Cost-effectiveness of broadly neutralizing antibodies (bNAbs) for PMTCT in resource-limited settings

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On behalf of the CEPAC-IMPAACT Collaboration

IMPAACT Network Meeting
June 13, 2019

Supported by the IMPAACT Network; National Institute of Allergy and Infectious Diseases (T32 AI007433); Eunice Kennedy Shriver National Institute of Child Health and Human Development (R01 HD079214)

bNAbs for PMTCT

- 180,000 infant infections/year: gaps in PMTCT cascade
  - Undetected maternal HIV; loss to f/u and variable adherence postpartum; incident maternal infection
- bNAbs may fill in some of these gaps:
  - May reduce postpartum MTCT for ~3 months after dose (PrEP)
  - May also provide post-exposure prophylaxis for intrapartum MTCT
- With maternal ART and infant ARVs, bNAb trial would need:
  - Very large sample size
  - Enrolment of difficult to reach “high-risk” population
  - Long duration of follow-up
- Model: If bNAbs prevent MTCT, avoiding costly lifelong pediatric care and ART, would they be worth the cost?

Rollins N STI 2012; UNAIDS 2016; Voronin Y. PLoS Med, 2014; South Africa 2016 DHHS Survey; Drake A, 2014 PLoS Med; Myer L CID 2017

Objective

To evaluate the long-term clinical impact and cost-effectiveness of bNAb infant prophylaxis compared to standard oral ARV prophylaxis for PMTCT in South Africa, Zimbabwe, and Côte d'Ivoire.

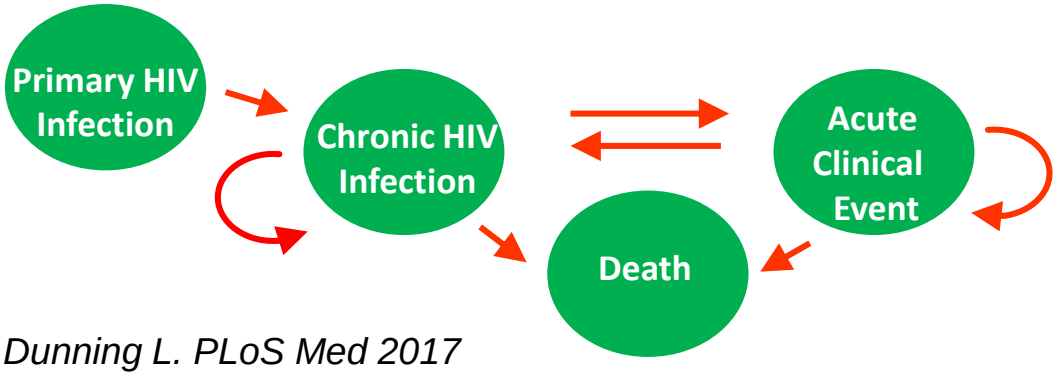
Funded by: IMPAACT Network (DR 808)

Collaborators: Caitlin Dugdale, Andrea Ciaranello, Coleen Cunningham, Genevieve Fouda, Barney Graham, Sallie Permar, and Lynda Stranix-Chibanda

Today: Brief overview of methods; selected examples of preliminary results and ways models can inform study design and implementation planning

Cost-effectiveness of Preventing AIDS Complications (CEPAC)

- CEPAC-Pediatrics computer simulation model of HIV infection, diagnosis, and treatment among children
- Simulate individuals from birth through death
  - MTCT: IU/IP/PP. By maternal acute/chronic HIV, ART use, RNA (<50 c/mL, 50-1000 c/mL, or ≥1000 c/mL)
  - Pediatric HIV outcomes: RNA and CD4; EID, linkage to ART; ART impact on RNA, CD4, morbidity, mortality
  - Use inputs from published literature and clinical trials to project long-term clinical and economic outcomes for children beyond the horizons and populations of clinical studies

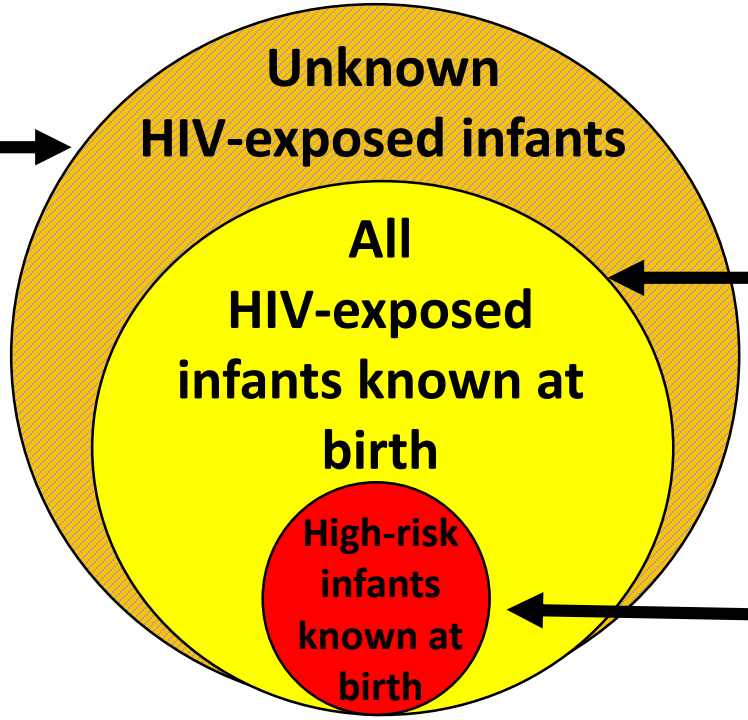


Ciaranello A. PLoS Med 2012; Dunning L. PLoS Med 2017

Modeled population(s)

*High-risk infants (per WHO 2016 Treatment Guidelines) include those recognized at birth to have:
- Mothers on ART <4 weeks prior to delivery
- Mothers with VL >1000 c/mL within 4 weeks of delivery
- Mothers with incident HIV infection during pregnancy

Unknown HIV-exposed infants (e.g., unknown maternal HIV; unrecognized incident maternal HIV) are not captured in yellow or red. *Could be captured by an "all infants" strategy.*



Some "low-risk" infants later face high MTCT risks postpartum with maternal viremia (LTFU or ART non-adherence)

bNAb use for highest risk infants most likely to be effective and cost-effective

Prophylaxis strategies

Prophylaxis strategy	Dose/administration
Standard of care **(SOC; <u>comparator</u>)**	Oral infant prophylaxis for 6 or 12 weeks (low/high risk) With maternal ART
SOC + single dose bNAb **(single-dose bNAb)***	At birth (= 3m duration of protection)
SOC + two doses of bNAb **(two-dose bNAb)***	At birth + 3 months (= 6m duration of protection)

Each bNAb strategy is IN ADDITION TO SOC, which includes lifelong maternal ART
Infant prophylaxis: NVP x 6 weeks– low risk, NVP/ZDV x 12 weeks – high risk

Settings and outcomes

- Settings: South Africa, Côte d'Ivoire, and Zimbabwe
  - Range of prevalence, access to care, healthcare costs
  - Today: preliminary results for South Africa

- Outcomes:
  - 1- and 5-year child survival
  - Overall MTCT risk
    - Intrauterine/intrapartum MTCT
    - Postpartum MTCT
  - Child life expectancy
  - Short-term (budget impact) and lifetime HIV-related costs
  - ICER: incremental cost-effectiveness ratio ($/year of life saved)

Selected model inputs – PMTCT cascade for South Africa

- Maternal HIV prevalence: *31%,* incidence: *3%/year*
- HIV status known in pregnancy: *78-89%*
- PMTCT (ART) coverage: *95%*
- Breastfeeding: *66%,* mean duration: *6 months*
- Retention through 12 months postpartum: *71%*
- Viral suppression (<1,000c/ml)
  - At delivery: *91%*
  - At 12 months postpartum: *85%*
- MTCT risks (from literature; L. Mofenson/Spectrum)

South Africa NDOH 2017; Golden LM 2018; South Africa NDOH 2016; UNAIDS 2017; West NS 2019; Myer 2018; Myer 2017.

Model inputs – bNAb prophylaxis

Input parameter	Value	Source
bNAb uptake (offer & accept)	54-92%	Vaccine uptake, DHS 2016
Postpartum MTCT risk reduction (bNAb efficacy)*	80% Range: 0-100%	Assumption (% of virus neutralized)**
Duration of bNAb effect	3 months after each dose	IMPAACT P1112
Cost	$50 Range: $20-100	Assumption (adult HIV vaccine models)*** $10/g; dose 80-100mg

*** Multiplier on PP MTCT risk at current infant ARV and maternal ART use.**

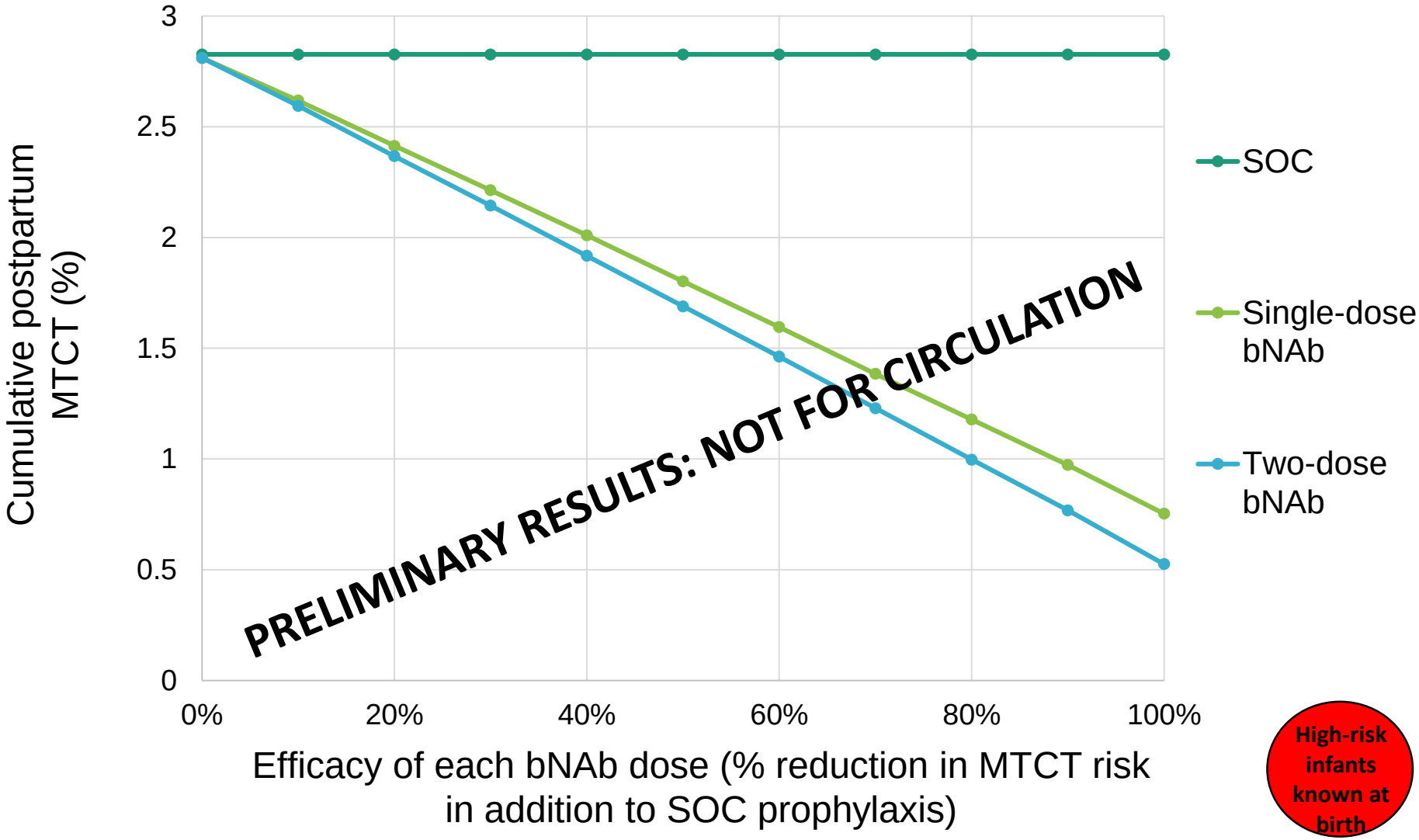
** Josh Tu; Nakamura AIDS 2013

******* Harmon PloS One 2016, Moodley Medicine 2016, Voronin JAIDS 2017

Model inputs – Selected costs

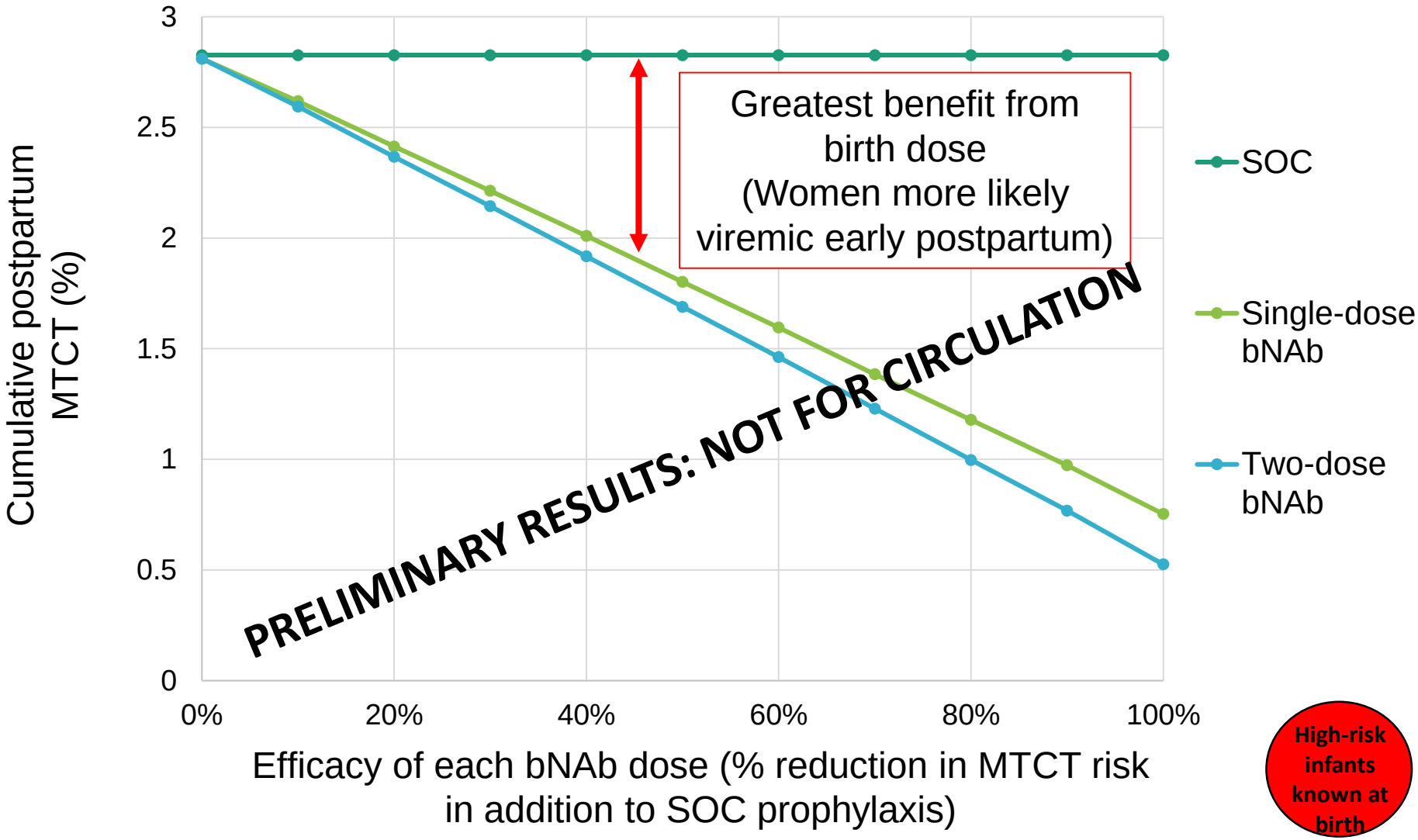
Cost parameter	Value	Source
NVP +/- ZDV, per month	$5-$15	Global Fund 2019
1st line pediatric ART (ABC + 3TC + LPV/r), per month	$13 - $23	Global Fund 2019; CHAI 2016
Pediatric HIV care	$19 - $155 per month Additional $10 - $1,700 for specific clinical events	Previous CEPAC cost derivations for South Africa

Results: Known high-risk infants - Postpartum MTCT



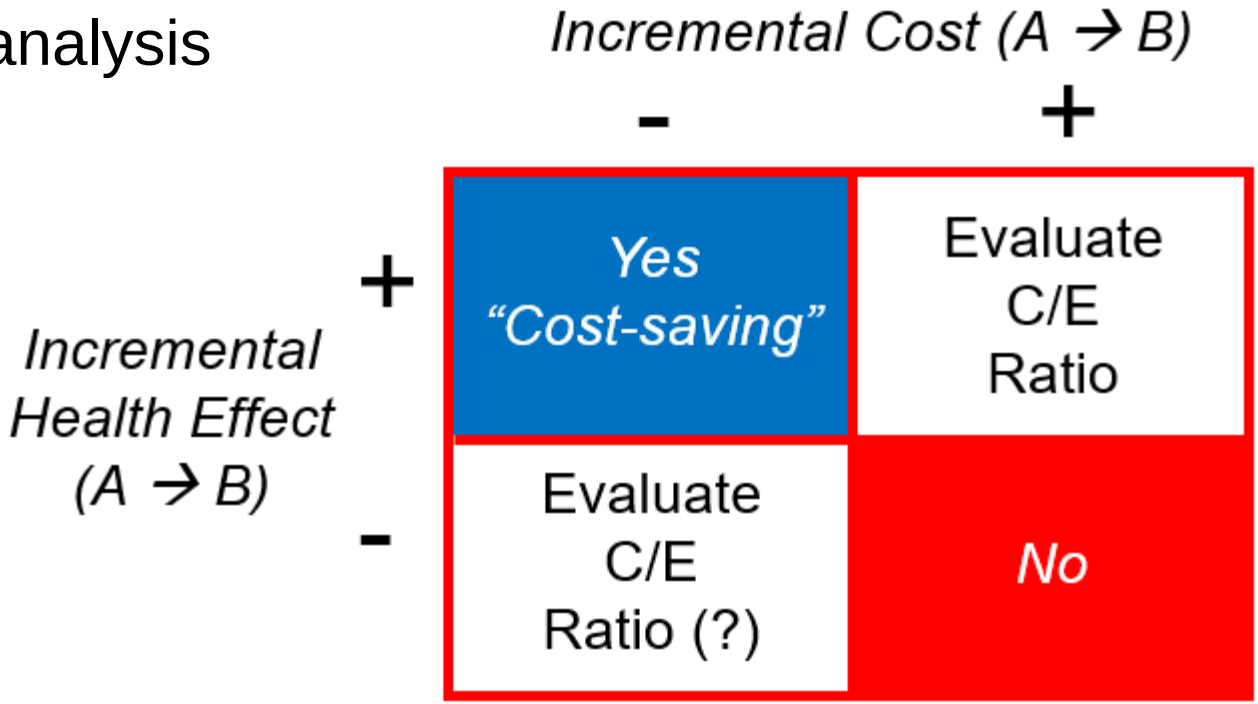
High-risk infants known at birth

Results: Known high-risk infants - Postpartum MTCT



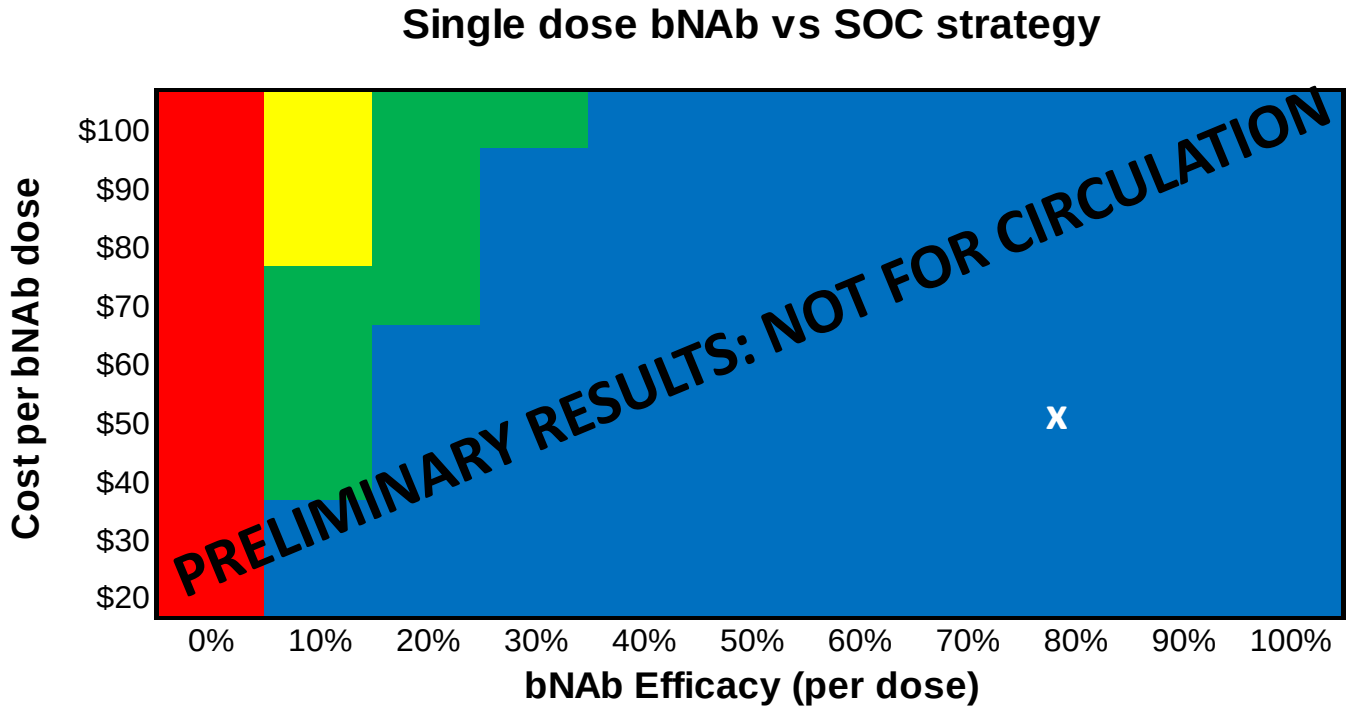
Cost-effectiveness analysis

- Cost-effective ≠ cheap, ≠ cost-saving
- Value for money
- Incremental analysis



- ICER: $\frac{\text{(Cost B – Cost A)}}{\text{(Life-years B – Life-years A)}}$

Results: Known high-risk infants - Cost-effectiveness

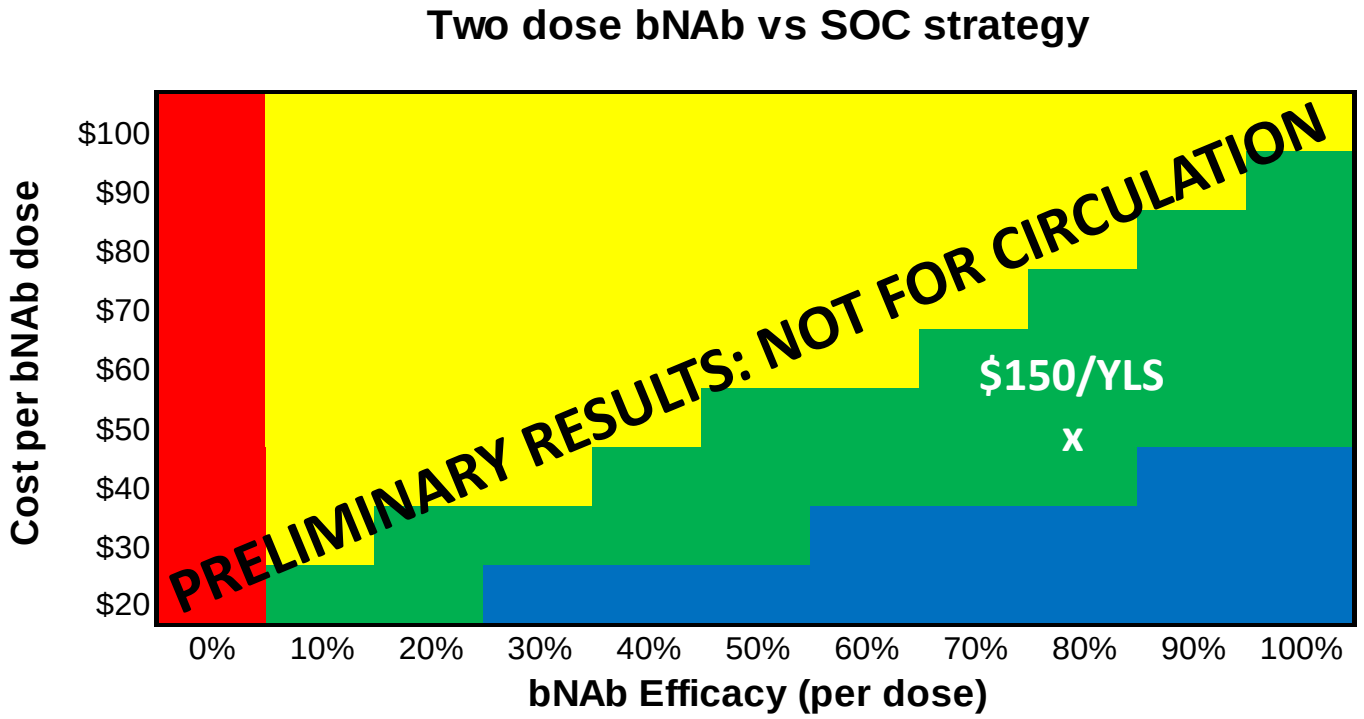


Incremental cost-effectiveness ratio (ICER) of bNAb strategy compared to SOC strategy, expressed in $/year of life saved (YLS)

- SOC less expensive and equally effective
- ICER >$6150/YLS
- ICER $500-$6150/YLS
- ICER <$500/YLS
- bNAb strategy is cost-saving relative to SOC

High-risk infants known at birth

Results: Known HIV-exposed infants - Cost-effectiveness



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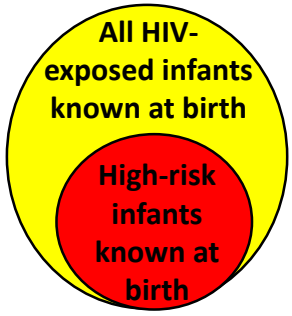

Next steps for modeling

- Vary all model input data and assumptions in sensitivity analyses
- Budget impact (1-5 years):
  - Affordability at program/population-level
  - Total costs; when offsets occur
- Interaction with EID cascade
  - Require negative EID first: may reduce resistance, at expense of access
  - Impact of bNAbs on later NAT and RDT results
- Zimbabwe and Côte d'Ivoire
- Strategy: offer to all infants

Preliminary conclusions

- Compared to SOC in South Africa, across a range of cost and efficacy assumptions:
  - When offered to known high-risk infants, bNAbs may be cost-effective, and are often cost-saving due to costly pediatric HIV infections averted
  - When offered to all known HIV-exposed infants, bNAbs may be cost-effective (ICER <$500/YLS); less often cost-saving
- Model-based analyses can inform both pre-trial design and (if effective) post-trial implementation of novel strategies, by:
  - Identifying key target populations and implementation strategies (dosing, EID)
  - Estimating potential population-level benefits
  - Quantifying potential short- and long-term costs and savings

Thank you

CEPAC-Pediatric Research Team

Elaine Abrams
Audrey Bangs
Ingrid Bassett
Andrea Ciaranello
Sophie Desmonde
Lorna Dunning
Julia Foote
Kenneth Freedberg
Adi Gandhi
Taige Hou
Emily Hyle
Valeriane Leroy
Nicole McCann
Landon Myer
Anne Neilan
A. David Paltiel
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Supported by:

The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network; Eunice Kennedy Shriver National Institute of Child Health and Human Development (R01 HD079214), National Institute of Allergy and Infectious Diseases (T32AI007433)

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