DEPARTMENT OF GLOBAL HEALTH

UNIVERSITY of WASHINGTON

RISK OF ADVERSE INFANT OUTCOMES ASSOCIATED WITH MATERNAL TUBERCULOSIS IN A LOW BURDEN SETTING

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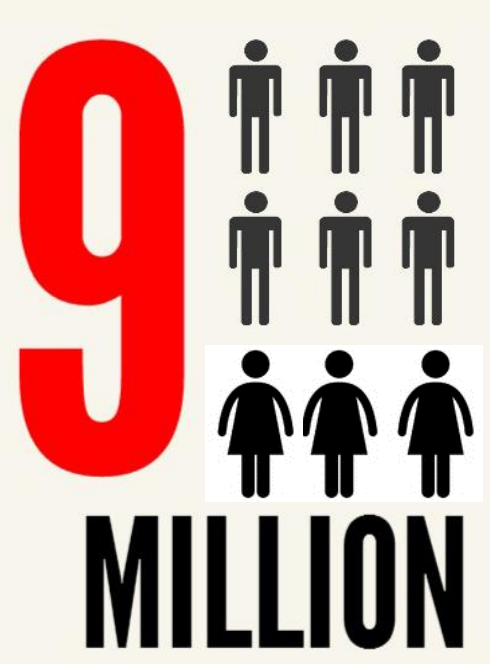
UW Medicine
UW SCHOOL OF MEDICINE
DIVISION OF ALLERGY & INFECTIOUS DISEASES

SCHOOL OF PUBLIC HEALTH
Department of Epidemiology

Background



- Globally, 9 million incident TB cases/year
  - 3.3 million were women
- WA State incidence of TB is 3/100,000
  - Foreign born 75%
  - Women account for 43% of incident TB cases
- Majority of TB cases in women occur during child-bearing years

WHO, 2014
CDC, 2012
WA State DOH, 2014
Mathad, CID 2012

Background

- Burden of TB is high among pregnant women

	Mean (95% uncertainty range)	Rate per 1000 pregnant women (95% uncertainty range)	Percentage of global burden
All countries combined	216 500 (192 100–247 000)	2·1 (1·8–2·4)	..
African Region	89 400 (74 200–110 500)	3·6 (3·0–4·5)	41%
Region of the Americas	4800 (3900–6000)	0·4 (0·3–0·5)	2%
Eastern Mediterranean Region	28 500 (19 700–41 900)	2·3 (1·6–3·4)	13%
European Region	4900 (3800–6300)	0·6 (0·5–0·8)	2%
South-East Asia Region	67 500 (52 000–87 100)	2·4 (1·9–3·1)	31%
Western Pacific Region	21 400 (19 400–23 700)	1·1 (1·0–1·2)	10%

Table 2: **Total number of active tuberculosis cases in pregnant women, rate per 1000 pregnant women and percentage of global burden by WHO region and combined**

Based on total population, crude birth weight, age distribution, case notification by age/sex

Sugarman, Lancet Global Health 2014

Background

- Pregnancy may increase risk
  - Postpartum risk ~2x higher than non-pregnant
  - Physiologic, immunologic, and hormonal changes
  - TB symptoms may be masked → delayed diagnosis

- Risk of adverse neonatal outcomes associated with maternal TB
  - Small for gestational age, low birth weight, prematurity

- Limited data using population based estimates of adverse infant outcomes in low TB prevalence settings

Zenner, AJRCCM 2012
Singh, CID 2007
Carter, Chest 1994
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Cross sectional population-based study in Taiwan:

- **SGA OR 1.22**
- **LBW OR 1.35**
- **Prematurity OR 0.97**

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Methods

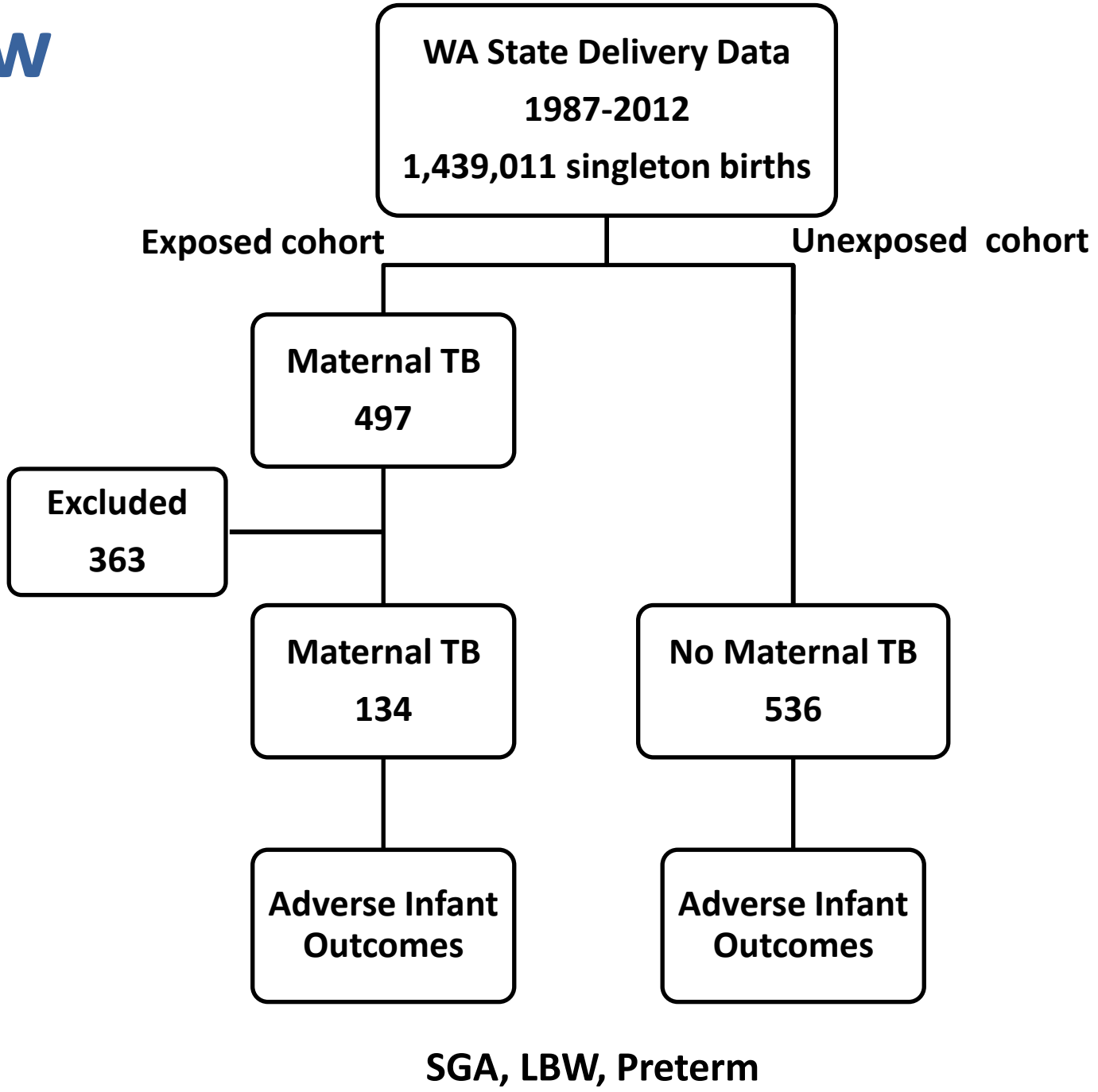
- Study Design: Retrospective maternal-infant birth cohort
- Study Population: Women with singleton births in WA state 1987-2012 and their infants
  - Maternal hospital data linked to infant birth certificate data
  - Birth Events Records Database (BERD)
- Exposure: Maternal TB as identified by TB-associated ICD-9 codes at delivery hospitalization
  - Frequency matched 1:4 to randomly selected women without TB

Methods

- Outcome: Risk of infant SGA, LBW, prematurity associated with maternal TB

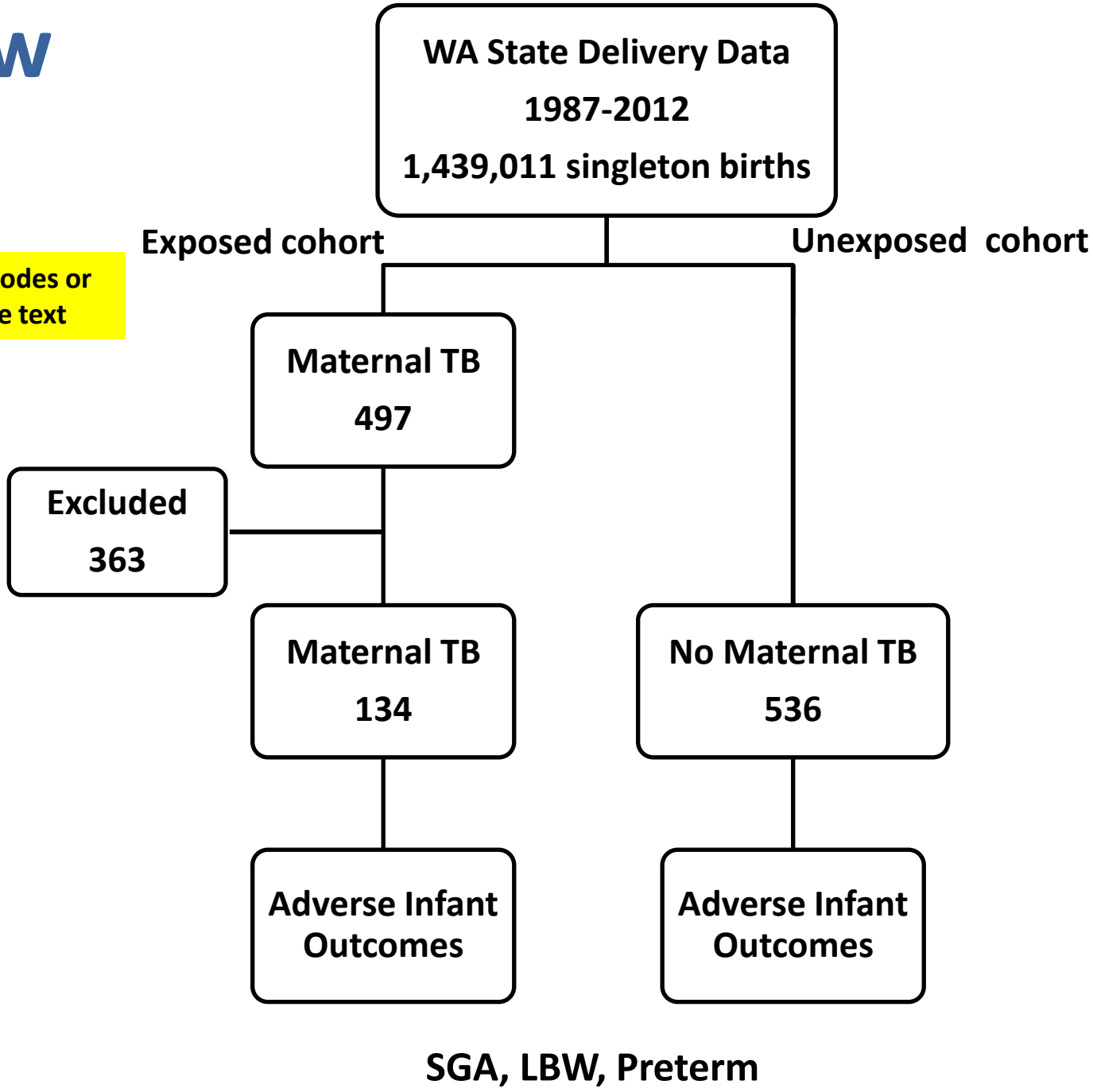
- Analysis:
  - Descriptive statistics
  - Estimated Relative Risks with multinomial logistic regression
  - Model adjusted for maternal age, income, parity

Study Flow


WA State Delivery Data
1987-2012
1,439,011 singleton births
Exposed cohort
Unexposed cohort
Maternal TB
497
Excluded
363
Maternal TB
134
No Maternal TB
536
Adverse Infant Outcomes
Adverse Infant Outcomes
SGA, LBW, Preterm

Study Flow

Any maternal TB ICD-9 codes or TB in birth certificate free text



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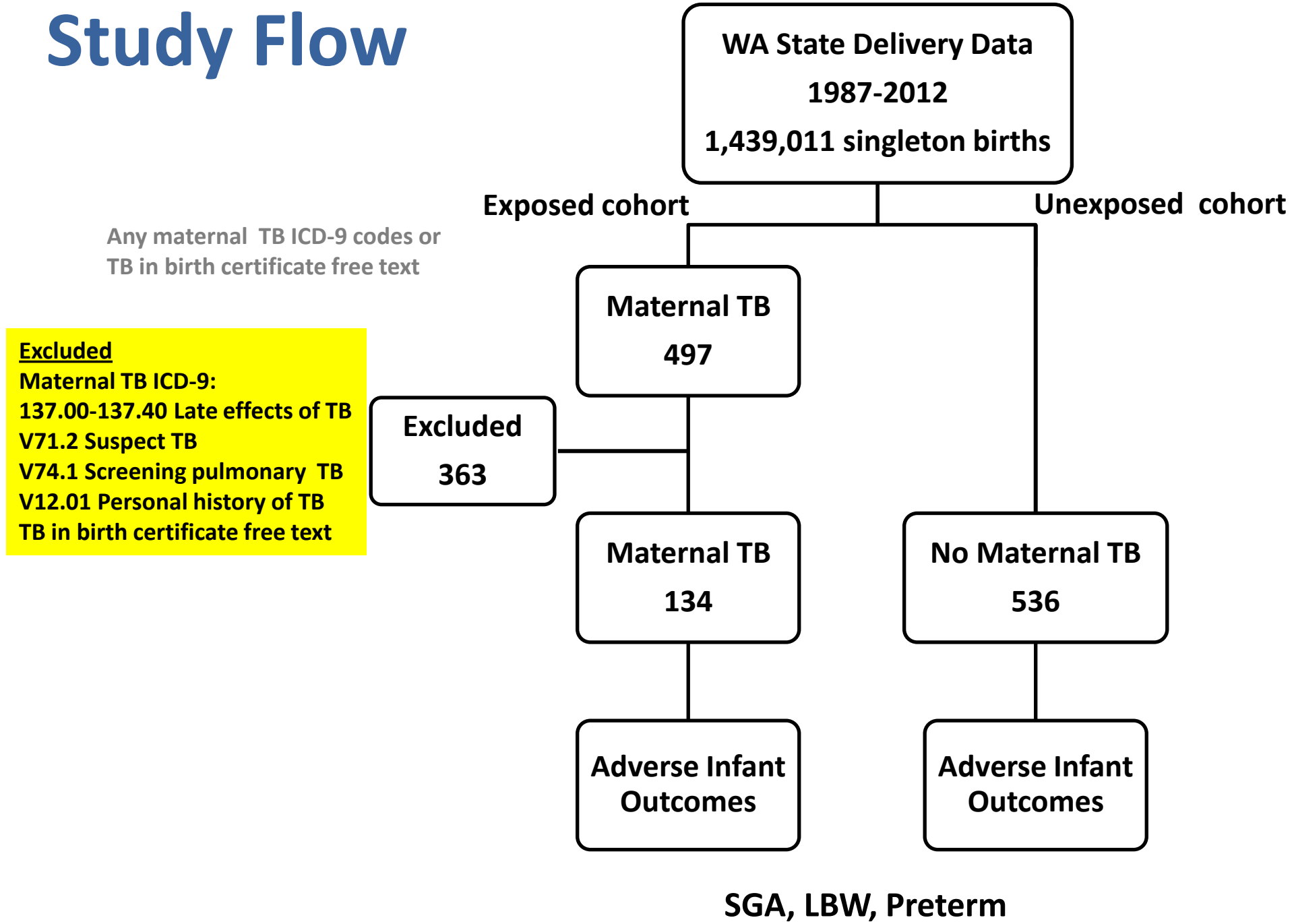
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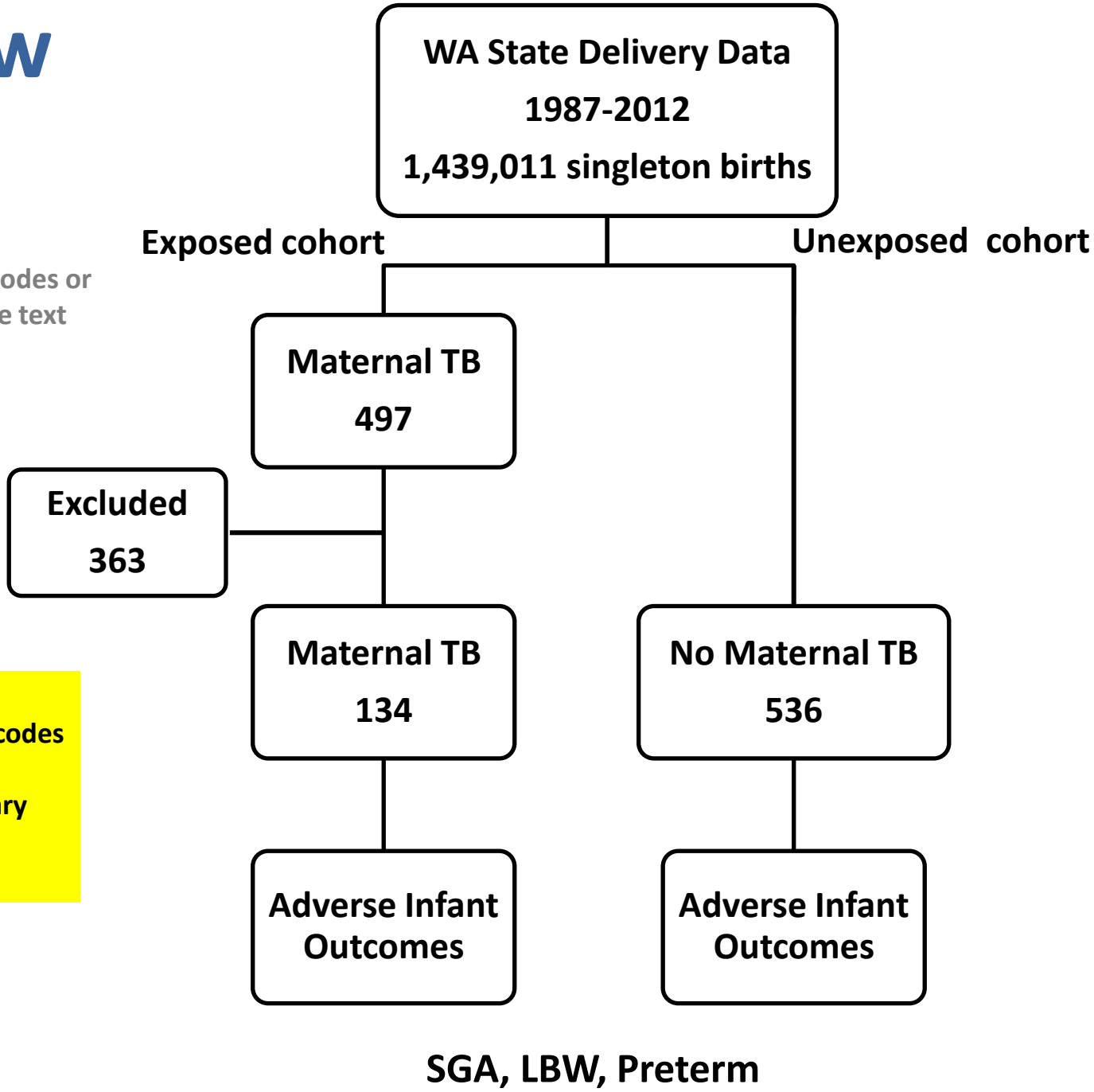
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13.00-17.99 Extra-pulmonary
18.00-18.99 Disseminated
647.30-647.34 TB in pregnancy
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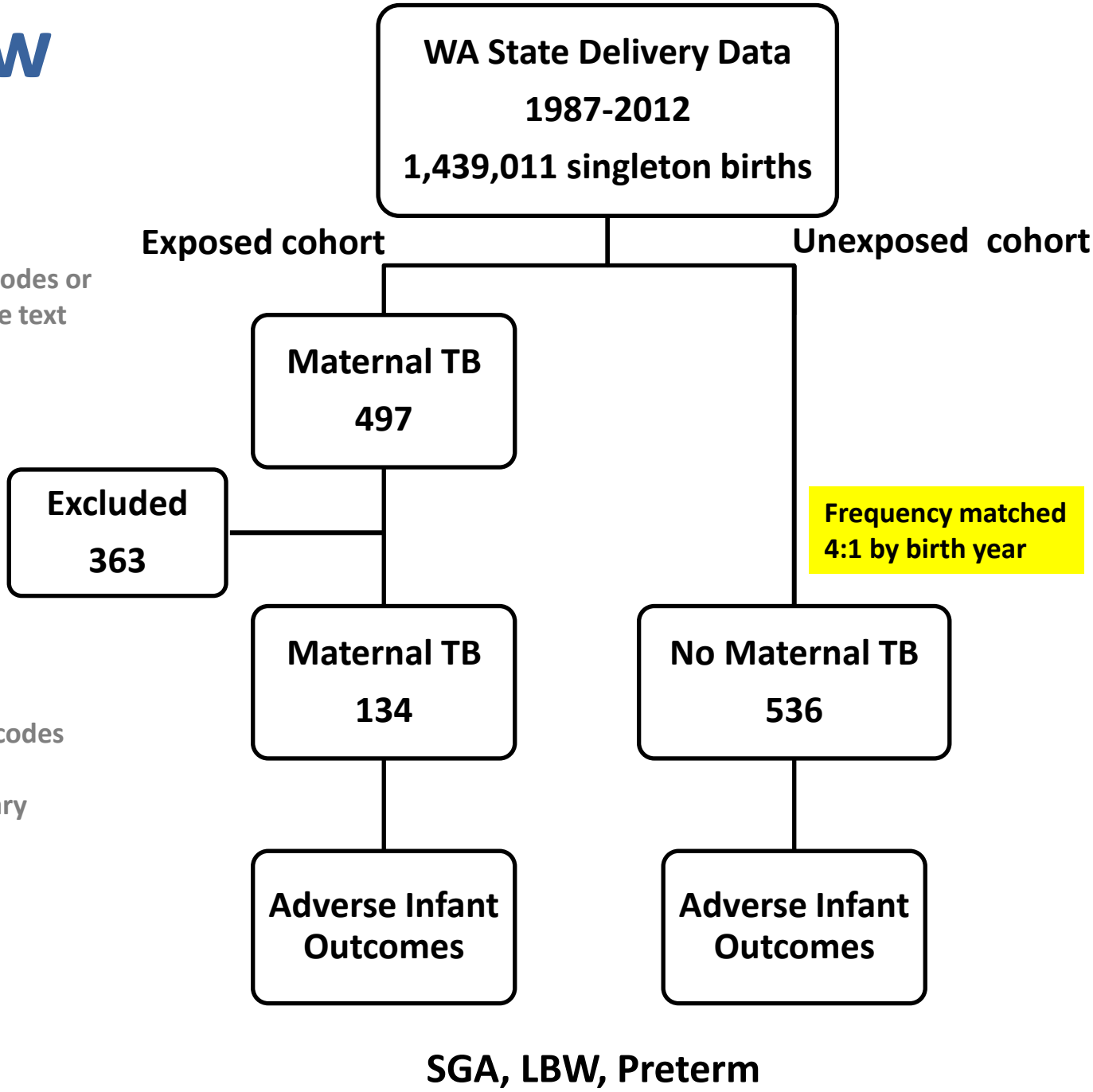
Study Flow



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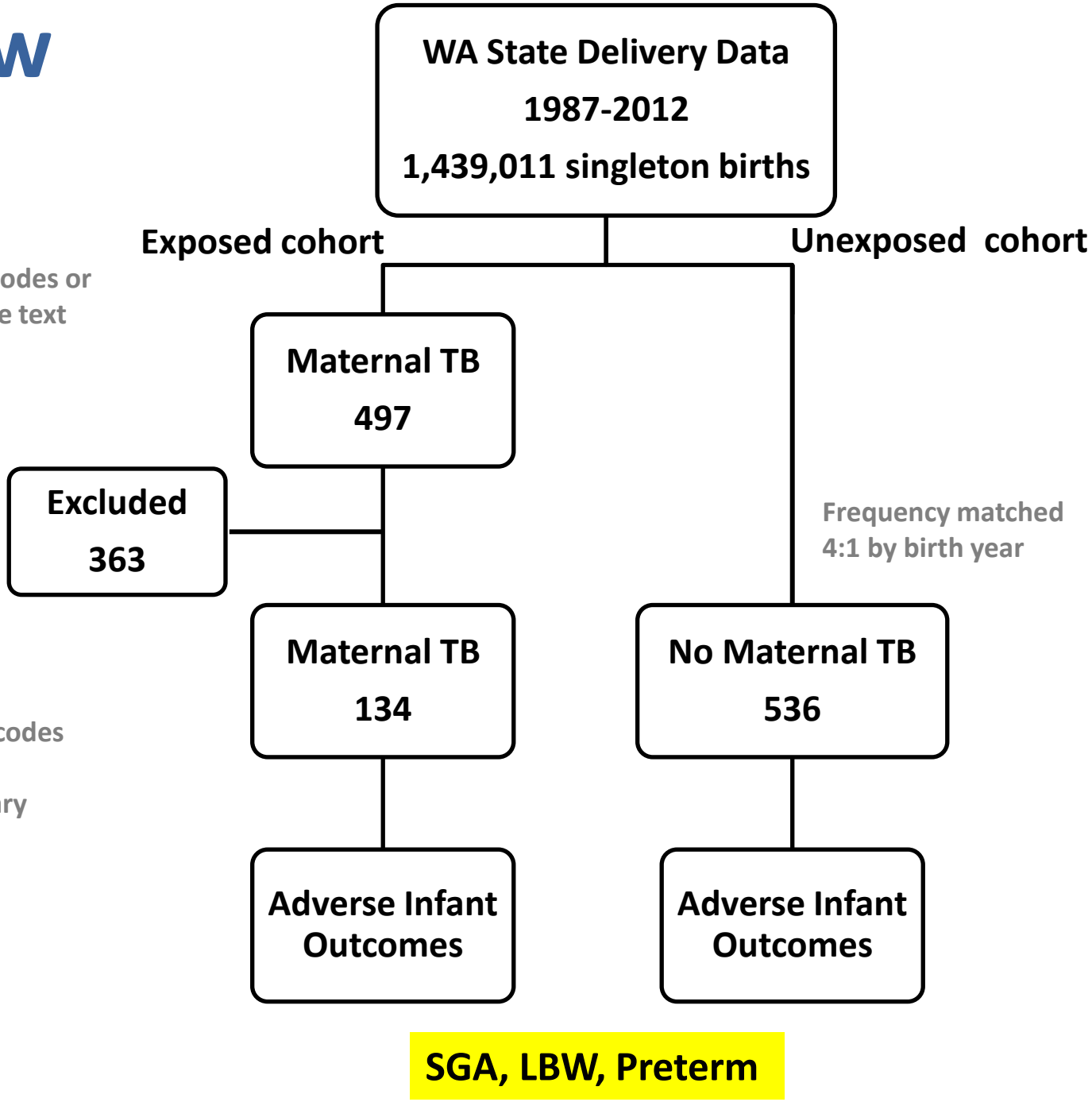

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Results

Maternal characteristic	Maternal TB N=134		No Maternal TB N=536	
	N(%), or median (IQR)		N(%), or median (IQR)	
Age (years)	26	(22-31)	27	(23-32)
Race				
White	27	20.5	415	79.4
Black	14	10.6	13	2.5
Asian	33	25.0	28	5.4
Hispanic	52	39.4	47	9.0
Native American	6	4.6	20	3.8
High school graduate	35	40.7	291	82.9
Income* (in thousands)	34	26-40	37	31-48
Foreign born	56	41.8	55	10.3
Single marital status				
Parity				
0				
1				
≥2				

Pregnant women with TB more likely to be:

- **Non-white, foreign born**
- **Lower education, income**
- **Single, multiple previous pregnancies**

Results

Infant outcome	Maternal TB N=134		No Maternal TB N=536		Unadjusted Relative Risk		Adjusted** Relative Risk	
	N(%)		N(%)		uRR	95% CI	aRR	95% CI
Weight for gestational age								
SGA (<10%)	21	15.8	47	8.9	**1.95**	1.11-3.41	**1.87**	1.03-3.44
Typical (10-90%)	100	75.2	436	82.4	1.00	Referent	1.00	Referent
LGA (>90%)	12	9.0	46	8.7	1.13	0.58-2.23	1.01	0.46-2.21
Birth weight (grams)								
LBW (<2,500)	15	11.9	24	4.5	**2.63**	1.34-5.20	**2.41**	1.13-5.08
Typical (2500-3,999)	105	78.4	443	82.7	1.00	Referent	1.00	Referent
Macrosomia (≥4,000)	14	11.5	69	12.9	0.86	0.46-1.58	0.81	0.40-1.62
Gestational age (weeks)								
<37 (premature)	13	9.8	32	6.1	1.74	0.89-3.43	1.43	0.66-3.10
37-41	112	84.9	481	90				
≥42 (post term)	7	5.3	16	3.(				

*Numbers may not add up to totals because of missing d

** Adjusted for maternal age, parity, and income

Maternal TB associated with:

- **Small for gestational age**
- **Low birth weight**

Conclusions

- Maternal TB associated with small for gestational age and low birth weight in a low burden setting
  - Similar risk estimates of LBW, SGA, and prematurity to high TB burden, middle income setting (Taiwan)

- Better understanding of mothers at risk for TB and the adverse infant outcomes associated with maternal TB may inform potential targeted interventions in other low prevalence settings

- Reinforces the importance of close clinical follow-up of pregnant women with TB and their infants

Acknowledgements

- Bill O'Brien, Department of Epidemiology, University of Washington, for programming assistance

- Washington State Department of Health, for data access

Questions/Comments?

Additional slides

Strengths/Limitations

- Strengths:
  - Data from a large population-based cohort
  - Linked maternal-infant data

- Limitations:
  - HIV diagnoses unknown
  - Details of maternal TB diagnosis and treatment status unknown

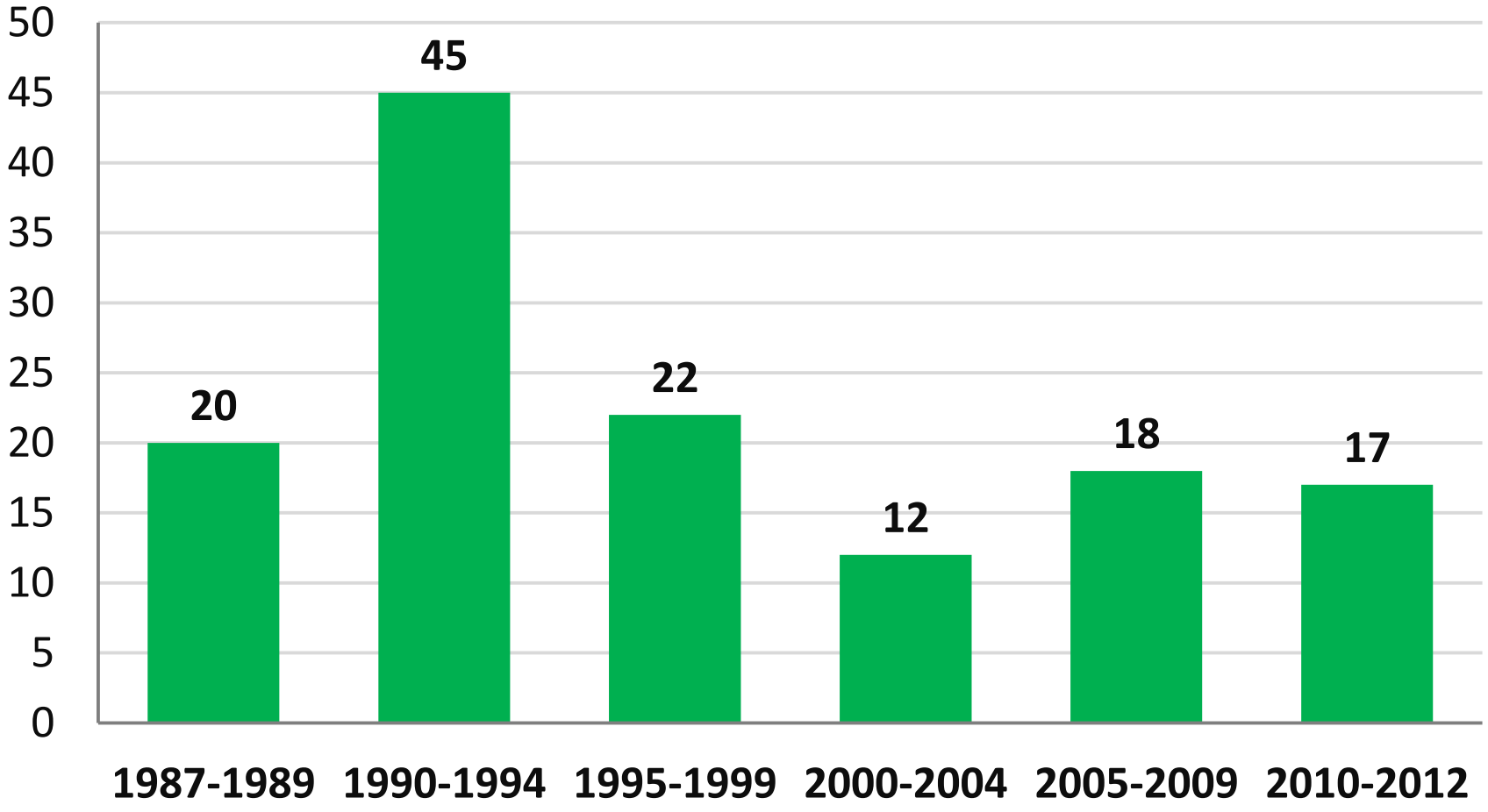
Methods

TB ICD-9 codes used to identify the maternal TB cohort delivering in Washington State, 1987-2012

ICD 9 code	Description	Maternal TB N=134	
		n	%
10.00-18.99	Anatomic TB ICD-9 codes		
11.90-11.92	Pulmonary	17	12.7
13.00-17.99	Extra-pulmonary	6	4.5
18.00-18.99	Disseminated	1	0.8
647.30-647.34	TB in pregnancy	110	82.1

Results

Frequency of maternal TB cases at delivery Washington state, 1987-2012



Distribution of maternal birthplace

Maternal TB

No Maternal TB