Maternal immunosuppression and adverse birth outcomes in a linked cohort of women living with HIV delivering in the UK

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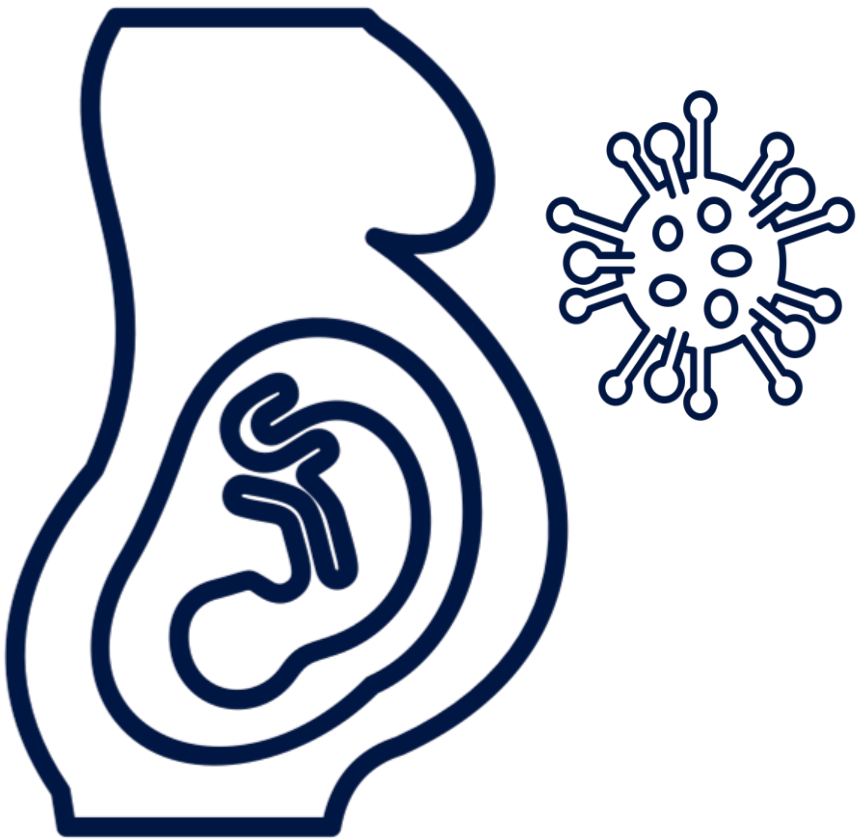
Background



- Untreated HIV infection in pregnancy is rare in the UK
- Minority of women will have a recent history of immunosuppression at the time of pregnancy
- Women with untreated HIV infection in pregnancy may be at risk of adverse perinatal outcomes
- This risk may be greater for women with advanced HIV disease

Wedi et al, Lancet HIV, 2016

Aims

1) To describe and compare adverse birth outcomes (ABO) in pregnancies where women had evidence of immunosuppression in the 12 months before and/or during pregnancy with pregnancies in women with no evidence of immunosuppression.
2) To evaluate relative risk for adverse birth outcomes associated with maternal immunosuppression, after adjusting for covariates
3) To estimate population-level impact of maternal immunosuppression on adverse birth outcomes

Data Sources

DATA LINKAGE

- **Population-level surveillance** of all pregnancies to women with diagnosed HIV
- Data reported by NHS antenatal care providers

- **Observational study** of people with diagnosed HIV
- Data from 25 participating sexual health centres
- Data abstracted from patient record system

Methods – adverse birth outcomes

- Stillbirth (SB): intrauterine death at ≥ 24 gestational weeks
- Preterm birth (PTB): <37 gestational weeks
- Low birthweight (LBW): <2500g
- Small for gestational age (SGA): birthweight <10th percentile based on gender-specific UK-WHO growth standards

Methods – study population

Immunosuppression markers defined as women with:

Year prior to pregnancy

- ≥1 report of an AIDS defining illness

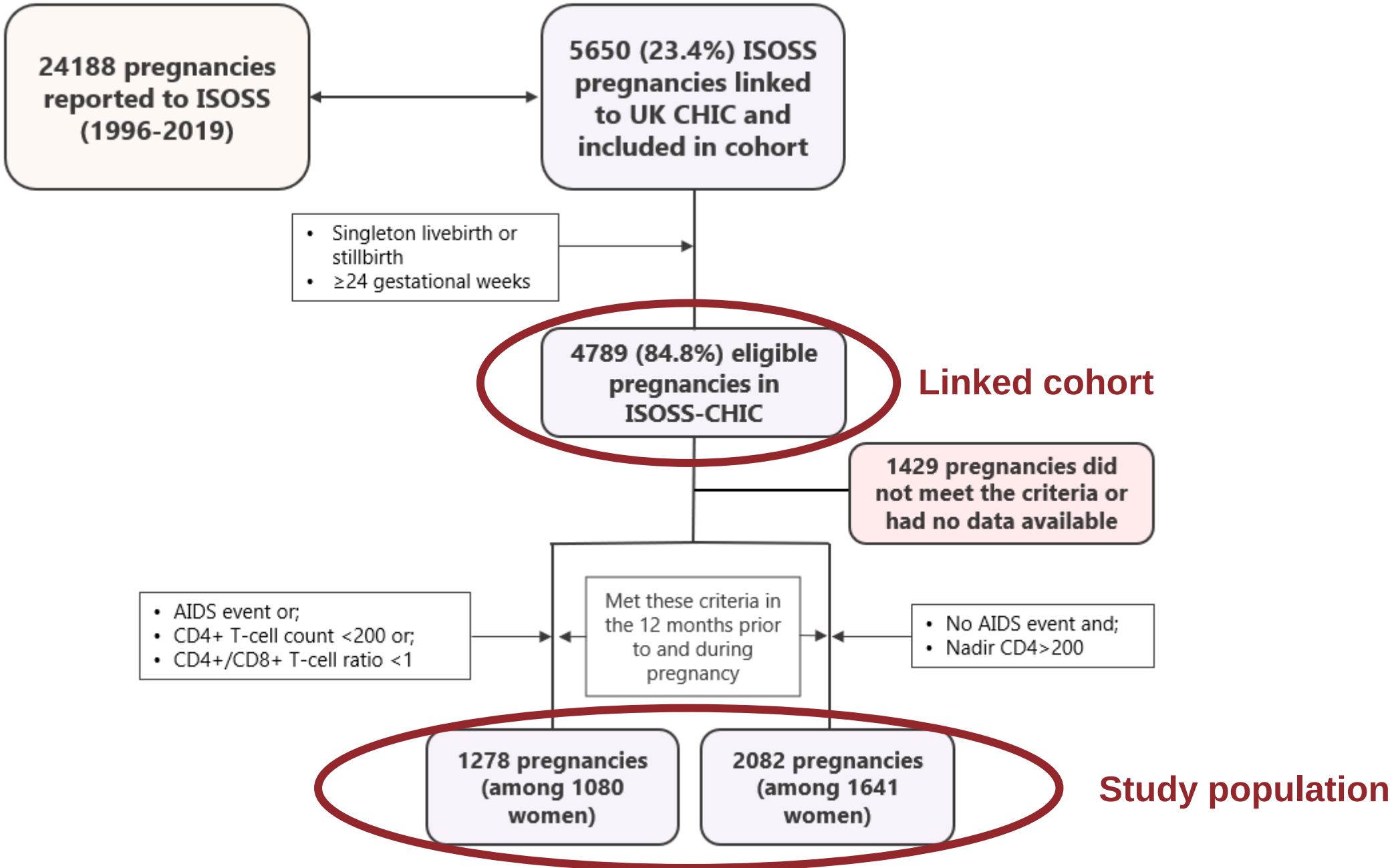
During pregnancy

- ≥1 CD4 cell count <200 cells/mm^3
- ≥1 report of an AIDS defining illness
- CD4+/CD8+ T-cell count ratio <1

Control group

- Pregnancies to women with no history of an AIDS-defining illness and with a nadir CD4 count >200 cells/mm^3

Selecting the study population



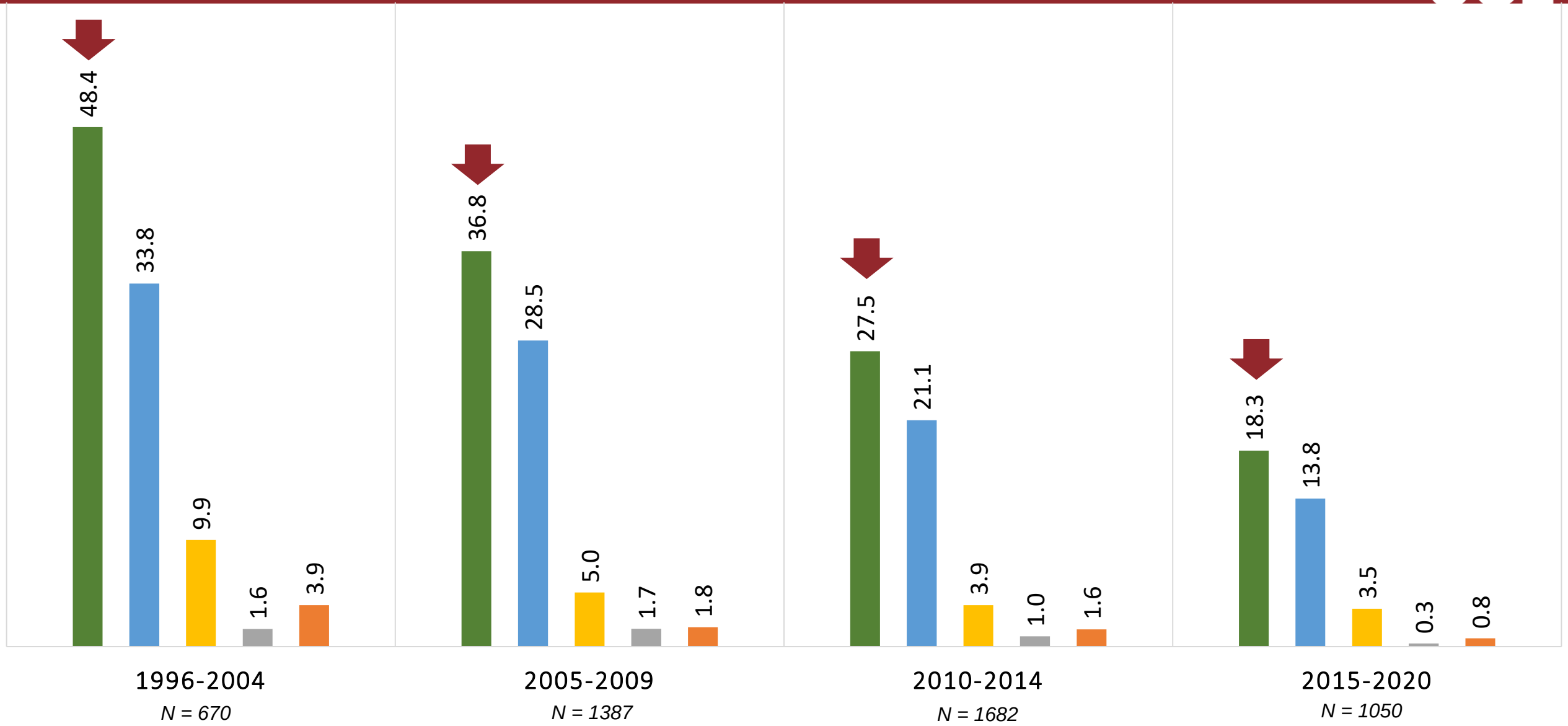
Methods - statistical analysis

- Characteristics of pregnancies in the study population were described using likelihood-ratio tests
- Multivariable logistic regression models were selected using Lasso regression and estimated adjusted odds ratios for each adverse birth outcome
- Population-level impact was estimated using the population attributable fraction (PAF):

$$\mathbf{PAF = pc\ (RRadj-1)/RRadj}$$

pc *is the prevalence of the exposure among cases and* ***RRadj*** *is the adjusted odds ratio*

Prevalence of maternal immunosuppression markers over time



Characteristics of pregnancies to women in the study population

	Immunosuppression markers (*n*=1278) (%)	**Control group** (*n*=2082) (%)	***P*-value**
Estimated year of delivery			
<2015	1110 (86.8)	1527 (73.3)	<0.001
2015-2019	168 (13.2)	555 (26.7)	
Parity since diagnosis			
1	305 (23.9)	458 (22.0)	0.003
2	462 (36.2)	704 (33.8)	
3+	511 (40.1)	854 (44.1)	
ART			
PI-based regimens	764 (61.0)	1059 (51.3)	<0.001

Overview of adverse birth outcomes

Adverse birth outcome	Prevalence	%
Stillbirth	36 / 3360	1.07
Adverse birth outcome (excl. SB)	959 / 3360	28.5
Preterm birth	434 / 3324*	13.1
Low birthweight	437 / 3324*	13.1
Small for gestational age	519 / 3319*†	15.6

*livebirths only
†5 livebirths with gestational age but missing birthweight

406/1278 (31.8%) of pregnancies affected by immunosuppression had ≥1 adverse birth outcomes (excl.SB)

553/2082 (26.6%) of pregnancies in the control group had ≥1 adverse birth outcomes (excl. SB)

Effect estimates for maternal immunosuppression on adverse birth outcomes

	Pregnancies to women with immunosuppression (N=1278) (%)		*Pregnancies to women in control group (N=2082) (%)*		*OR*	*(95% CI)*	*aOR*	*(95% CI) *†*
Stillbirth	18	(50.0)	18	(50.0)	1.64	(0.85-3.16)	1.62	(0.72-3.98)
Livebirth	1260	(37.9)	2064	(62.1)				
Composite outcome (excl. stillbirth)								
No adverse birth outcome	878	(36.3)	1529	(63.7)	1		1	
Adverse birth outcome	406	(42.3)	553	(57.7)	**1.29**	**(1.11-1.50)**	**1.35**	**(1.13-1.60)**
Preterm birth								
No	1069	(36.5)	1857	(63.5)	1		1	
Yes	209	(48.2)	225	(51.8)	**1.61**	**(1.32-1.98)**	**1.48**	**(1.17-1.88)**
Small for gestational age								
No	1062	(37.9)	1738	(62.1)	1		1	
Yes	195	(37.6)	324	(62.4)	0.98	(0.82-1.20)	1.18	(0.94-1.47)
Low birthweight								
No	1078	(36.9)	1845	(63.1)	1		1	
Yes	200	(45.8)	237	(54.2)	**1.44**	**(1.18-1.77)**	**1.44**	**(1.12-1.83)**

*Adjusted for estimated year of delivery, PI use in pregnancy, parity since diagnosis and hypertensive disorders

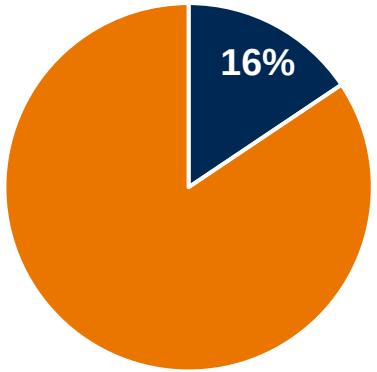
† Validated using non-percentile-based bootstrap with 1000 repetitions

Population-level impact of maternal immunosuppression on adverse birth outcomes estimated by population attributable fractions

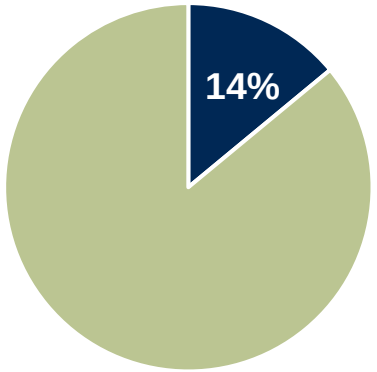
Study population (N=3360)

- 16% of 434 PTB outcomes were attributable to maternal immunosuppression

Preterm birth



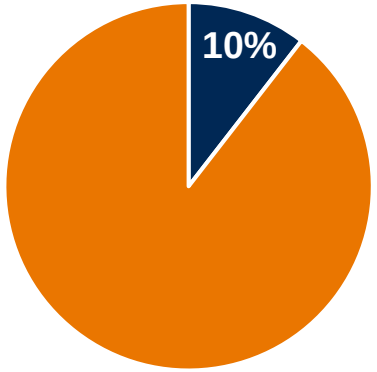
Low birthweight

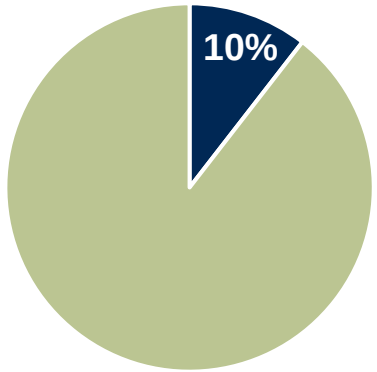


- 14% of 437 LBW outcomes were attributable immunosuppression

Linked cohort (N=4789)

- 10% of 630 PTB outcomes were attributable to maternal immunosuppression





- 10% of 607 PTB outcomes were attributable to maternal immunosuppression

Conclusions & limitations

- Overall 26.7% (1278/4789) of pregnancies in our linked cohort were in women who had evidence of immunosuppression markers in the 12 months prior to pregnancy and/or during pregnancy
- Maternal immunosuppression was associated with increased odds of PTB and LBW but not SGA or stillbirth
- 10% of PTB and LBW outcomes were attributable to maternal immunosuppression
- Limitations include unmeasured confounding and possible selection bias
- Maternal immunosuppression markers as estimated in our study, could also be a marker for women who are at greater risk of adverse birth outcomes based on other risk factors

Acknowledgements

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- For any queries, please get in touch: l.bukasa@ucl.ac.uk

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