Association between RBC transfusions and NHL: a meta-analysis of observational studies

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Introduction

- The incidence of NHL is increasing
- Unexplained reasons
- Transfusion is increasing
- Meta-analysis of observational studies

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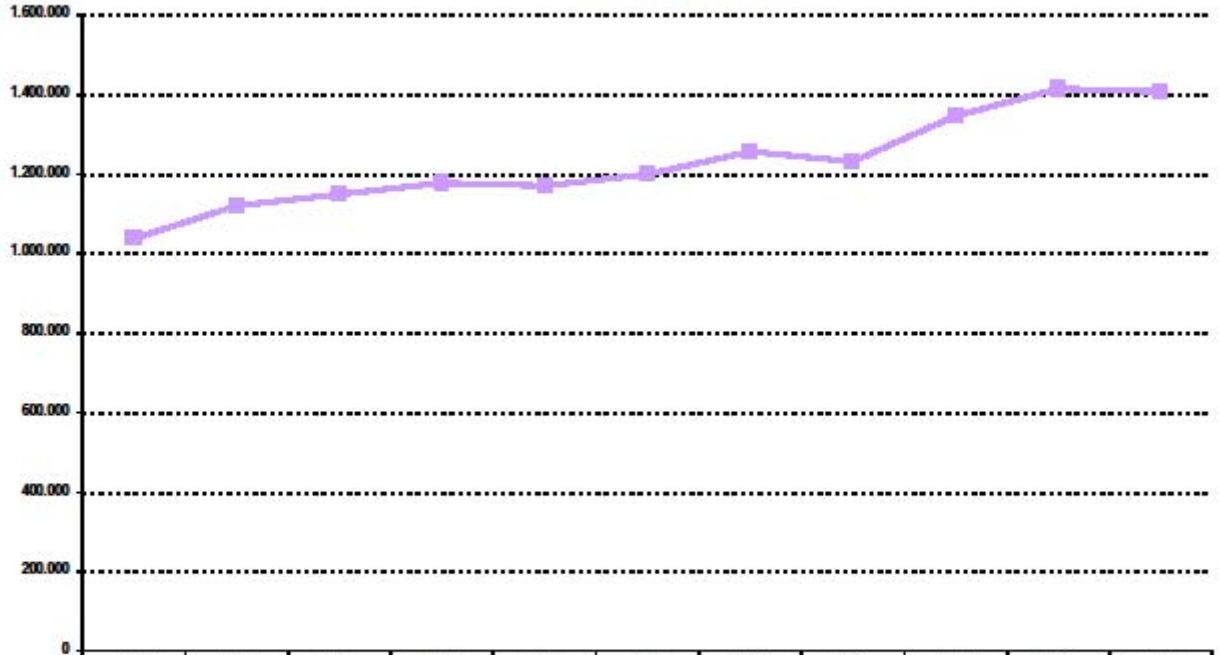
Introduction

TRANSFUSION HEMATÍES Y SANGRE TOTAL 1994-2004
TOTAL NACIONAL



	1.994	1.995	1.996	1.997	1.998	1.999	2.000	2.001	2.002	2.003	2.004
U.Hematíes + ST	1.036.308	1.117.627	1.147.945	1.178.271	1.168.099	1.196.963	1.254.831	1.231.131	1.343.955	1.412.753	1.406.855

Fuente: Ministerio de Sanidad y Consumo. D.G. Salud Pública
Plan Nacional de Hemoterapia

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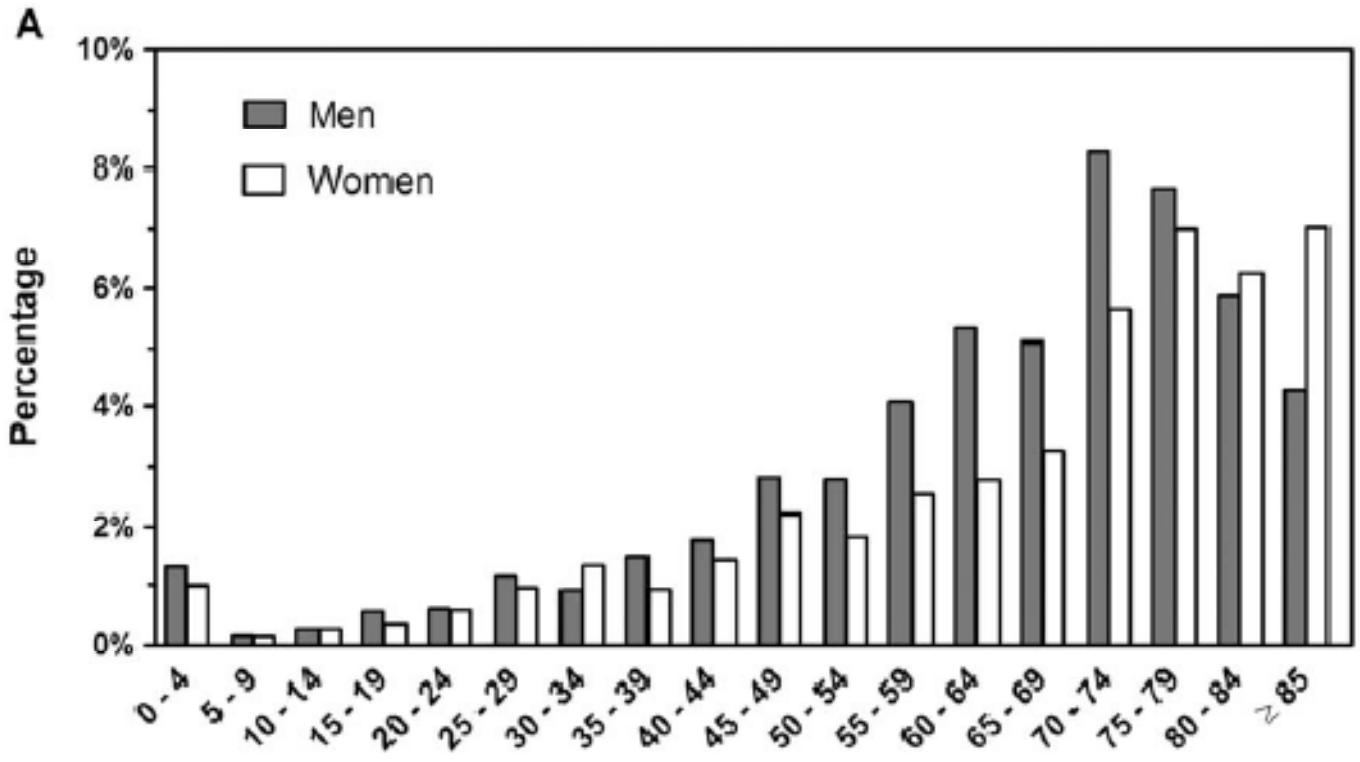
Introduction



Bosch et al. Transfusion 2011;51:105-16

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Introduction
Observational studies

- Case-control studies = Retrospective

- Cohort studies = Prospective

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Methods
Literature search

- PubMed/MEDLINE
  - Through December 2009
  - “non-Hodgkin lymphoma” AND “blood transfusion”
  - Full articles

- Cochrane database

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Methods
Inclusion criteria

- English language
- Epidemiologic observational studies
  - Case-control
  - Cohort
- Reproted an association between RBC transfusion and NHL

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Methods
Exclusion criteria

- Hodgkin lymphoma
- Multiple myeloma
- Autologous RBC transfusions
- Only abstract
- Old publications of the same study

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Methods
Data extraction

- Case-control studies
  - Source and definition of cases and controls
  - Years of inclusion
  - RR (95% CI)
  - Variables used for adjustment
- Cohort studies
  - Source of cohort
  - Years of follow-up
  - Source of the expected incidence of NHL
  - RR (95% CI)
  - Variables used for adjustment
- Contact with authors asking missing information
- **M**eta-analysis of **O**bservational **S**tudies (MOS) group

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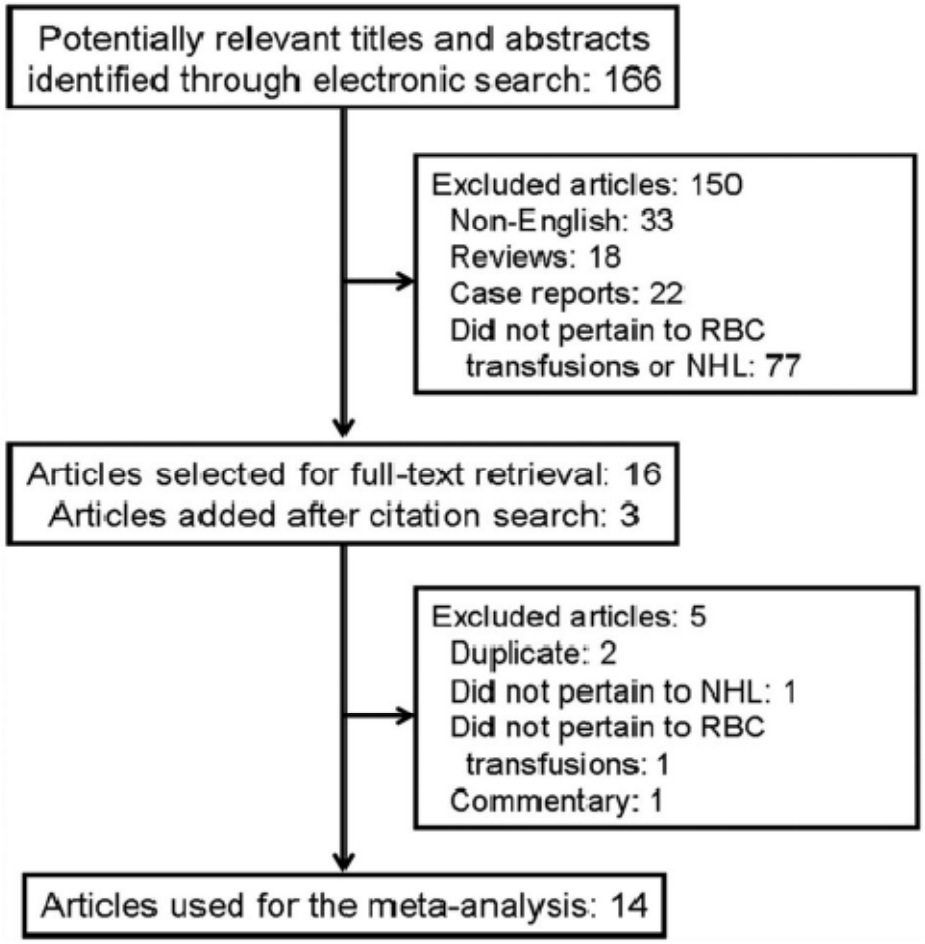
Methods
Data synthesis and analysis

- RR (95% CI)
- Fixed-effects model and random-effects model
- Subset analysis
  - Sex
  - Lymphoma subtype
  - Year of transfusion
- Heterogeinity
  - Q-test statistic
  - Quantity I^2

Results
Search results



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Results
Case-control studies

Author	Year	Cases	Controls
Brandt	1996	280	1827
Adami	1997	361	705
Nelson	1998	378	378
Maguire-Boston	1999	37	174
Tavani	1999	385	1297
Chow	2002	1591	2515
Zhu	2003	1511	1910
Zhang	2004	600	712
Cerhan	2008	759	589

Results
Cohort studies

Author	Year	Median follow-up	Total cohort	Cases observed
Blomberg	1993	10 y	8,249	7
Memon	1994	25 y	340,227	4
Cerhan	2001	12 y	418,342	40
Hjalgrim	2007	Varied	5,652,918	2,853
Erber	2009	10 y	NR	939

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Results
Quality assessment

Author	Year	Selection	Comparability	Outcome	Exposure	Total
Cohort studies						
Blomberg[14]	1993	4	1	2	—	7
Memon[18]	1994	4	0	2	—	6
Cerhan[15]	2001	4	2	2	—	8
Hjalgrim[17]	2007	4	2	3	—	9
Erber[16]	2009	4	2	3	—	9
Average		4	1.4	2.4	—	7.8
Case-control studies						
Brandt[6]	1996	3	2	—	2	7
Adami[5]	1997	4	2	—	3	9
Nelson[10]	1998	4	2	—	2	8
Maguire-Boston[9]	1999	3	2	—	3	8
Tavani[11]	1999	3	2	—	2	7
Chow[8]	2002	4	2	—	2	8
Zhu[13]	2003	3	2	—	2	7
Zhang[12]	2004	4	2	—	2	8
Cerhan[7]	2008	3	2	—	3	8
Average		3.4	2	—	2.3	7.7

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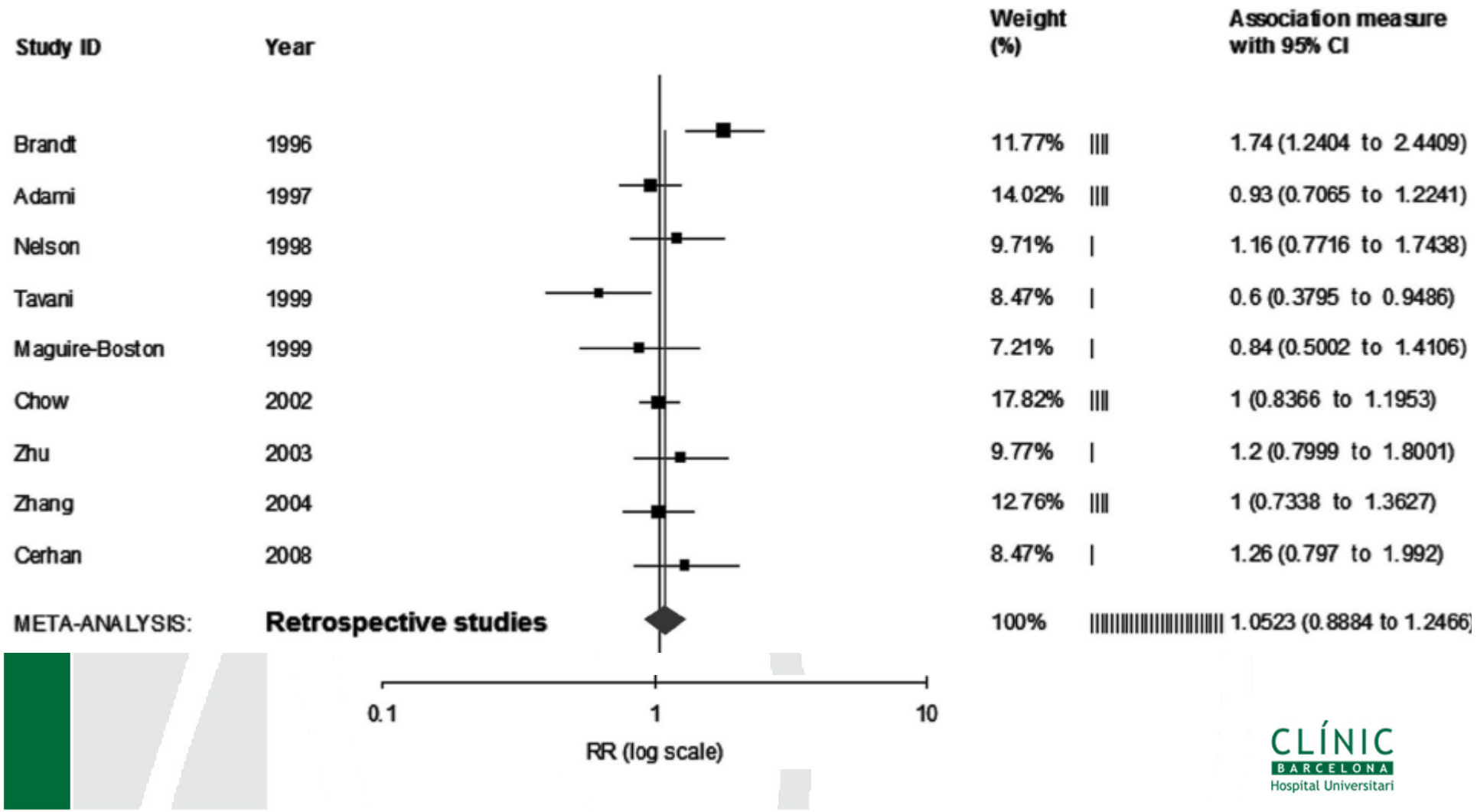
Results
Case-control studies. Outcome



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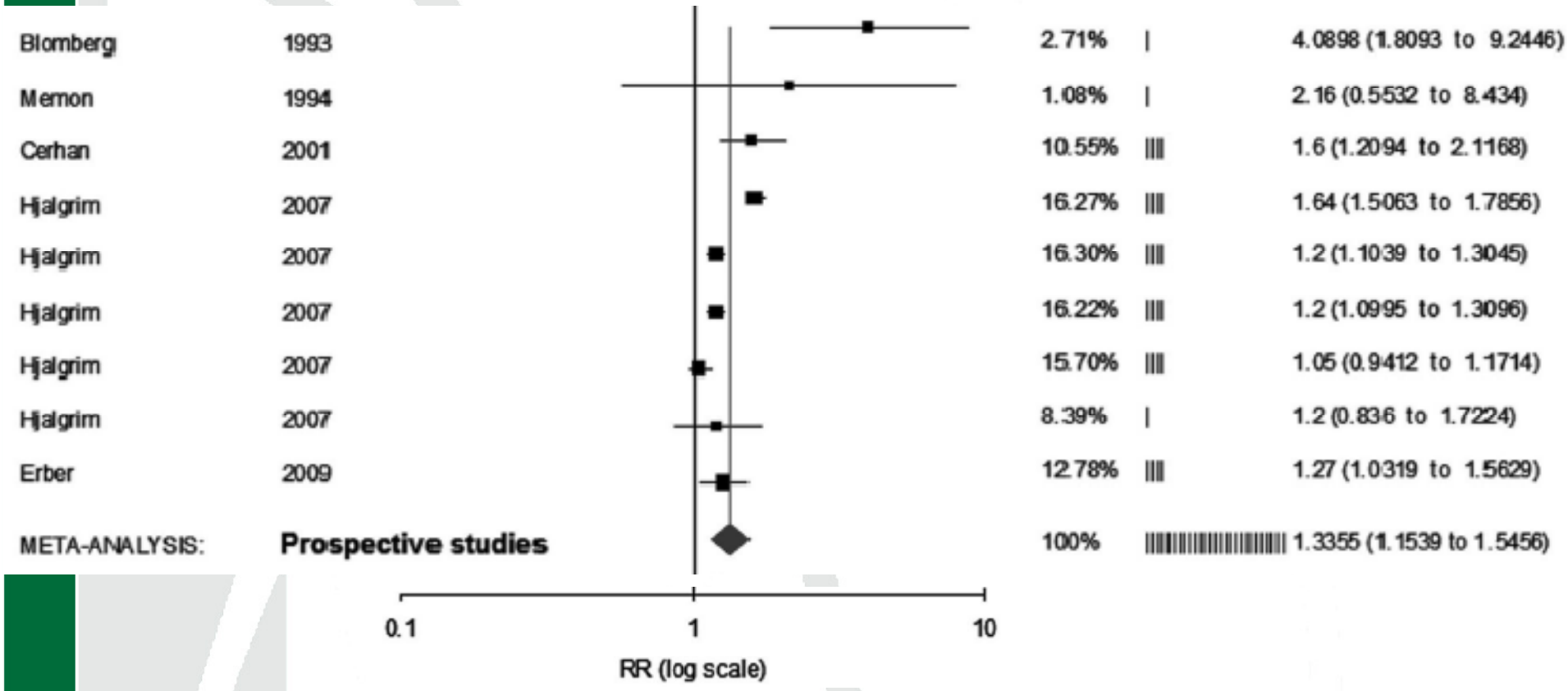
Results
Cohort studies. Outcome



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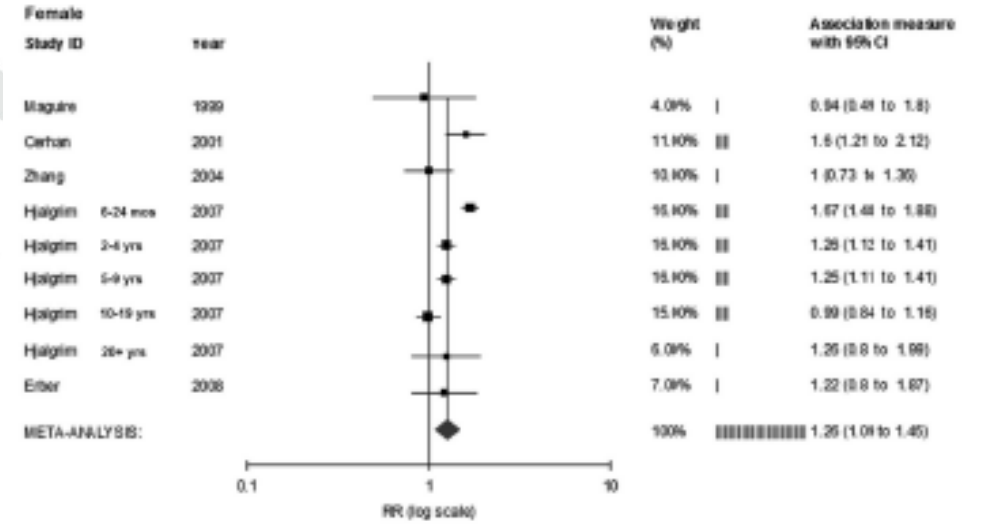
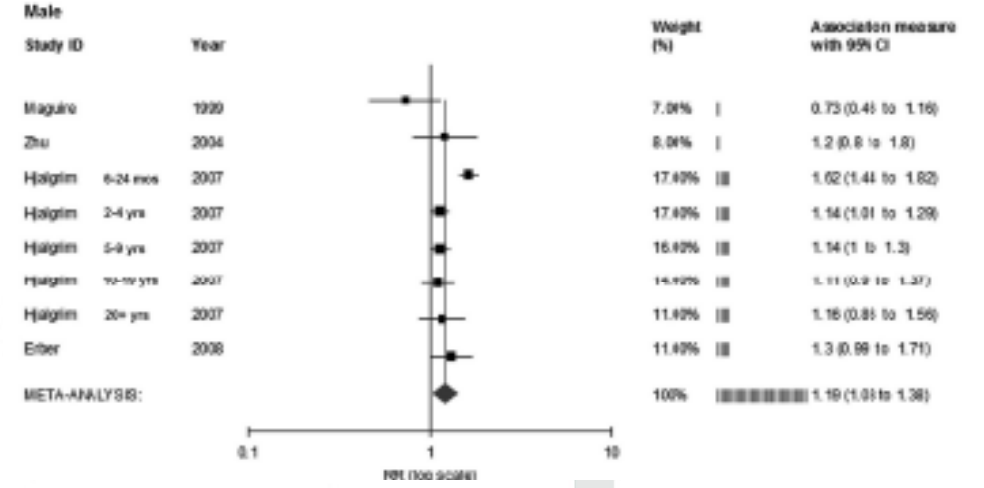
Results
Subset analysis. Sex





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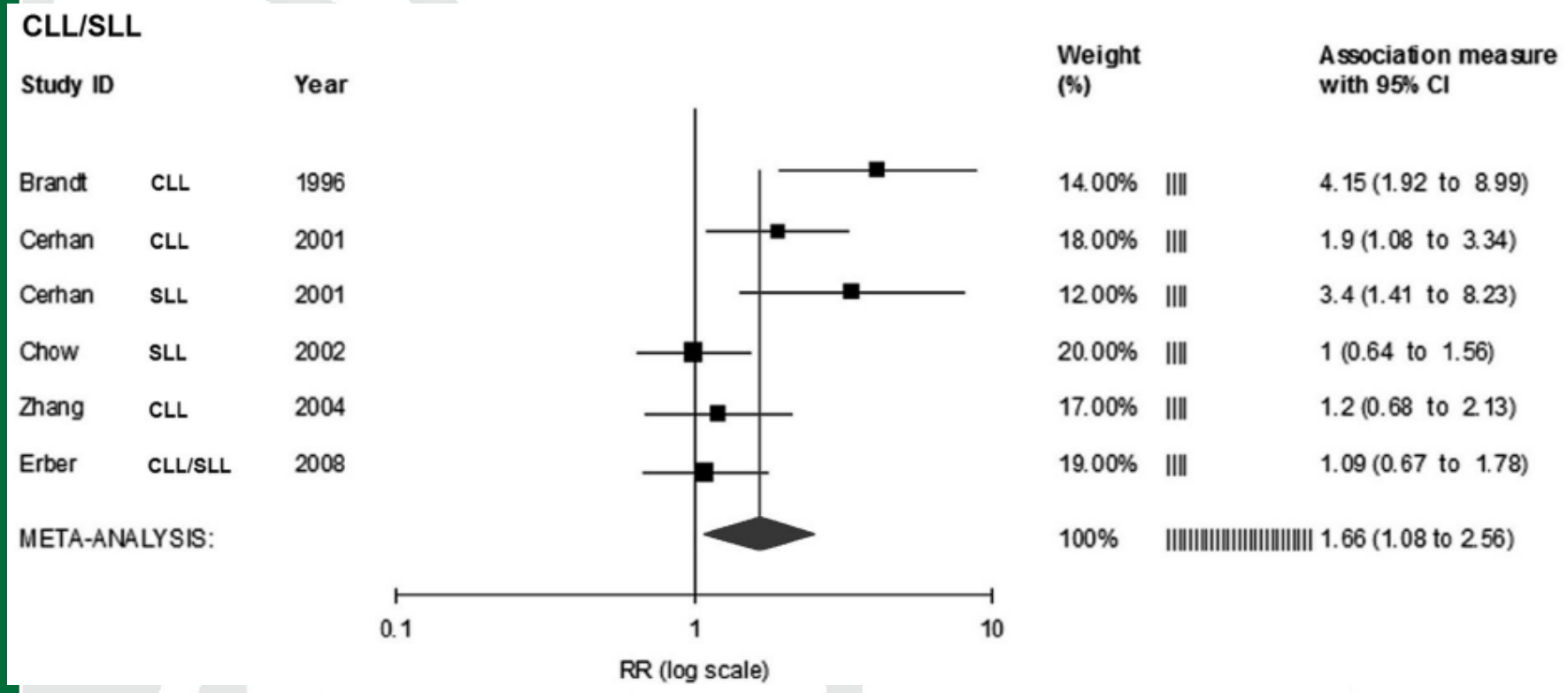
Results
Subset analysis. Lymphoma subtype



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Results
Subset analysis. Others

Subset	Statistical association
Year of transfusion (before or after 1992)	Yes
Transfusion latency	Highly variable No formal analysis
Number and type of transfusions	Highly variable No formal analysis
Reasons for transfusion	Highly variable No formal analysis

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Discussion
Etiology of NHL

- Autoimmune diseases
- Chronic infections
- Congenital and acquired immunodeficiencies
- Diabetes mellitus
- Pesticides

- In general, immune dysregulation

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Blood Reviews (2007) 21, 327–348

ELSEVIER

www.elsevierhealth.com/journals/blre

REVIEW

Transfusion-related immunomodulation (TRIM): An update

Eleftherios C. Vamvakas [a], Morris A. Blajchman [b,*]

[a] *Department of Pathology and Laboratory Medicine, University of Ottawa, Faculty of Medicine, Canada*
[b] *Department of Pathology and Molecular Medicine, McMaster University Medical School, and Canadian Blood Services, Hamilton, Ontario, Canada*

Discussion
Statistical association

- Authors found a statistical association between RBC transfusion and development of NHL
  - Case-control studies did not
  - Cohort studies did
  - Small sample size, confounding variables, recall bias
- No association with sex
- High association with CLL/SLL→ further attention
- No association with year of transfusion

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Discussion
Limitations

- Age of RBCs was not analyzed
- Quality of published studies
  - Self-reporting questionnaires
  - Platelet/plasma transfusion
  - Latency and reasons for transfusion
- Confounding variables
  - HIV
  - Autoimmune diseases

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