IN THE NAME OF GOD

Zanjan University of Medical Sciences

Title: Correlation between vaccination status and the risk of childhood acute lymphoblastic leukemia

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Epidemiology of Leukemia

- Leukemia is one of the most common cancer in children and teens, accounting for almost 1 out of 3 cancers.
- About 3 out of 4 leukemia among children and teens are acute lymphocytic leukemia (ALL).
- Most of the remaining cases are acute myeloid leukemia (AML).

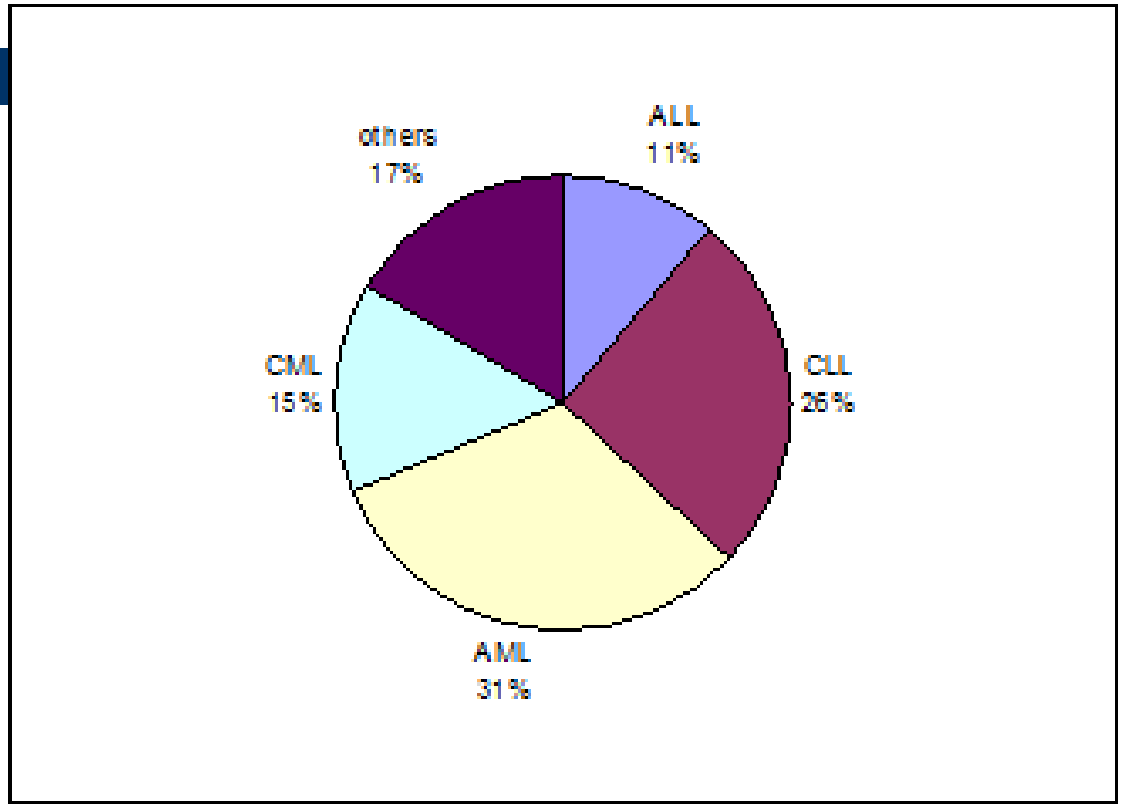
Demographics of Leukemia Patients (2001 Data)

CLL=Chronic Lymphocytic

ALL=Acute Lymphocytic

CML=Chronic Mylogenous

AML=Acute Mylogenous



Total Reported Cases = 31,500

Source from *Leukemia, Lymphoma, Myeloma Facts 2001*

Epidemiology of Leukemia

- ALL is most common in early childhood, peaking between 2 and 5 years of age.

- AML tends to be more spread out across the childhood years, but it's slightly more common during the first 2 years of life and during the teenage years.

Risk factors and etiology

- Ionizing radiation during prenatal and postnatal life
- Paternal smoking
- Exposure to household pesticides
- Benzene·
- Genetic and epigenetic factors
- Gene deletion
- Gene mutation
- Chromosomal translocation

Risk factors and etiology

- immune dysfunction may play an important role in the etiology of childhood leukemia.
- Leukemia is essentially a malignancy of the immune system.
-

Risk factors and etiology

- Early exposure to infections may modulate the development of immune system and may be protective for childhood ALL.

- Greaves in 1997 stated that both the pattern and timing of infections in early life is critical to the developmental programming of the immune system.

Risk factors and etiology

- Current lifestyles
- Improvement of hygiene
- less exposure to infections

- causes defect in appropriate development of immune system.

Risk factors and etiology

- Genetic predisposition
- Inappropriate development of immune system

- Results in an abnormal immunological response thus increasing the risk of leukemia

Risk factors and etiology

- Vaccination due to its role in stimulating the immune system, has been considered a potential modifier of the risk of childhood leukemia.
- Vaccination timing and dosage
-

Pediatric Vaccination Schedule

Vaccines are important to prevent getting serious illnesses. Here is a list of recommended pediatric vaccines from birth to age 18.
Please talk with your child's doctor about the vaccines your child needs and when.

Vaccines	Birth	1 Month	2 Months	4 Months	6 Months	12 Months	15 Months	18 Months	19–23 Months	2–3 Years	4–6 Years	7–10 Years	11–12 Years	13–18 Years
DTaP			•	•	•		▬	▬			•		•	
HepA						▬	▬	▬	▬					
HepB	•	▬	▬	▬	▬	▬	▬	▬	▬					
Hib			•	•	•	▬	▬							
HPV													•	
Influenza					Yearly									
IPV			•	•	▬	▬	▬	▬	▬		•			
MMR						•	•				•			
MCV4													•	Booster
PCV			•	•	•	▬	▬							
RV			•	•	•									
Varicella						•	•				•			

● Given at these ages

▬ The vaccine can be given once during the age range

DTaP (Diptheria, Tetanus and Pertussis)
HepA (Hepatitis A)
HepB (Hepatitis B)
Hib (*Haemophilus Influenzae* Type b)
HPV (Human Papillomavirus)
Influenza (Flu)
IPV (Polio)
MMR (Measles, Mumps and Rubella)
MCV4 (Meningococcal)
PCV (Pneumococcal)
RV (Rotavirus)
Varicella (Chickenpox)

Sources: The American Academy of Pediatrics, the Centers for Disease Control

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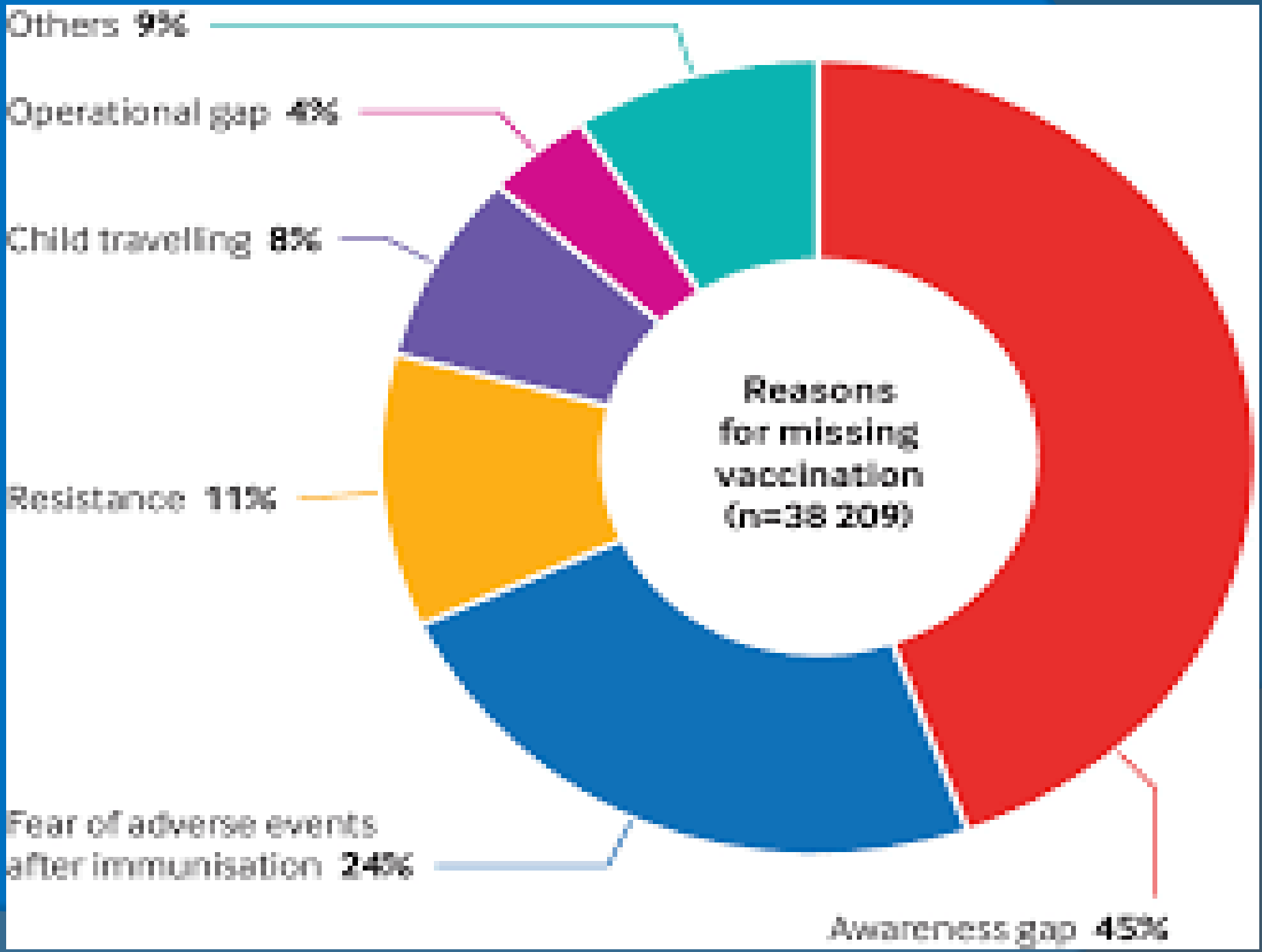
Others 9%
Operational gap 4%
Child travelling 8%
Resistance 11%
Fear of adverse events after immunisation 24%
Awareness gap 45%
Reasons for missing vaccination (n=38 209)

Vaccination

- A study from Australia reported
- A increased risk of ALL leukemia with vaccination against diphtheria, pertussis (whooping cough), and tetanus

- While other studies did not support such an association.
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Vaccination

- Also, studies from USA, Canada and Finland have reported:
- A reduced risk of leukemia with Bacille Calmette–Guerin (BCG) vaccination.

- However, a study in New Zealand showed no effect.

Aim of present study

- Analyzing the correlation between diphtheria, pertussis, tetanus (DPT), poliomyelitis, MMR, hepatitis B, BCG and *Haemophilus influenzae* type b (Hib) vaccination and risk of ALL leukemia.

Material and Methods

Search Strategy

- Scopus,
- PubMed,
- Google Scholar,
- Science-Direct,
- Web of Science,
- ProQuest,
- ClinicalTrials.gov,
- Directory of Open Access Journals,

Search Strategy

- Immunization or immunized
- Vaccines or vaccine or vaccination or vaccinated
- Risk or risks or association or correlation or odds
- leukemia or leukaemia or leukemic or leukaemic
- child or children or childhood or baby or infant or infants or newborn or neonates or pediatrics or pediatric

Selection criteria: inclusion criteria

- Studies reported:
- the association of early vaccination with leukemia in children under 20 years old and vaccines were included in this study.
- .

Selection criteria: Exclusion criteria

- (i) unreliably extracted data;
- (ii) leukemia cases reported in adults;
  (iii) overlapped data sets;
- (iv) abstract-only articles,

- All studies identified were reviewed independently for eligibility.

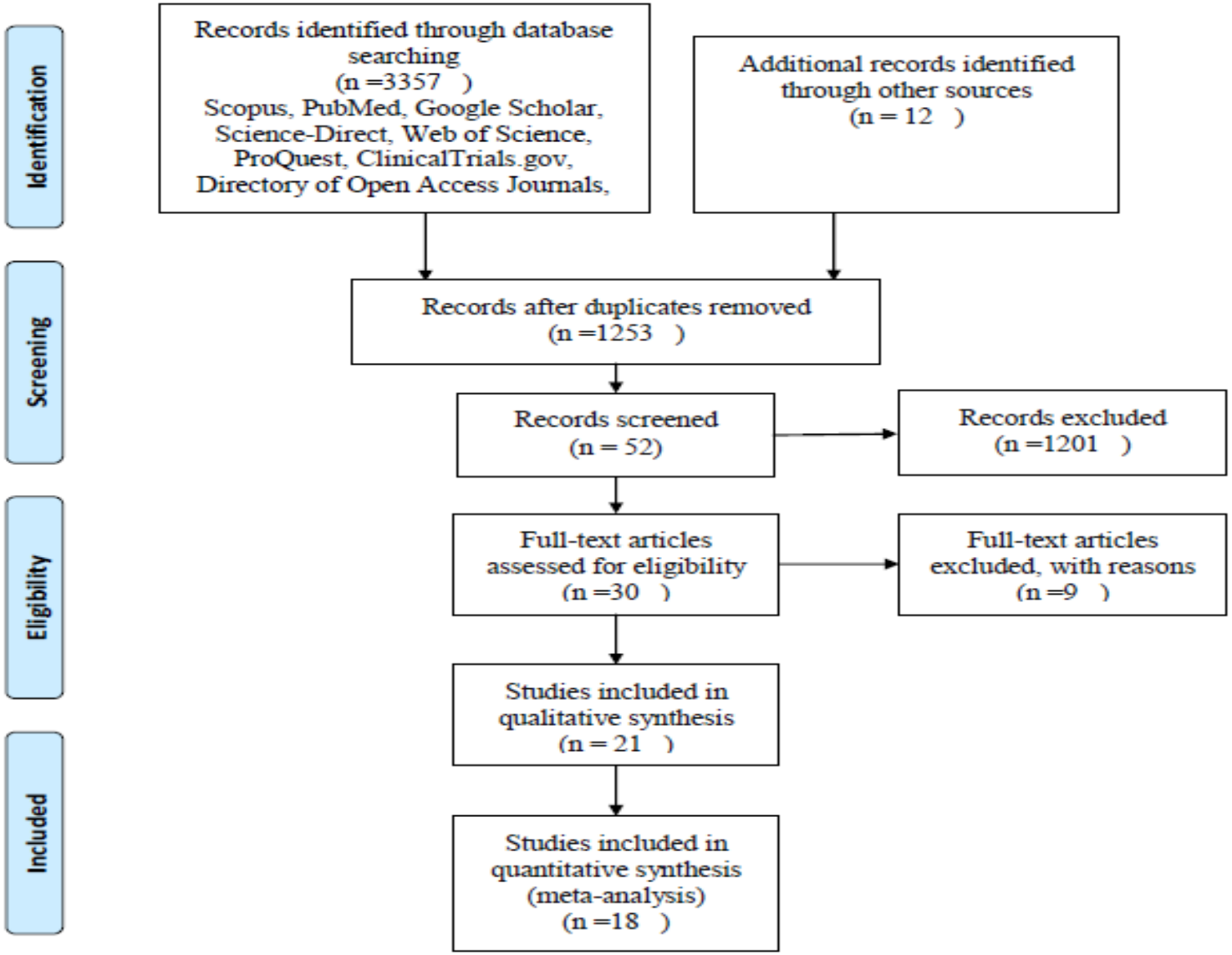


Figure 1. PRISMA flow diagram of studies' screening and selection.

Statistical methods

- Comprehensive Meta-analysis software STATA version 14 was used.
- Summary odds ratios (ORs)
- 95% confidence intervals [CIs]
  Heterogeneity: Q statistic and I-squared tests.
- Heterogeneity was considered statistically significant if the P-value was < 0.1 or I-squared value was > 50%

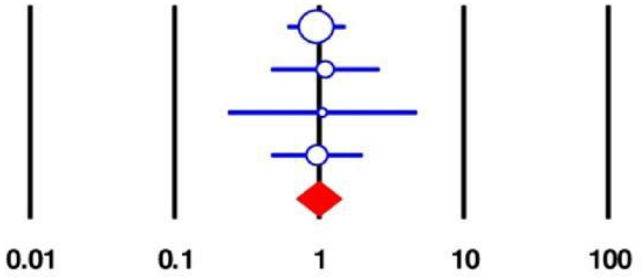
- Results

Forest plot showing meta-analysis of polio sip vaccination

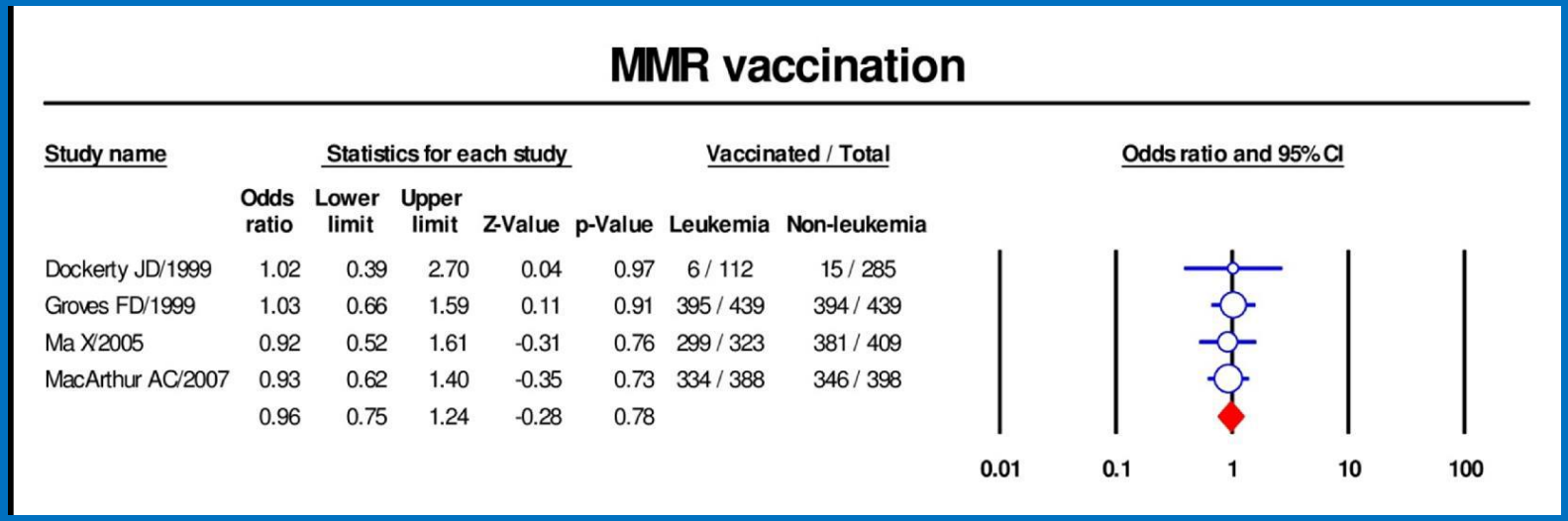
Polio sip vaccination

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	Vaccinated / Total: Leukemia	Vaccinated / Total: Non-leukemia
Dockerty JD/1999	0.95	0.60	1.52	-0.20	0.85	80 / 117	197 / 284
Groves FD/1999	1.10	0.46	2.62	0.22	0.83	429 / 439	428 / 439
Ma X/2005	1.05	0.23	4.74	0.07	0.95	320 / 323	405 / 409
MacArthur AC/2007	0.97	0.47	2.00	-0.09	0.93	371 / 386	384 / 399
	0.98	0.70	1.39	-0.09	0.93		

Odds ratio and 95% CI



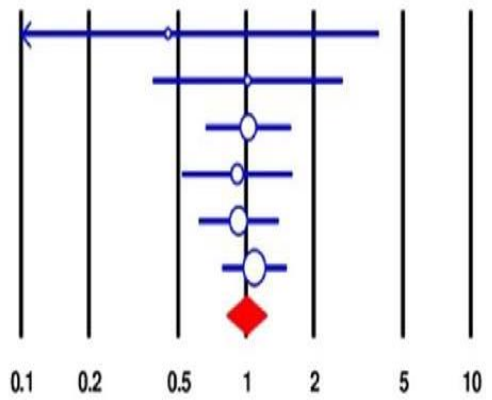
Forest plot showing meta-analysis of MMR vaccination



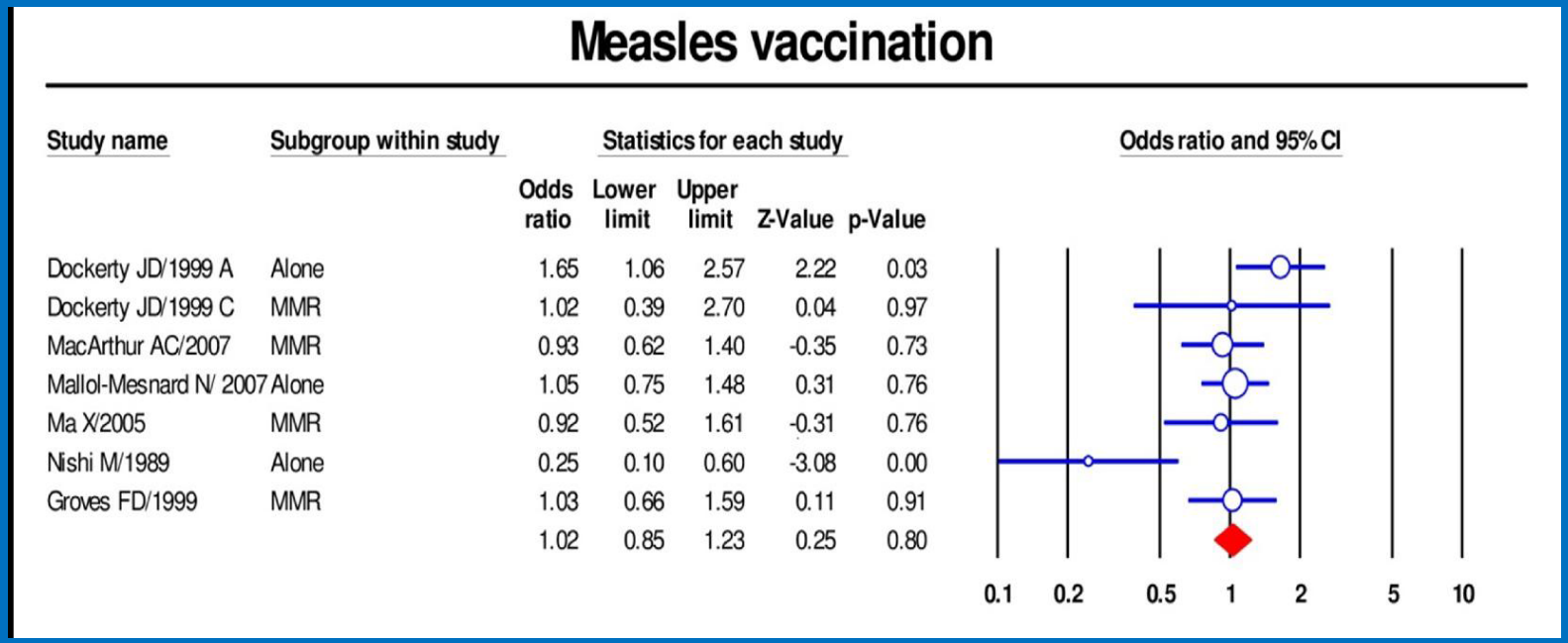
Forest plot showing meta-analysis of rubella vaccination

Rubella vaccination

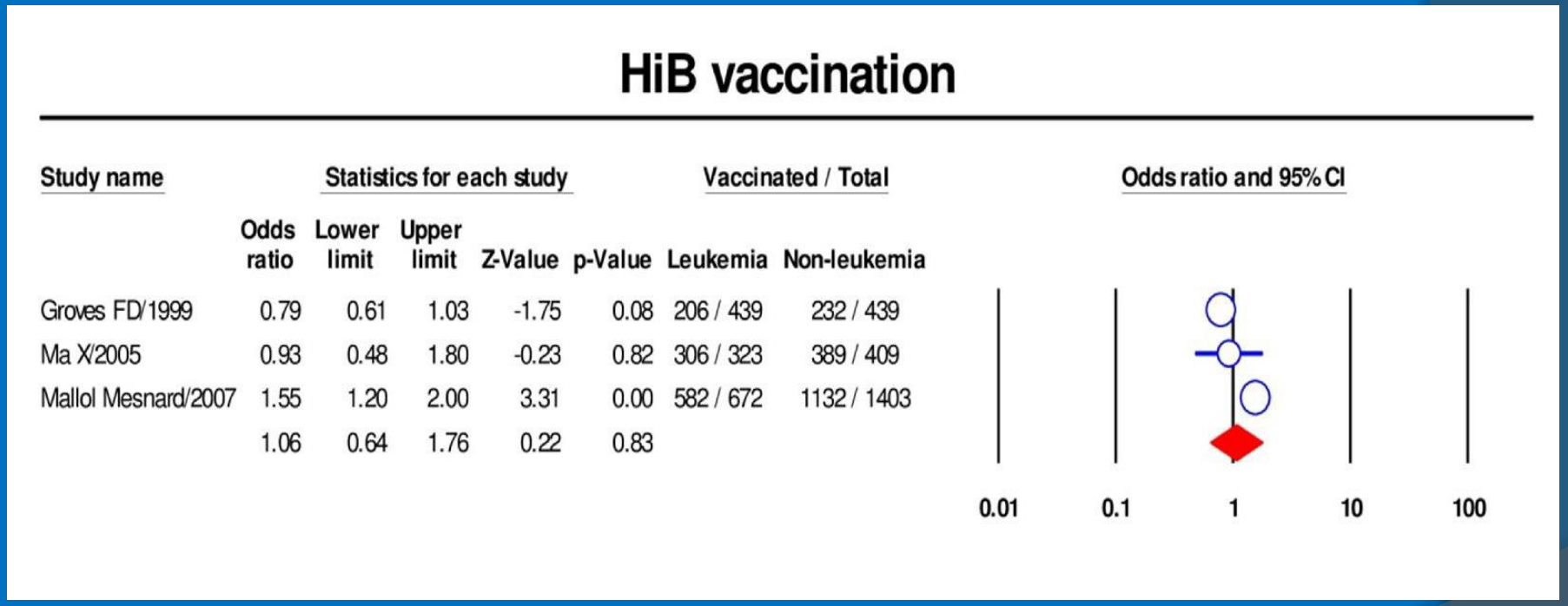
Study name	Subgroup within study	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	Vaccinated / Total: Leukemia	Vaccinated / Total: Non-leukemia
Dockerty JD/1999 A	Alone	0.45	0.05	3.90	-0.72	0.47	1 / 115	5 / 262
Dockerty JD/1999 C	MMR	1.02	0.39	2.70	0.04	0.97	6 / 112	15 / 285
Groves FD/1999	MMR	1.03	0.66	1.59	0.11	0.91	395 / 439	394 / 439
Ma X/2005	MMR	0.92	0.52	1.61	-0.31	0.76	299 / 323	381 / 409
MacArthur AC/2007	MMR	0.93	0.62	1.40	-0.35	0.73	334 / 388	346 / 398
Mallol-Mesnard N/ 2007	Alone	1.09	0.78	1.52	0.52	0.60	540 / 596	1104 / 1229
		1.00	0.82	1.23	0.03	0.98		



Forest plot showing meta-analysis of measles vaccination



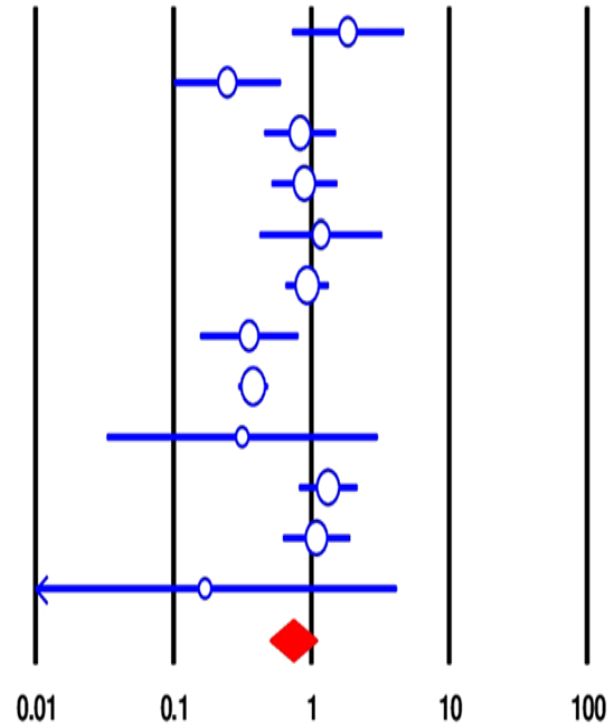
Forest plot showing meta-analysis of HiB vaccination



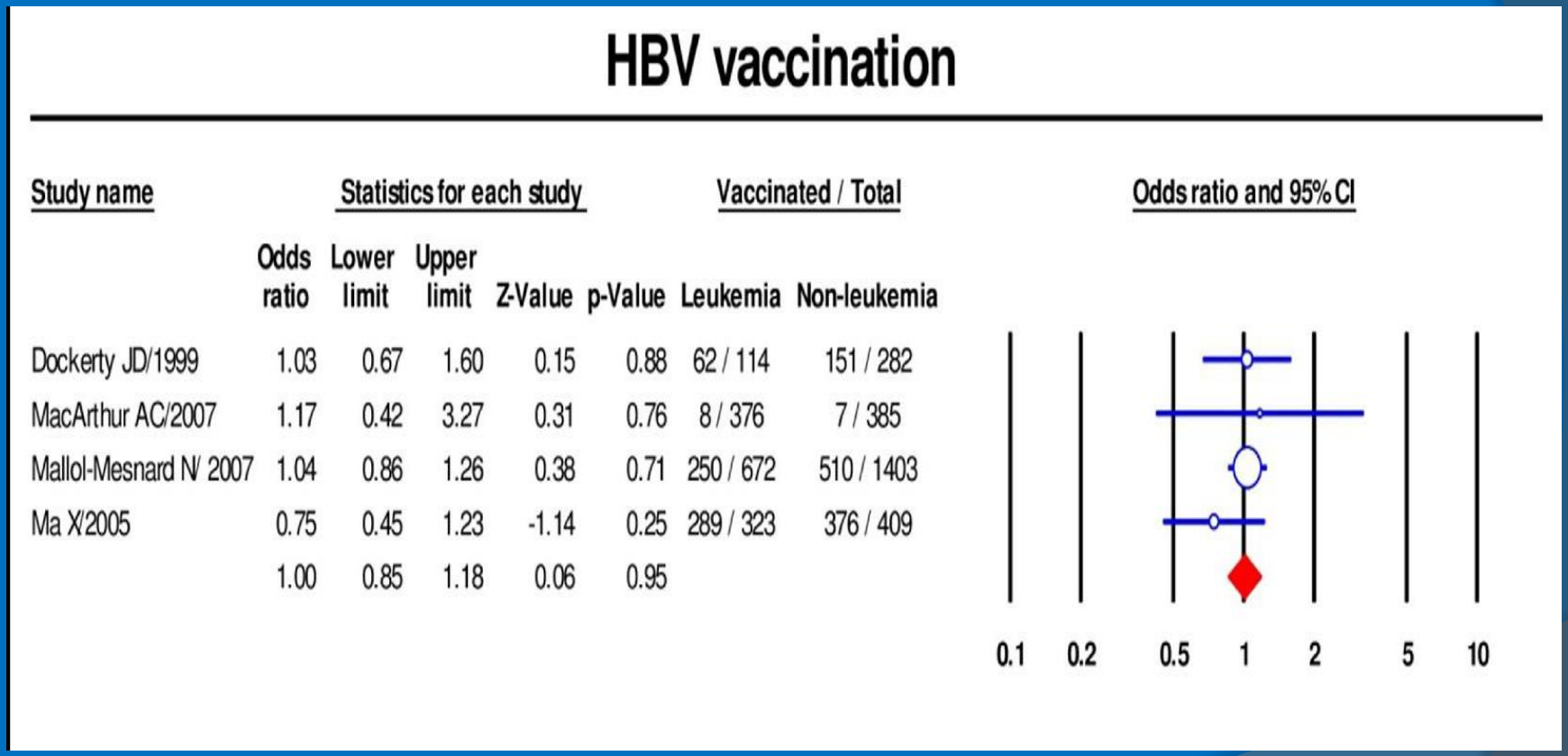
Forest plot showing meta-analysis of BCG vaccination

BCG vaccination

Study name	Odds ratio	Lower limit	Upper limit	p-Value	Vaccinated / Leukemia	Total / Non-leukemia
Dockerty JD/1999	1.84	0.72	4.71	0.20	8 / 120	11 / 295
Nishi M/1989	0.25	0.10	0.60	0.00	48 / 63	117 / 126
Salonen T/1976	0.83	0.46	1.51	0.54	348 / 373	352 / 373
Von Kries R/2000	0.89	0.51	1.54	0.68	107 / 129	273 / 323
MacArthur AC/2007	1.17	0.42	3.27	0.76	8 / 376	7 / 385
Mallol-Mesnard N/ 2007	0.93	0.65	1.34	0.71	624 / 672	1309 / 1403
Crispen RG/1976	0.35	0.16	0.81	0.01	6 / 112	85350 / 620114
Davignon L/1971	0.38	0.30	0.48	0.00	96 / 287	1092400 / 1917000
Sutherland I/1982	0.32	0.03	3.03	0.32	1 / 4	13598 / 26465
Mathe/1974	1.32	0.81	2.16	0.26	76 / 130	67 / 130
Petridou/1997	1.09	0.62	1.91	0.76	22 / 153	40 / 300
Comstock GW/1975	0.17	0.01	4.17	0.28	0 / 1	5524 / 8340
	0.73	0.50	1.08	0.12		



Forest plot showing meta-analysis of HBV vaccination



Discussion

- The main finding of present study was that childhood vaccination status was not significantly correlated with the risk of ALL.

- However, inconsistencies in existing findings with respect to vaccination and childhood leukaemia have been reported.

- Some studies reported decreased
- risks of leukemia associated with measles vaccination, DTP vaccination, Haemophilus influenzae type B (Hib) vaccination, and BCG vaccination for tuberculosis (16).

- Timely completion of early childhood immunizations may decrease the risk of
- leukemia through general improvements in immune functioning.

- The reasons for inconsistent results may be related to “Exposure assessment” in different studies.

- Few studies:
- Written vaccination records

- Most studies used:
- Interviews with parents
- Self-administered questionnaires by parents.
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Thanks for
your attention