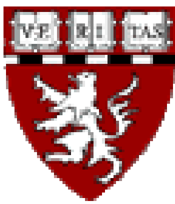

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Optimizing Pediatric HIV Testing WHO/CEPAC Collaboration

CENTS Webinar
February 5, 2019

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CEPAC
Cost-effectiveness of Preventing AIDS Complications

World Health Organization

Outline

1. Background and rationale
2. CEPAC-Pediatric model and prior EID analyses
3. Research question 1: screening for HIV exposure in immunization clinics
4. Research question 2: case-finding at entry points beyond PMTCT and immunization clinics
5. Web-based decision support tool

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Background

- WHO currently recommends EID testing at ~6 weeks for all infants known to be HIV-exposed
- Current EID reaches <50% of all HIV-exposed infants
    - Mothers identified with HIV: imperfect linkage to EID
    - Mothers not identified with HIV (not tested or infected after last test in pregnancy)
- Immunization programs (EPI) reach many infants in the first months of life
- Opportunities exist to test children aged 2-10 presenting at many entry points
- Low rates of test positivity may yield high absolute numbers of children identified
- Benefit and value of testing at each site may differ depending on the epidemic context (between and within countries)

Rationale

- Operational research to address these unknowns is difficult to conduct in a robust way
- Generalizability can be limited by the epidemic and health system differences
- Modelling provides an opportunity to address current and future uncertainty to inform normative guidelines and to support program planning

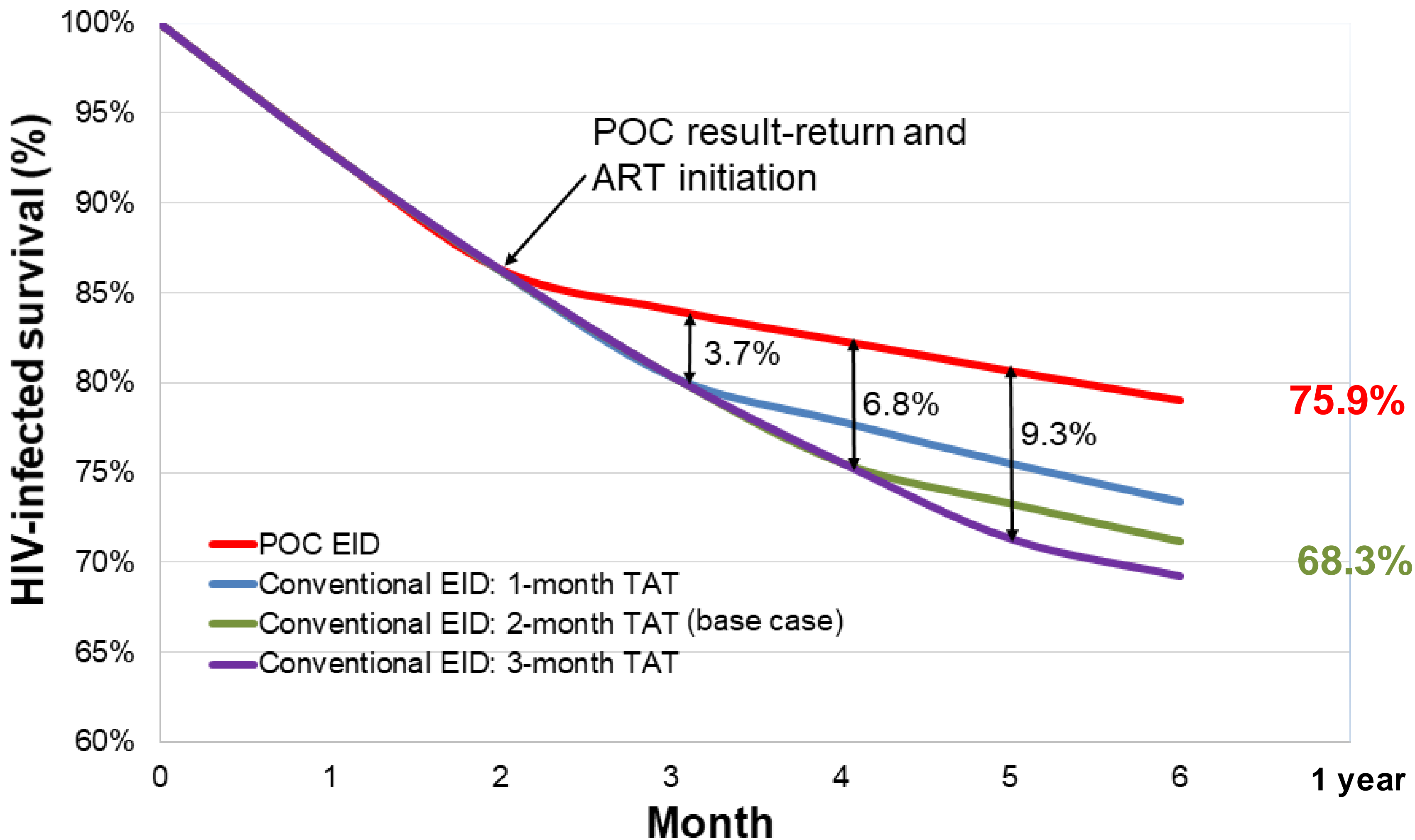
Goal: to undertake evidence-based modelling to develop a user-friendly web interface that will support programme managers in designing their pediatric HIV testing strategies

CEPAC-Pediatric Model

- Monte Carlo microsimulation model
- Infants enter at birth: HIV-unexposed, HIV-exposed/uninfected, HIV infected
- Monthly risks of HIV infection (breastfeeding), disease progression
- ART efficacy, toxicity, costs
- Detailed modules for EID (virologic tests for infants), antibody-based testing (all ages)
  - Includes presentation to care, ART initiation, retention
  - Past work: timing and frequency of EID, point-of-care

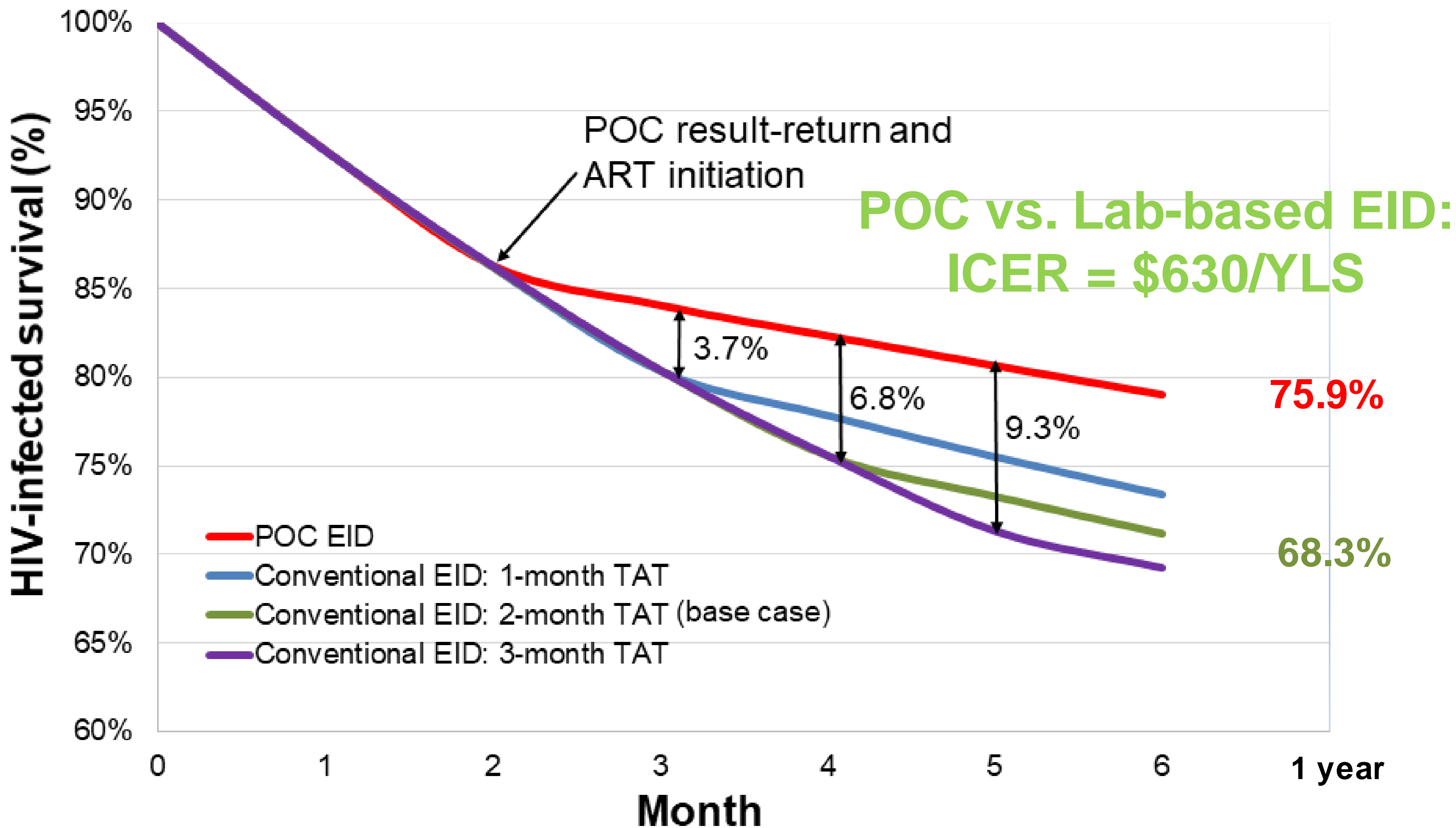
Frank Lancet HIV 2018; Dunning PLoS Med 2017; Francke JID 2016; Ciaranello AIDS 2015

CEPAC-Pediatric Model: Point-of-care EID in Zimbabwe



Frank Lancet HIV 2018

CEPAC-Pediatric Model: Point-of-care EID in Zimbabwe



Frank Lancet HIV 2018

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Research Question 1

- What is the clinical impact and cost-effectiveness of routine HIV screening for exposure and testing of HIV-exposed infants at immunization visits?

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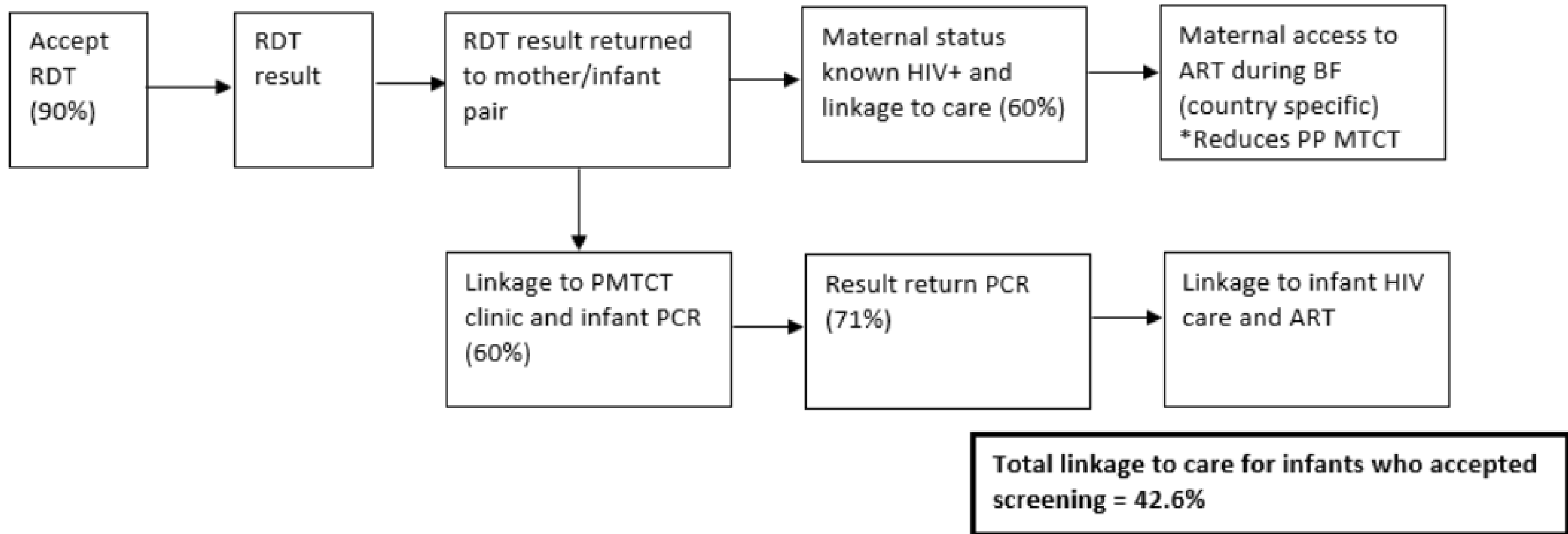
Modeled Strategies

- Routine 6-week *EID*
  - PCR testing for infants known to be HIV-exposed who present to 6-week PMTCT/EID visit
- *Screen-and-test*
  - PCR testing for infants known to be HIV-exposed who present to 6-week PMTCT/EID visit
  - If not known to be exposed, maternal RDT at 6-week immunization visit, with referral to EID if positive
- Focus countries: Côte d'Ivoire, South Africa, Zimbabwe

Dunning et al, in progress

Screen-and-test Strategy

Structure for all 3 countries; sample linkage values for South Africa:



Dunning et al, in progress

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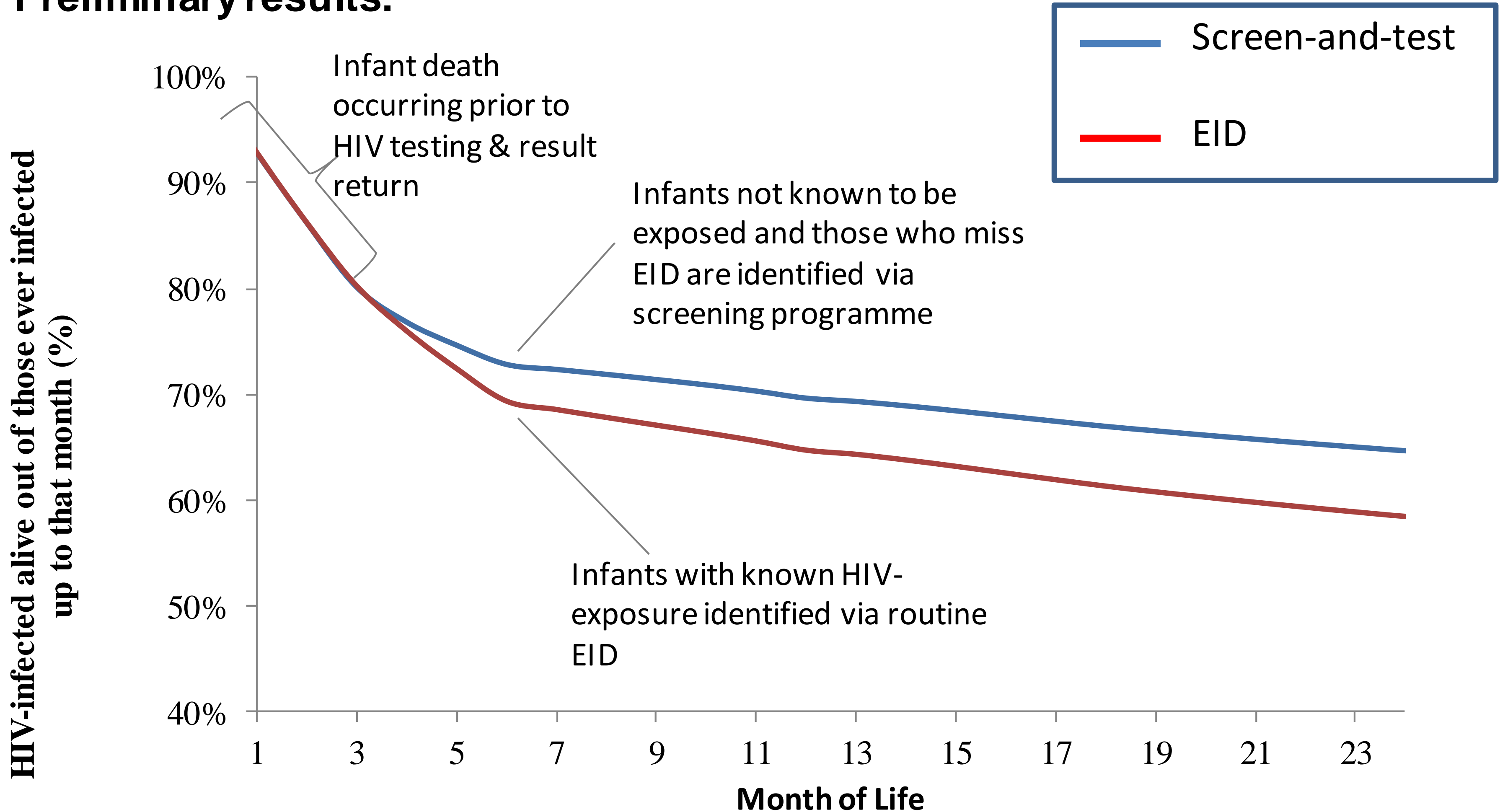
Selected Inputs

Parameter	South Africa	Zimbabwe	Côte d'Ivoire
Maternal prevalence	30.8%	16%	3.5%
Maternal incidence post-partum (risk per year)	3%	2%	0.7%
Maternal knowledge of HIV status if HIV-infected	90%	77%	58%
ART coverage during pregnancy if known to be HIV-infected	95%	84%	80%
EID coverage for infants with known HIV-exposure at birth	73%	58%	41%
Immunization coverage (6w-10w)	78%	95%	98%
Result return and linkage to PMTCT clinic (PCR; maternal ART) after RDT	60%	60%	60%
Linkage to HIV care for infants found to be HIV-infected at routine EID and identified via screening	71%	71%	71%
ART coverage during breastfeeding if mother's status becomes known	95%	84%	80%
Screening program cost	$10	$10	$10

UNAIDS; Drake 2014; Desmonde 2017; Granho 2016; Woldesenbet 2015; GAVI/WHO 2016; Hsaio 2013; PEPFAR 2014

Survival curve: HIV-infected infants (South Africa)

Preliminary results



Dunning et al, in progress

Preliminary results

Identification of Infants by Age 5 (South Africa)

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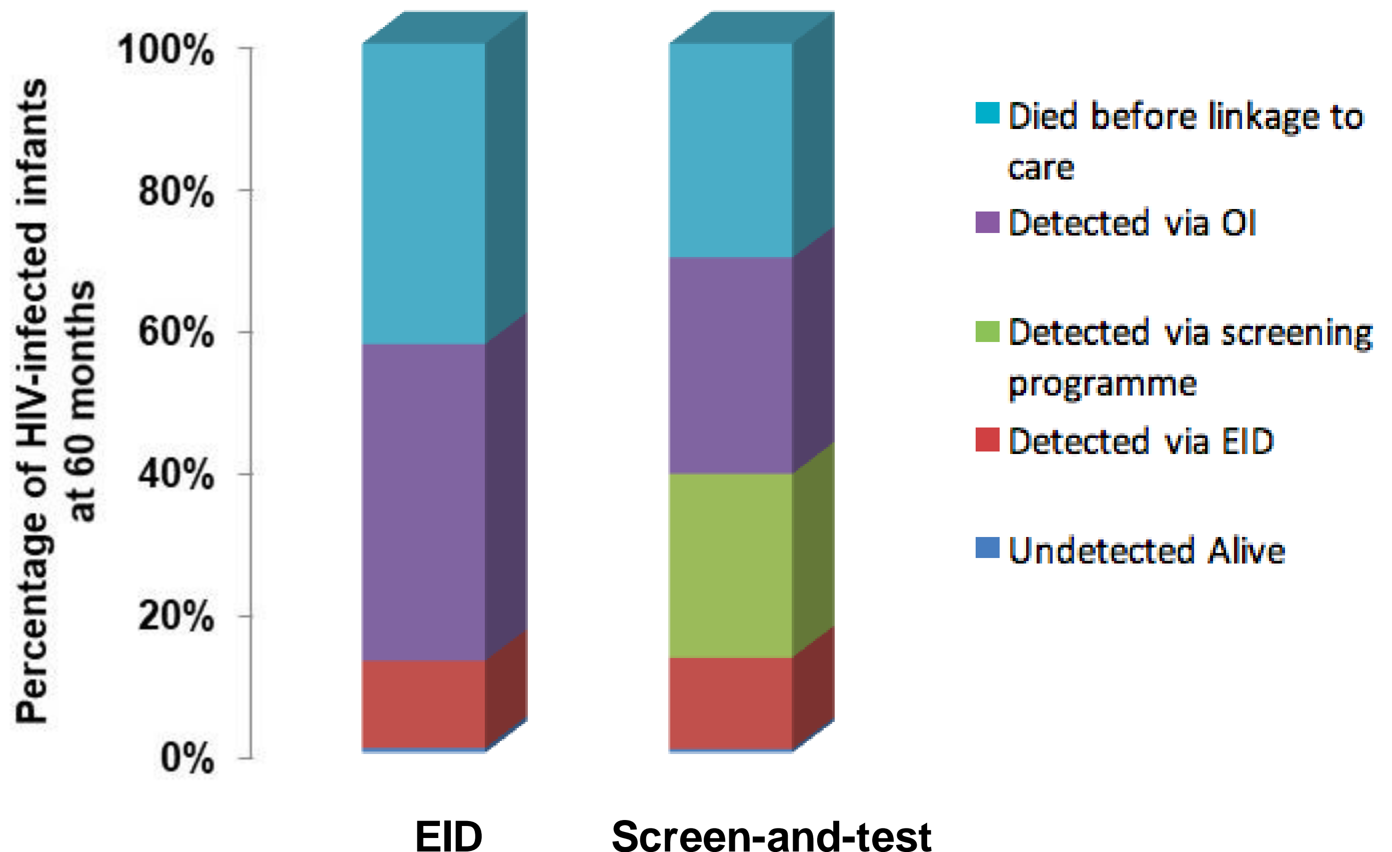
Preliminary results:



Dunning et al, in progress

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Preliminary results

Cost-effectiveness (South Africa)

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Lifetime projections (undiscounted) – preliminary results			
Strategy	**HIV-infected life expectancy (years)**	**Birth cohort life expectancy (years)**	**Lifetime costs (2016 USD per person)**
EID	19.45	63.29	260
Screen-and-test	21.46	63.36	285

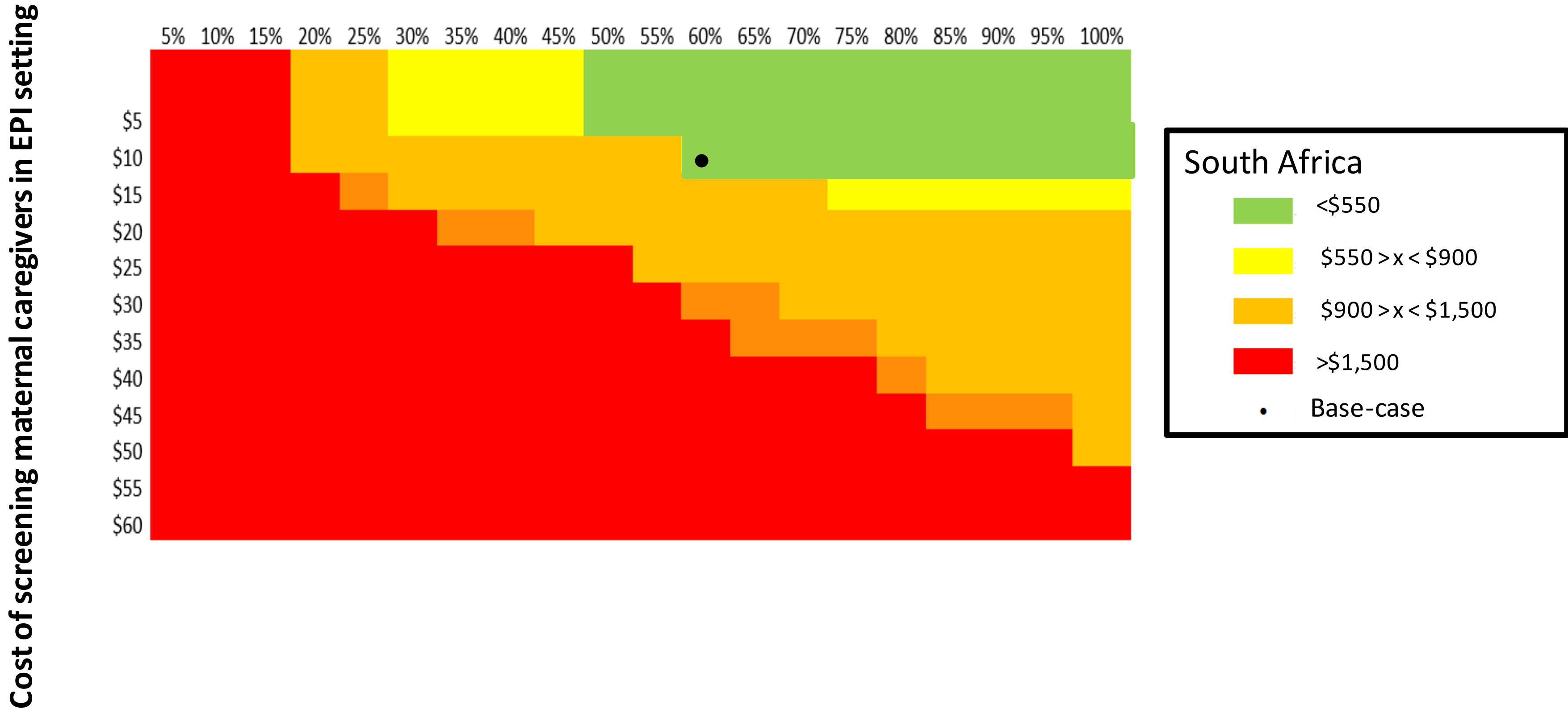
- Cost-effectiveness (birth cohort costs and LE, discounted at 3%/year)
  - *Screen-and-test* vs. *EID*: ICER = $500/YLS
- How should “cost-effective” be defined?
  - Older: 1x or 3x *per-capita* GDP (WHO-CHOICE)
  - Newer: goal = better reflect opportunity cost
    - Based on empiric data (UK, extrapolated to SSA): $500/DALY
    - ICER of already-funded programs (e.g., 2nd-line ART, $900/LYS)
    - Investment case (South Africa: $550-800/DALY)

Dunning et al, in progress; Ochalek BMC Global Health 2018, Woods Value Health 2016, Meyer-Rath PLoS One 2017

Two-way Sensitivity Analyses: ICER of *screen-and-test vs. EID*

Preliminary results

Preliminary results:



Research Question 2

- What is the clinical impact and cost-effectiveness of testing for HIV at TB clinic, malnutrition wards, inpatient wards, outpatient departments?

Data inputs required for each setting

- Age distribution of children presenting to care
- HIV prevalence (previously undiagnosed) by age
- Uptake of testing (universal)
- Mortality risks:
  - HIV-infected, diagnosed and treated
  - HIV-infected, not diagnosed or treated
  - HIV-uninfected (higher mortality due to underlying condition)
- Result return rate
- Linkage to care at each strategy
- Access to ART for infants presenting to care
- Impact of early vs. deferred ART (e.g., TB)

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Data Concerns

- Despite many available reports, limited data:
  - Data not stratified by age
  - Routine vs. targeted testing
  - Often not reported:
    - Number of refusals at testing site
    - Linkage to care
    - Retention in care
    - Diagnosis after opportunistic disease (counterfactual)
    - Comorbidities and impact on survival
    - Data from non-hospital or nutrition setting, e.g. TB clinics, OVC services, co-located maternal ART visits

Kankasa 2009, Fergusson 2009, Weigel 2009, McCollum 2010 & 2011, Mutanga 2012, Ramirez-Avila 2013, Rytter 2015, Ferrand 2016, Cohn 2016, Simon 2017, Sinclare 2017, Macken 2017, EGPAF 2017

Testing in a Range of Settings

- Create a series of look-up tables
- Report CE of testing vs. not testing at various ages and prevalence of undiagnosed HIV
  - Representing different entry points
  - Representing different setting histories of maternal prevalence, PMTCT, EID, ART coverage
- Motivate collection of additional data about undiagnosed HIV prevalence

Preliminary results

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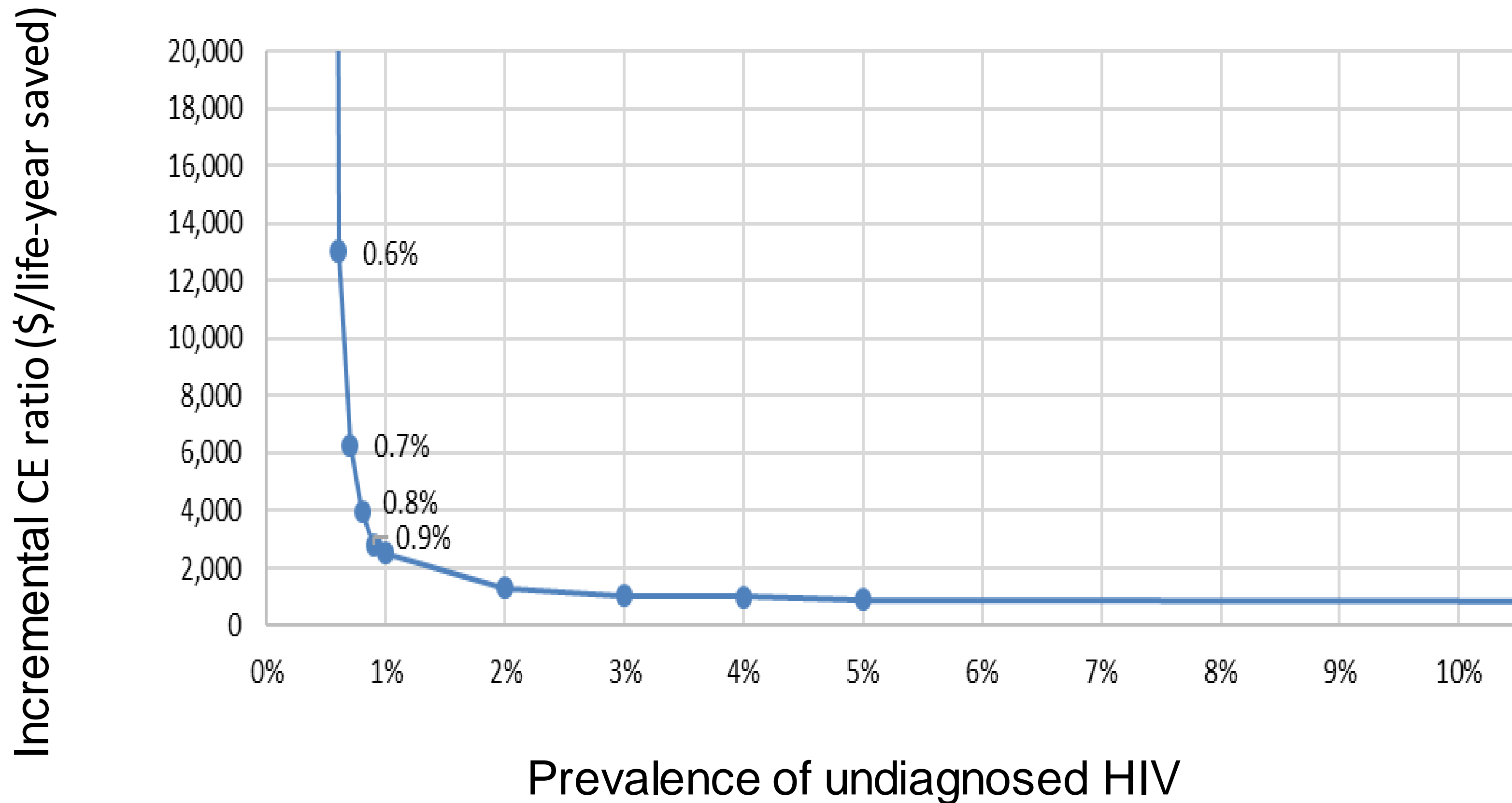
Structure of Preliminary Results

Sample model results for 5-year old children in South African general population



Webtool: Research Question 1
Screen-and-test vs. *EID*

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Preliminary results

Select a Country
South Africa

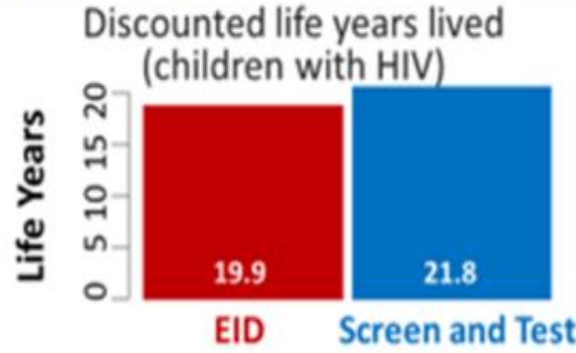
Cost inputs (US Dollars)

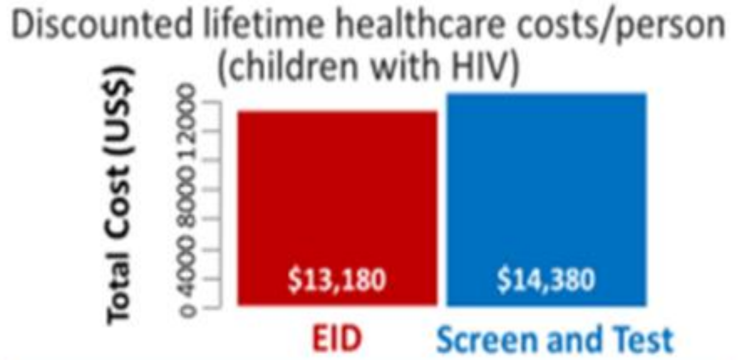
Input	Value
Lab EID test	$20
POC EID test	$25
1st-line ART/month	$15
2nd-line ART/month	$26

Population profile

Input	Value
Maternal HIV prev	36%
PMTCT coverage	96%
EID coverage	80%
Breastfeeding prob	55%
Breastfeeding duration	12m

Cost-Effectiveness | Survival | Costs | HIV cases avoided





Policy Recommendation:
Screen and Test

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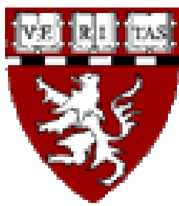
Preliminary results

Feedback and Discussion

- Parameters of interest for EPI and other settings
  - Resource requirements for screening in each setting
  - Linkage after screening in each setting
- Outcomes of interest for web tool



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Thank You

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