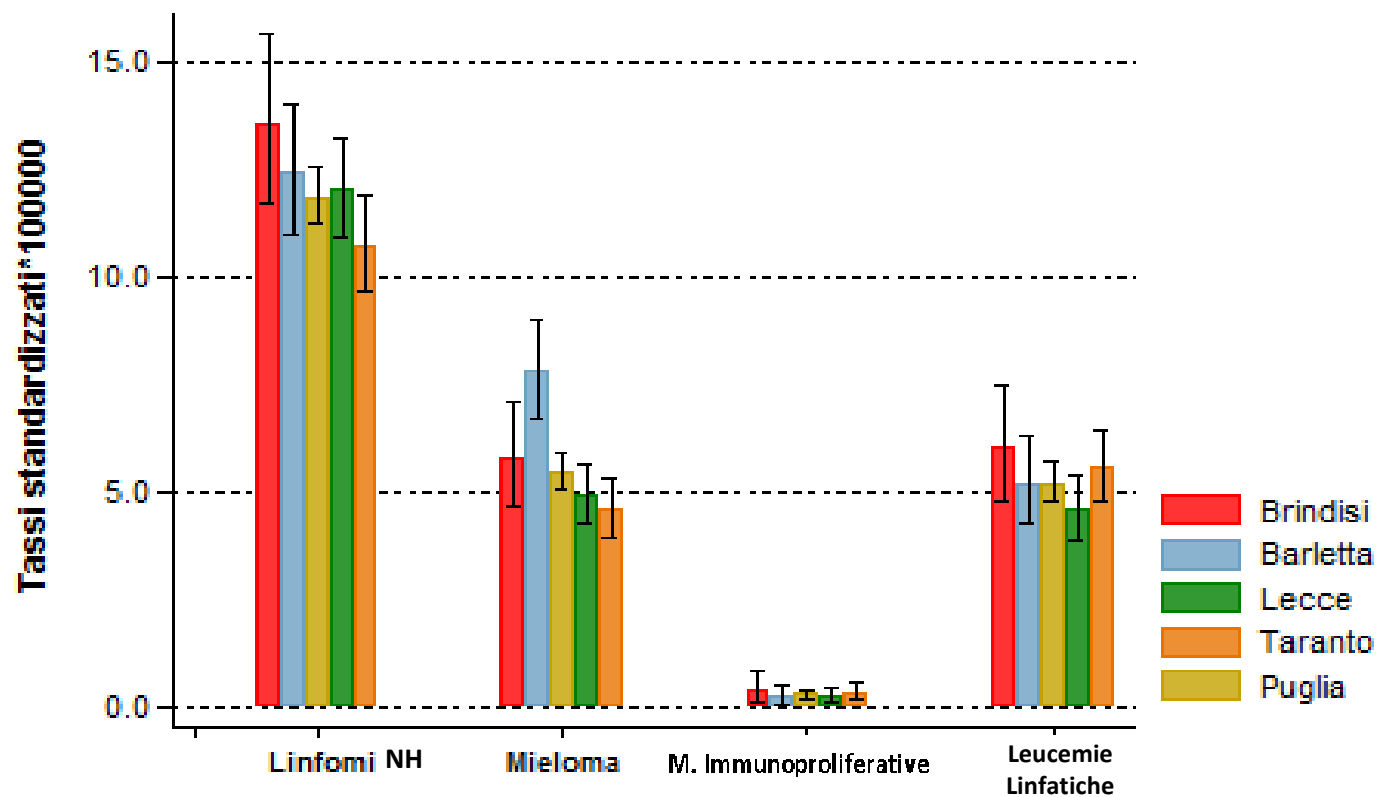
# RISULTATI

Tassi di incidenza standardizzati per sesso - Puglia  
(pop europea)



# RISULTATI

## Tassi di incidenza standardizzati per provincia (pop europea)



# TASSI STANDARDIZZATI DIRETTI - PUGLIA

Tassi per 100000

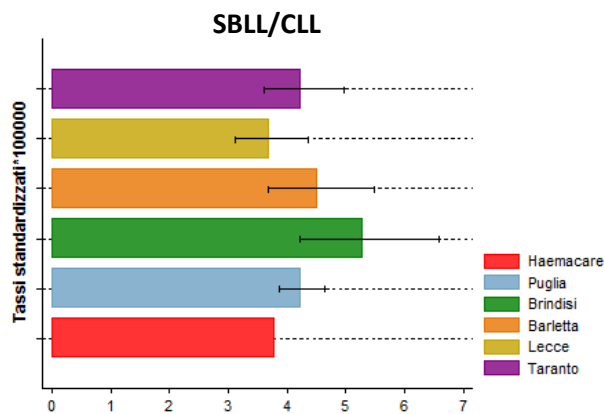
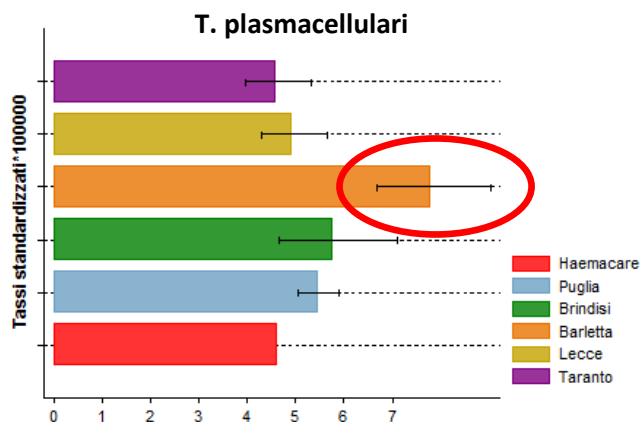
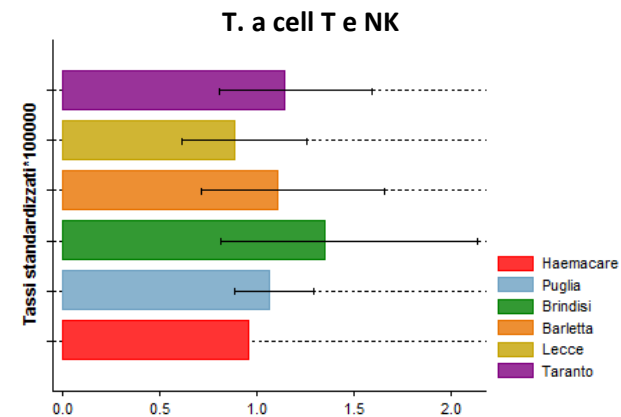
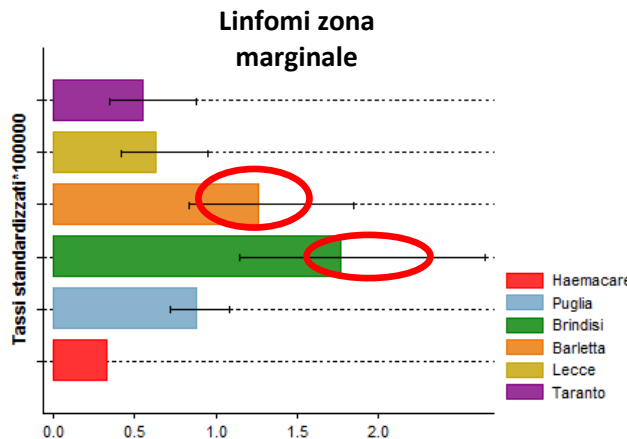
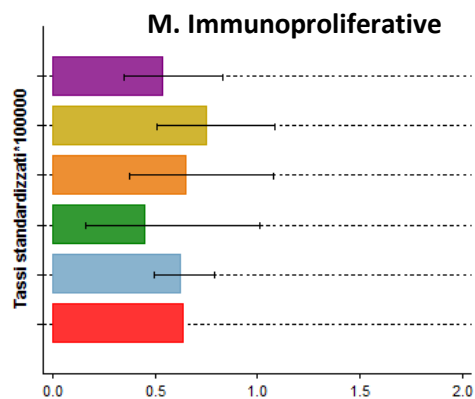
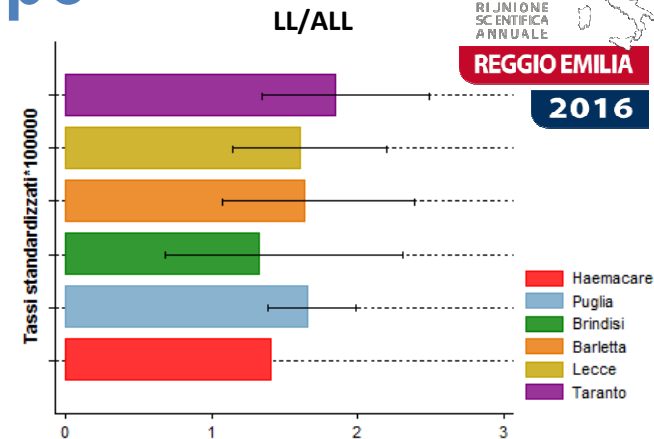
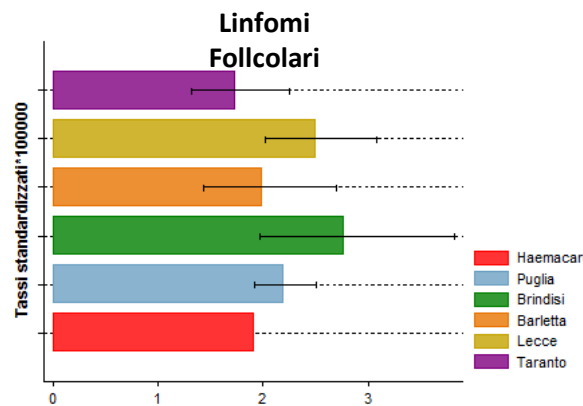
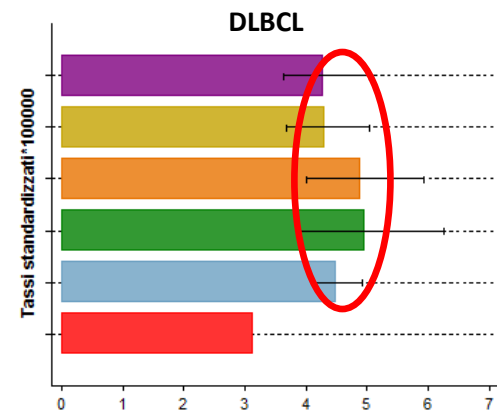
TIPO HAEMACARE	N.	TSD ( pop europea)	Tasso Haemacare	TSD (pop mondiale)	Tasso Modena
SBLL/CLL	534	4.2 (3.9-4.6)	3.8	2.9 (2.7-3.2)	3.3
Immunoproliferative diseases	81	0.6 (0.5-0.8)	0.6	0.4 (0.3-0.6)	1.1
Mantle cell/centrocytic	30	0.3 (0.2-0.4)	0.4	0.2 (0.1-0.3)	0.4
Follicular B-cell limphoma	246	2.2 (1.9-2.5)	1.9	1.6 (1.4-1.9)	2.0
Diffuse B-cell limphoma	529	4.5 (4.1-5.0)	3.2	3.7 (3.4-4.1)	4.8
Burkitt lymphoma/leukemia	24	0.3 (0.2-0.4)	0.2 <sup>2</sup>		
Marginal zone lymphoma	102	0.9 (0.7-1.1)	0.4	0.6 (0.5-0.8)	1.5
Mature B Leukemia	21	0.2 (0.1-0.3)		0.1 (0.1-0.2)	0.2
Plasma cell neoplasms	730	5.5 (5.1-5.9)	4.7	3.7 (3.4-4.0)	
Mature T e NK cell neoplasms	121	1.1 (0.9-1.3)	1.0	0.8 (0.7-1.0)	2.2
Lymphoblastic lymphoma/acute (precursor cell) lymphatic leukemia	130	1.7 (1.4-2.0)	1.4	2.0 (1.7-2.5)	
Lymphoma NOS	54	0.4 (0.3-0.6)	1.7	0.3 (0.2-0.4)	
NHL NOS	121	1 (0.8-1.2)	2.7	0.7 (0.6-0.9)	
<b>Totale</b>	<b>2723</b>				

# TASSI STANDARDIZZATI DIRETTI - PUGLIA

Tassi per 100000

TIPO HAEMACARE	N.	TSD ( pop europea)	Tasso Haemacare	TSD (pop mondiale)	Tasso Modena
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NHL NOS	121	1 (0.8-1.2)	2.7	0.7 (0.6-0.9)	
<b>Totale</b>	<b>2723</b>				

# Tassi standardizzati diretti per istotipo



Tassi standardizzati  
(pop europea)

# SIR PUGLIA PER LNH, LEUCEMIE LINFATICHE E MIELOMA (riferimento ITACAN- SUD ITALIA 2006-2009)

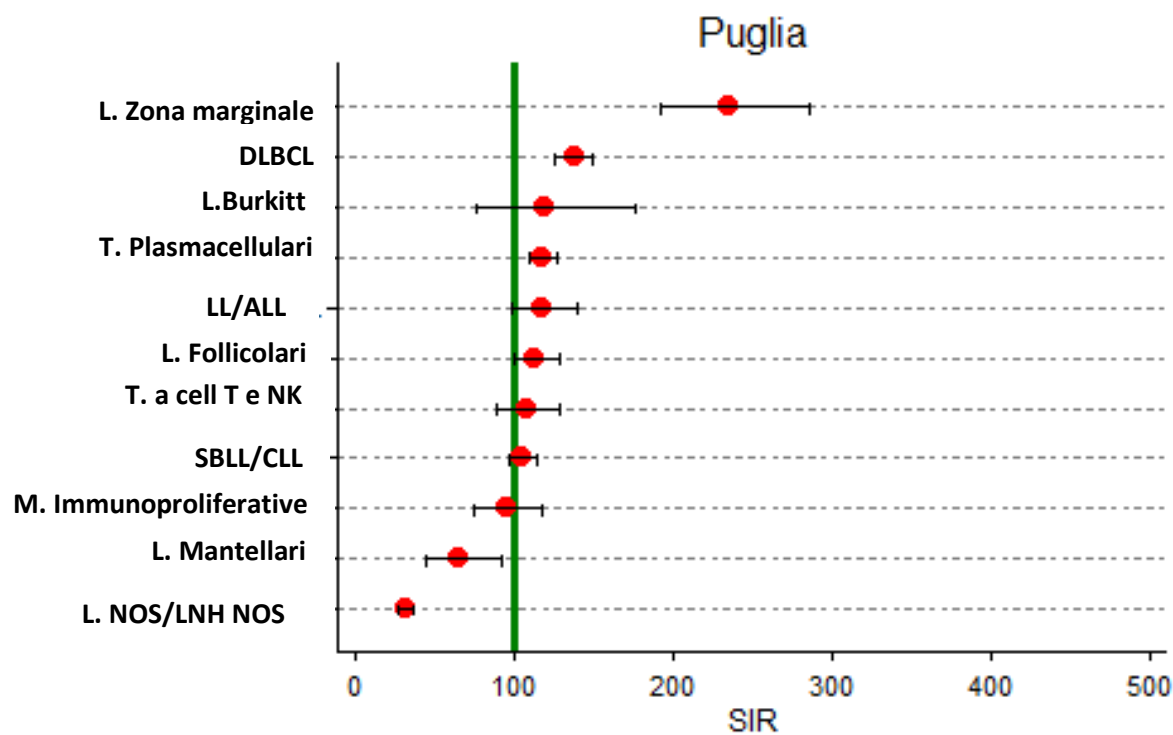


	Osservati	Attesi	SIR (IC)
<b>Leucemie linfatiche acute</b>	<b>111</b>	<b>101.9</b>	<b>108.9 (89.6-131.2)</b>
<b>Leucemie linfatiche croniche</b>	<b>455</b>	<b>376.7</b>	<b>120.8 (110.0-132.4)</b>
<b>Linfomi non Hodgkin</b>	<b>1364</b>	<b>1545.0</b>	<b>88.3 (83.7-93.1)</b>
<b>Mielomi-M. immunoproliferative</b>	<b>771</b>	<b>672.0</b>	<b>114.7 (106.8-123.1)</b>

AIRTUM

ITACAN: Tumori in Italia, Versione 2.0. Associazione Italiana dei Registri TUMori  
(<http://www.registri-tumori.it>).

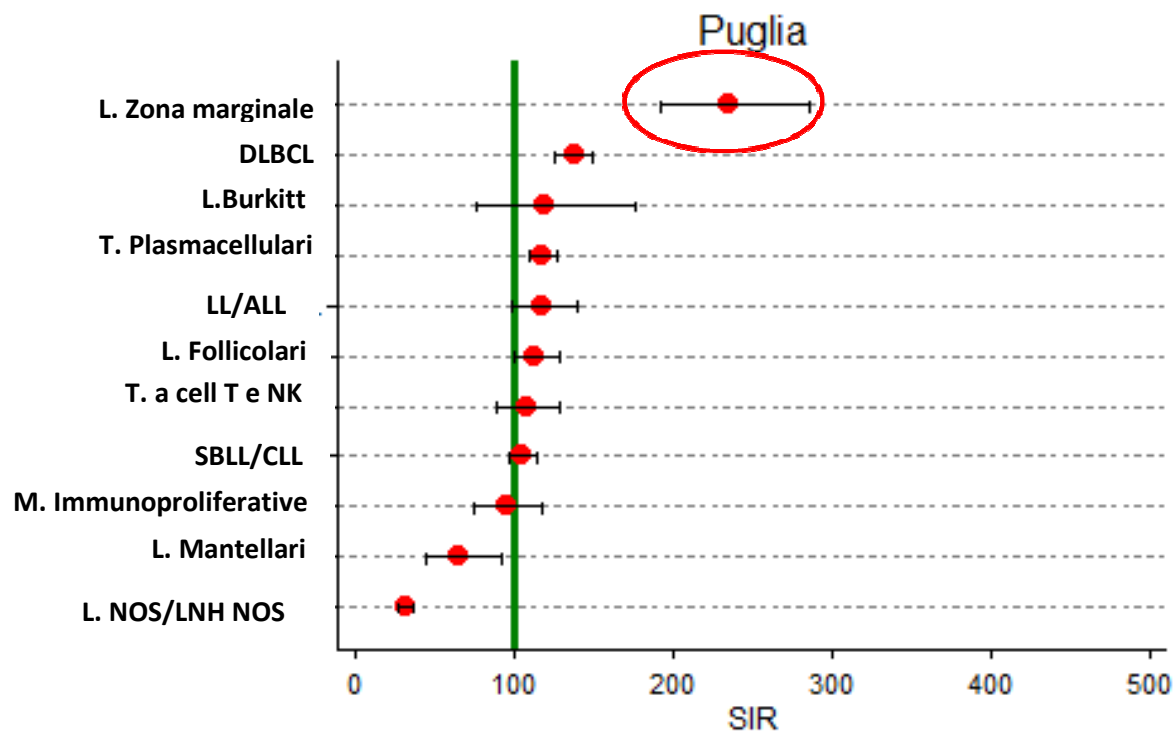
# RAPPORTI STANDARDIZZATI DI INCIDENZA (SIR)



	SIR (IC)
<b>SBLL/CLL</b>	<b>104.8</b> (96.1-114.1)
<b>Immunoproliferative diseases</b>	<b>94.4</b> (75.0-117.4)
<b>Mantle cell/centrocytic</b>	<b>64.6</b> (43.6-92.2)
<b>Follicular B-cell lymphoma</b>	<b>113.2</b> (99.5-128.3)
<b>Diffuse B-cell lymphoma</b>	<b>137.2</b> (125.7-149.4)
<b>Burkitt lymphoma/leukemia</b>	<b>118.5</b> (75.9-176.3)
<b>Marginal zone lymphoma</b>	<b>235.3</b> (191.9-285.7)
<b>Plasma cell neoplasms</b>	<b>117.5</b> (109.1-126.4)
<b>Mature T e NK cell neoplasms</b>	<b>107.5</b> (89.2-128.4)
<b>Lymphoblastic lymphoma/acute (precursor cell) lymphatic leukemia</b>	<b>116.9</b> (97.7-138.9)
<b>Lymphoma NOS/NHL NOS</b>	<b>31.3</b> (26.9-36.3)

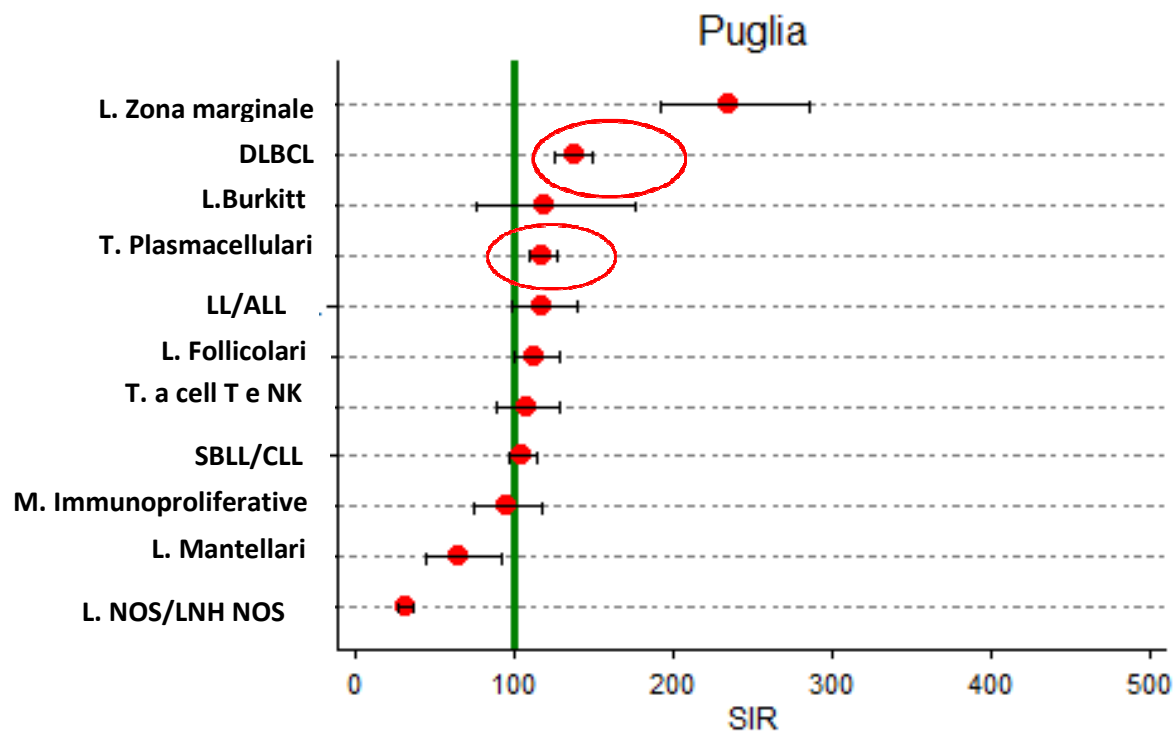


# RAPPORTI STANDARDIZZATI DI INCIDENZA (SIR)



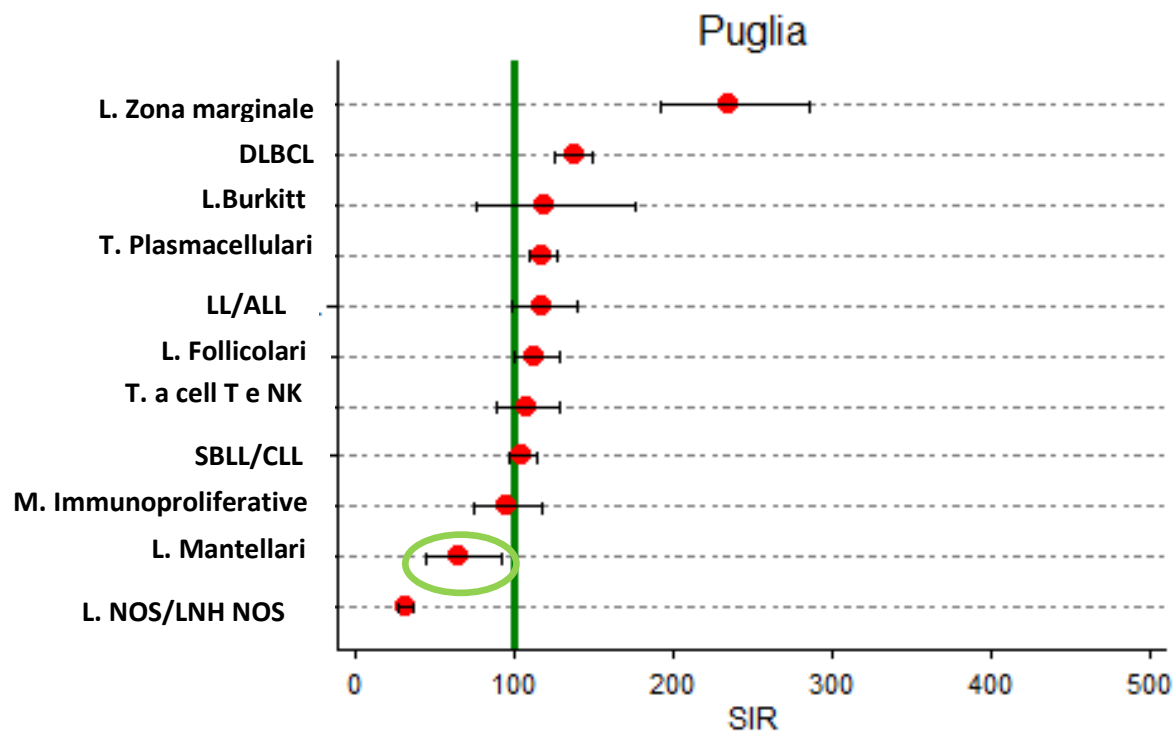
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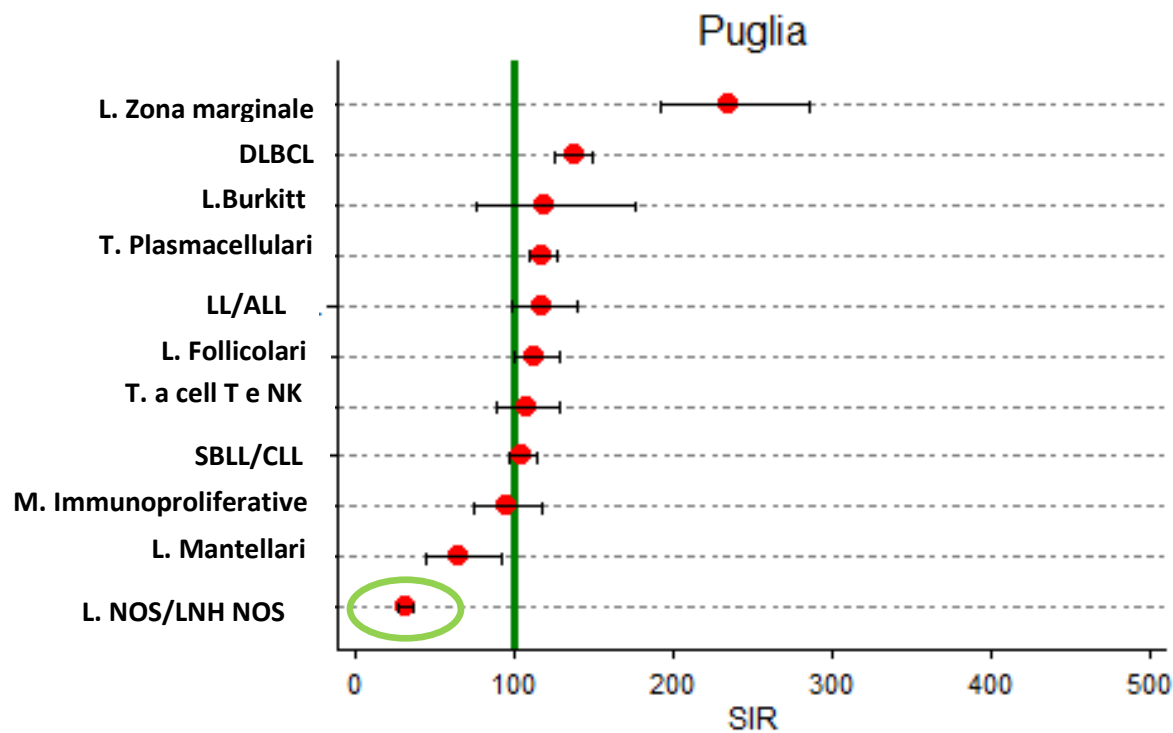
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<b>Lymphoma NOS/NHL NOS</b>	<b>31.3</b> (26.9-36.3)

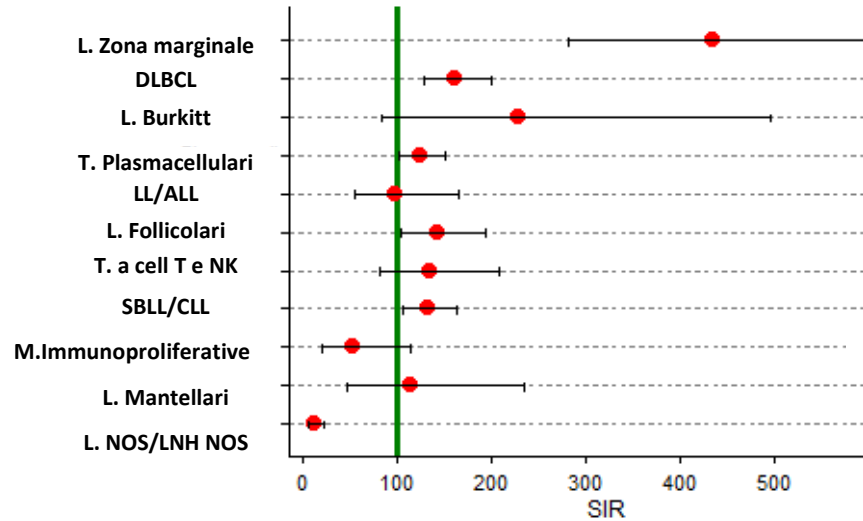
# RAPPORTI STANDARDIZZATI DI INCIDENZA (SIR)



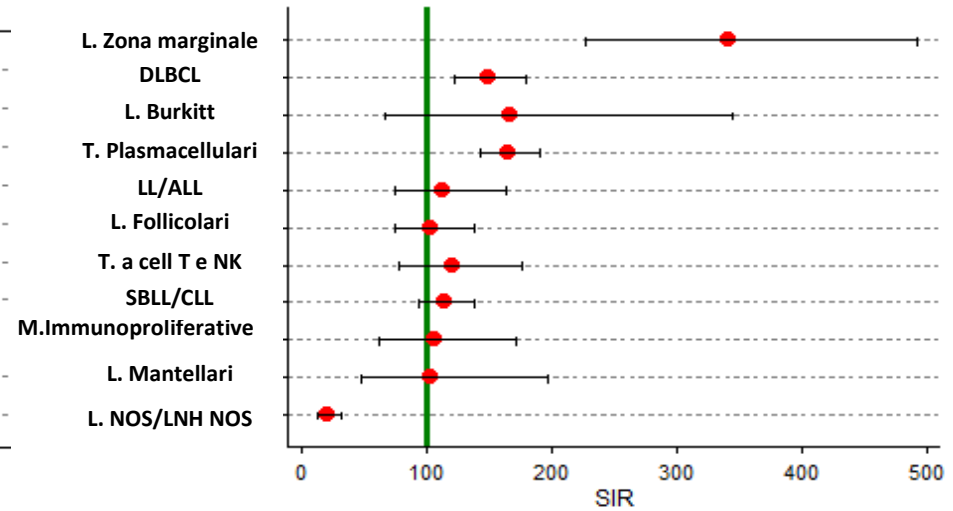
	SIR (IC)
<b>SBLL/CLL</b>	<b>104.8</b> (96.1-114.1)
<b>Immunoproliferative diseases</b>	<b>94.4</b> (75.0-117.4)
<b>Mantle cell/centrocytic</b>	<b>64.6</b> (43.6-92.2)
<b>Follicular B-cell lymphoma</b>	<b>113.2</b> (99.5-128.3)
<b>Diffuse B-cell lymphoma</b>	<b>137.2</b> (125.7-149.4)
<b>Burkitt lymphoma/leukemia</b>	<b>118.5</b> (75.9-176.3)
<b>Marginal zone lymphoma</b>	<b>235.3</b> (191.9-285.7)
<b>Plasma cell neoplasms</b>	<b>117.5</b> (109.1-126.4)
<b>Mature T e NK cell neoplasms</b>	<b>107.5</b> (89.2-128.4)
<b>Lymphoblastic lymphoma/acute (precursor cell) lymphatic leukemia</b>	<b>116.9</b> (97.7-138.9)
<b>Lymphoma NOS/NHL NOS</b>	<b>31.3</b> (26.9-36.3)

# SIR PROVINCE PUGLIESI

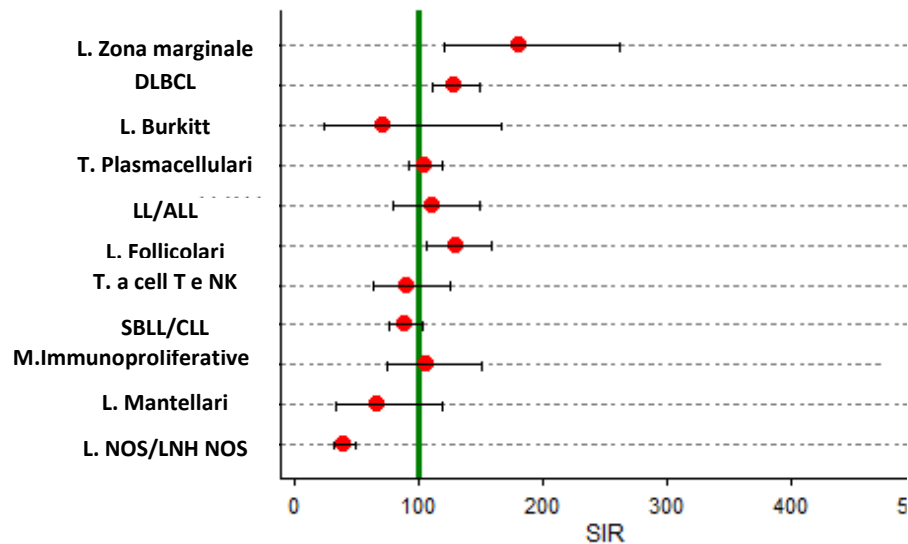
RTBR



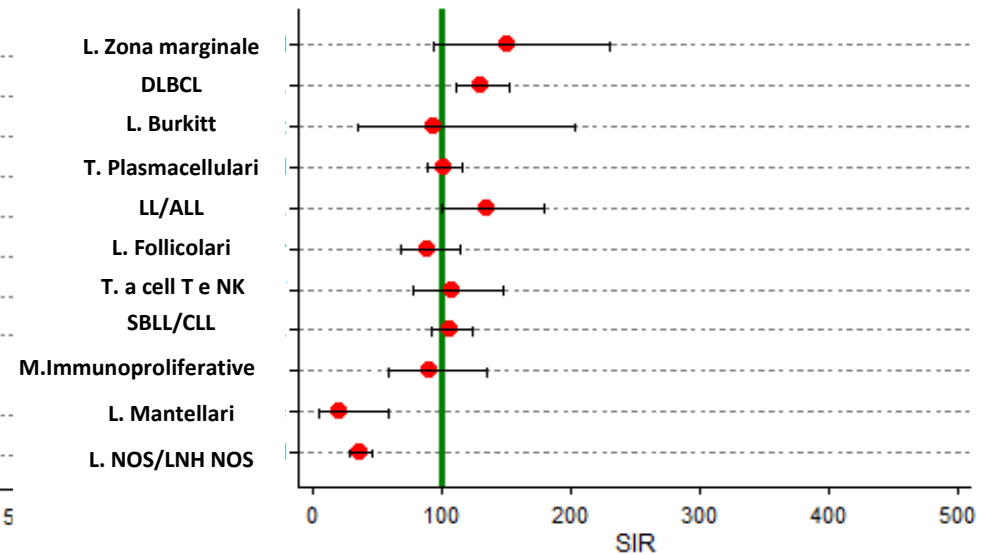
RTBT



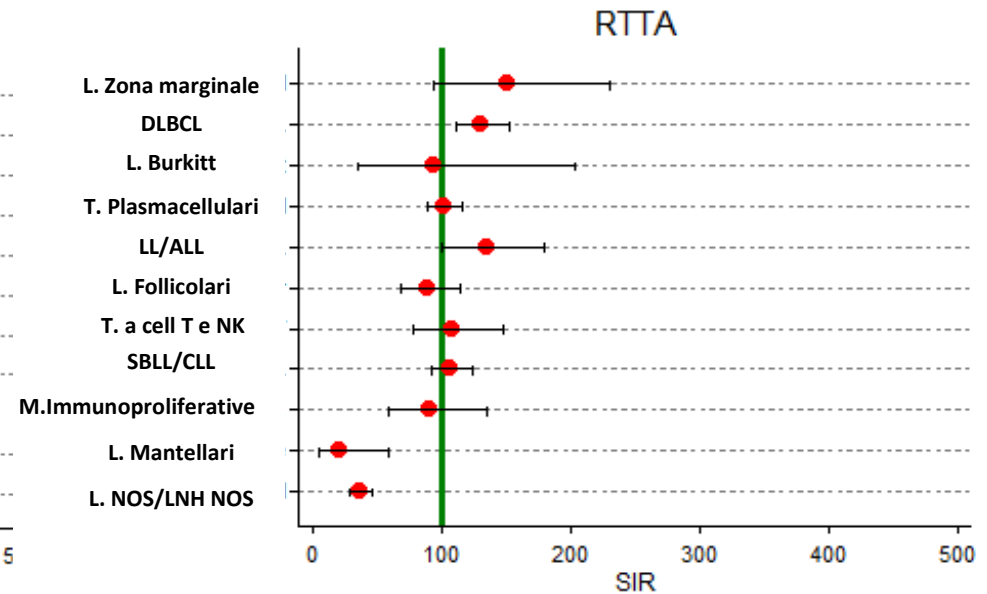
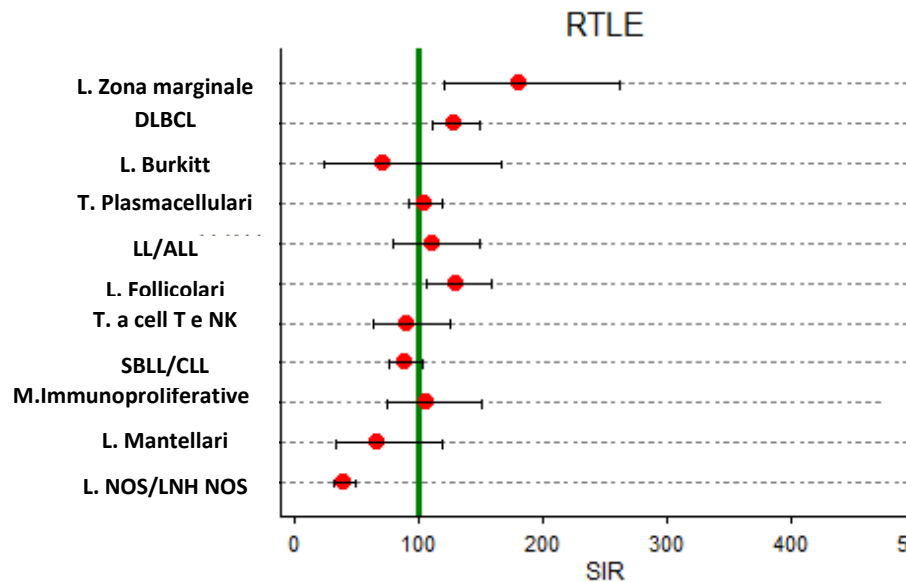
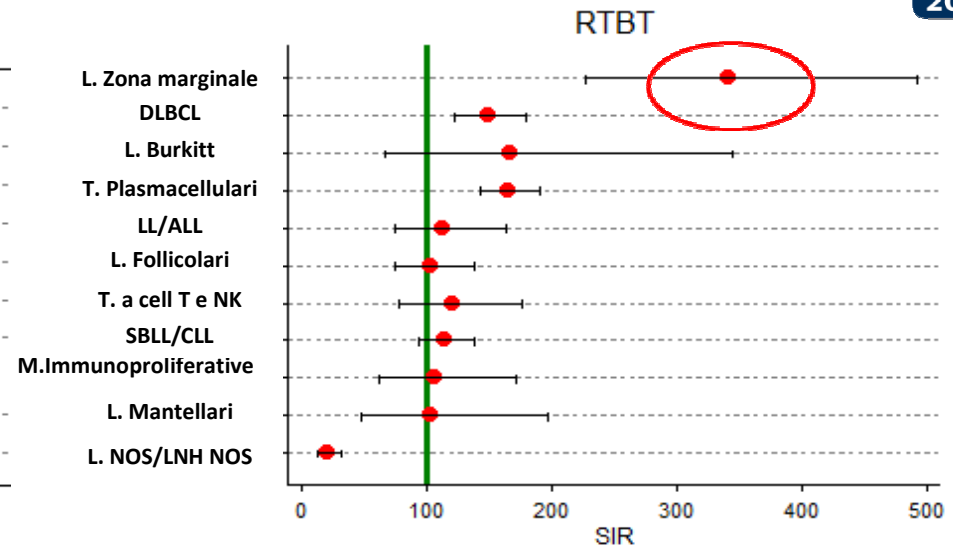
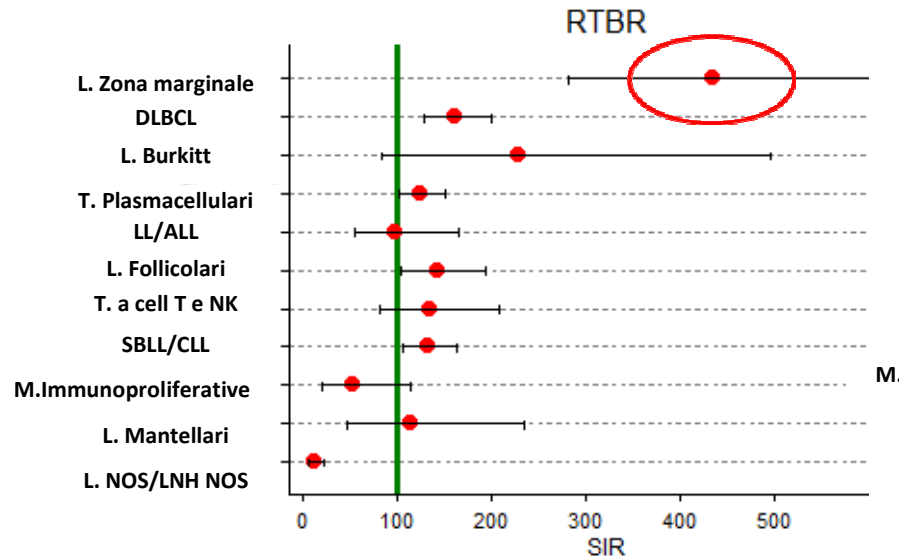
RTLE



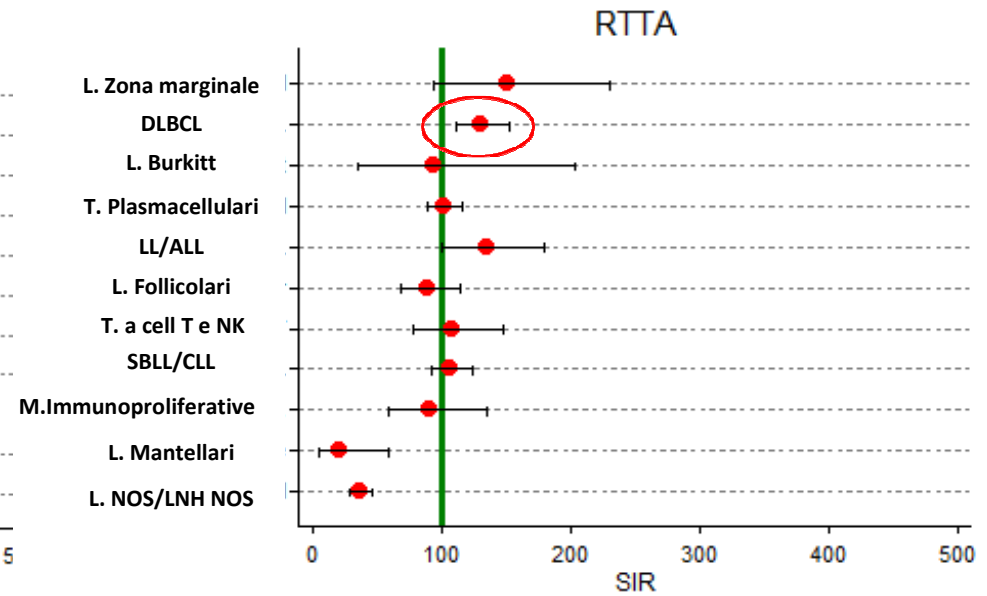
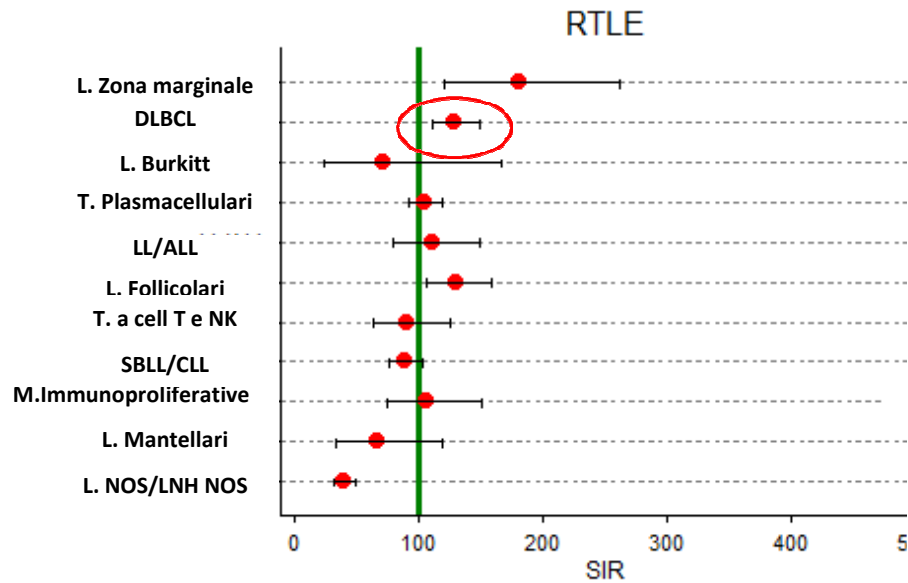
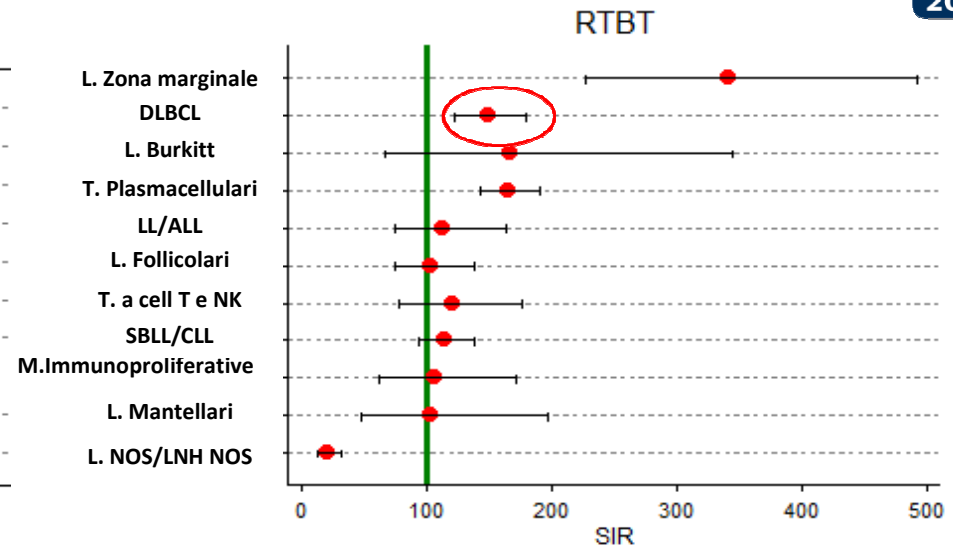
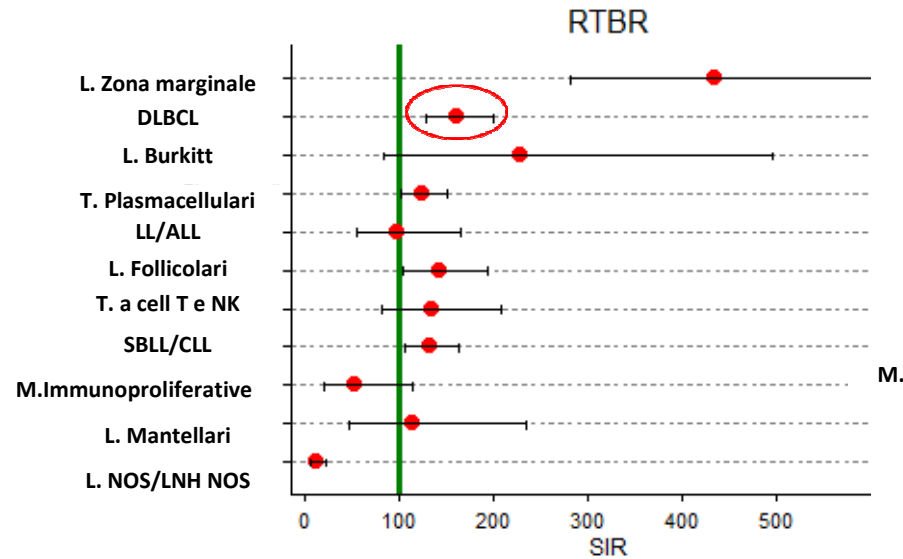
RTTA



# SIR PROVINCE PUGLIESI

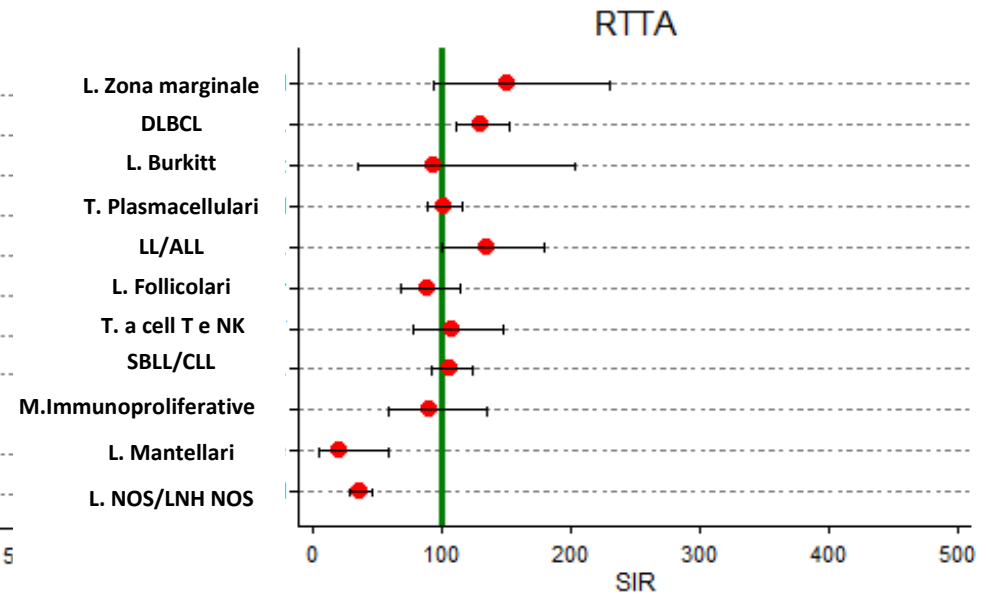
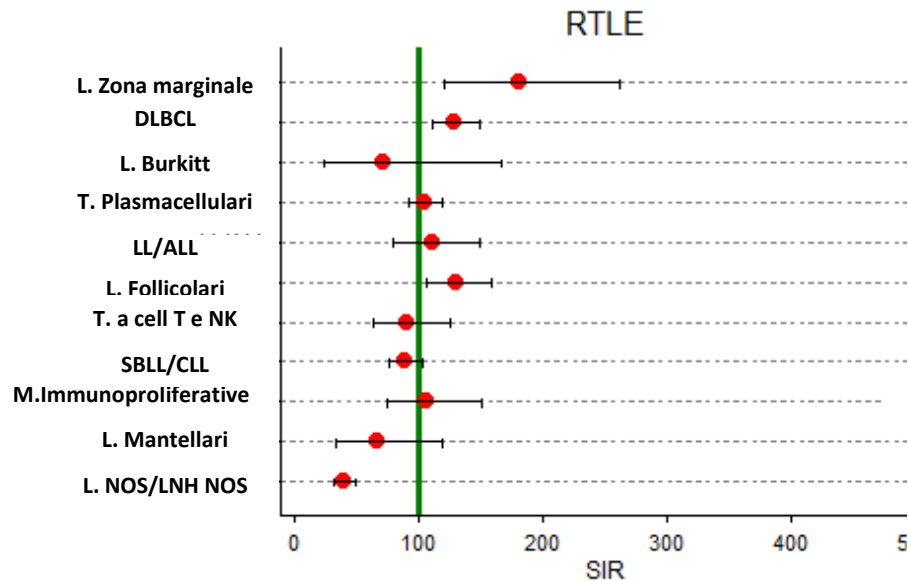
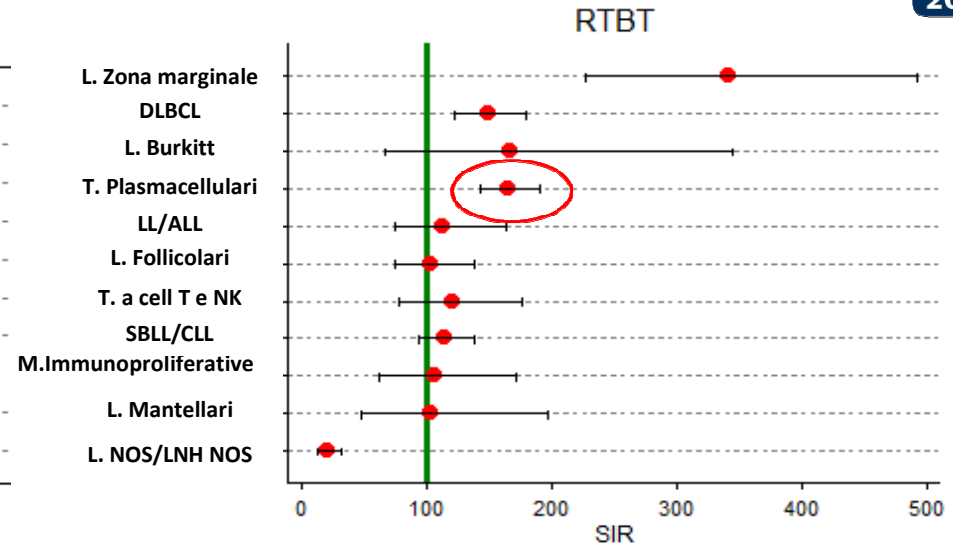
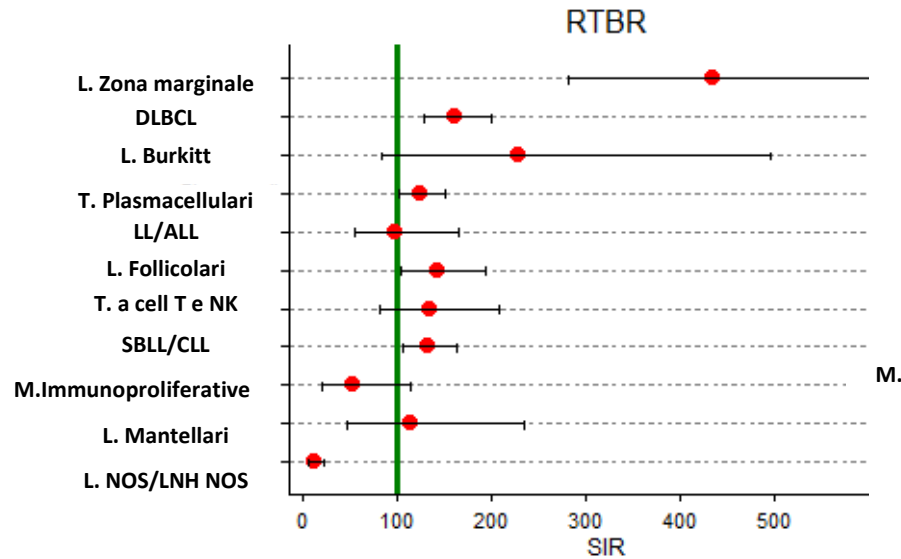


# SIR PROVINCE PUGLIESI





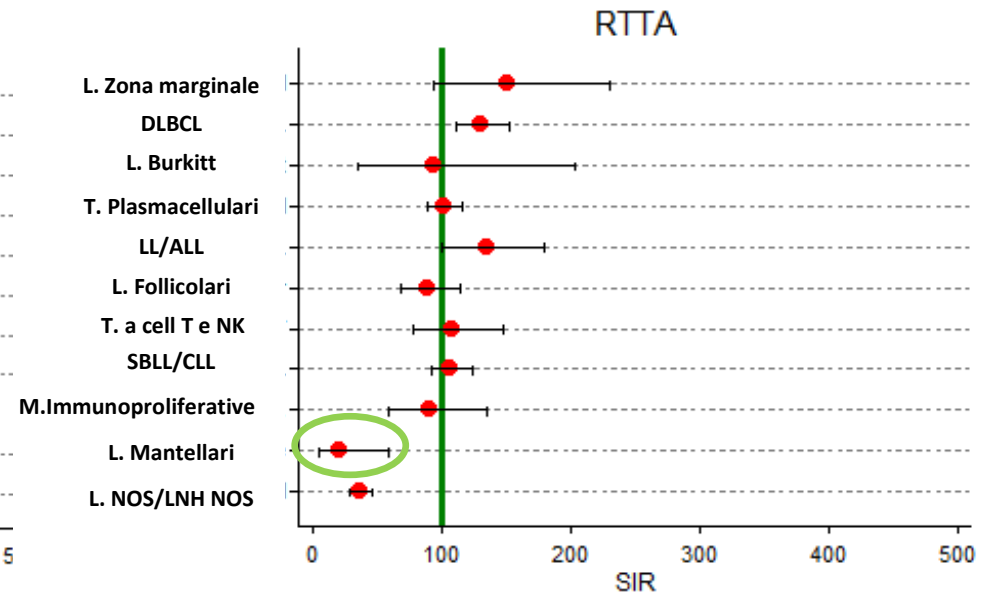
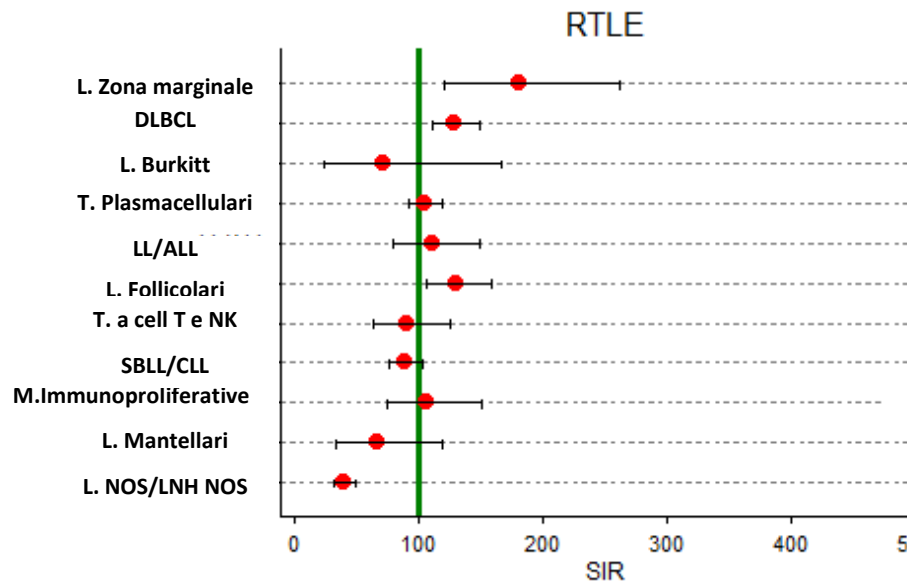
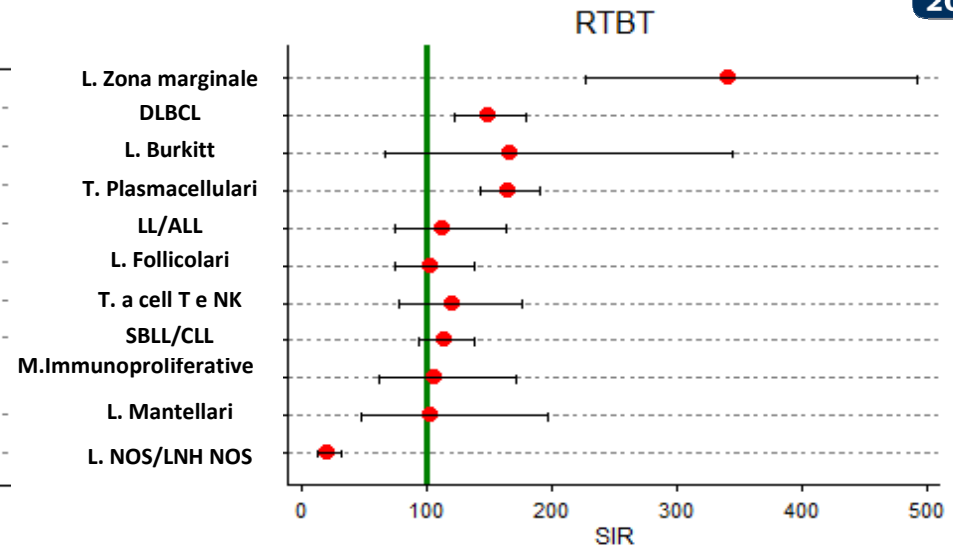
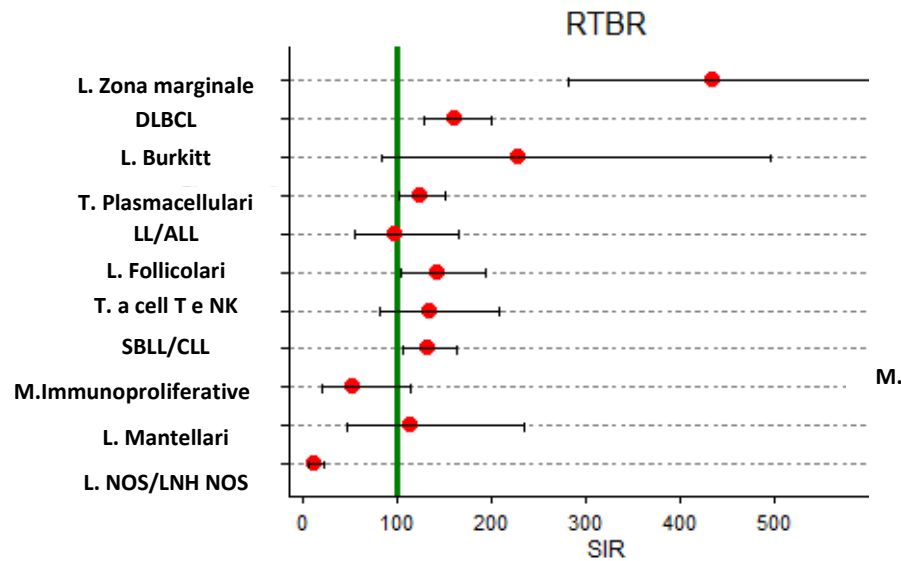
# SIR PROVINCE PUGLIESI



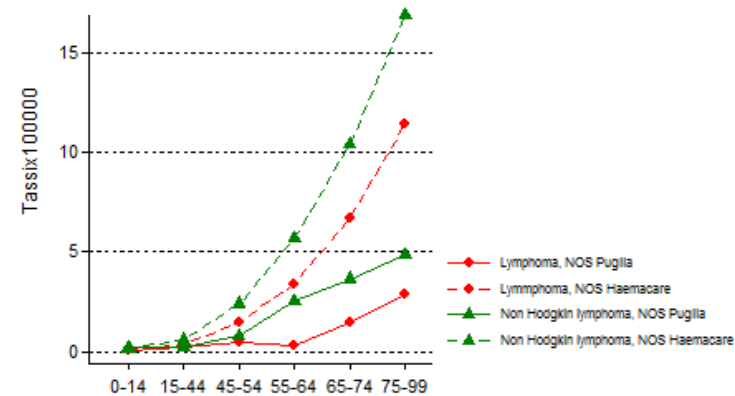
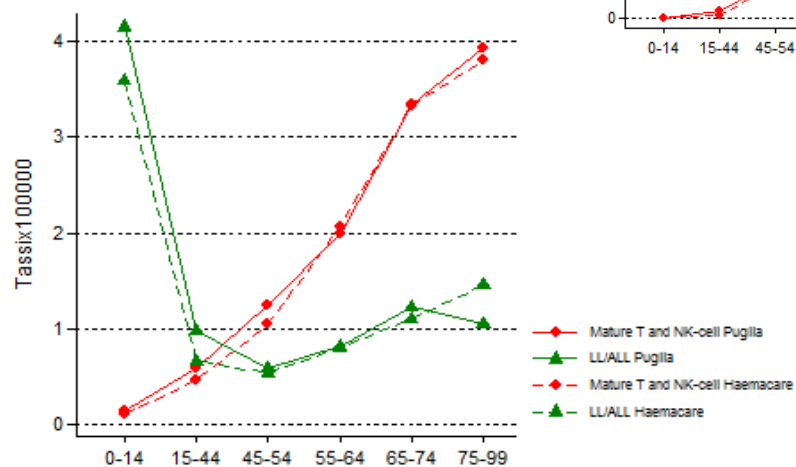
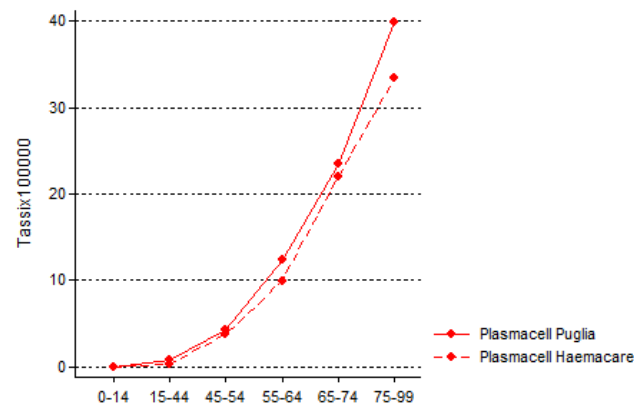
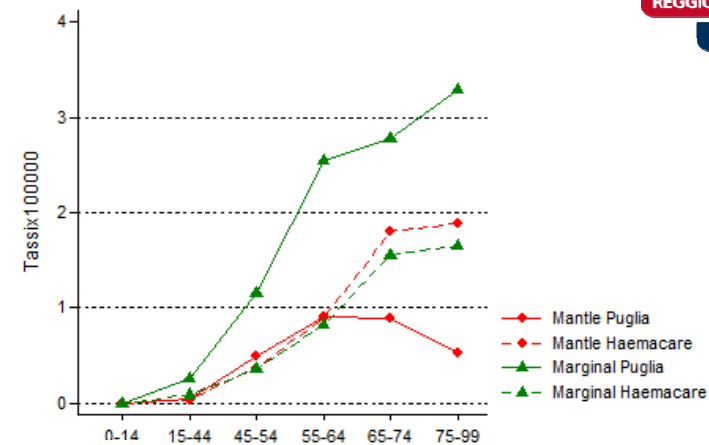
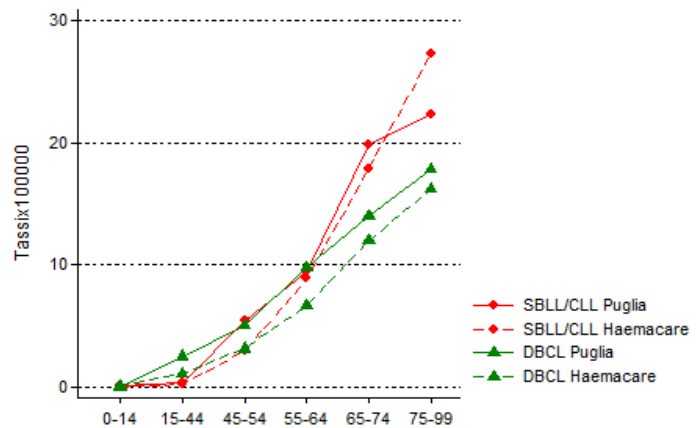
# BASE DI DIAGNOSI T. PLASMACELLULARI

Base diagnosi	RTBR		RTBT		RTLE		RTTA		Totale	
	N.	%	N.	%	N.	%	N.	%	N.	%
DCO	4	3.9	4	2.1	7	3.0	5	2.5	20	2.7
CLINICA	5	4.8	1	0.5	14	5.9	10	5	30	4.1
STRUMENTALE	1	1.0	0	0.0	7	3.0	27	13.3	35	4.8
MARKER	4	3.9	9	4.7	2	1.0	5	2.5	20	2.7
CITOLOGICA	18	17.5	10	5.2	23	9.8	54	26.7	105	14.4
ISTOLOGICA	71	68.9	167	87.5	181	77.3	101	50	520	71.3
<b>Totale</b>	103		191		234		202		730	

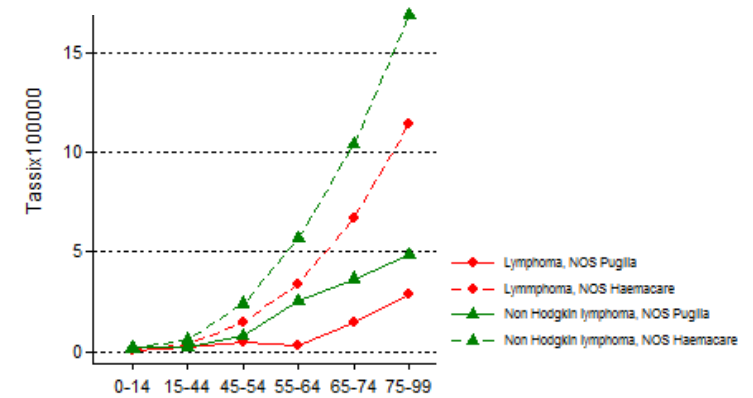
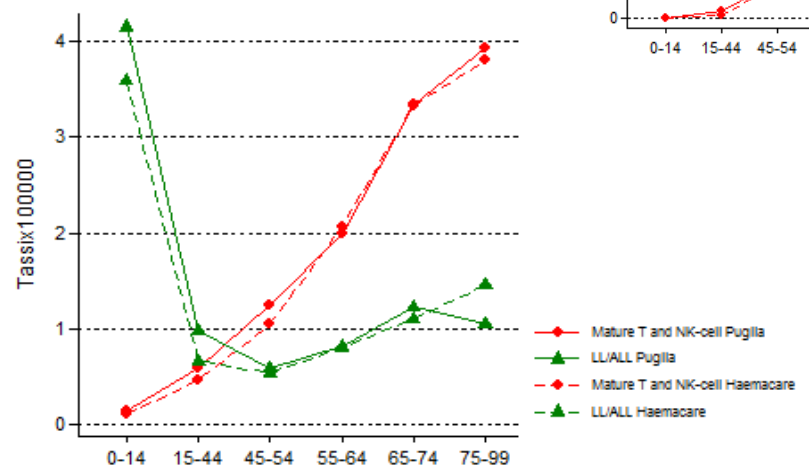
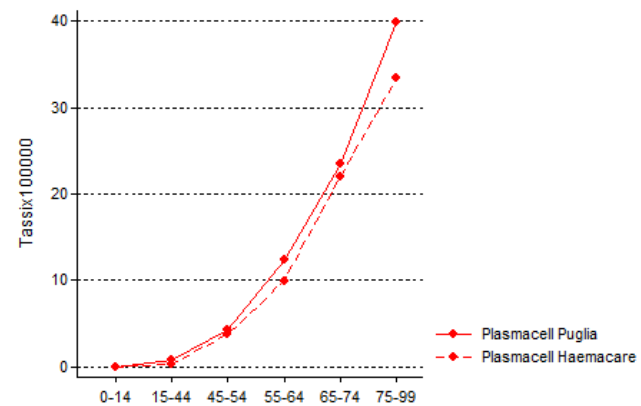
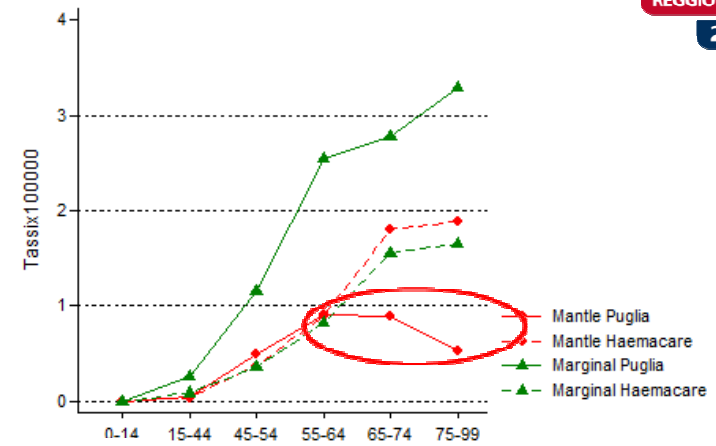
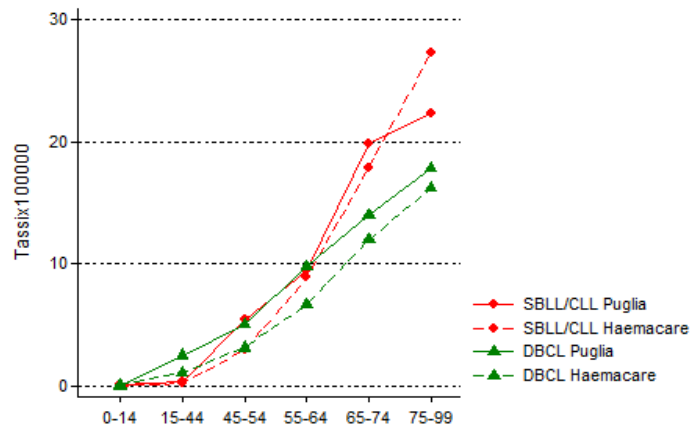
# SIR PROVINCE PUGLIESI



# TASSI PER CLASSE DI ETA'



# TASSI PER CLASSE DI ETA'



# CONCLUSIONI

- Primi dati di incidenza pugliesi per istotipo di Linfomi non Hodgkin, leucemie linfatiche, tumori plasmacellulari.
- In Puglia si sono rilevati eccessi di linfomi della zona marginale, DLBCL e tumori plasmacellulari rispetto allo studio Haemacare. SIR in difetto riguardano invece i linfomi mantellari.
- Analizzando i casi per provincia si evidenzia un eccesso di linfomi della zona marginale nelle Asl BR e BT e in misura minore nelle Asl LE e TA , un eccesso di mielomi nella Asl BT. Nella Asl TA si rileva un'incidenza di linfomi mantellari significativamente inferiore all'atteso.
- Si osserva che l'analisi per grandi gruppi diagnostici (slide 16) rileva un difetto di LNH e un eccesso di leucemie linfatiche croniche di difficile interpretazione.

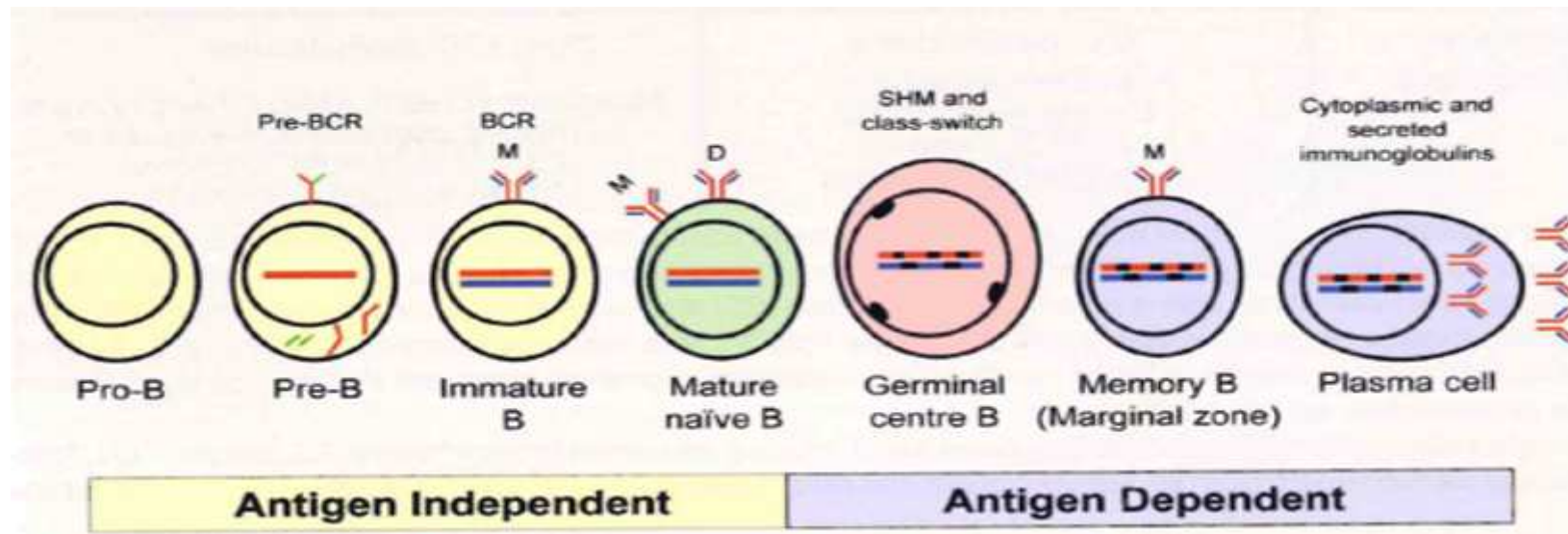
# CONCLUSIONI



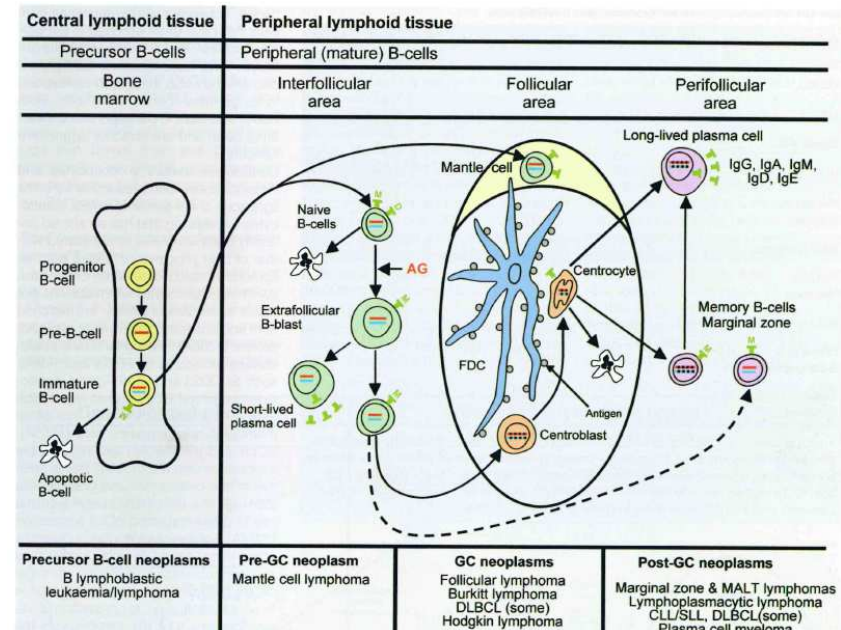
- E' necessario tenere presente che nello studio Haemacare la percentuale di forme NOS è più alta rispetto a quella calcolata per la Puglia.  
Ciò determina una sovrastima dei SIR per gli istotipi specifici di LNH e leucemie stimati nel nostro studio.
- Rispetto allo studio di Luminari et al., relativo alla provincia di Modena, i tassi rilevati in Puglia sono risultati sempre più bassi.
- Le maggiori differenze si riscontrano per i DLBCL e i linfomi della zona marginale in cui i tassi della provincia di Modena sono nettamente superiori a quelli rilevati in Puglia.



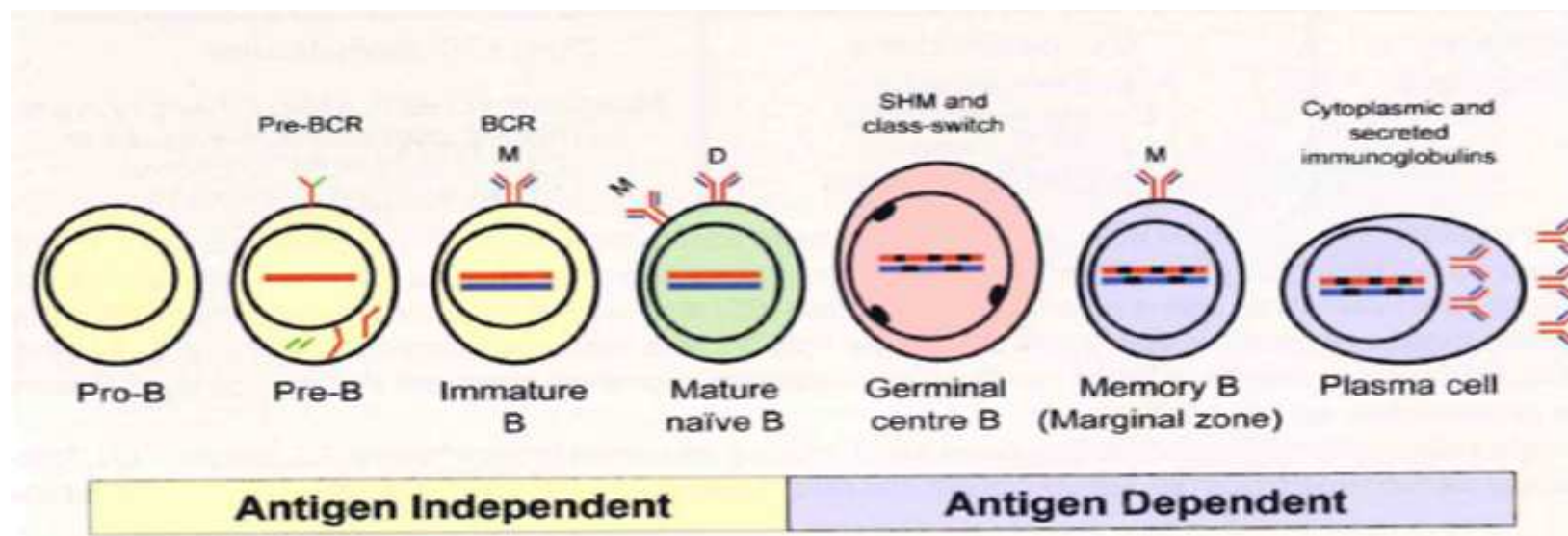
# IPOSTESI PER SUCCESSIVI APPROFONDIMENTI



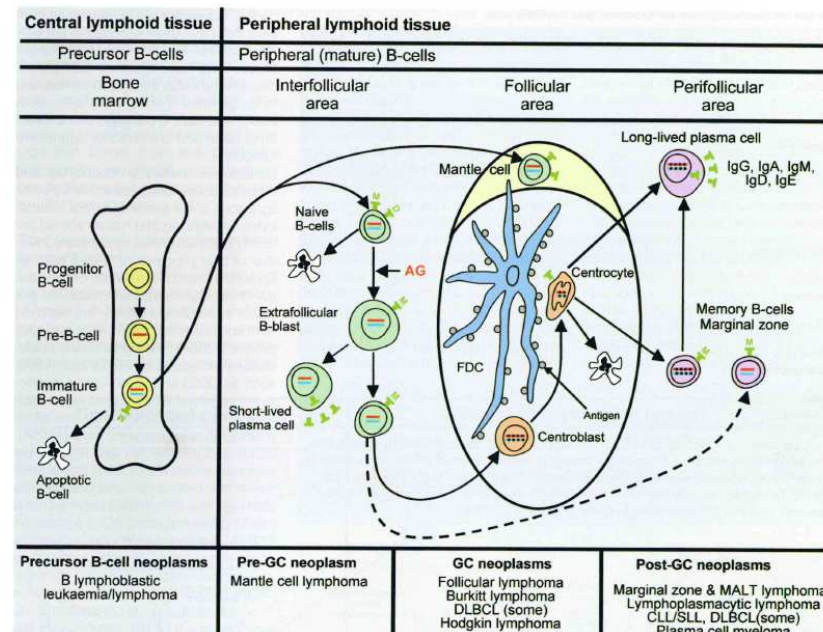
I linfomi della zona marginale sono neoplasie che originano da cellule già esposte alla stimolazione antigenica e si distinguono in nodali, splenici e mucosa associati (MALT).



# IPOSTESI PER SUCCESSIVI APPROFONDIMENTI



Un'ipotesi suggestiva è che l'eccesso di linfomi marginali nodali e splenici rilevato nelle Asl BR e BT possa essere correlato alla diffusione dell'infezione da HCV ed allo stato di infiammazione cronica ad essa correlato.



## Gruppo di lavoro Registro Tumori Puglia

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Grazie per l'attenzione

