

Divergent Roles of Peripheral Leukocytes Before Preparing for Pregnancy and Before Conception in Spontaneous Abortion: A Population-based Retrospective Cohort Study

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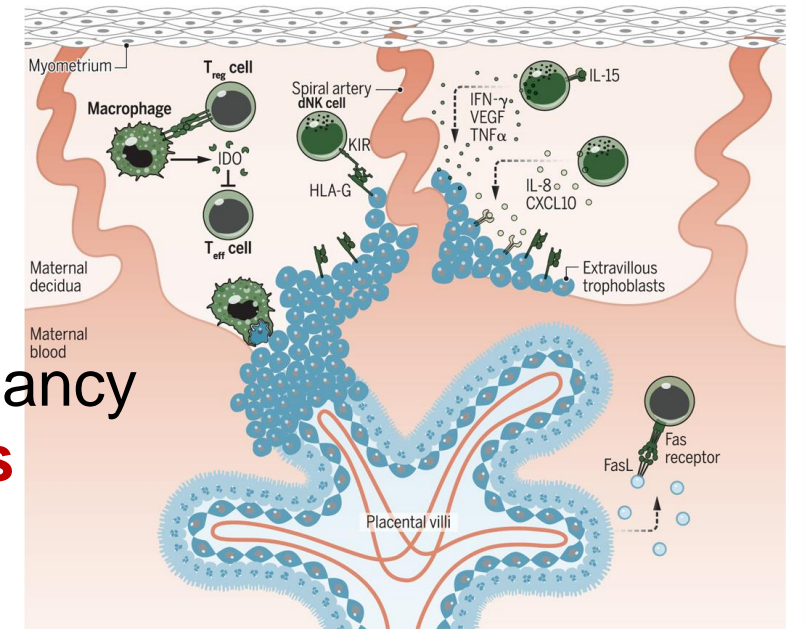
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BACKGROUND

- **Spontaneous abortion (SAB)**
 - The most common complication of early pregnancy
 - Pathogenesis: fetal factors + **maternal factors** + paternal factors
- **Immunity**
 - One of the most booming fields in reproduction
 - Leukocytes at the maternal-fetal interface
 - Maintaining placental development and function
 - Fighting against infection
 - Minimizing the risk of fetal attack by maternal immune system
 - **No lab-based evidence of peripheral leukocytes (PLs)**



Source: Stephanie E. Ander *et al.* *Sci. Immunol.* 2019.

BACKGROUND

• Problem Formation

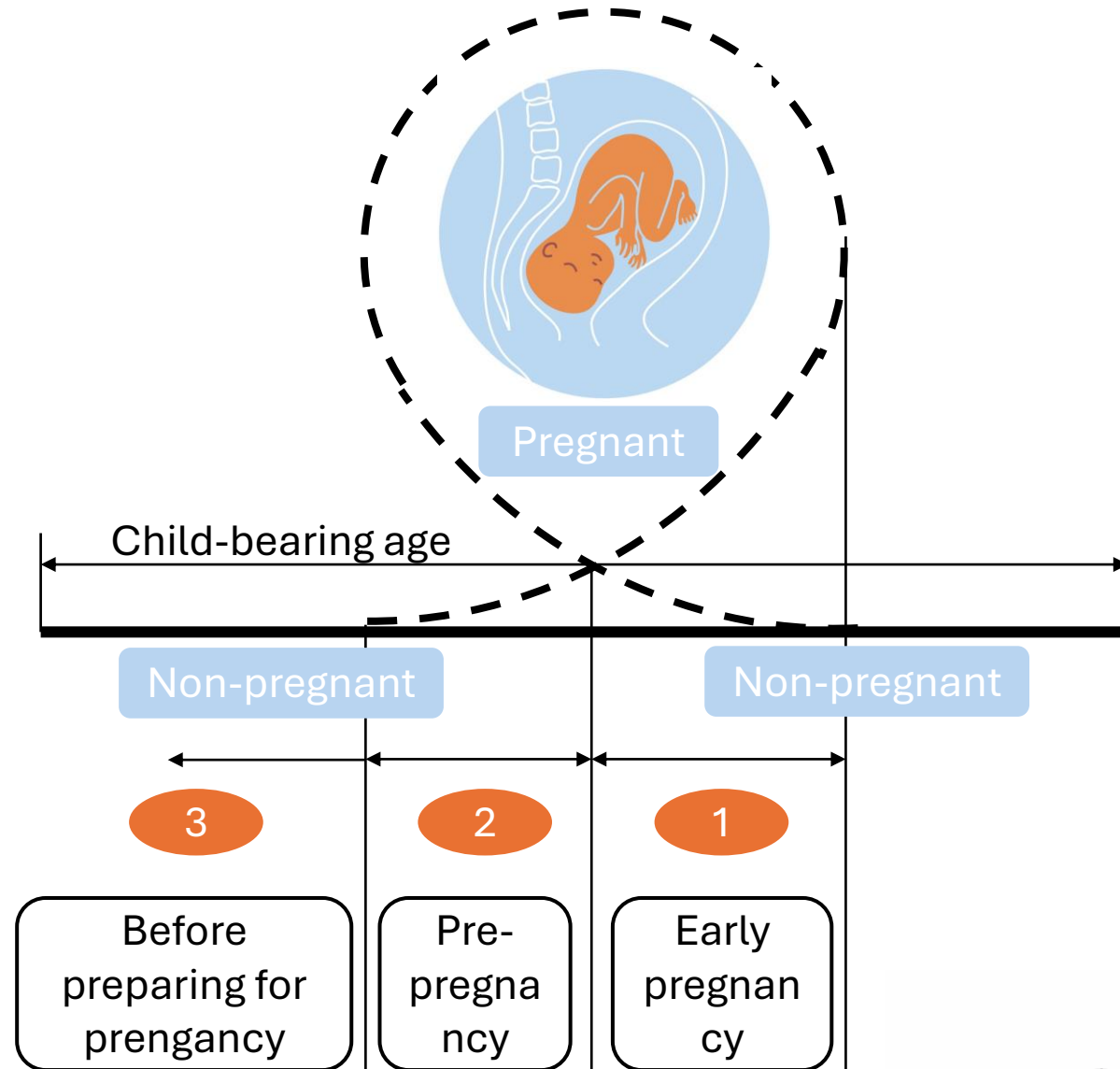
- **Low pre-pregnancy PLs** were associated with increased risk of SAB
 - Increased risk of periconceptional infection
 - Inadequate recruitment at the maternal-fetal interface during and after embryo implantation.
 - Others mechanism?
 - Shared immunogenetic basis between mother and fetus?
 - Innate and adaptive immunity memory?

Source: Domínguez-Andrés J, et al. Physiological reviews. 2023.

BACKGROUND

• Problem Formation

- Is PLs before preparing for pregnancy associated with the risk of SAB?
- Before preparing for pregnancy \neq Before conception
- **Immunological preparation for maternal and fetal functioning after conception**



METHODS

- **Study design:** retrospective cohort study
- **Data sources and collection**
 - National Free Pre-pregnancy Checkups Project
 - Preconception health examination
 - Early-pregnancy follow-up
 - Outcome follow-up
 - **238 716 women** who had participated the project **twice**

METHODS

- **Exposure and Outcome**

- **Exposure**

- **PLs before preparing for pregnancy:** PLs determined at the pre-pregnancy health examination of the first participation
 - **Pre-pregnancy PLs:** PLs determined at the second participation

- **Outcome**

- **SAB at the second participation:** fetal death occurring before the 28th week of gestation

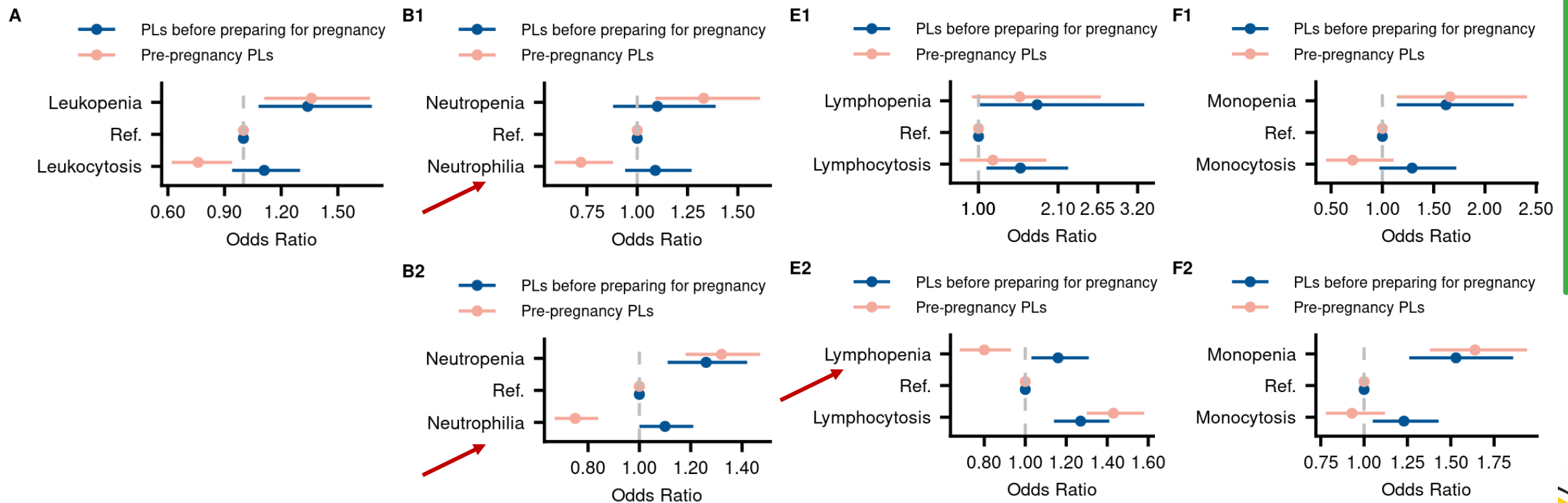
METHODS

- **Statistical methods**

- Odds ratio (OR) with 95% confidence interval (CI)
 - Logistic regression
 - Adjusted for the imbalance caused by baseline characteristics via **inverse probability weighting (IPW)**
- Non-linear dose-response relationship
 - Restricted cubic splines
- Data analysis software: R

RESULTS

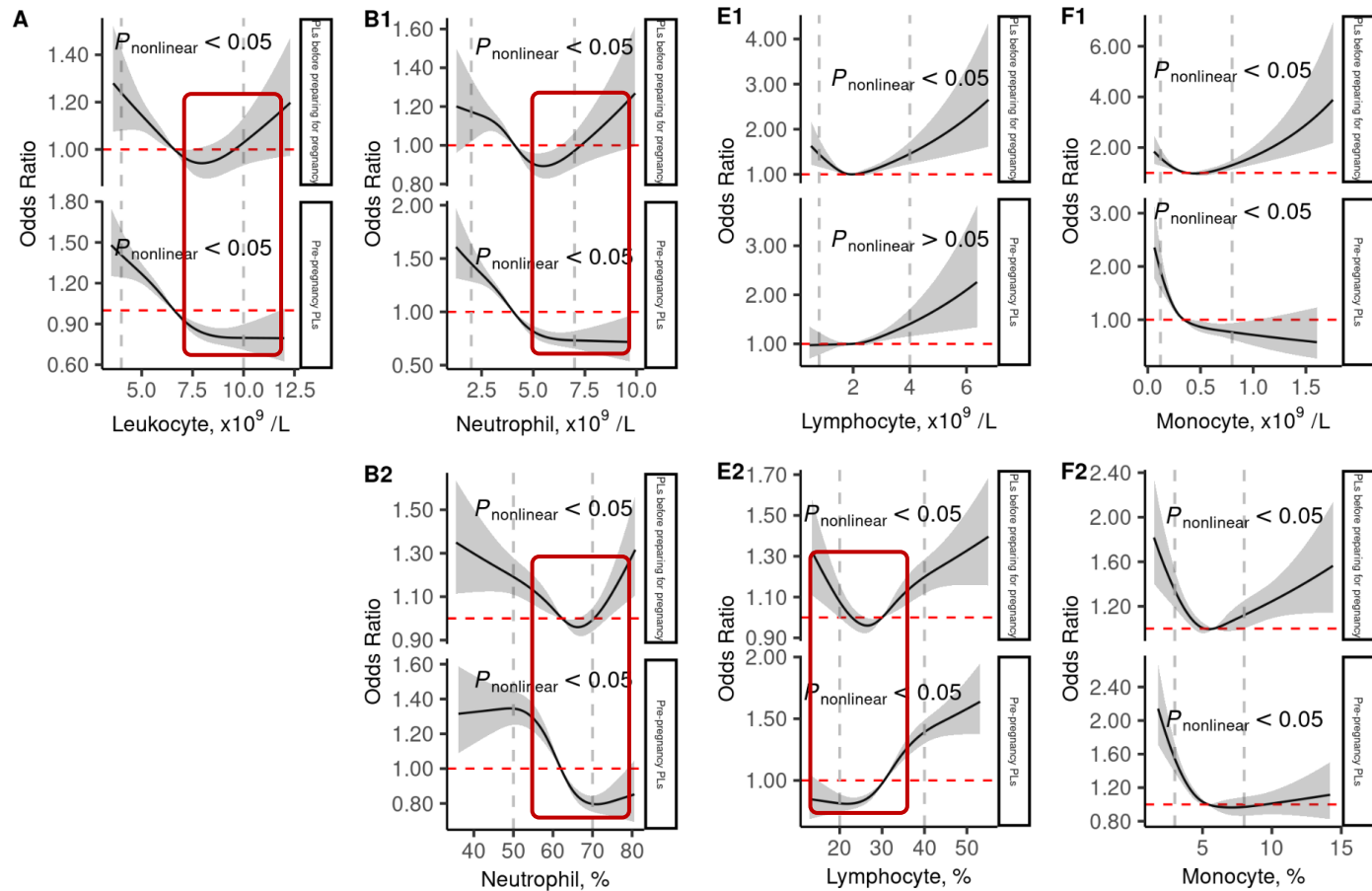
- **Figure 1.** Inverse-probability weighted ORs of PLs before preparing for pregnancy and before conception for the risk of SAB.



Legend: 1 = PLs in count; 2= PLs in ratio. A = leukocyte; B = neutrophil; E = lymphocyte; F = monocyte.

RESULTS

- **Figure 2.** Exposure-response relationship between PLs before preparing for pregnancy and before conception and the risk of SAB



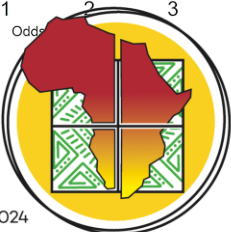
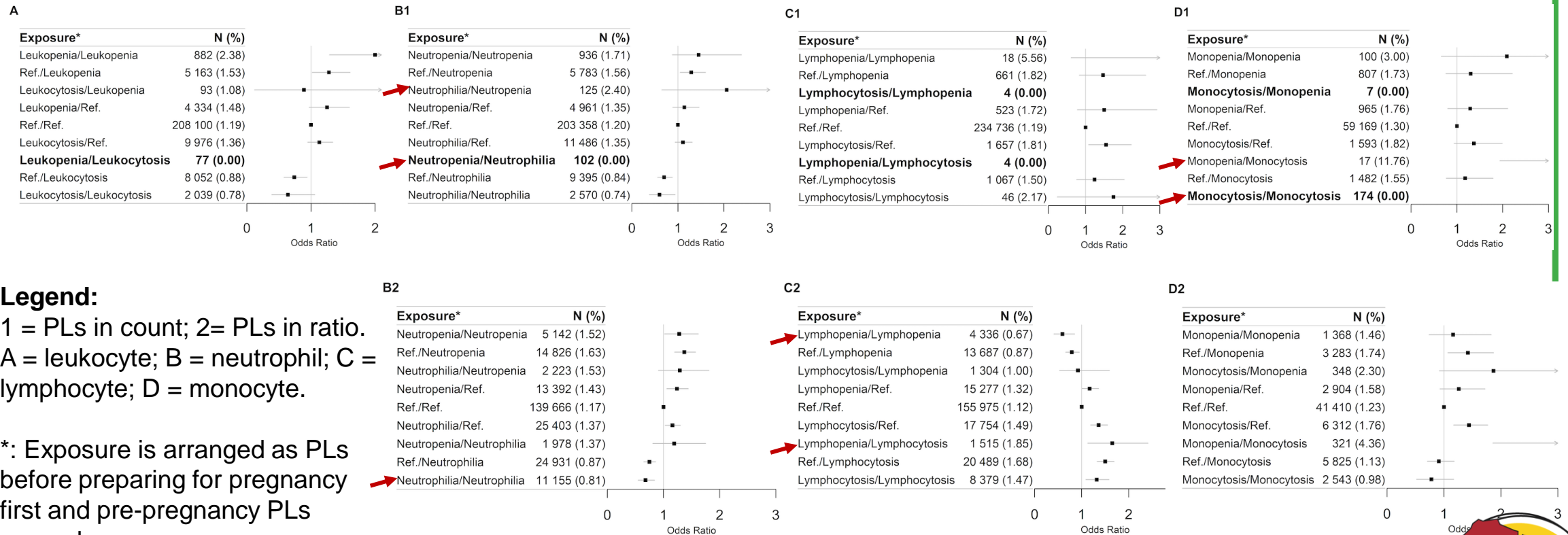
Legend:

1 = PLs in count; 2= PLs in ratio.
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RESULTS

- **Figure 3.** Inverse-probability weighted ORs for the risk of SAB according to PLs before preparing for pregnancy and pre-pregnancy PLs

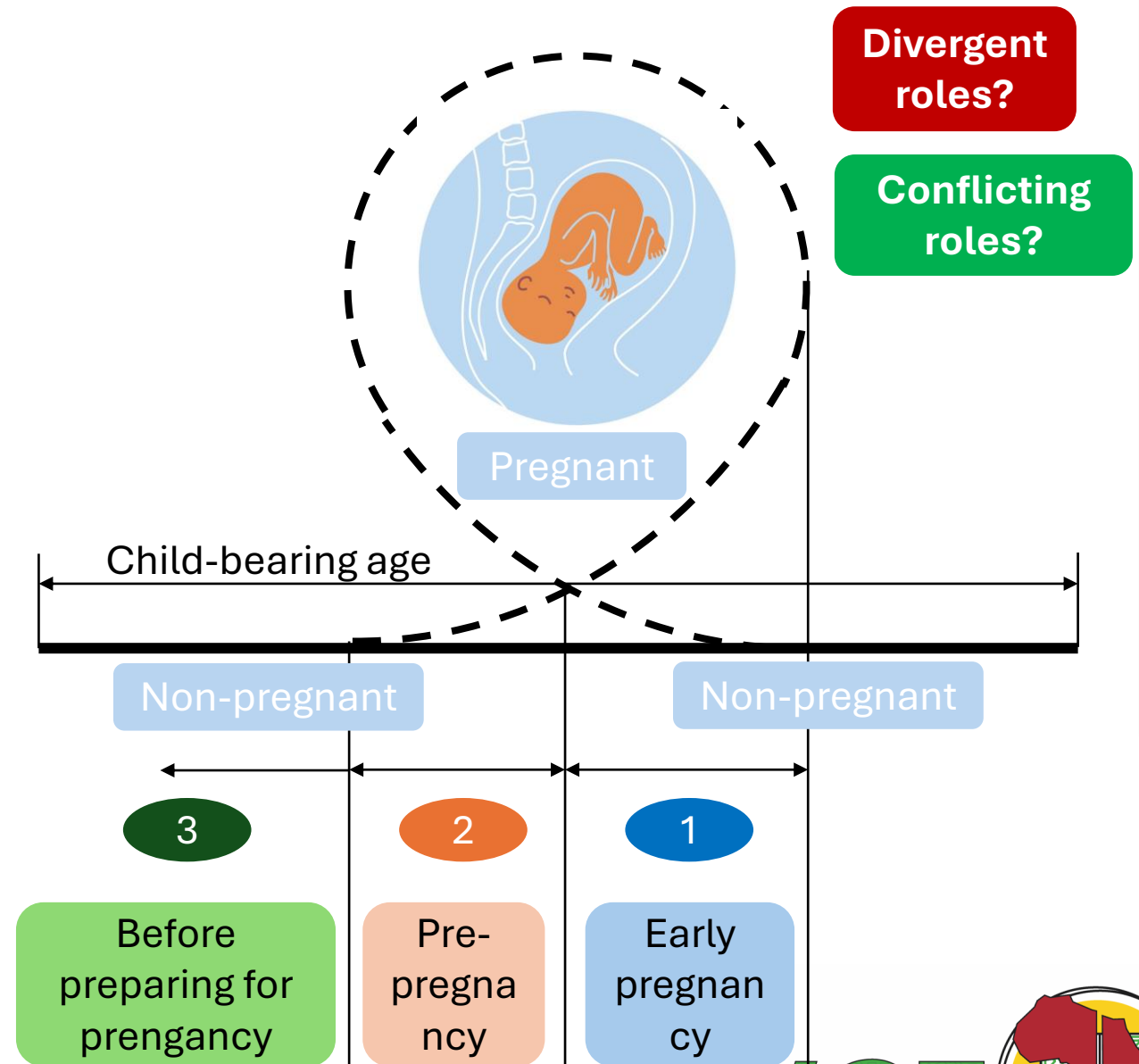


CONCLUSIONS

- Maintaining placental development and function
- Fighting against infection
- Minimizing the risk of fetal attack by maternal immune system

- Providing sufficient leukocytes needed by maternal-fetal interface to maintain placental development and function
- Fighting against periconceptional infection
- Ability to shift the Th1/Th2/Th17 and Treg paradigms

- Indicating exposure possibility to environmental pathogens
- Immunogenetic basis?
- Immunological memory?



CONCLUSIONS

1

- PLs before preparing for pregnancy and before conception have **divergent roles** in the development of SAB.

2

- More efforts is needed to **forward** the immune window of pregnancy from periconception to a period before preparing for pregnancy.



Thanks !

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