Benefit-Risk Conceptual Framework for In Utero Exposure to Immunosuppressive Medications

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Johnson&Johnson

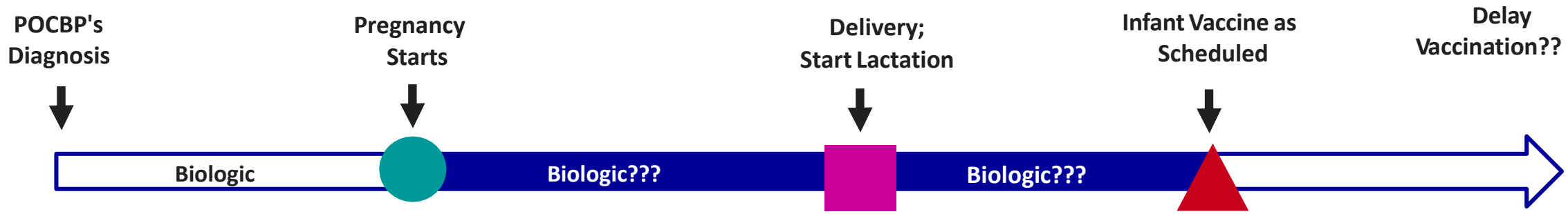
Disclosure

Laura M. Bozzi, MS, PhD, is an employee of Johnson & Johnson and holds stock in Johnson & Johnson. All views expressed are her own.

Background

- Biologic exposure → potential childhood live vaccine delay (infant at risk), but not using a biologic puts the pregnant person at risk

- Little is known about whether biologics cross the placenta or are in the breastmilk



- **<u>Goal:</u>** Develop a conceptual framework for exposure to biologics in utero
  - Evidence-based approach to support pregnant person/infant safety and benefit-risk
  - Help inform future decision-making for biologics

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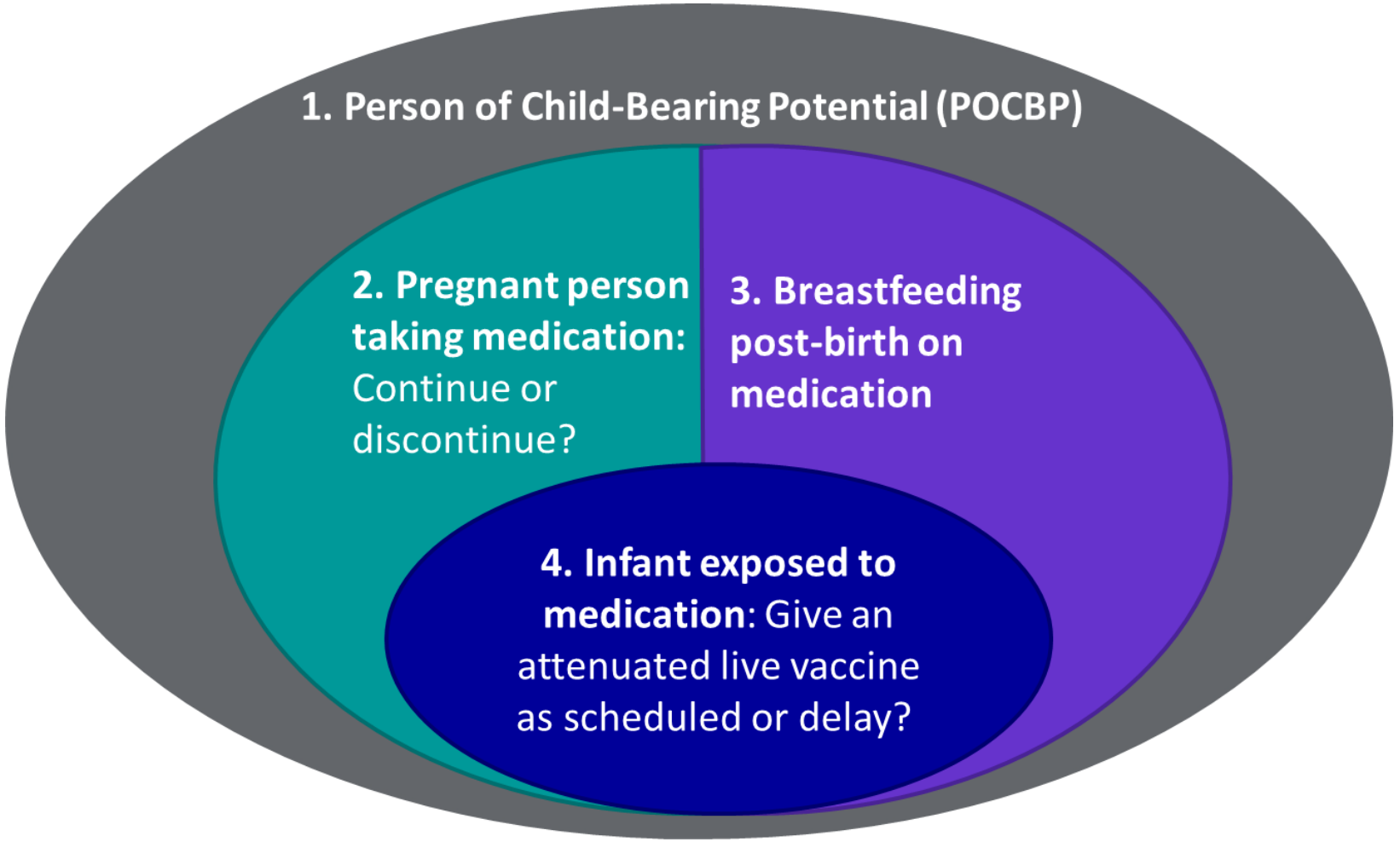
POCBP: Person of Child-Bearing Potential

Nested Conceptual Model for Benefit-Risk Assessment for Pregnant People and Infants Exposed to Immunosuppressive Medications



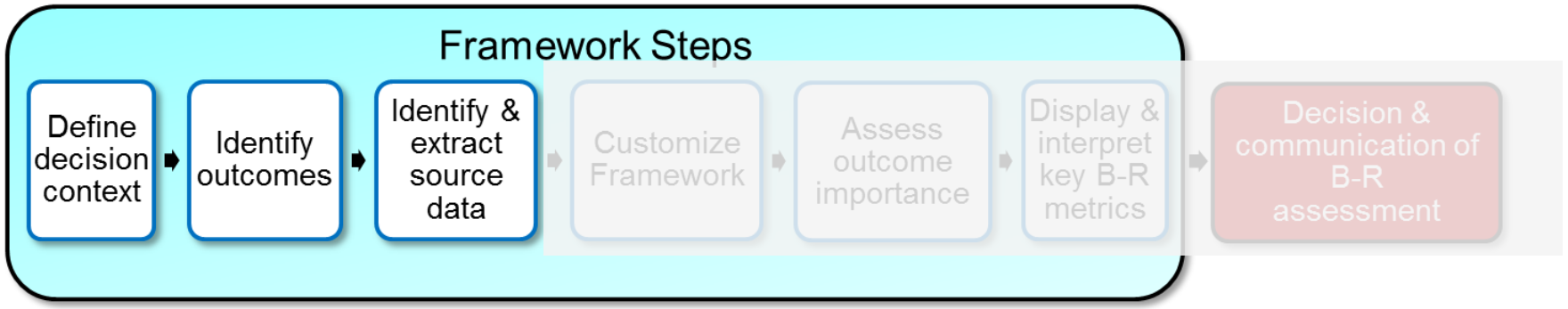
Today's discussion will focus on Scenario 4, within the context of Scenario 2

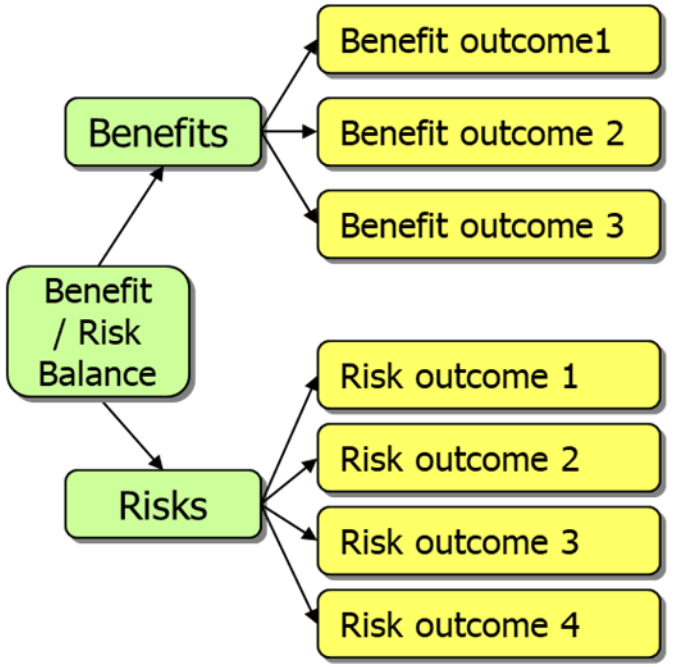
Adapted from Bozzi LM, Jacobson MH, Yost E, et al. A Benefit-Risk Conceptual Framework for Biologic Use During Pregnancy: A Mini-Review. *Clin Pharmacol Ther*. 2024;115(6):1251-1257. doi:10.1002/cpt.3239

Tackling this problem:

Using a Benefit-Risk (B-R) Framework

PhRMA BRAT Framework



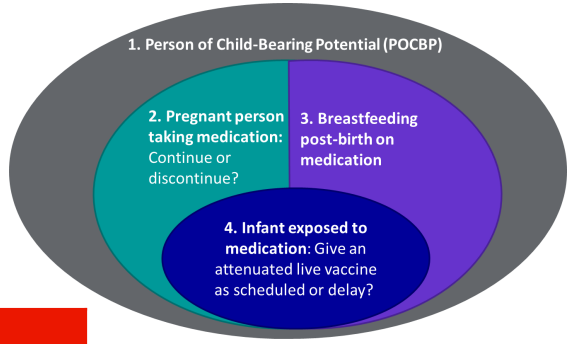


BRAT: Benefit-Risk Action Team

Coplan, P.M., et al., *Development of a framework for enhancing the transparency, reproducibility and communication of the benefit-risk balance of medicines.* Clin Pharmacol Ther, 2011. **89**(2): p. 312-5.; Levitan BS et al. Application of the BRAT framework to case studies: observations and insights. *Clin Pharmacol Ther*. 2011;89(2):217-224. doi:10.1038/clpt.2010.280

Scenario 2 Decision Context:

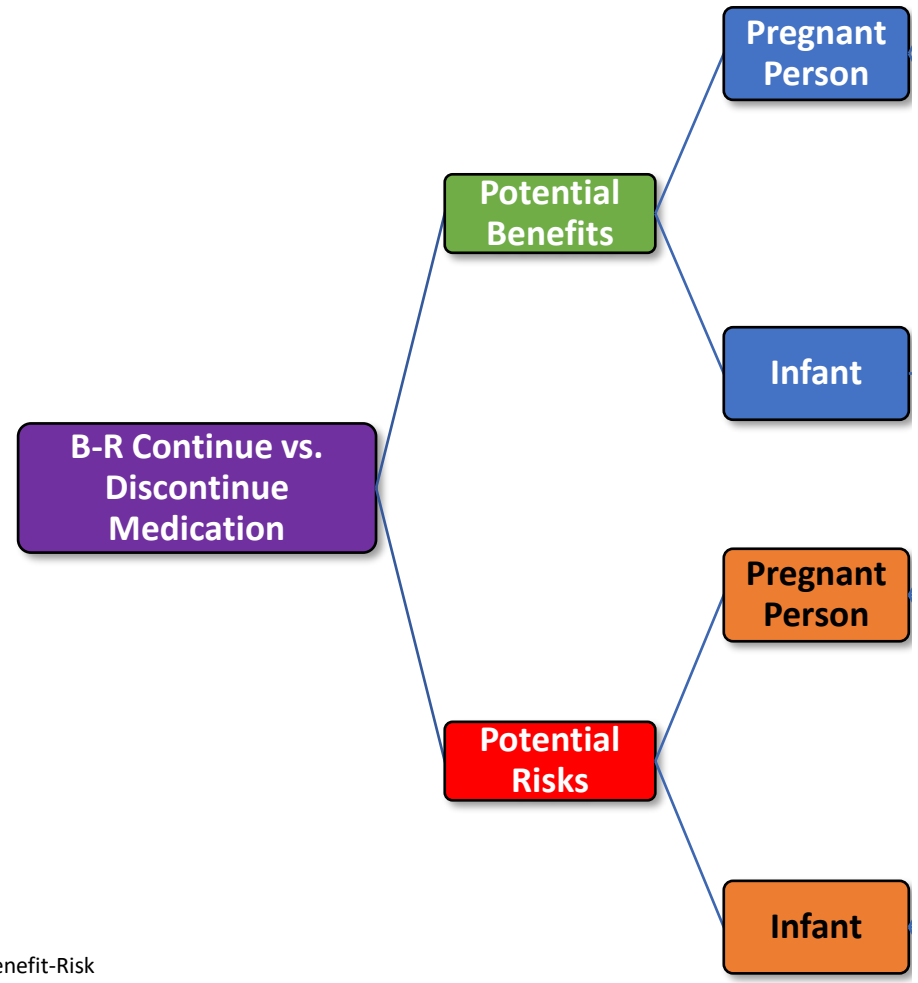
Use of medications while pregnant



Term	Definition
Treatment	Continuing biologic therapy during pregnancy
Comparator	Discontinuing biologic therapy
Population	Two participants: the pregnant person and infant
Indication	Any autoimmune condition that warrants use of biologics. The framework can be applied to an individual indication.
Time-frame	Conception to infant one year of age
Decision-maker	Pregnant person and their physician
Subgroups of interest	Includes disease severity, rate of transplacental passage, and medical/obstetrical history

Value Tree

Continue vs. discontinue immunosuppressive medications while pregnant



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B-R: Benefit-Risk

Scenario 2 Value Tree

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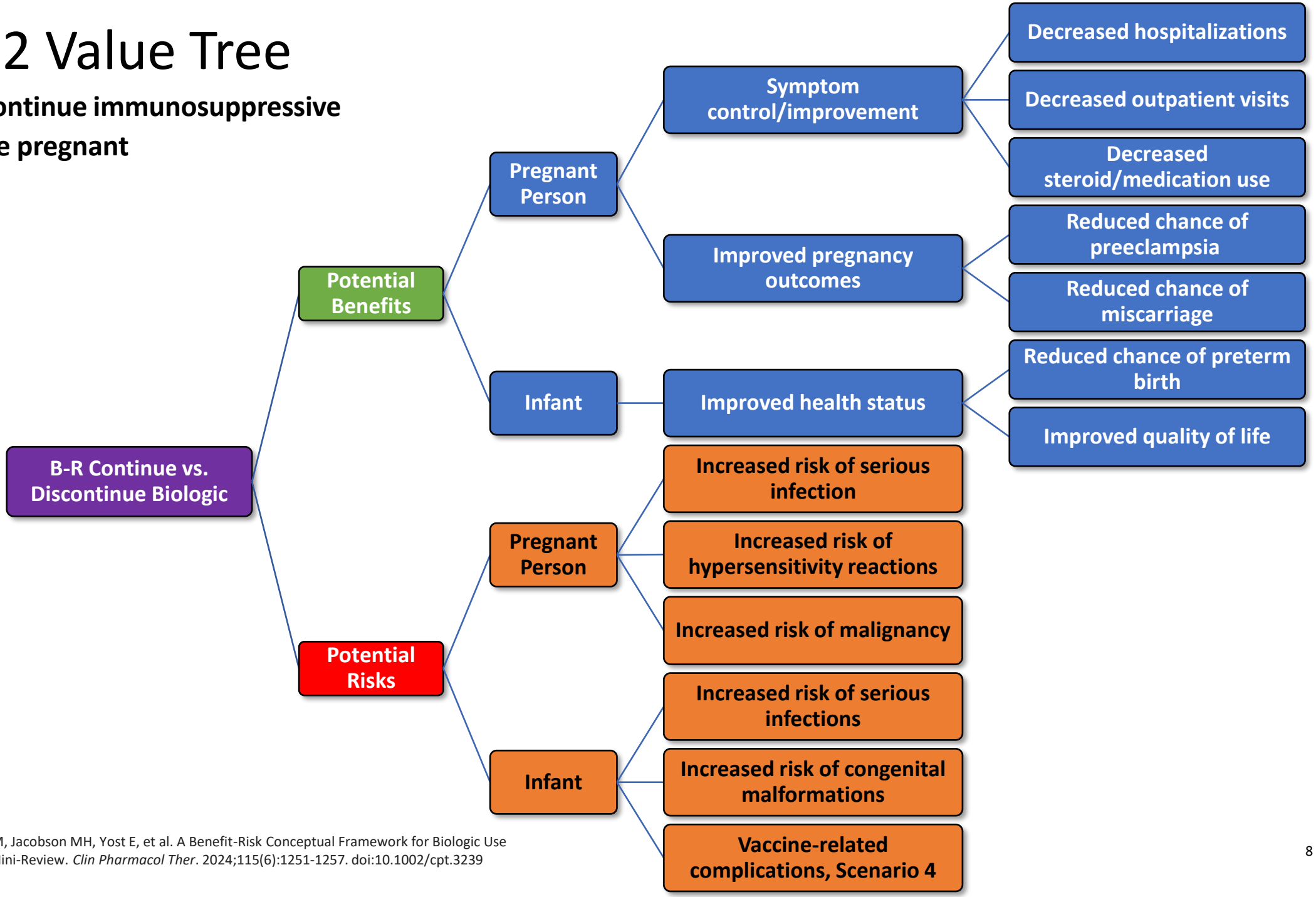

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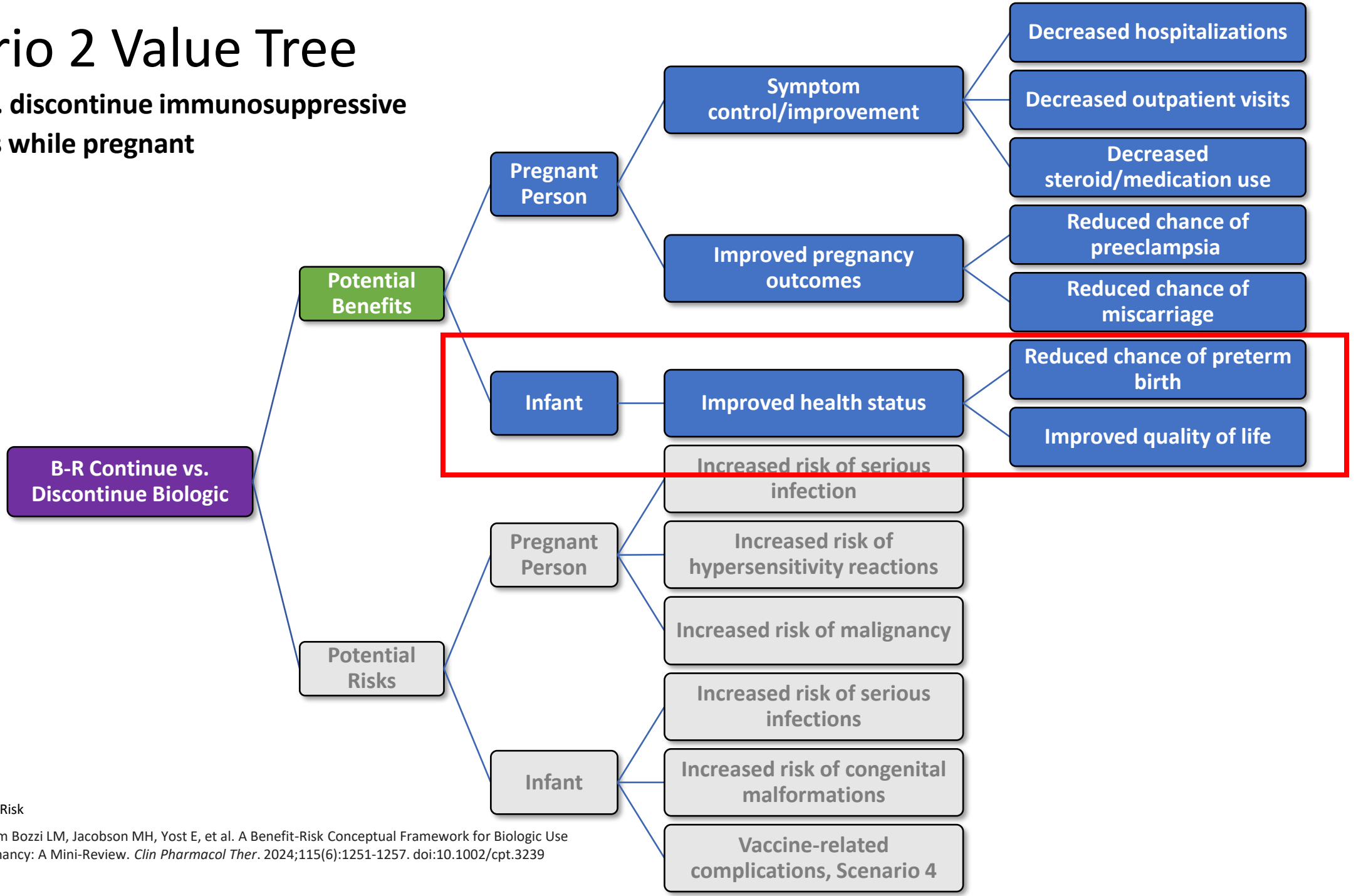

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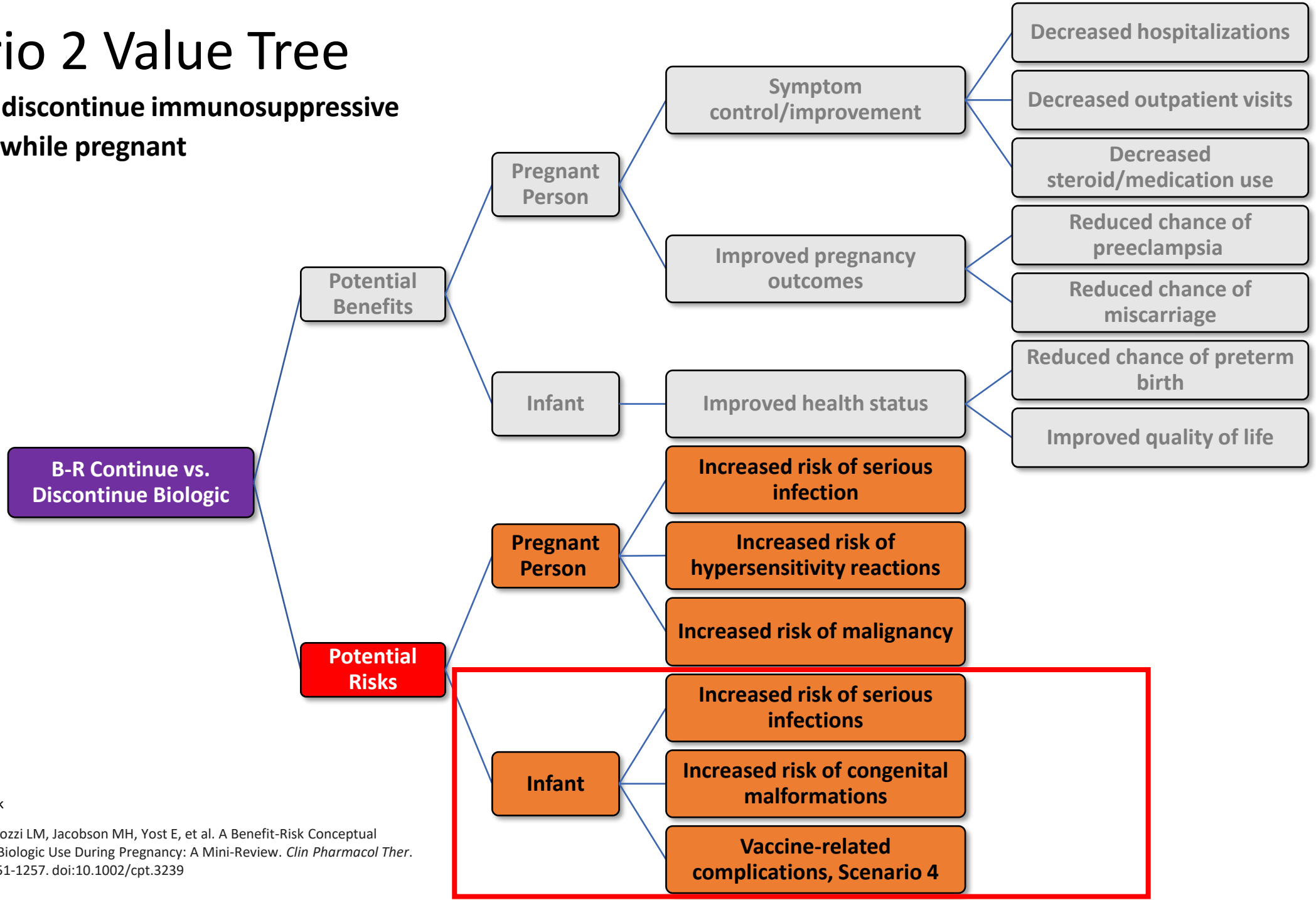

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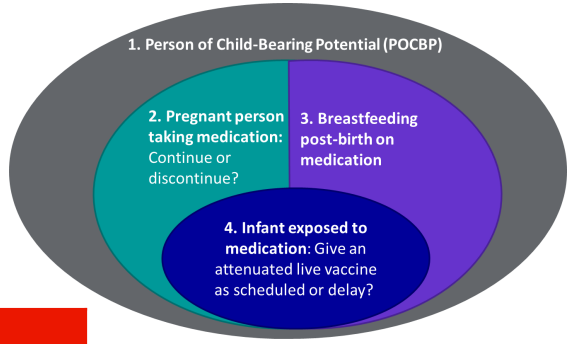
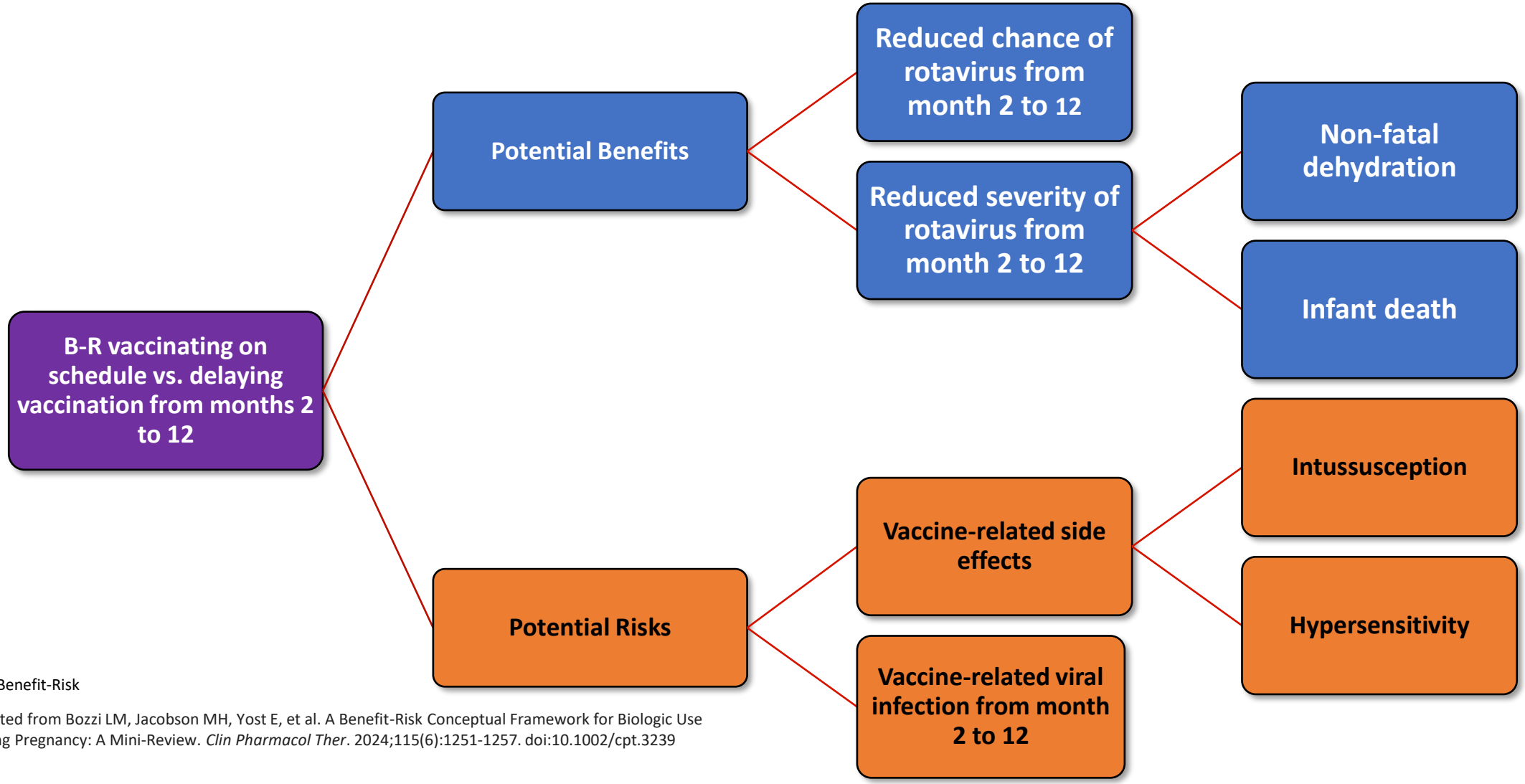
Scenario 4 Decision Context:

Attenuated live vaccine in infants exposed to medications, adapted for rotavirus



Term	Definition
Treatment	Attenuated live vaccination on schedule
Comparator	Attenuated live vaccination delayed 12 months
Population	Infant exposed to biologic (via in utero or breastfeeding)
Indication	Rotavirus prevention
Time-frame	Birth to infant two years of age
Decision-maker	Infant's clinician/caregiver, informed by regulatory/clinical guidelines
Subgroups of interest	Infant exposed to biologic in utero alone; infant exposed to biologic via breastfeeding alone; infant exposed to biologic in utero and breastfeeding

Value Tree of the Benefits and Risks of Administering the Rotavirus Vaccine as Scheduled in Infants Exposed to Medications (Scenario 4)



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Where are we going?

Data Needed

- Benefit-risk is often quantified using clinical trial data.
- In the case of Scenario 2, benefit-risk assessment of biologic use can partially be quantified through claims or registry data. Limitations include:
  - Maternal and infant data linkage
  - Lack of long-term follow-up
  - Missing or incomplete capture of outcomes of interest
- For Scenario 4, where are we going to get the data?

Expertise Needed

- Multi-functional stakeholder expertise
  - Immunology
  - Pediatrics
  - Gynecology
  - Neonatology
  - Perinatology
  - Obstetrics
  - Epidemiology
  - Statistics
  - Patients/Parents

Proposal: The BRIITE Consortium (Benefit-Risk of Infant Immunosuppressive Treatment Exposure)

- **Need:** Due to the complexity and limitations of real-world data, the unmet need for guidance, and the cross-disciplinary nature of the research questions
- **Goal:** To inform future evidence-based analyses to quantify the framework and assist/support clinical recommendations
- **Value:** By validating the framework across diverse stakeholders, the consortium would allow for standardization and acceptance of the framework for application to specific indications and biologics

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Pregnancy & Lactation Advisory Group