Modeling HIV Prevention Modalities for Children

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Outline

- Modeling and cost-effectiveness analyses
- Examples of model-based analyses in PMTCT and pediatric HIV
- Proposed application of modeling methods to emerging questions in PMTCT: example of immunoprophylaxis
- Next steps and future collaborations

Role of Model-based Analyses

- Balance of risks and benefits (costs and benefits)
- Questions not amenable to trials or cohort studies
  - Long follow up would be needed
  - Ethics and feasibility concerns
  - Difficult to ascertain outcomes (e.g., for those not in care)
- Integrate current data from multiple sources
- Explicitly vary uncertain data parameters, to determine if policy conclusions will change

Model-based Analyses

- Project different kinds of outcomes
  - Clinical and epidemiologic outcomes
  - Short-term costs (budget impact analysis)
  - Long-term costs (cost-effectiveness analysis)

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CEPAC-Pediatric Model

- Adult: 1993 (Ken Freedberg); Pediatric: 2009+: IMPAACT, NIAID, EGPAF, NICHD, WHO
- Monte Carlo simulation model (individual agent)
  - Birth through entire lifetime
  - Enter as intrauterine-infected, intrapartum-infected, HIV-exposed/ uninfected (at risk for postpartum infection), HIV-unexposed
  - CD4- and age-stratified OI and mortality risks; modified by ART
- Data: from clinical trials, cohorts, published literature
  - Clinical data: East African research cohort data; calibrated to pooled analyses from 8 sub-Saharan African countries, P1060
  - Costs: testing, HIV and OI care, ART, laboratory tests
- Project short- and long-term OI risk, survival, ART use, costs; compare clinical outcomes and cost-effectiveness

Ciaranello, PLoS ONE 2013; Ciaranello, AIDS 2015; Francke, JID 2016

CEPAC Early Infant Diagnosis (EID) Analyses

- Analyses conducted for WHO 2015 guidelines
- What is the value of birth testing, in addition to or instead of currently-recommended 6-week testing?
  - Role for 10-week testing, alone or with birth testing?

EID in the CEPAC Model

- Simulate all steps in the EID cascade
- HIV detection: EID or opportunistic infection (OI)
- Nucleic acid test (NAT) at select ages
  - Birth, 6 weeks, 10 weeks, and combinations
- Selected input parameters (all varied widely)
  - Sensitivity:
    - 0% first month after infection (except IU detectable at birth)
    - 100% thereafter
  - Specificity: 98.8%
  - Assay cost: $25

Penazzato, WHO Technical EID Updates, 2013 and 2015; UNITAID; South Africa NHLS; estimation of phlebotomist and counselor time and salary (Myer, personal communication)

First Modeled Scenario for WHO Guidelines

- Infants of women known to be living with HIV
- South Africa
- 90% ART coverage for PMTCT
- 80% breastfeeding (median 12 months)
- Guideline-concordant EID uptake: 100% testing uptake, result return, linkage to care

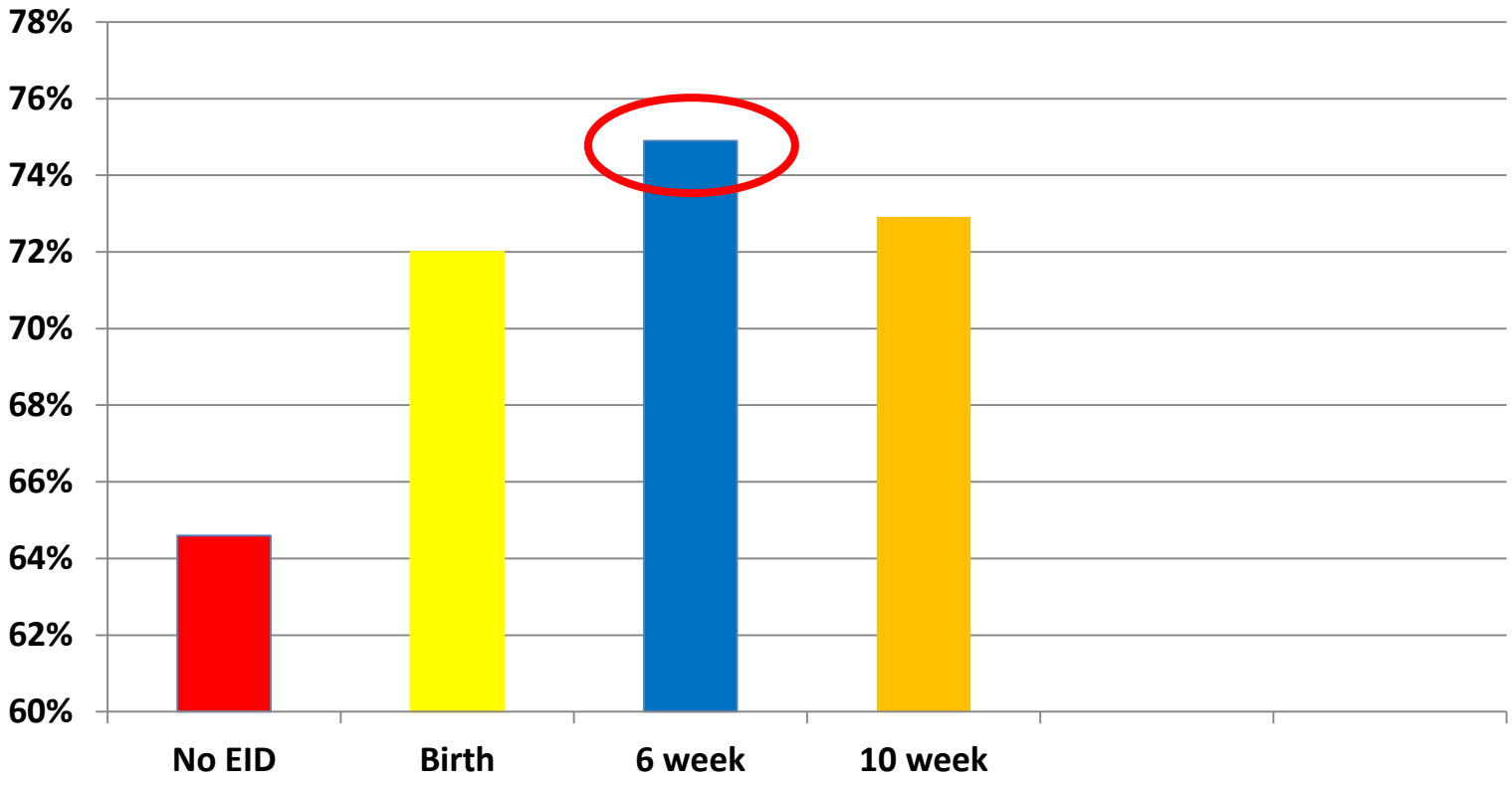
Francke, JID 2016; UNAIDS Global Reports; assumptions

Infant Transmission Results

- Overall risk: 4.9%
  - 1.8% intrauterine infection
  - 1.2% intrapartum infection
  - 1.9% postpartum infection
- 95.1% HIV-exposed/uninfected

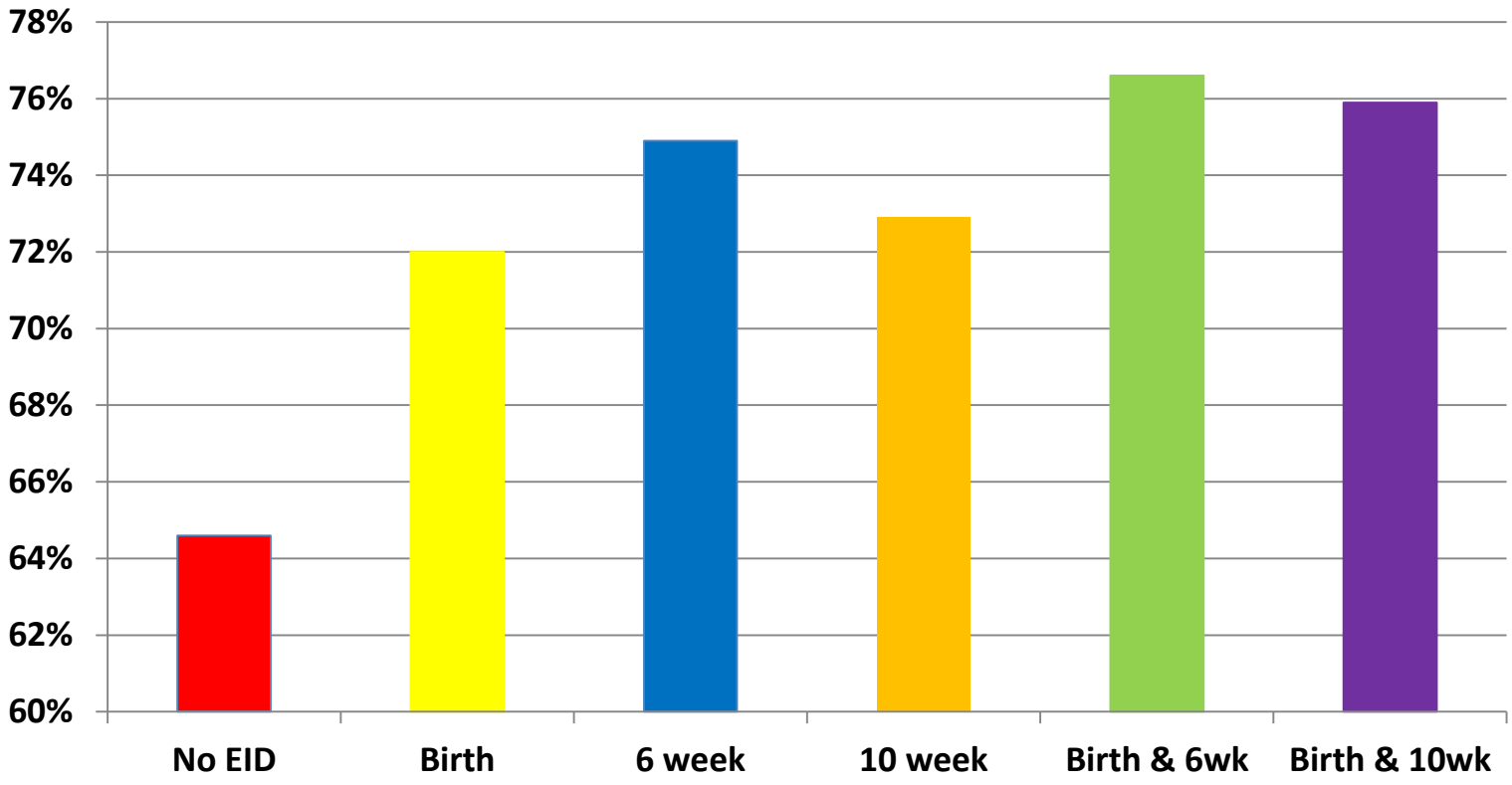
Francke, JID 2016

One-year Survival (HIV-infected): Testing Once



Francke, JID 2016

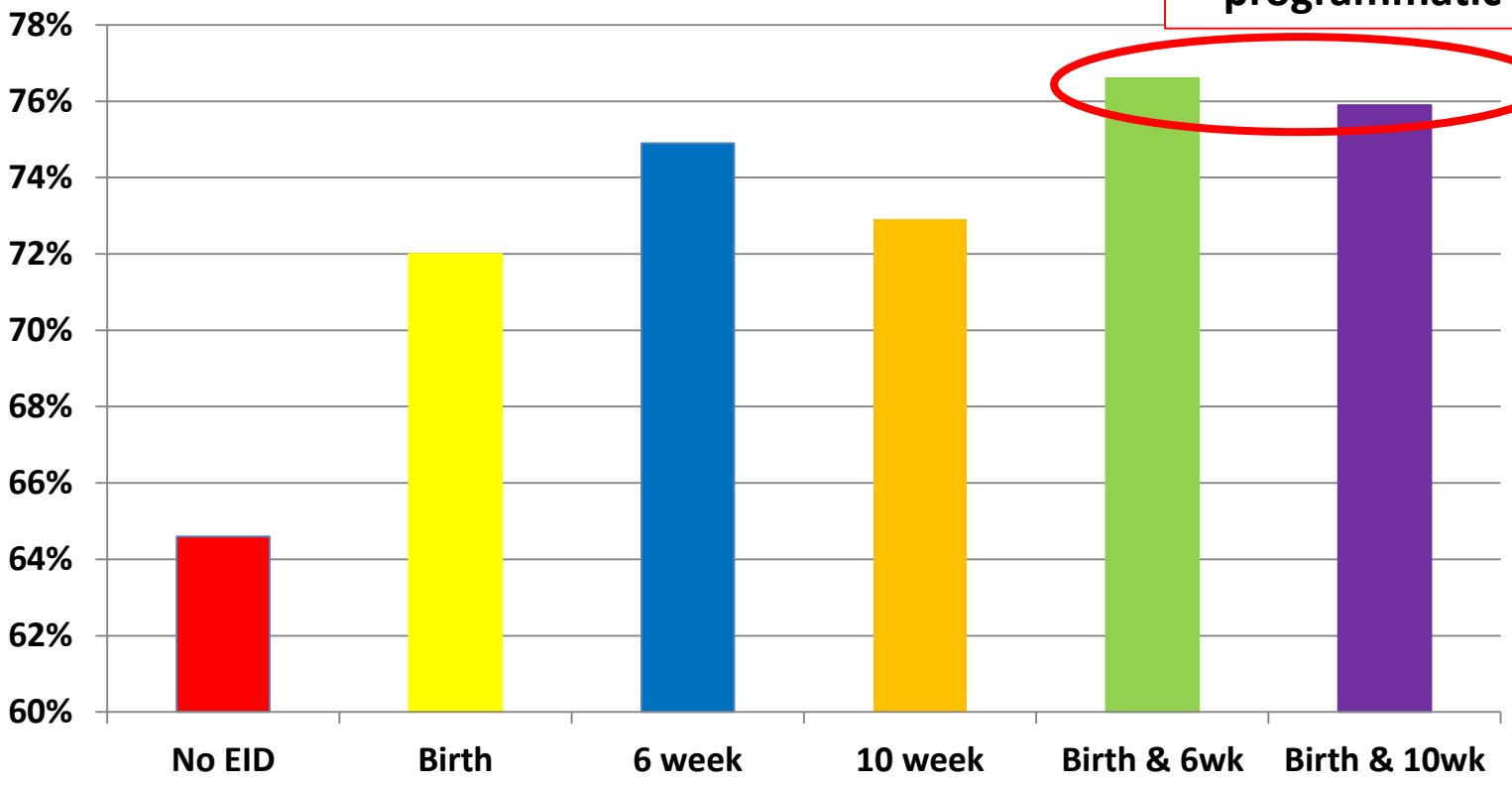
One-year Survival (HIV-infected): Testing Twice



Francke, JID 2016

One-year Survival (HIV-infected)

Choose based on programmatic factors



Francke, JID 2016

Additional Outcomes

- Short-term costs
- Long-term (lifetime) costs
- Life expectancy
- Lifetime projections: cost-effectiveness ratios in $/year of life saved (YLS)
  - No EID: Comparator
  - Birth: dominated (inefficient use of resources)

Francke, JID 2016

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- Lifetime projections: cost-effectiveness ratios in $/year of life saved (YLS)
  - No EID: Comparator
  - Birth: dominated (inefficient use of resources)
  - 6 weeks vs. no EID: $1,250/YLS
  - Birth & 6 weeks vs. 6 weeks: $2,900/YLS
- Less than 50% GDP (0.5 x $6,500 = $3,250)

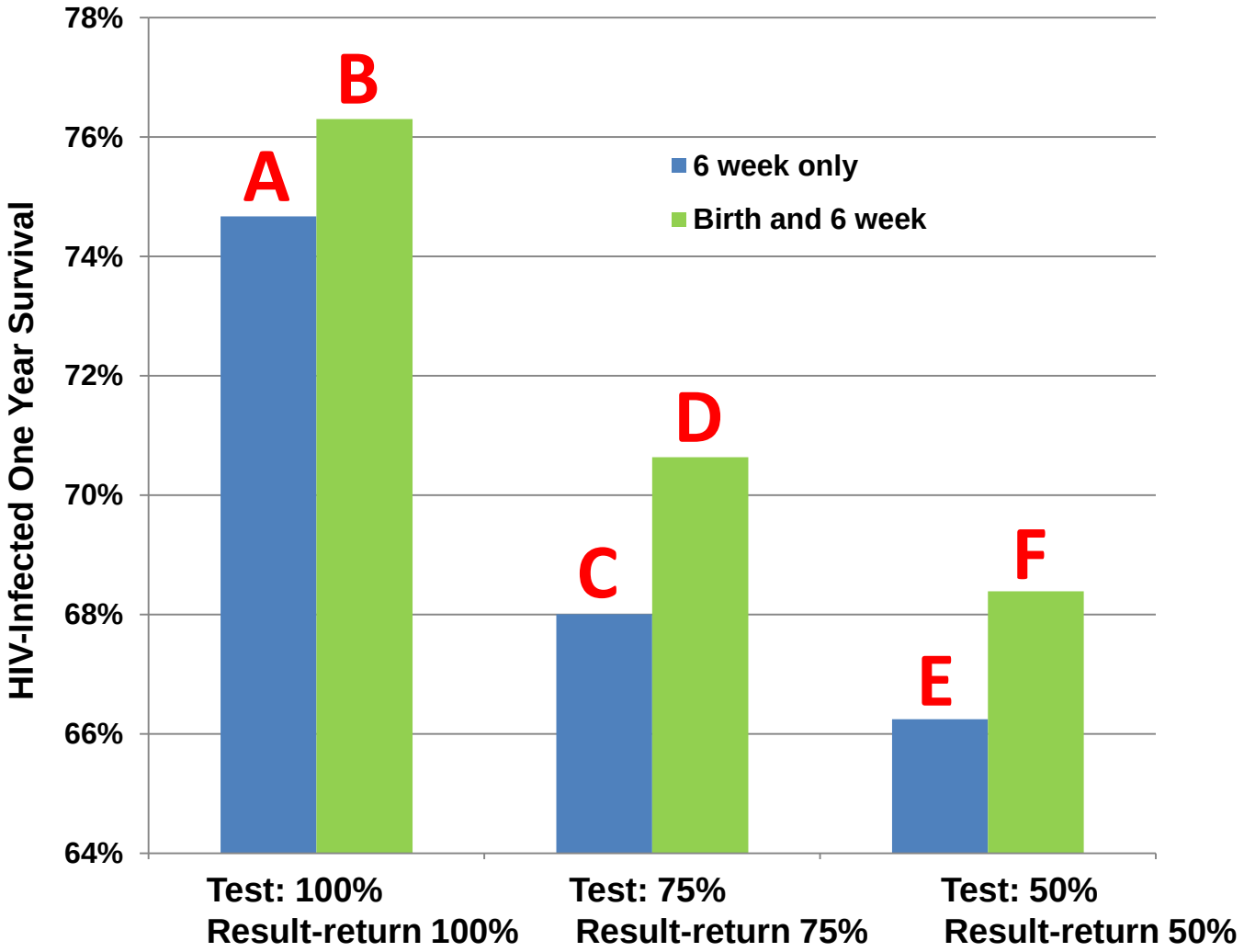
Francke, JID 2016

Key Findings (WHO 2015) - 1

- Testing once: 6 weeks is clinically and economically superior to birth or 10 weeks
- Testing twice: markedly improves outcomes and is cost-effective in South Africa, compared to 6 weeks alone

Francke, JID 2016

Capacity to Examine Tradeoffs in Implementation: Example



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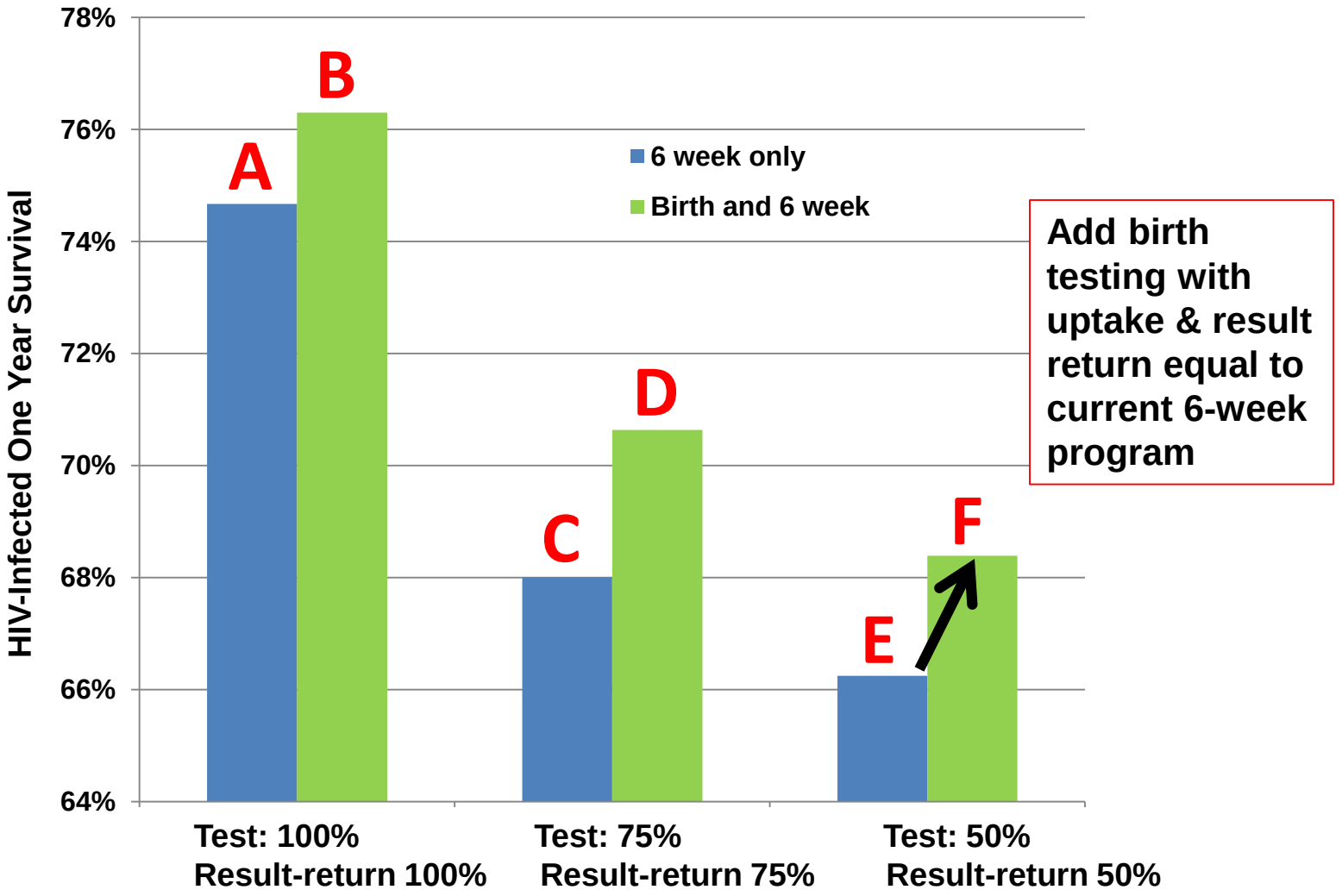

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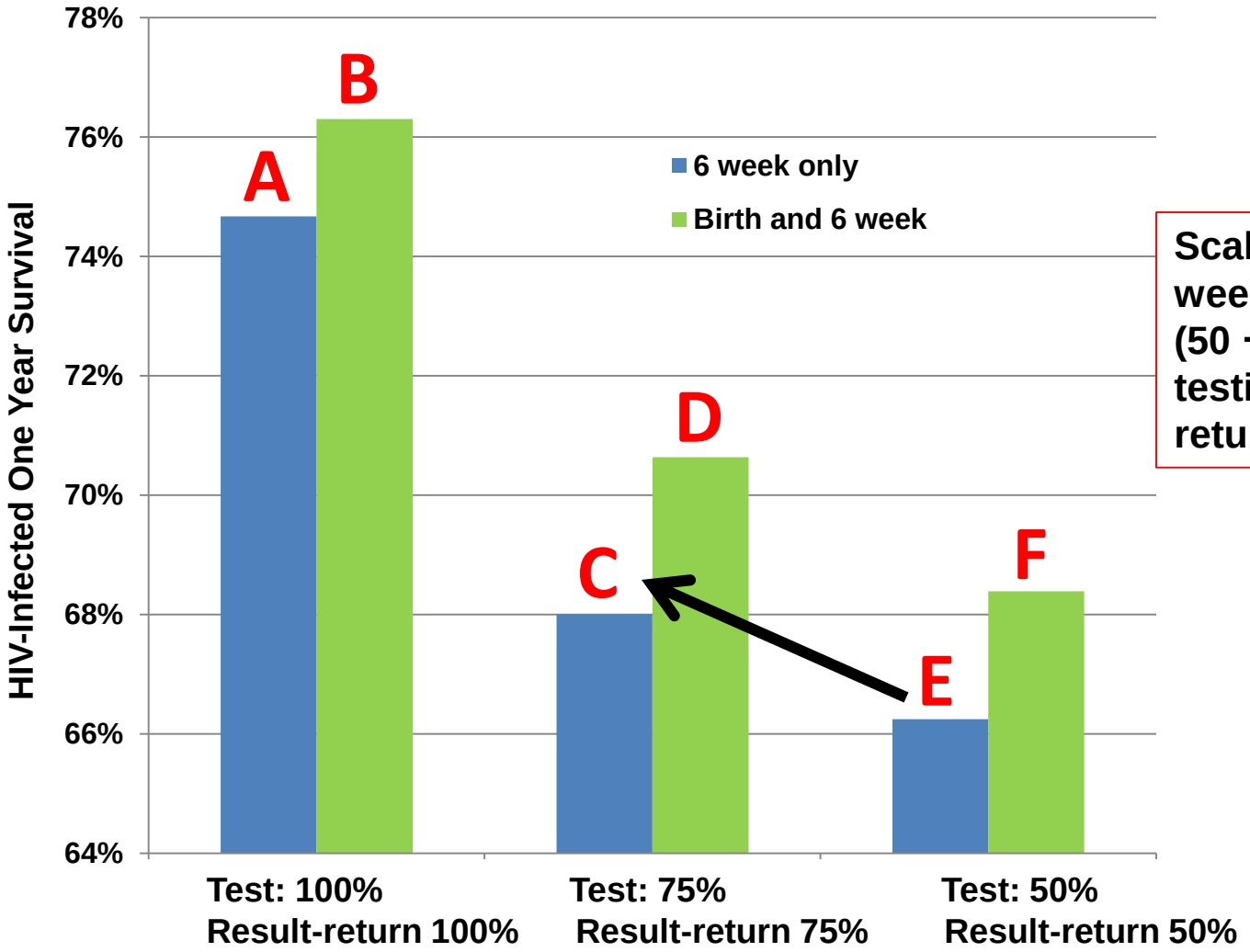

Scale up 6-week program (50 → 75% testing, result return)

Francke, JID 2016

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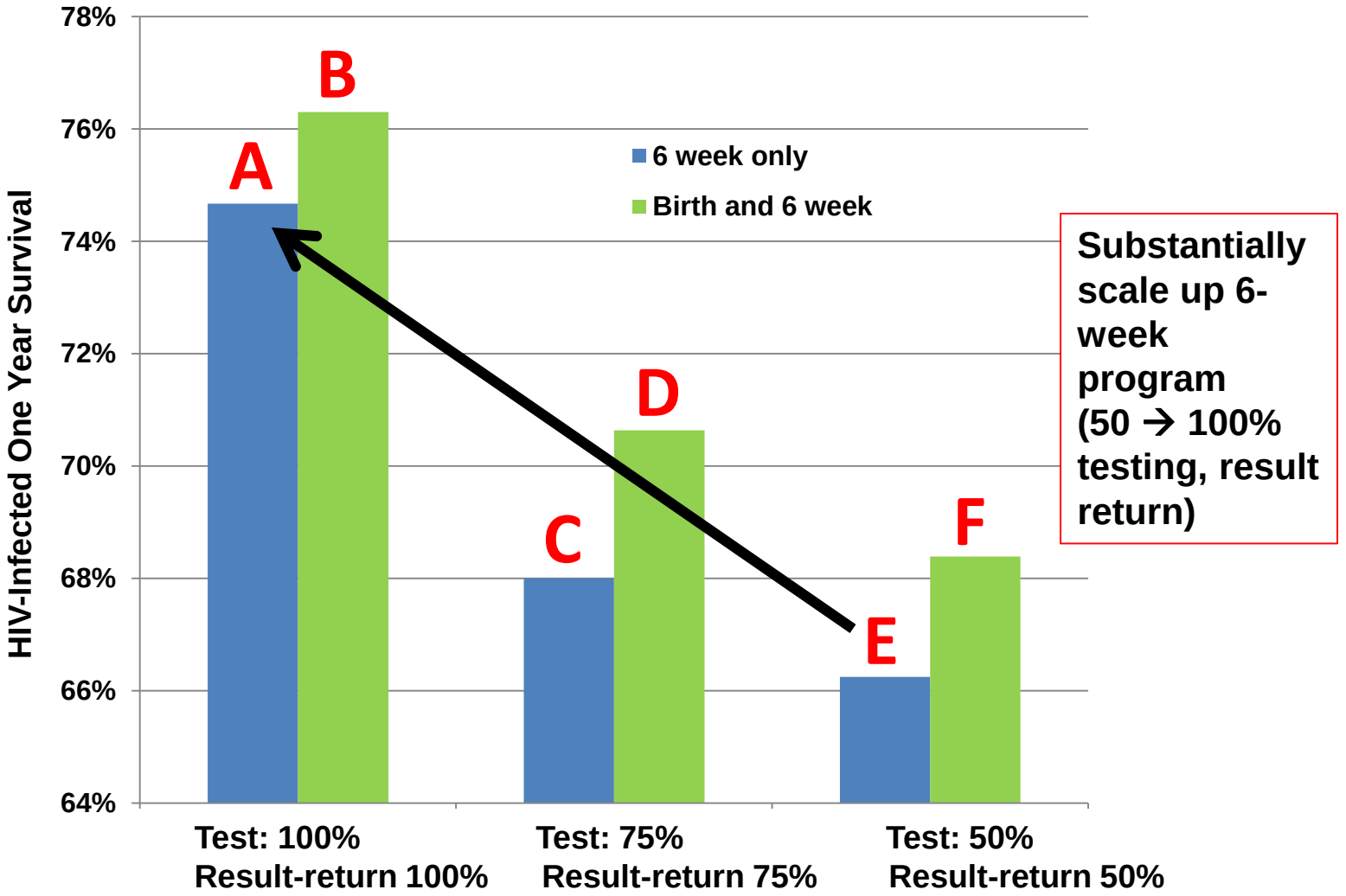

Francke, JID 2016

Key Findings (WHO 2015) - 2

- If scale-up costs are comparable, programs with incomplete 6-week EID coverage should scale up 6-week programs before adding birth testing

Francke, JID 2016

Key Findings (WHO 2015) - 3

- Avoiding loss to follow-up after birth testing is critical
  - Negative birth test only rules out intrauterine infection; later testing is needed to evaluate intrapartum and early postpartum infections
  - If >37% of infants with negative birth test fail to return at 6 weeks, survival benefits of adding birth testing are lost

Francke, JID 2016

Additional Analyses (IMPAACT, EGPAF, NIAID, NICHD, WHO, March of Dimes)

- EID
  - Confirmatory testing (Dunning)
  - Impact of PMTCT scale-up on the value of birth testing (Frank)
  - Point-of-care EID assays in Zimbabwe (Frank)
  - Screening for HIV exposure at immunization visits (Dunning)
- Pediatric and adolescent
  - First-line ART, NEVEREST3 and MONOD trials (Desmonde)
  - Adolescent HIV testing in the US (Neilan)
- PMTCT
  - Zimbabwe: reaching “eMTCT,” CE of Options A, B, B+
  - South Africa: point of care CD4, MCH-ART trial (Dugdale)
  - PROMISE sub-study (Dugdale)

Dunning, CROI/submitted, Frank, IAS/HIV pediatrics 2017; Desmonde, CROI 2017
Neilan, Submitted; Dugdale, ongoing; Ciaranello, PLoS Med 2012, CID 2013, AIDS 2015, PLoS ONE 2015

Thank You

CEPAC-Pediatric Team: Elaine Abrams, Ingrid Bassett, Alex Bulteel, Andrea Ciaranello, Sophie Desmonde, Caitlin Dugdale, Lorna Dunning, Simone Frank, Emily Hyle, Taige Hou, Valeriane Leroy, Landon Myer, Anne Neilan, Robert Parker, Kunjal Patel, Martina Penazzato, George Seage, Djora Soeteman, Milton Weinstein, Rochelle Walensky, Kenneth Freedberg

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Cost-effectiveness Analysis

- Cost-effective ≠ saves money
- Cost-effective ≠ cheap
- A more effective intervention is often more expensive. → Is the additional benefit worth the additional cost?
- "Value for money:" For any given health care budget, maximize the overall benefit conferred
- Many additional factors: feasibility, ethics/equity, political motivation, priority populations

Cost-effectiveness Analysis

- Two different outcomes
- Measured (e.g., from trial) or projected (modeled)
  - Cost (in dollars or other currency)
  - Effectiveness:
    - Life-years
    - Quality-adjusted life-years (QALYs)
    - (Infections averted, cases detected, patients initiated on ART, etc.)
- *Cost-effective: compared to what?*

Is It Worth It?

Incremental Health Effect (A → B)	Incremental Cost (A → B): −	Incremental Cost (A → B): +
+	*Yes*	Evaluate C/E Ratio
-	Evaluate C/E Ratio (?)	*No*

Cost-Effectiveness Ratios

- Incremental cost-effectiveness ratio (A → B):

$$\frac{\text{Additional Resource Use (\$)}}{\text{Additional Health Benefits (YLS)}}$$

- $/Year of life saved (YLS)
- Lower ratio: more cost-effective
- What are we willing to pay for 1 year of healthy life?
  - WHO: <1x GDP = very CE; <3x GDP = cost-effective
  - Too high: Move towards 50% GDP
  - Equity: Compare to current programs (ART: $500-1,500/YLS)

Commission on Macroeconomics and Health, WHO 2013; Schillcutt, Pharmacoeconomics 2010; Revill and Sculpher, BMJ 2013; Braithwaite, JIAS 2011; Woods, Value in Health 2016

Summary: CE Analysis

- One of many factors in decision-making
  - Affordability
  - Ethics, political will, feasibility, priority populations
- Formal methodology to assess value for investment and guide allocation of scarce resources
- In guideline development, a useful adjunct to empiric clinical data and model-projected clinical and epidemiologic outcomes

Schillcutt, Pharmacoeconomics 2010; Revill and Sculpher, BMJ 2013