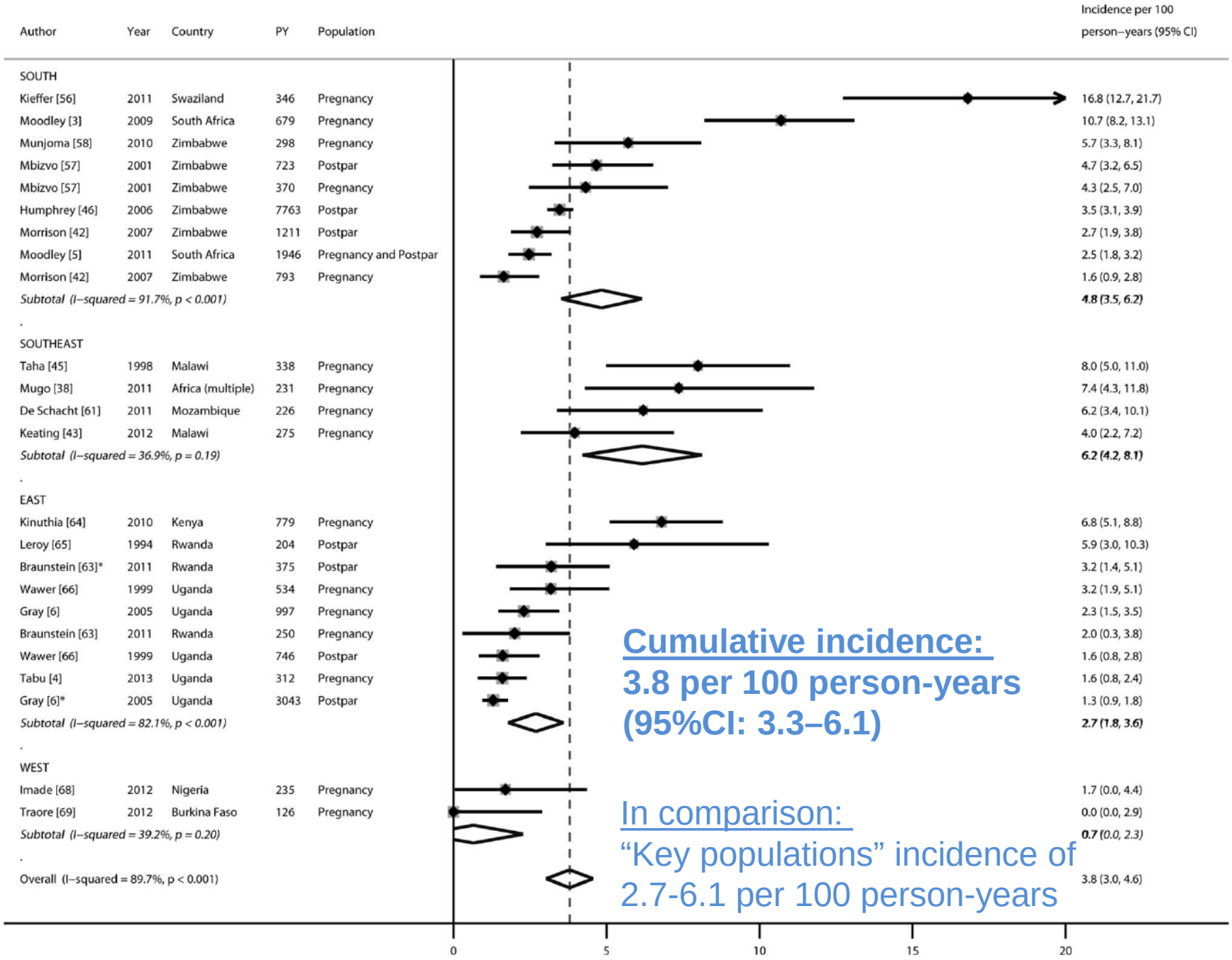
HIV Prevention in Pregnancy

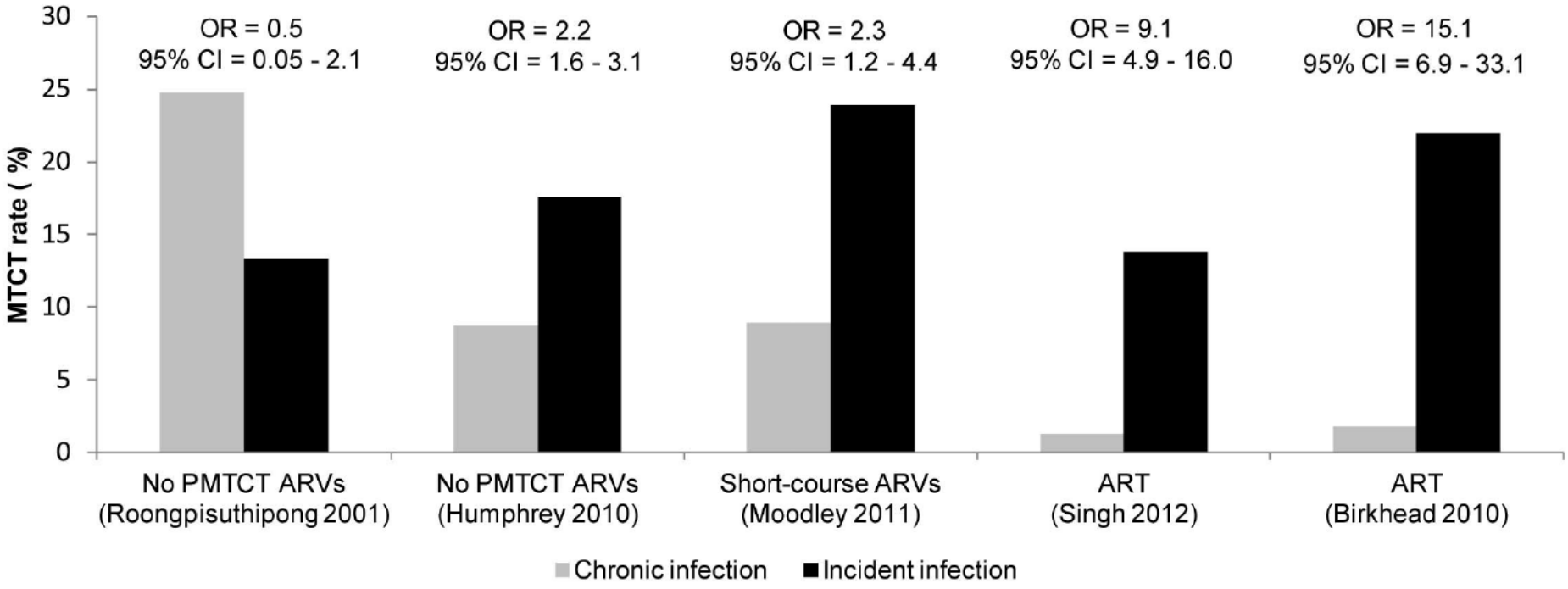


Cumulative incidence:
3.8 per 100 person-years
(95%CI: 3.3–6.1)

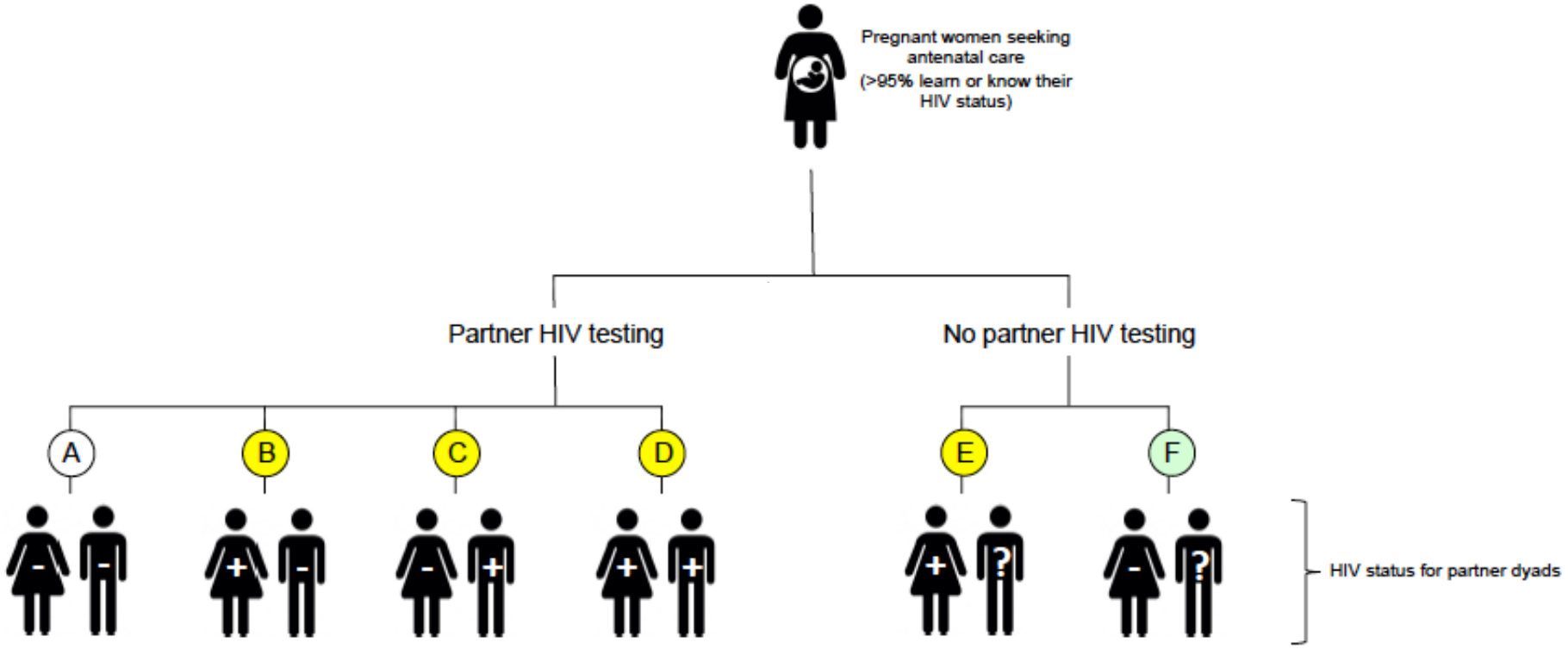
In comparison:
"Key populations" incidence of 2.7-6.1 per 100 person-years

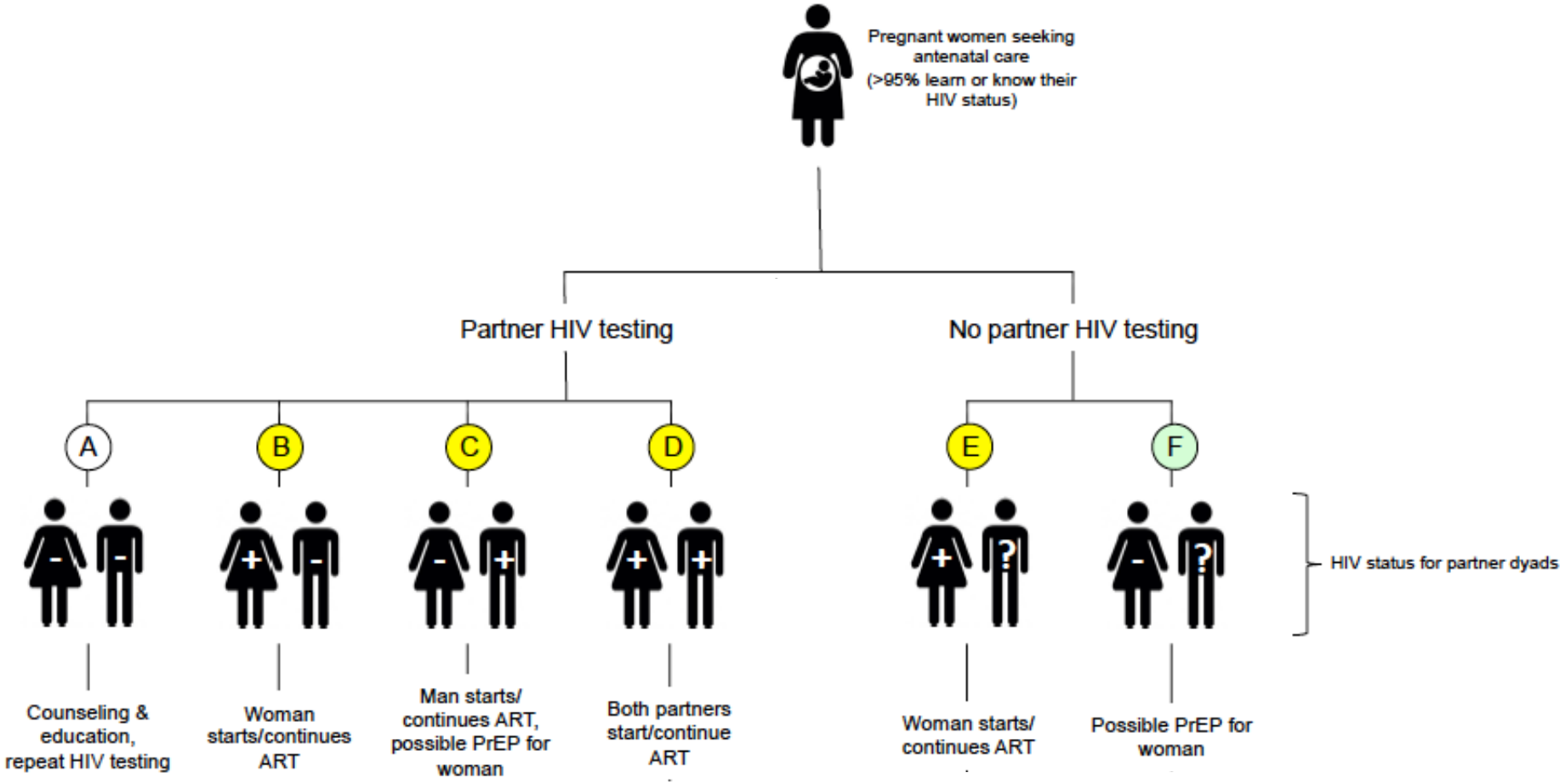
Drake, *PLoS Med* 2014

Acute HIV infection associated with greater MTCT risk



Drake, *PLoS Med* 2014


Pregnant women seeking antenatal care (>95% learn or know their HIV status)
Partner HIV testing
No partner HIV testing
A
B
C
D
E
F
- -
+ -
- +
+ +
+ ?
- ?
HIV status for partner dyads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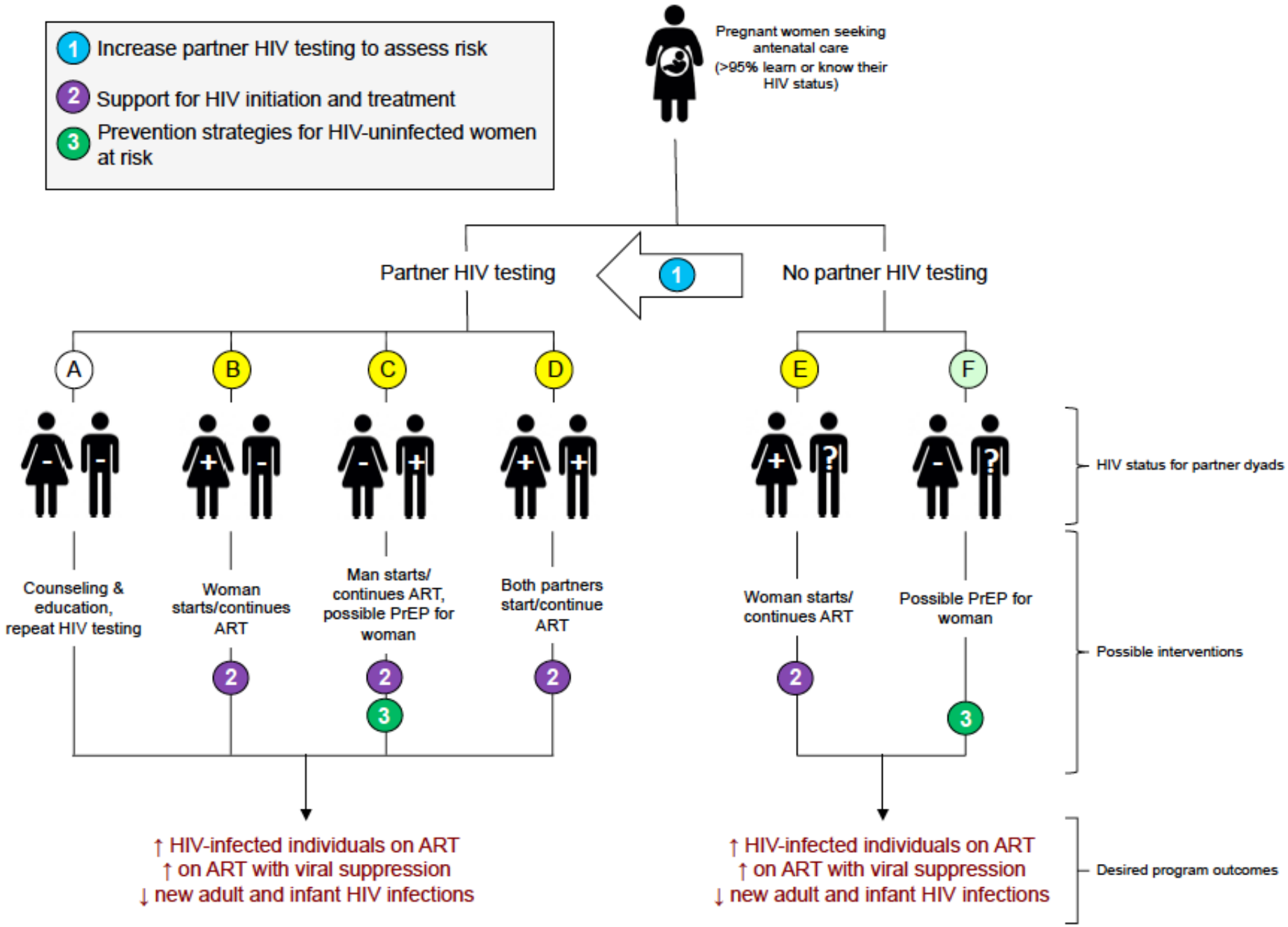
HIV status for partner dyads
Counseling & education, repeat HIV testing
Woman starts/continues ART
Man starts/ continues ART, possible PrEP for woman
Both partners start/continue ART
Woman starts/ continues ART
Possible PrEP for woman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2 Support for HIV initiation and treatment
3 Prevention strategies for HIV-uninfected women at risk
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Both partners start/continue ART
Woman starts/ continues ART
Possible PrEP for woman
HIV status for partner dyads
Possible interventions
↑ HIV-infected individuals on ART
↑ on ART with viral suppression
↓ new adult and infant HIV infections
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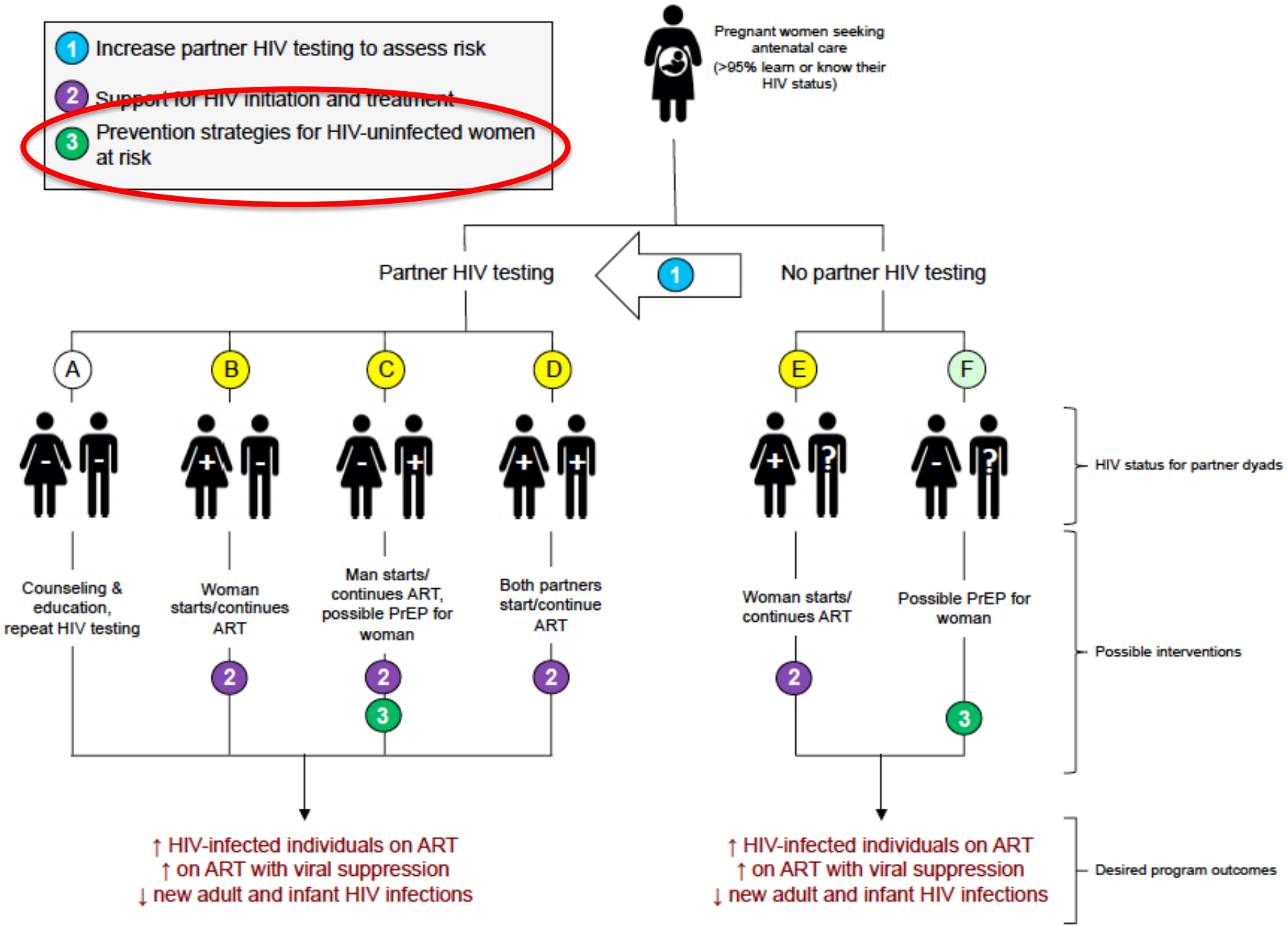
Desired program outcomes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Desired program outcomes

PrEP WHO Guidelines

Antiretroviral drugs for HIV prevention

The updated guidelines include a new recommendation on the use of oral pre-exposure prophylaxis (PrEP) to prevent the acquisition of HIV. WHO has expanded its earlier recommendations to offer PrEP to selected key populations. PrEP is now recommended for all populations at substantial risk of acquiring HIV, provisionally defined as an incidence of HIV greater than three per 100 person-years in the absence of PrEP.

3. CLINICAL GUIDELINES: ANTIRETROVIRAL DRUGS FOR HIV PREVENTION	
3.1 Oral pre-exposure prophylaxis for preventing the acquisition of HIV	Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk[2] of HIV infection as part of combination HIV prevention approaches *(strong recommendation, high quality evidence)*.

Key populations:
Sero-discordant couples
Commercial sex workers
Men who have sex with men
Intravenous drug users

Cost-effectiveness of PrEP in pregnancy and breastfeeding

- Conditional probability model
- Women in sub-Saharan Africa
  - Limited time window: first ANC visit to BF cessation
- Lifetime time horizon
- Health system perspective
- Model parameters
  - Medical literature
  - Program estimates from Zambia and Malawi
- Costs: PrEP program, HIV, preterm birth
  - 3% annual discount rate
  - Inflated to 2015 U.S. dollars

Price, *JAIDS,* in press

Key model parameters

HIV incidence in pregnancy, per 100py	4.7
HIV incidence in PP/BF, per 100py	2.9
MTCT risk if incident HIV, %	22.7
PTB risk on PrEP, %	20
PrEP effectiveness (RR HIV)	0.55
Cost PrEP, annual	$75
Cost PrEP program, annual	$240
Cost HIV care (incl ART), annual	$610

Price, *JAIDS,* in press

Base scenario

	Cost (per person)	Incremental Cost ($)	DALY (per person)	Incremental Effectiveness (DALY)	ICER ($/DALY)
PrEP	$453	+$330	3.16	–	**$980**
No PrEP	$123	–	3.49	+0.34	–

< $6462 / DALY = cost-effective
< $2154 / DALY = very cost-effective

In <u>one-way sensitivity analyses</u>, PrEP was no longer cost effective when:

- PrEP effectiveness was 22% or lower
- Risk for preterm birth was 30% or greater

Price, *JAIDS*, in press

IMPAACT 2009

Pharmacokinetics, Feasibility, Acceptability, and Safety of Oral Pre-Exposure Prophylaxis for Primary HIV Prevention during Pregnancy and Breast Feeding in Adolescents and Young Women

Participating sites

- **Uganda**
  - Baylor CRS
  - Makerere Uni-JHU CRS
- **Malawi:** Blantyre CRS
- **Zimbabwe**
  - Harare Family Care CRS
  - St. Mary's CRS
  - Seke North CRS
- **South Africa:** Shandukani CRS

PK component

PK Component (1)

- Approved by SLG in Feb 2016
- Designed to establish drug thresholds for optimal adherence to PrEP during pregnancy
  - Refines adherence outcome measure
  - Informs drug level-based counseling
- 15-20 participants in each of two groups:
  - Antepartum: 14-24 weeks gestation
  - Postpartum: 6-10 weeks postpartum
- Pregnant women ≥ 16 yrs eligible
- All participants agree to take daily TDF-FTC

PK Component (2)

- 12 weeks of PK monitoring, with weekly DBS specimens for drug levels
  - Followed by an observational period to 6 weeks postpartum
- Specimens to be shipped to U.S. for testing
- Intensive monitoring of drug adherence

PrEP Comparison Component

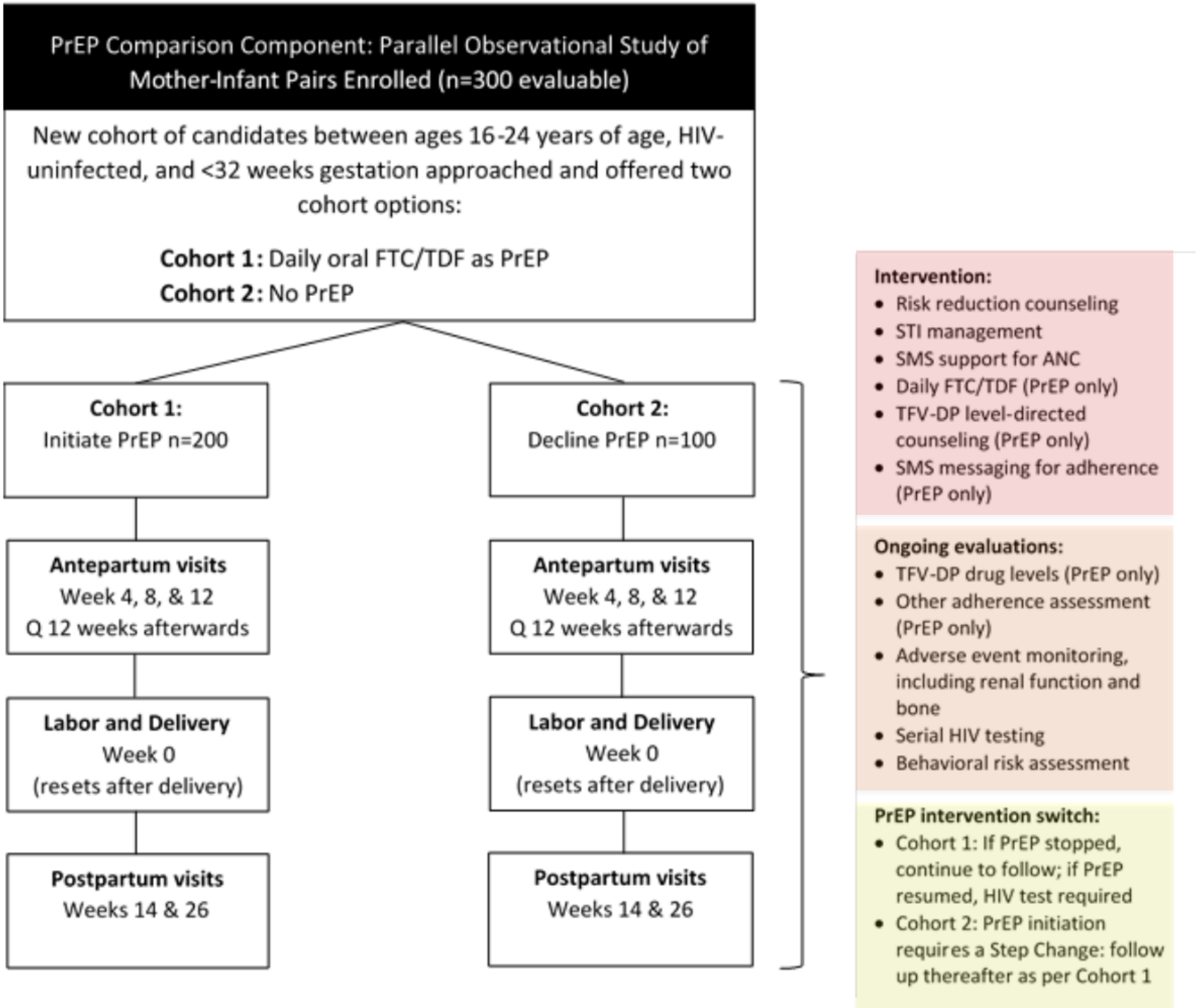
Primary Objectives

- To characterize PrEP adherence among HIV-uninfected women aged 16-24 years who initiate once-daily TDF-FTC in pregnancy

- To compare maternal and infant adverse events (including pregnancy outcomes) between women who initiate PrEP and those who decline PrEP

Secondary Objectives

- To identify individual, social, and structural barriers and facilitators to PrEP uptake during pregnancy
- To compare between the PrEP and non-PrEP cohorts:
  - Reported sexual risk behavior and incidence of STIs
  - HIV incidence
  - HIV drug resistance among HIV-infected mothers and infants


PrEP Comparison Component: Parallel Observational Study of Mother-Infant Pairs Enrolled (n=300 evaluable)
New cohort of candidates between ages 16-24 years of age, HIV-uninfected, and <32 weeks gestation approached and offered two cohort options:
Cohort 1: Daily oral FTC/TDF as PrEP
Cohort 2: No PrEP
Cohort 1: Initiate PrEP n=200
Cohort 2: Decline PrEP n=100
Antepartum visits Week 4, 8, & 12 Q 12 weeks afterwards
Antepartum visits Week 4, 8, & 12 Q 12 weeks afterwards
Labor and Delivery Week 0 (resets after delivery)
Labor and Delivery Week 0 (resets after delivery)
Postpartum visits Weeks 14 & 26
Postpartum visits Weeks 14 & 26
Intervention:
Risk reduction counseling
STI management
SMS support for ANC
Daily FTC/TDF (PrEP only)
TFV-DP level-directed counseling (PrEP only)
SMS messaging for adherence (PrEP only)
Ongoing evaluations:
TFV-DP drug levels (PrEP only)
Other adherence assessment (PrEP only)
Adverse event monitoring, including renal function and bone
Serial HIV testing
Behavioral risk assessment
PrEP intervention switch:
Cohort 1: If PrEP stopped, continue to follow; if PrEP resumed, HIV test required
Cohort 2: PrEP initiation requires a Step Change: follow up thereafter as per Cohort 1

Study population (n=300)

- At least 16 years and less than 25 years
- Confirmed pregnancy at any gestational age
- HIV negative by HIV RNA screening
- No history of chronic disease
- For PrEP cohort:
  - Willingness to take PrEP through pregnancy to 26 weeks postpartum
  - Access to cell phone to receive SMS messages

Study endpoints

- **Adherence**
  - Tenofovir diphosphate (TFV-DP) levels measured through dried blood spots.
- **Safety (maternal and pregnancy)**
  - Adverse pregnancy outcomes will include:
    - Stillbirth
    - Low birthweight <2500g
    - Preterm delivery <37 weeks gestation
  - Maternal AE outcome will be a composite:
    - Grade 3 or higher signs and symptoms
    - Grade 2 or higher chemistry abnormalities
    - Grade 3 or higher pregnancy-related diagnosis

Study endpoints

- **Safety (infant)**
  - Infant safety outcome measures:
    - Infant death
    - Creatinine clearance measured by Schwartz equation
    - Anthropometric growth
    - Lumbar spine and Whole Body bone mineral content
- **HIV-related outcomes**
  - HIV drug resistance in women who become infected while on PrEP
  - HIV drug resistance in infants who become infected while their mothers are on PrEP

Qualitative Component

- Provides deeper insight into feasibility
- In-depth individual interviews - up to 60 women
- Purposive sampling based on PrEP initiation and adherence
- Stratified by pregnancy or postpartum periods
- Protocol-specific training will be provided
  - Standard interview guides
  - Mock interviews with protocol team review
- Sites for qualitative component not yet selected

End