



PEPFAR-Funded Evaluations: Overview of Care and Treatment and PMCT Evaluations



Dr. Stefan Wiktor
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A Public Health Questions Approach to Unifying Strategic Information

Are we doing them on a large enough scale?

Determining Collective Effectiveness

OUTCOMES & IMPACTS MONITORING

Are collective efforts being implemented on a large enough scale to impact the epidemic (coverage; impact)? • **Surveys & Surveillance**

Are we doing them right?

Monitoring & Evaluating National Programs

OUTCOMES

Are interventions working/making a difference?
• **Outcome Evaluation Studies**

OUTPUTS

Are we implementing the program as planned?
• **Outputs Monitoring**

ACTIVITIES

What are we doing?
• **Process Monitoring & Evaluation, Quality Assessments**

Are we doing the right things?

INPUTS

What interventions and resources are needed?
• **Needs, Resource, Response Analysis & Input Monitoring**

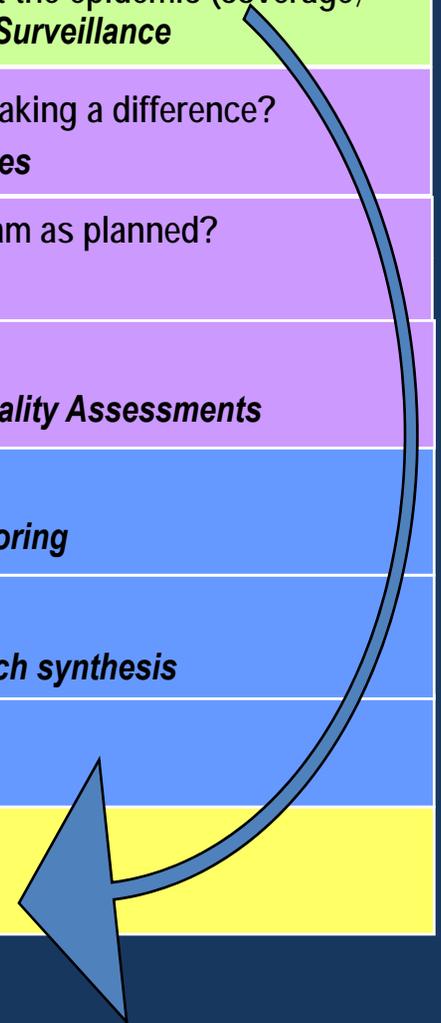
Understanding Potential Responses

What interventions can work (efficacy & effectiveness)?
• **Special studies, Operations res., Formative res. & Research synthesis**

What are the contributing factors?
• **Determinants Research**

Problem Identification

What is the problem?
• **Situation Analysis and Surveillance**



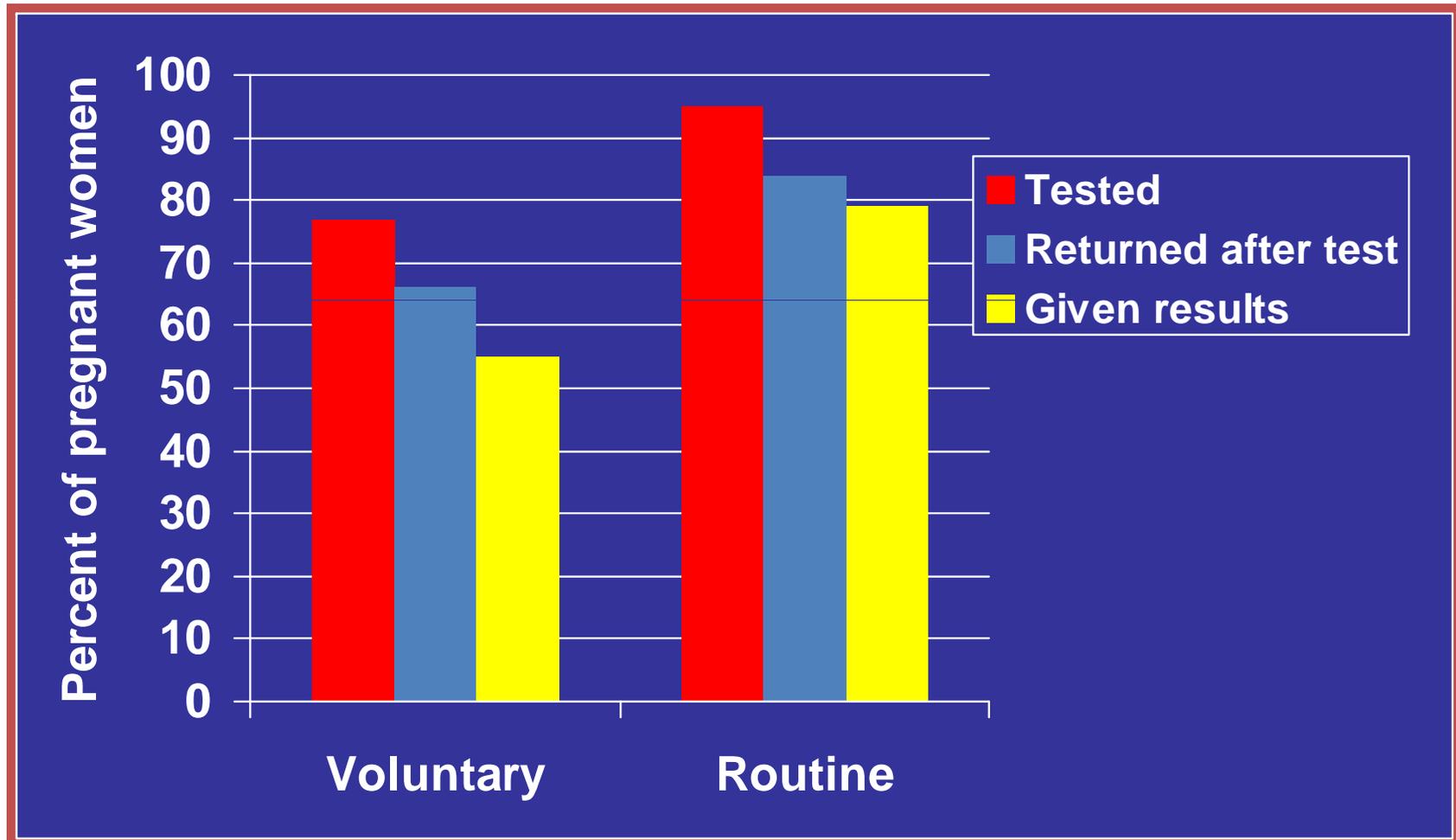


PMTCT in Botswana: Background

- 1999: Botswana started Africa's first free national PMTCT program
- By late 2002, PMTCT services available in all public ANC clinics at no cost
- Poor uptake: Only 49% of pregnant women tested for HIV
- 2003 survey indicated that women's knowledge of PMTCT predicted HIV test acceptance suggesting role for pre-test education as a factor to increase testing uptake
- 2004 CDC pilot in 4 large public antenatal clinics used new pre-test education system and "opt-out" routine testing



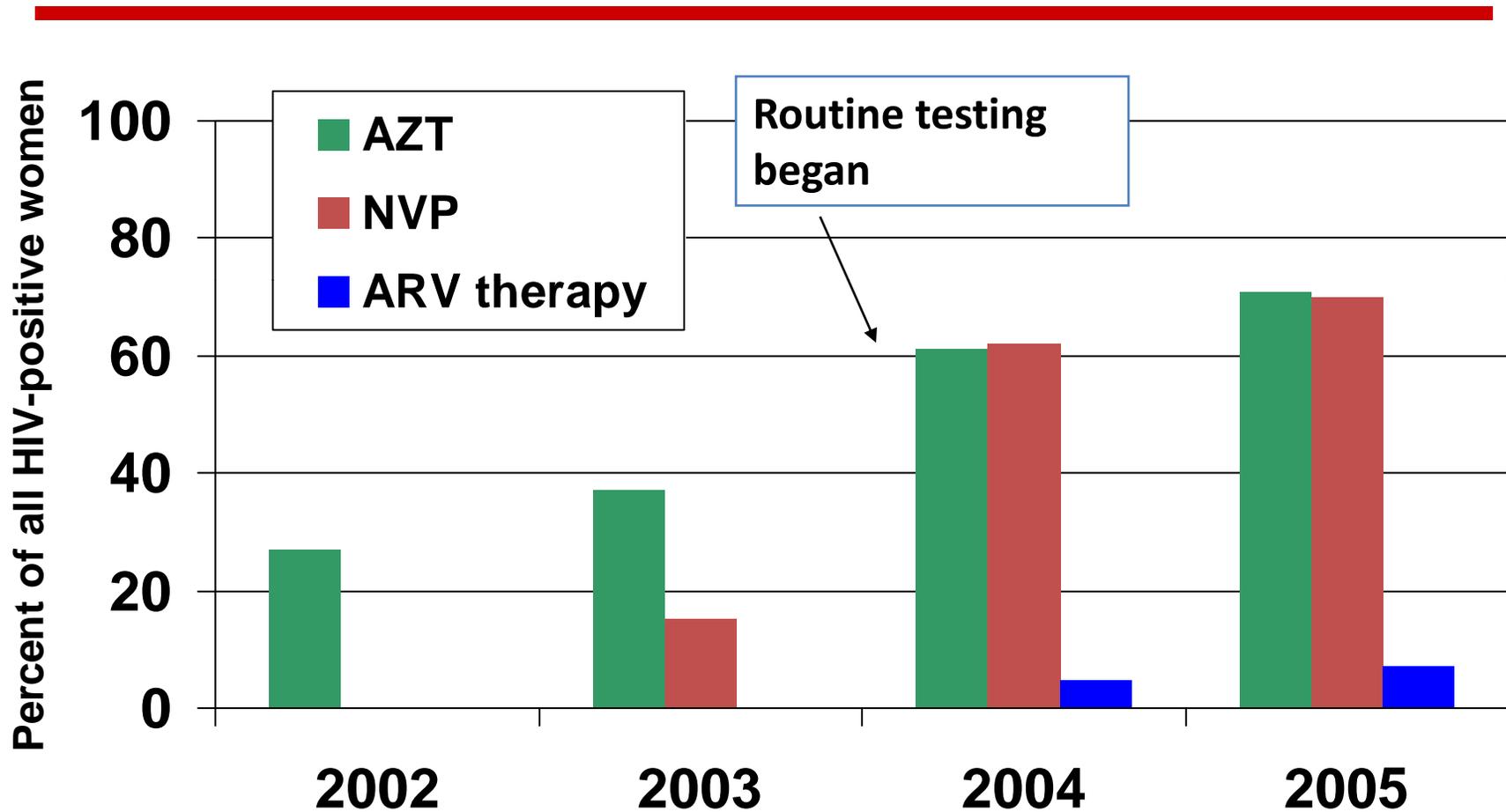
HIV testing in antenatal care using voluntary vs. routine testing strategies – Francistown, Botswana 2003-2004



(all differences $p < 0.05$)



Percent of all HIV-positive pregnant women receiving antiretrovirals during pregnancy, Botswana National PMTCT Program, 2002-2005





Broad Impact

- International recognition and broad dissemination
- Findings published in MMWR
- Data used in development of WHO generic PMTCT training curriculum
- Influenced many other country policies and programs

World AIDS Day — December 1, 2004

World AIDS Day 2004 focuses on the increasing vulnerability of women to human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) with the theme, Women, Girls, HIV, and AIDS. Globally, women account for nearly half of adults living with HIV. However, in some African countries, HIV prevalence is nearly five times greater among young women than men (1).

In the United States, women in racial/ethnic minority populations are especially vulnerable. In 2003, black and Hispanic women accounted for 25% of all U.S. women but 83% of women with diagnosed AIDS (2). Black women were 25 times more likely and Hispanic women six times more likely than white women to have diagnosed AIDS (2).

In 2002, surveys of U.S. adults indicated that one tenth had been tested for HIV during the previous year (3). CDC estimates one fourth of the approximately 900,000 persons living with HIV in the United States do not know that they are infected, are not receiving treatments, and might unknowingly transmit HIV to others (4).

CDC supports a combined biomedical and behavioral program to reduce HIV infections in the United States.

Introduction of Routine HIV Testing in Prenatal Care — Botswana, 2004

In 2003, approximately 37% of pregnant women in Botswana (2001 population: 1.7 million; approximately 40,000 births per year) (1) were infected with human immunodeficiency virus (HIV) (2). Since 2001, all prenatal clinics in Botswana have offered HIV screening and interventions for prevention of mother-to-child transmission of HIV (PMTCT), which can decrease vertical transmission of HIV from 35%–40% to 5%–10% (3). Historically, HIV testing in Botswana has been performed after individual pretest counseling, with patients actively choosing whether to be tested (i.e., an “opt-in” approach). In 2003, 52% of pregnant women receiving prenatal care nationwide learned their HIV status. In 2004, to increase use of free national PMTCT and antiretroviral treatment (ARV) programs, Botswana began routine, noncompulsory (i.e., “opt-out”) HIV screening in prenatal and other health-care settings. Concerns have been raised that routine testing in Africa might deter women from seeking prenatal care and might result in fewer women returning for their test results and HIV care after testing. To assess the early impact of routine testing on HIV-test accep-





The PEARL Study

- PMTCT Effectiveness in Africa:
Research and Linkages to Care
and Treatment
 - UAB – CIDRZ (Zambia)
 - U. Bordeaux – PAC-CI (Cote d'Ivoire)
 - U. Cape Town (RSA)
 - EGPAF and CBCHB (Cameroon)
- Elizabeth Stringer, MD, FACOG
 - Associate Professor of Obstetrics and Gynecology, UAB, Centre for Infectious Disease Research in Zambia (CIDRZ)
- 4-country effectiveness evaluation
- Facilities and their catchment populations randomly identified in each country
- Facility-based evaluations
 - Cord Blood Surveillance
 - Facility Survey
- Community-based evaluations
 - Community Survey
- Cost-effectiveness evaluation
- Funding:
 - PEPFAR - CDC-GAP (ZM, CI, RSA)
 - EGPAF (Cam)



Coverage of Nevirapine-Based Services to Prevent Mother-to-Child HIV Transmission in 4 African Countries

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IN 2001, A SPECIAL SESSION OF THE United Nations General Assembly set an ambitious goal for curbing the global spread of pediatric human immunodeficiency virus (HIV)—a 50% reduction in new infections by 2010.¹ Such an effort would require not only new scientific discoveries, but also substantial policy work, mobilization of huge new resources, and large-scale implementation of services in some

Context Few studies have objectively evaluated the coverage of services to prevent transmission of human immunodeficiency virus (HIV) from mother to child.

Objective To measure the coverage of services to prevent mother-to-child HIV transmission in 4 African countries.

Design, Setting, and Patients Cross-sectional surveillance study of mother-infant pairs using umbilical cord blood samples collected between June 10, 2007, and October 30, 2008, from 43 randomly selected facilities (grouped as 25 service clusters) providing delivery services in Cameroon, Côte d'Ivoire, South Africa, and Zambia. All sites used at least single-dose nevirapine to prevent mother-to-child HIV transmission and some sites used additional prophylaxis drugs.

Main Outcome Measure Population nevirapine coverage, defined as the proportion of HIV-exposed infants in the sample with both maternal nevirapine ingestion (confirmed by cord blood chromatography) and infant nevirapine ingestion (confirmed by direct observation).

Results A total of 27 893 cord blood specimens were tested, of which 3324 were HIV seropositive (12%). Complete data for cord blood nevirapine results were available on 3196 HIV-seropositive mother-infant pairs. Nevirapine coverage varied significantly by site (range: 0%-82%). Adjusted for country, the overall coverage estimate was 51% (95% confidence interval [CI], 49%-53%). In multivariable analysis, failed coverage of nevirapine-based services was significantly associated with maternal age younger than 20 years (adjusted odds ratio [AOR], 1.44; 95% CI, 1.18-1.76) and maternal age between 20 and 25 years (AOR, 1.28; 95% CI, 1.07-1.54) vs maternal age of older than 30 years; 1 or fewer antenatal care visits (AOR, 2.91; 95% CI, 2.40-3.54), 2 or 3 antenatal care visits (AOR, 1.93; 95% CI, 1.60-2.33), and 4 or 5 antenatal care visits (AOR, 1.56; 95% CI, 1.34-1.80) vs 6 or more antenatal care visits; vaginal delivery (AOR, 1.22; 95% CI, 1.03-1.44) vs cesarean delivery; and infant birth weight of less than 2500 g (AOR, 1.34; 95% CI, 1.11-1.62) vs birth weight of 3500 g or greater.

Conclusion In this random sampling of sites with services to prevent mother-to-child HIV transmission, only 51% of HIV-exposed infants received the minimal regimen of single-dose nevirapine.

JAMA. 2010;304(3):293-302

www.jama.com



Infant dose not administered
(n=120, 4%)

Documentation not available
(n=240, 8%)

Testing not offered
(n=273, 9%)

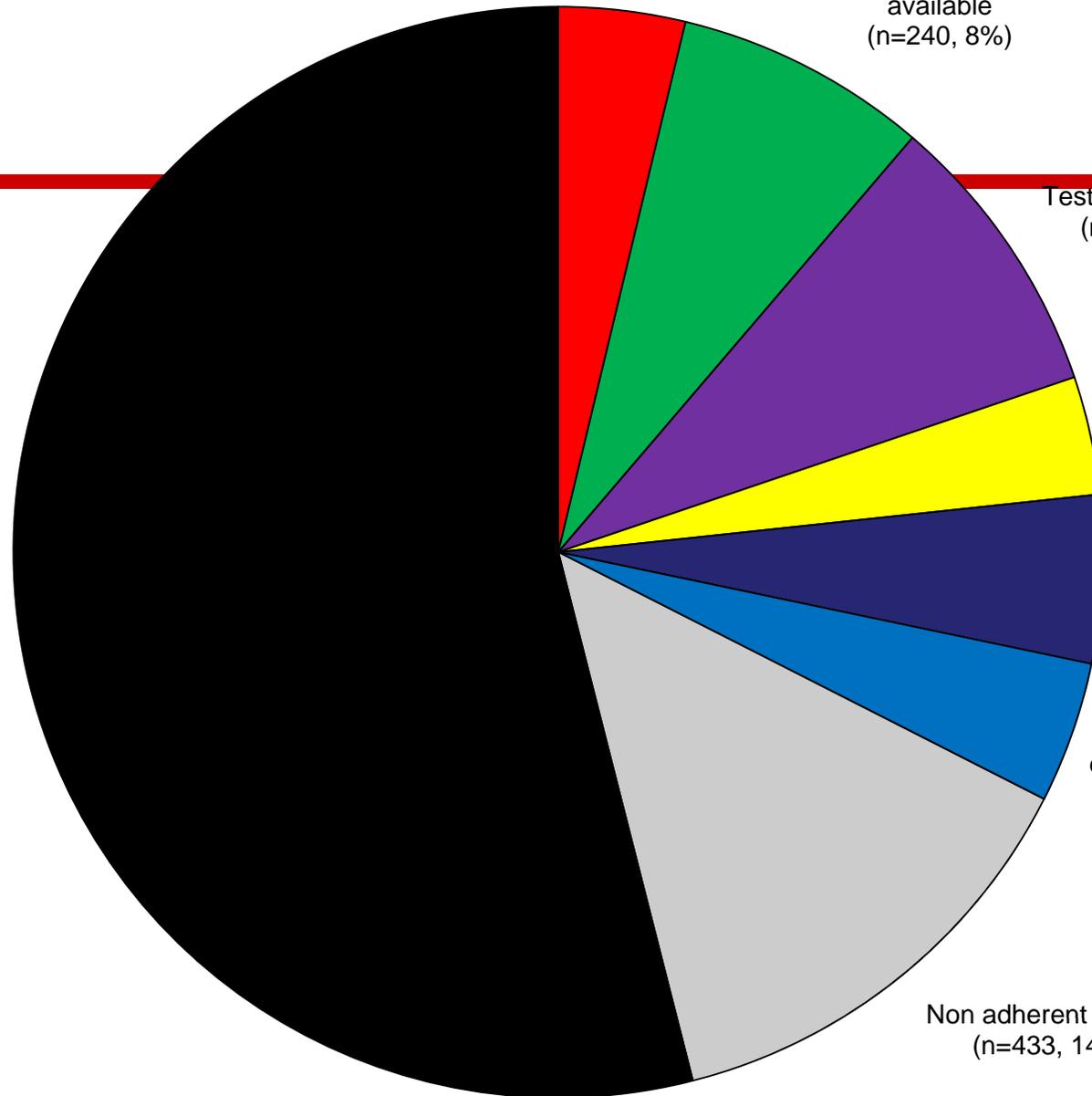
Testing not Accepted
(n=112, 4%)

Positive result not received
(n=159, 5%)

Maternal NVP not dispensed
(n=134, 4%)

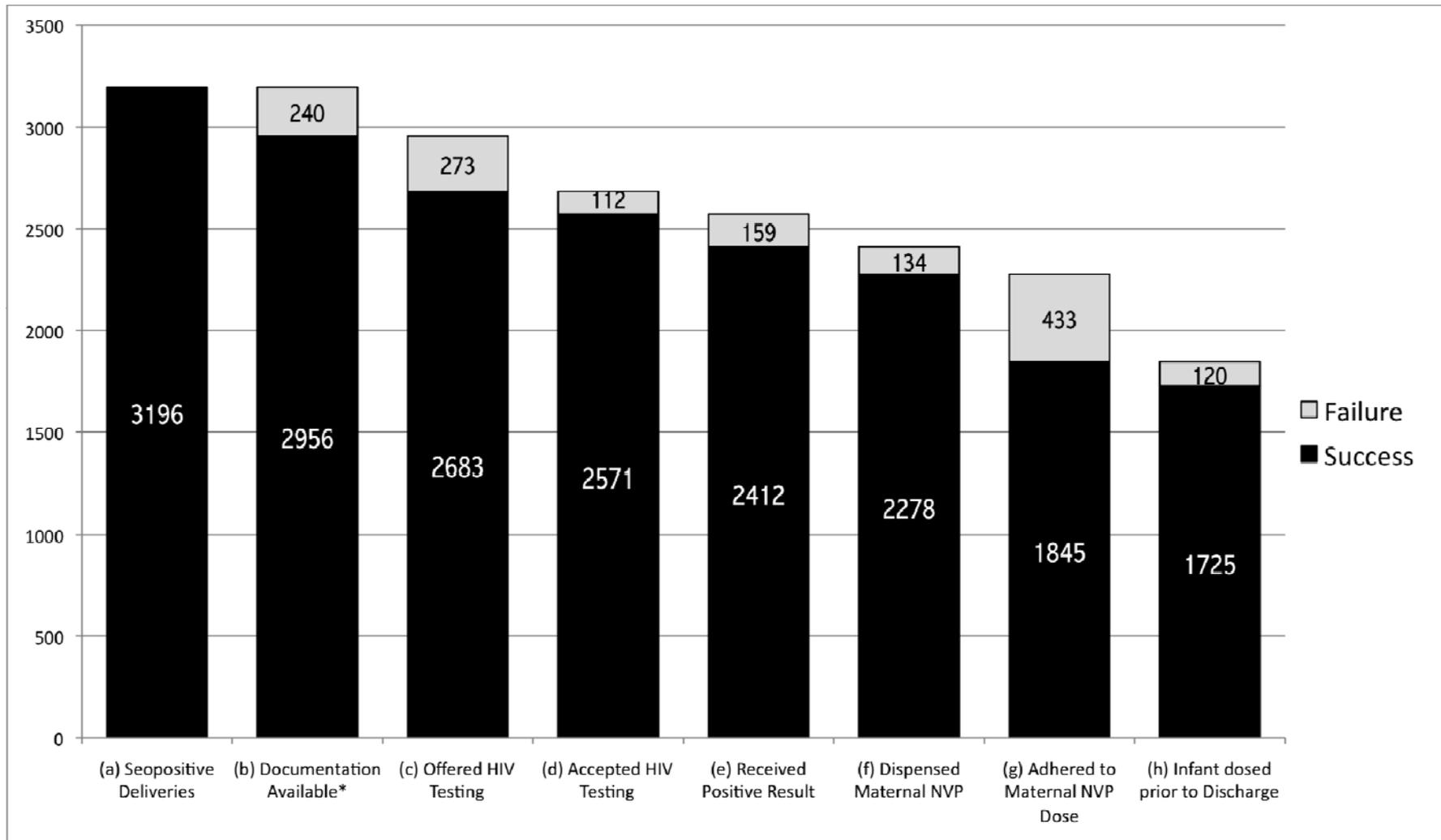
Non adherent to NVP
(n=433, 14%)

Successful prophylaxis
(n=1725, 54%)





PMTCT Coverage – all Countries



(128 no NVP results)



Conclusions

- In order for PMTCT to work, each mother-infant pair must negotiate a complex cascade of events
- Failures occur along each step of this pathway and should be systematically targeted
- Fixing the “coverage problem” would prevent as many infant HIV deaths as would rolling out more effective regimens – and should be taken just as seriously

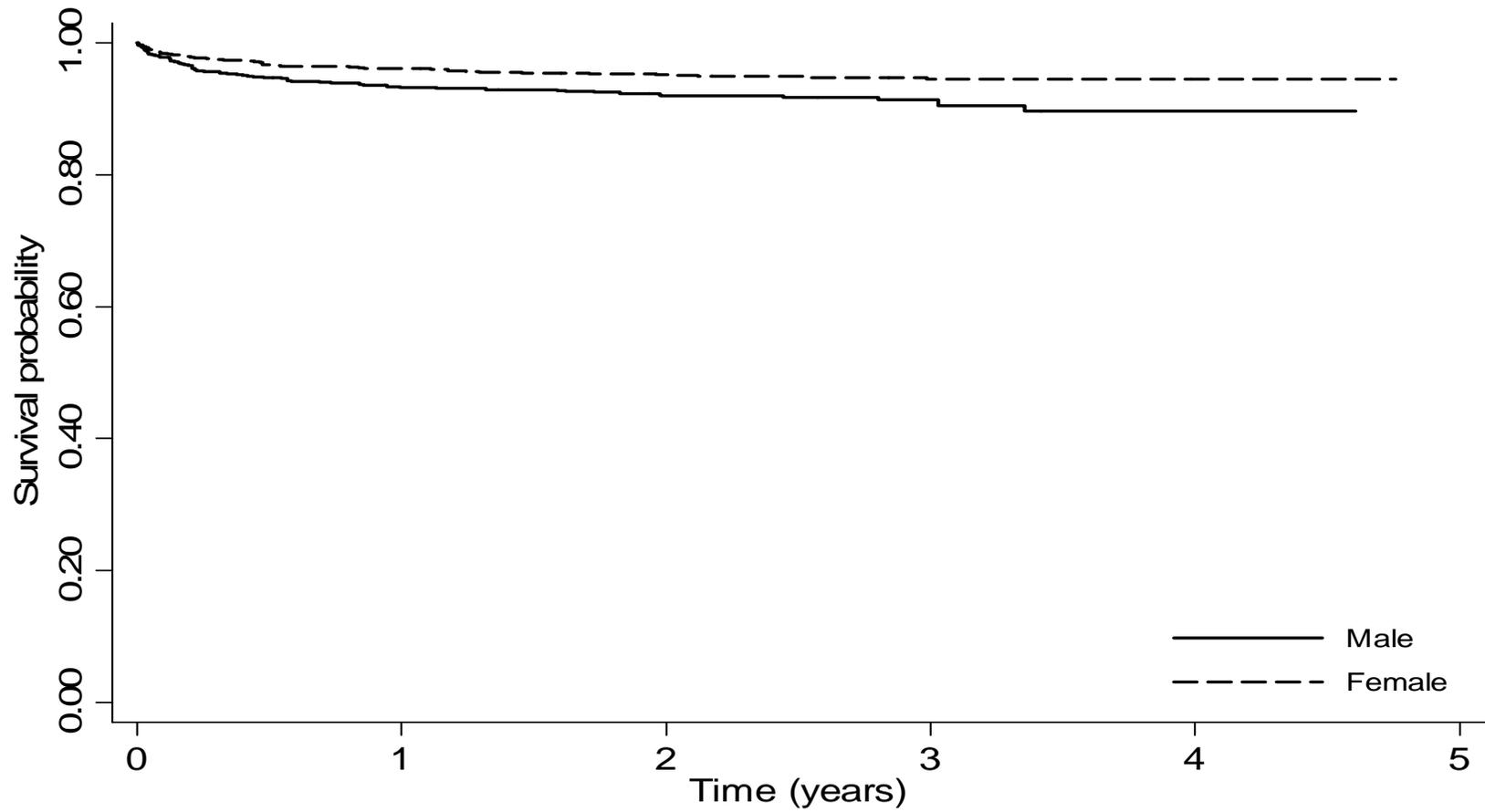


Treatment Outcomes of Adult Patients Enrolled in Mozambique's Rapidly Expanding Antiretroviral Therapy Program during 2004-2007

- In Mozambique, numbers of adult patients enrolled on antiretroviral therapy (ART) increased nearly 16-fold, from <5,000 to 79,500, during 2004-2007
- Nationally representative treatment outcomes not yet reported
- In 2008, we conducted a nationally-representative retrospective cohort evaluation, to:
 - Estimate mortality rates and attrition rates [numbers of patients dead or lost-to-follow-up (LTFU) per 100 person-years]
 - Identify baseline characteristics associated with outcomes
 - Describe CD4⁺ T-cell gains and weight gains over time



Survival Stratified By Sex



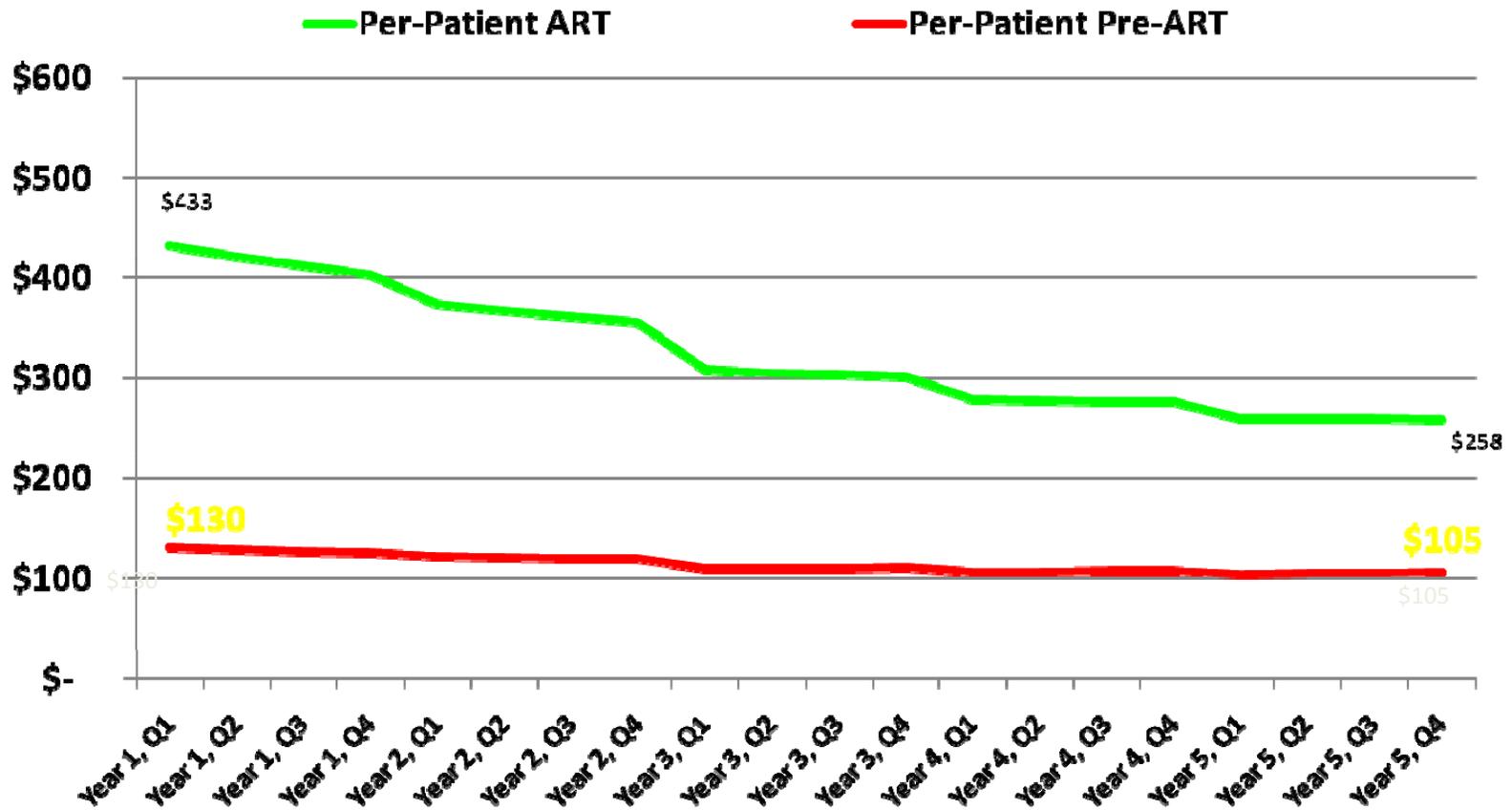


PEPFAR ART Costing Project: Background

- Centrally and country funded Public Health Evaluation study
 - 63 Sites in seven countries (Nigeria, Ethiopia, Uganda, Botswana, Vietnam, Mozambique, Tanzania)
 - Collaboration between CDC, USAID and PEPFAR country program
- Objectives
 - Estimate the annual per-patient cost of out-patient HIV treatment
 - Inform PEPFAR planning and resource requirements for treatment scale-up
 - Identify factors that drive costs
 - Create cost projection models for use at country and OGAC levels



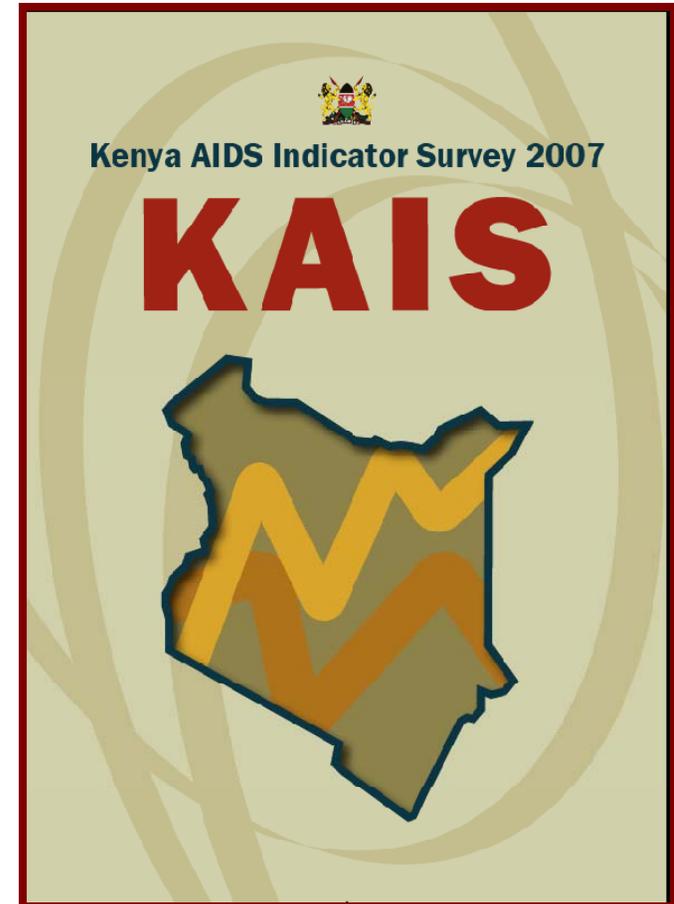
Per-Patient Costs (PEPFAR, Direct) over 5 years, Mozambique





Kenya AIDS Indicator Survey

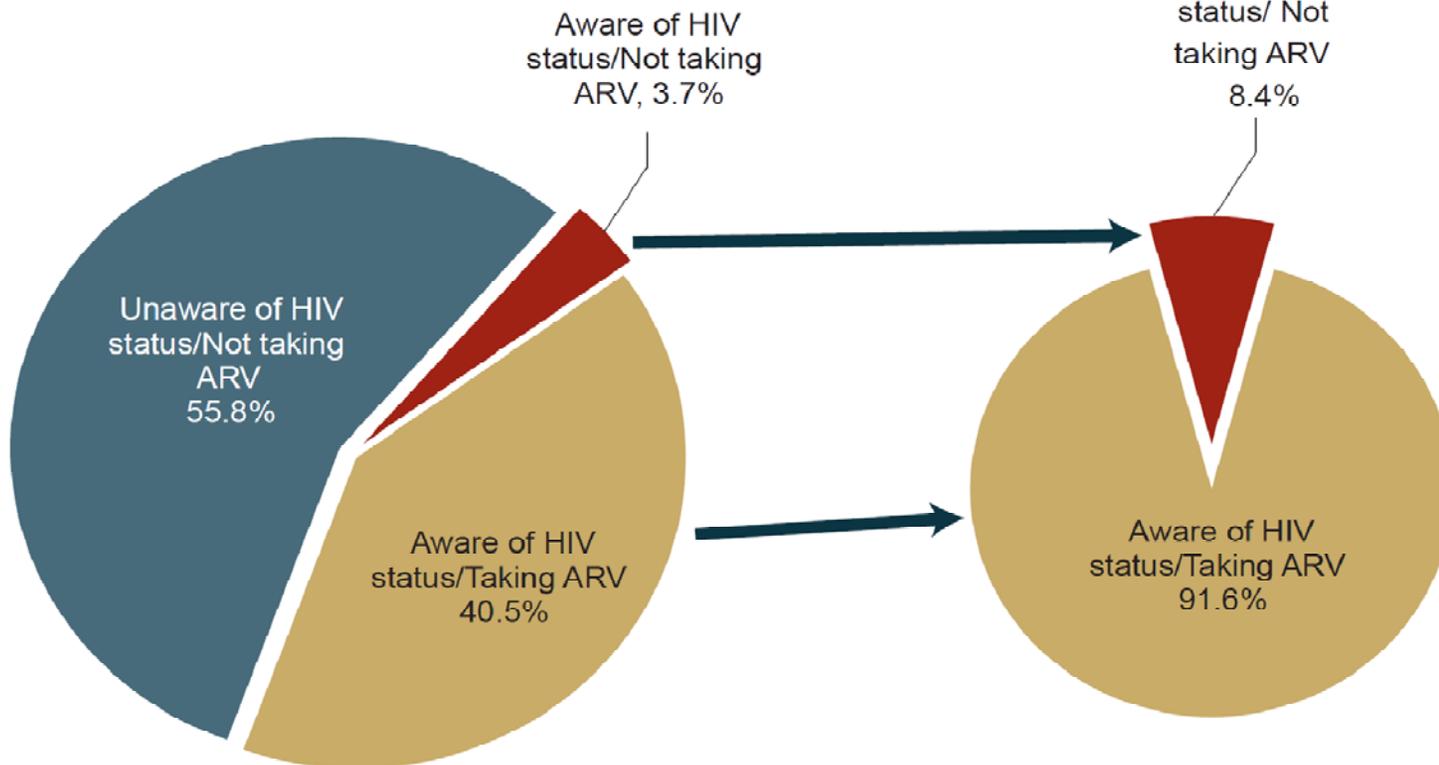
- Nationally representative household survey of persons aged 15-64
- Informed consent for interview, blood draw, storage
- Included testing for HIV, CD4, HSV-2, and syphilis
- Test results returned to patients





Coverage of Antiretroviral (ARV) Therapy among Eligible HIV-infected Participants

Eligibility criterion: $CD4 \leq 250$ cells/ μ l





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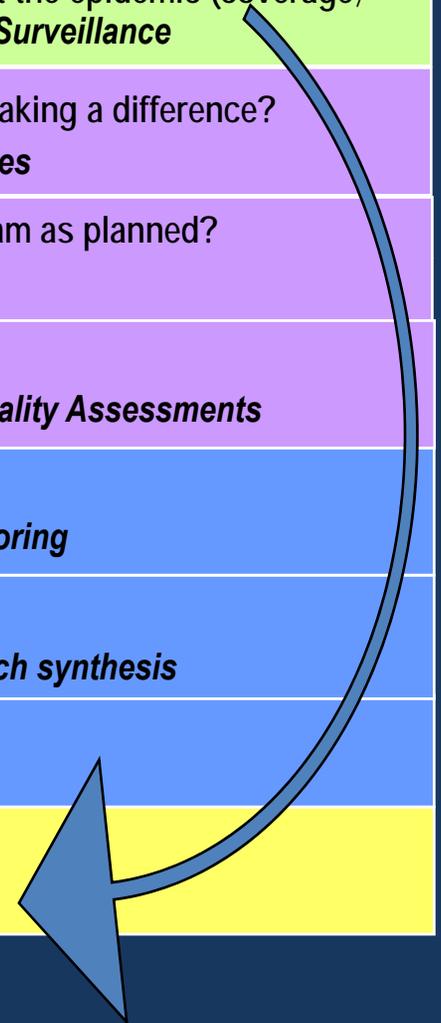
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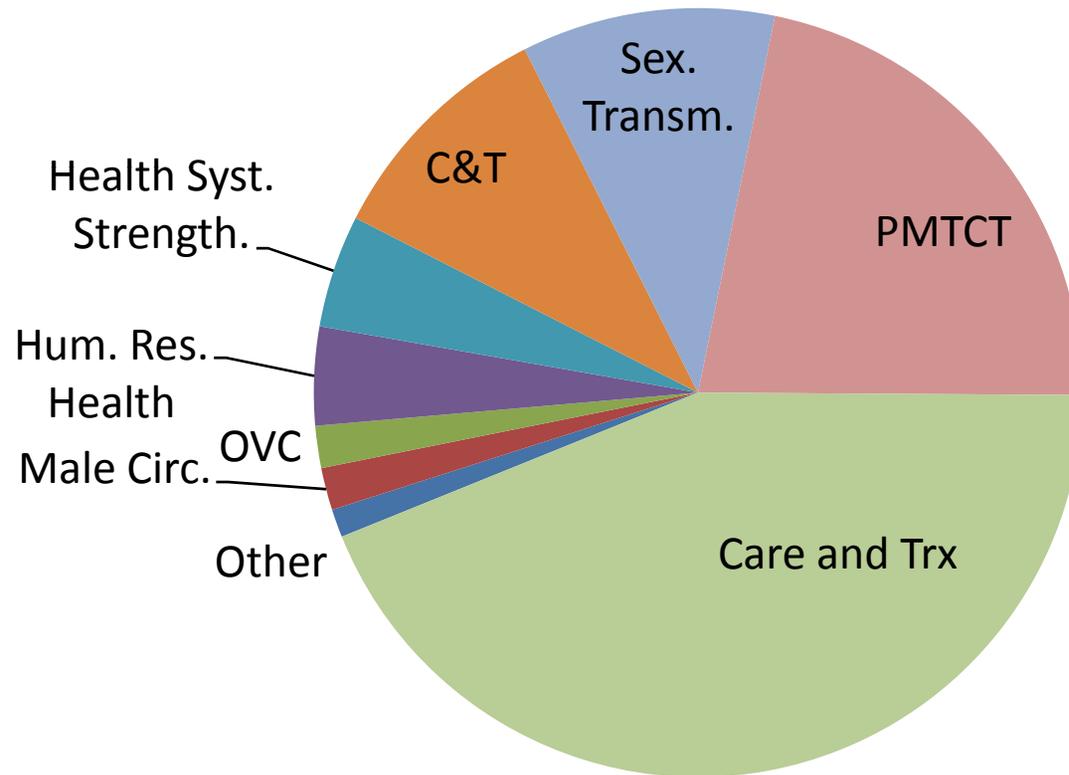
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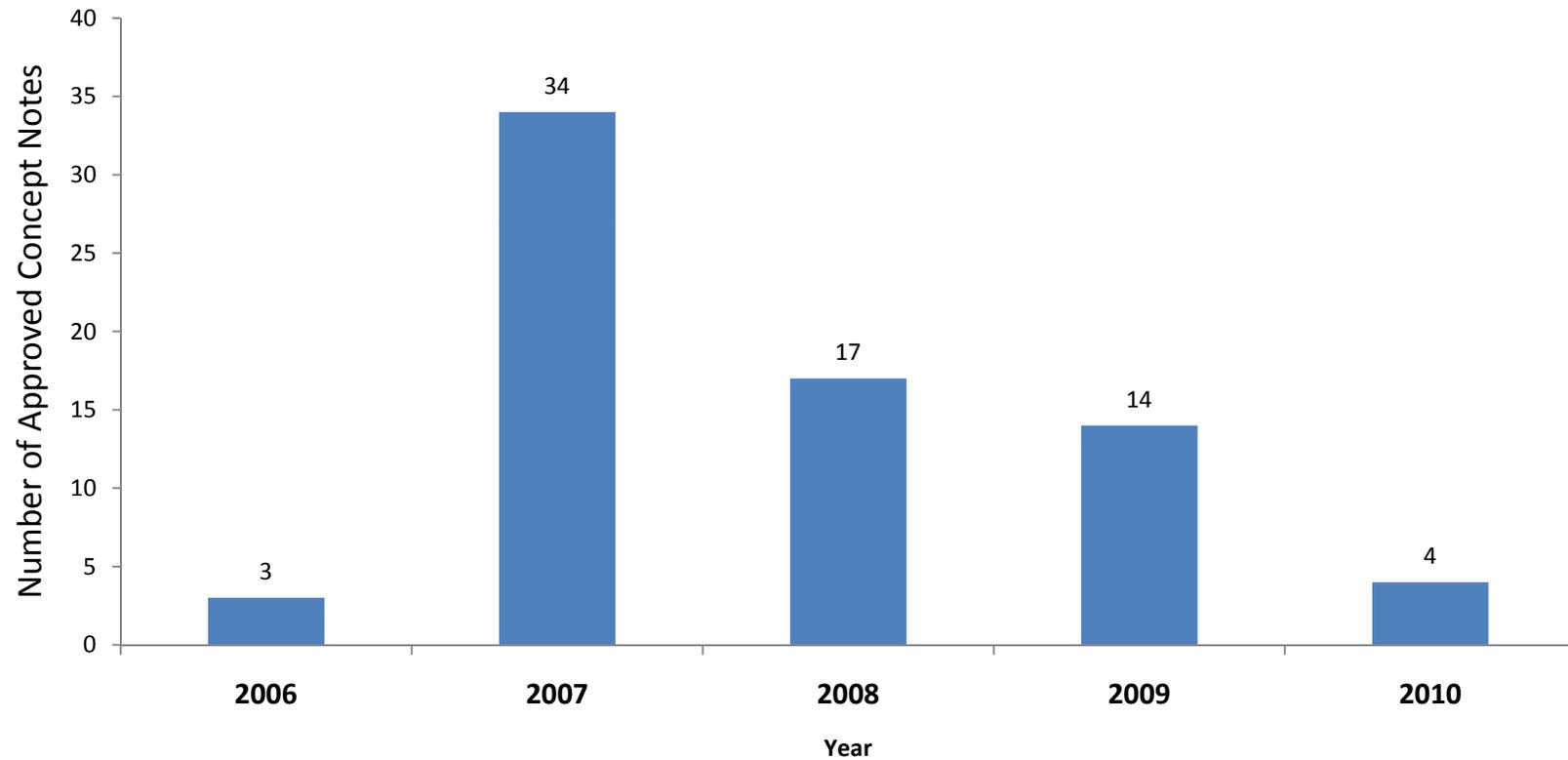


Distribution of PHEs by program area (n=169)



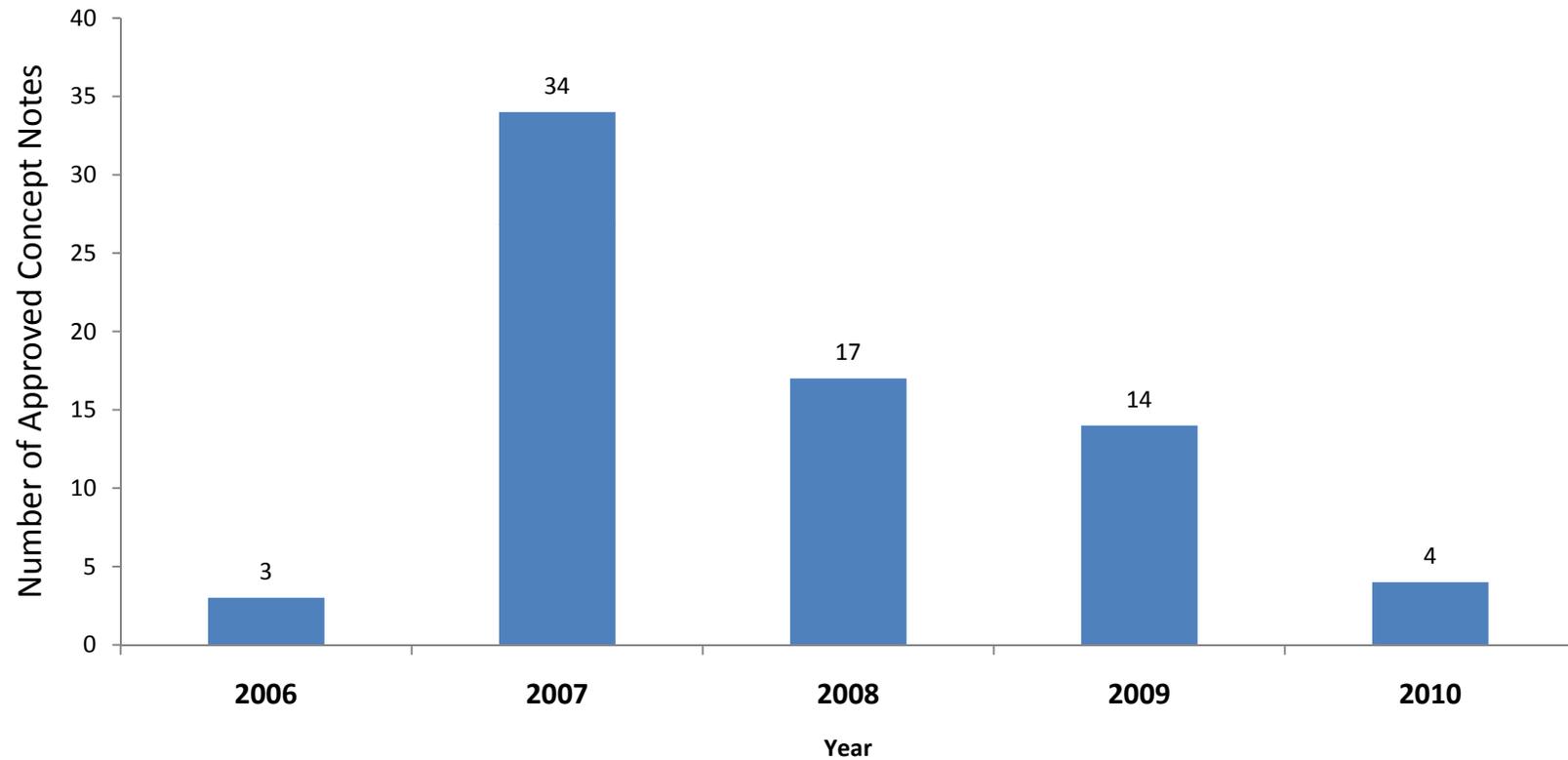


Distribution of approved CART PHE Concepts by Year (n=72)





Distribution of approved CART PHE Concepts by Year (n=72)

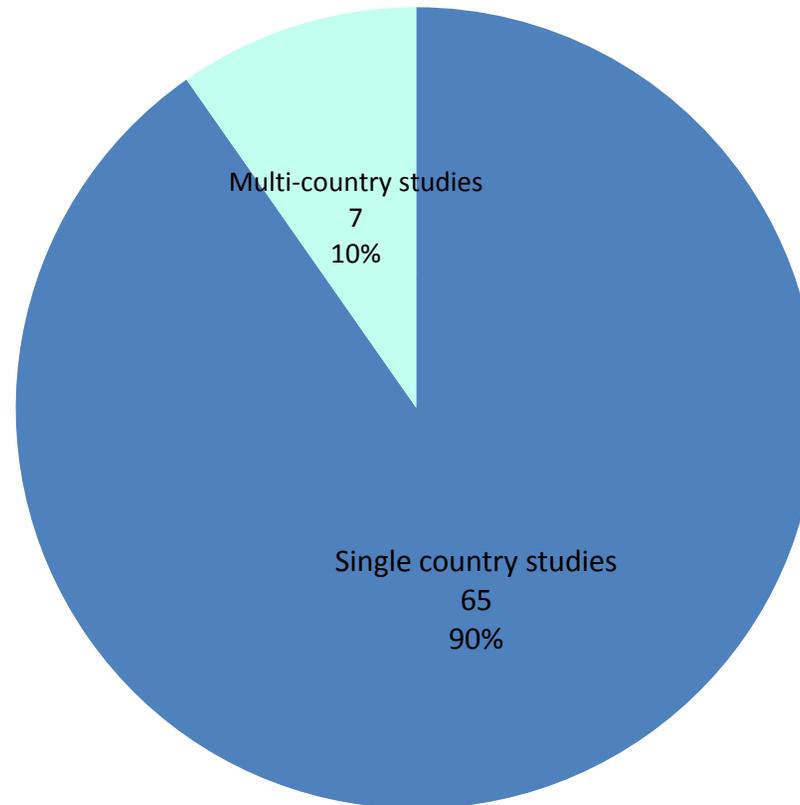




CART PHE Studies Single Country v. Multi-Country

(2006-2010)

n=72*

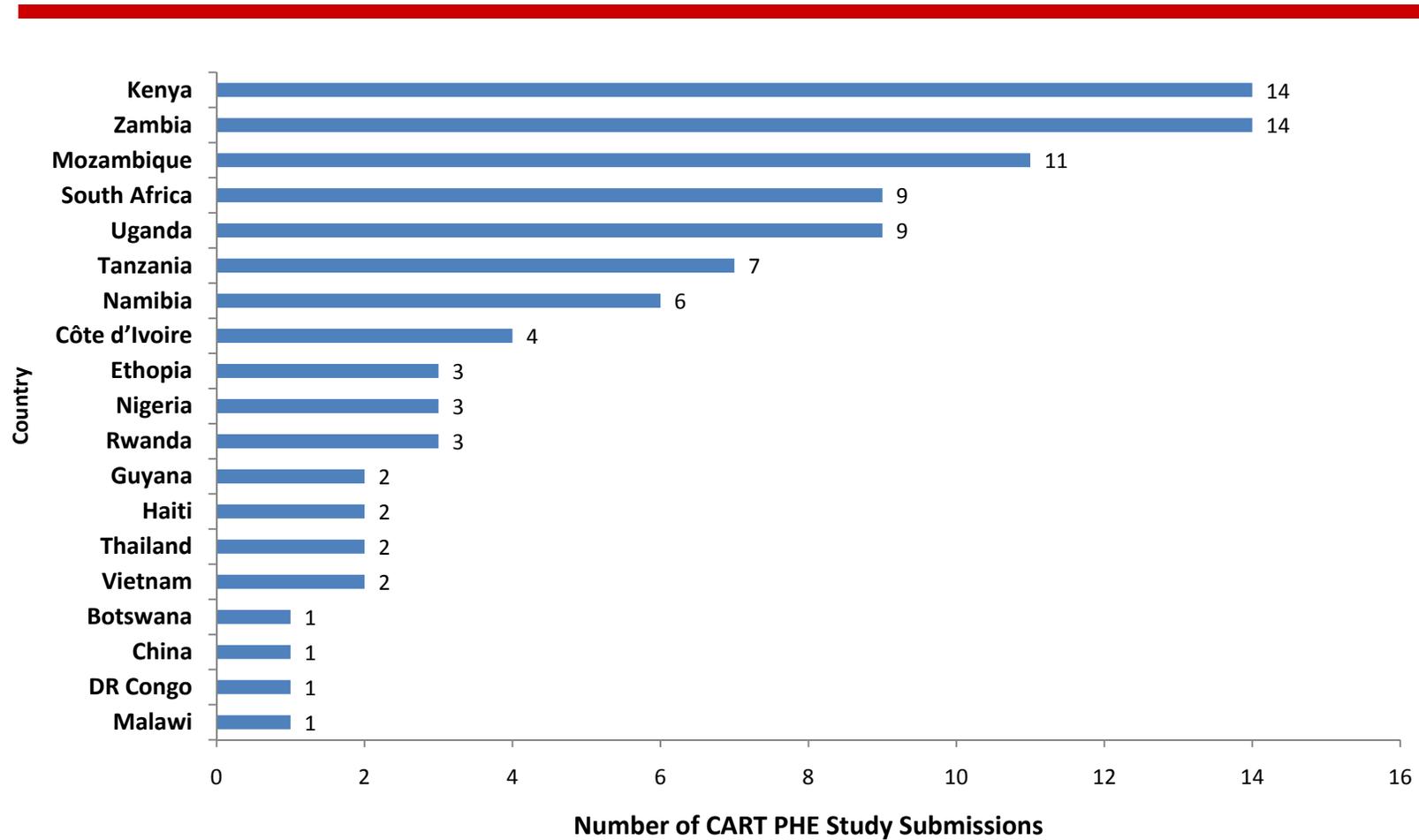


*Multi-country protocols are listed as separate submissions by protocol title



Distribution of CART PHE Studies by Country

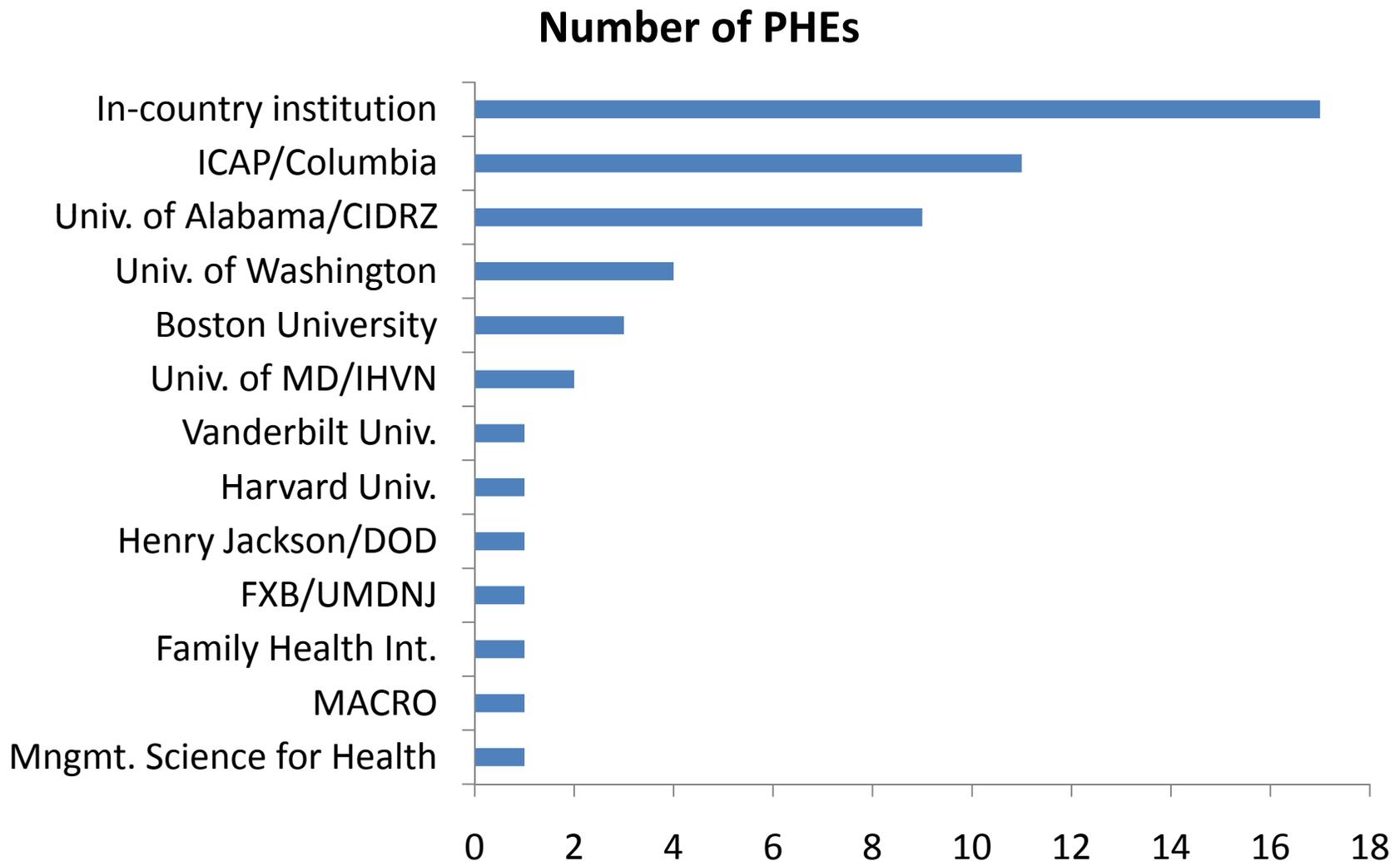
2006-2010 (n=95*)



*Multi-country studies are listed with all country locations of study

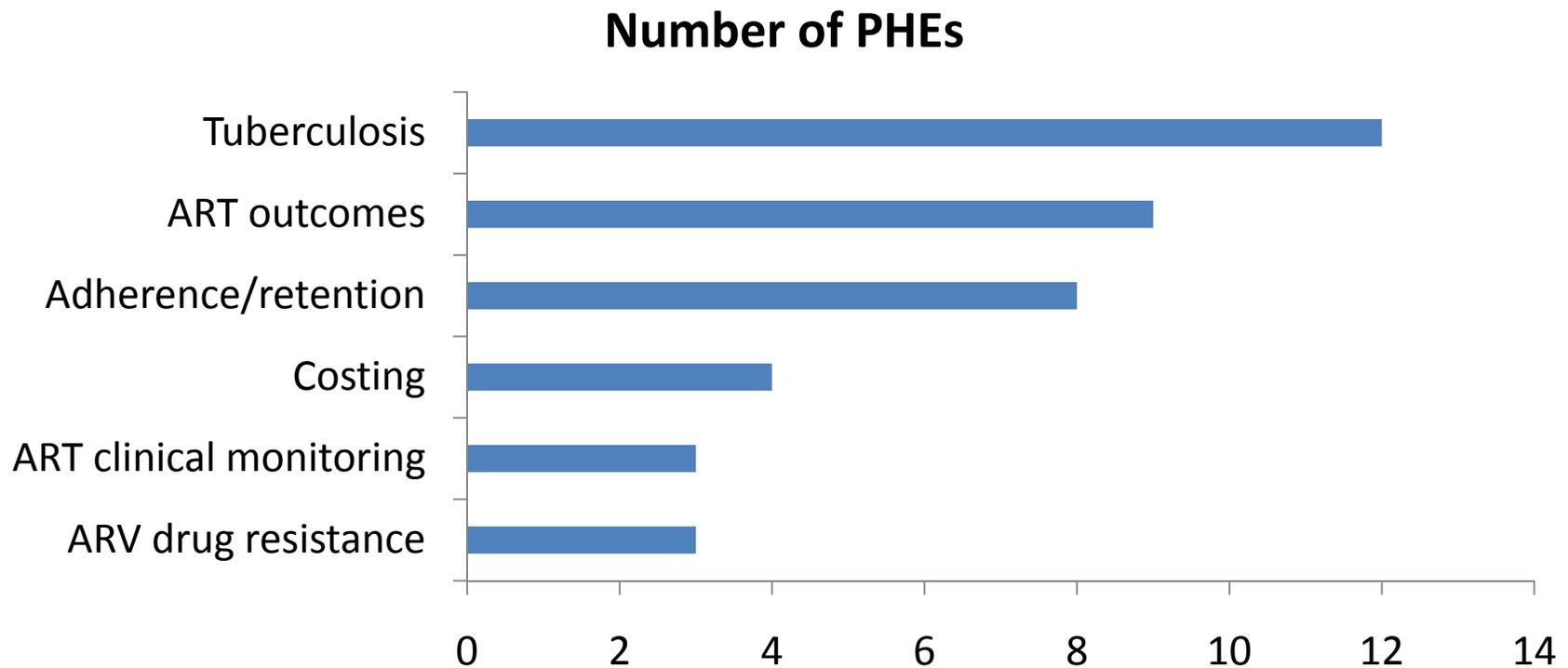


Distribution of implementing partners: Care and treatment PHEs





Distribution of implementing partners: Care and treatment PHEs

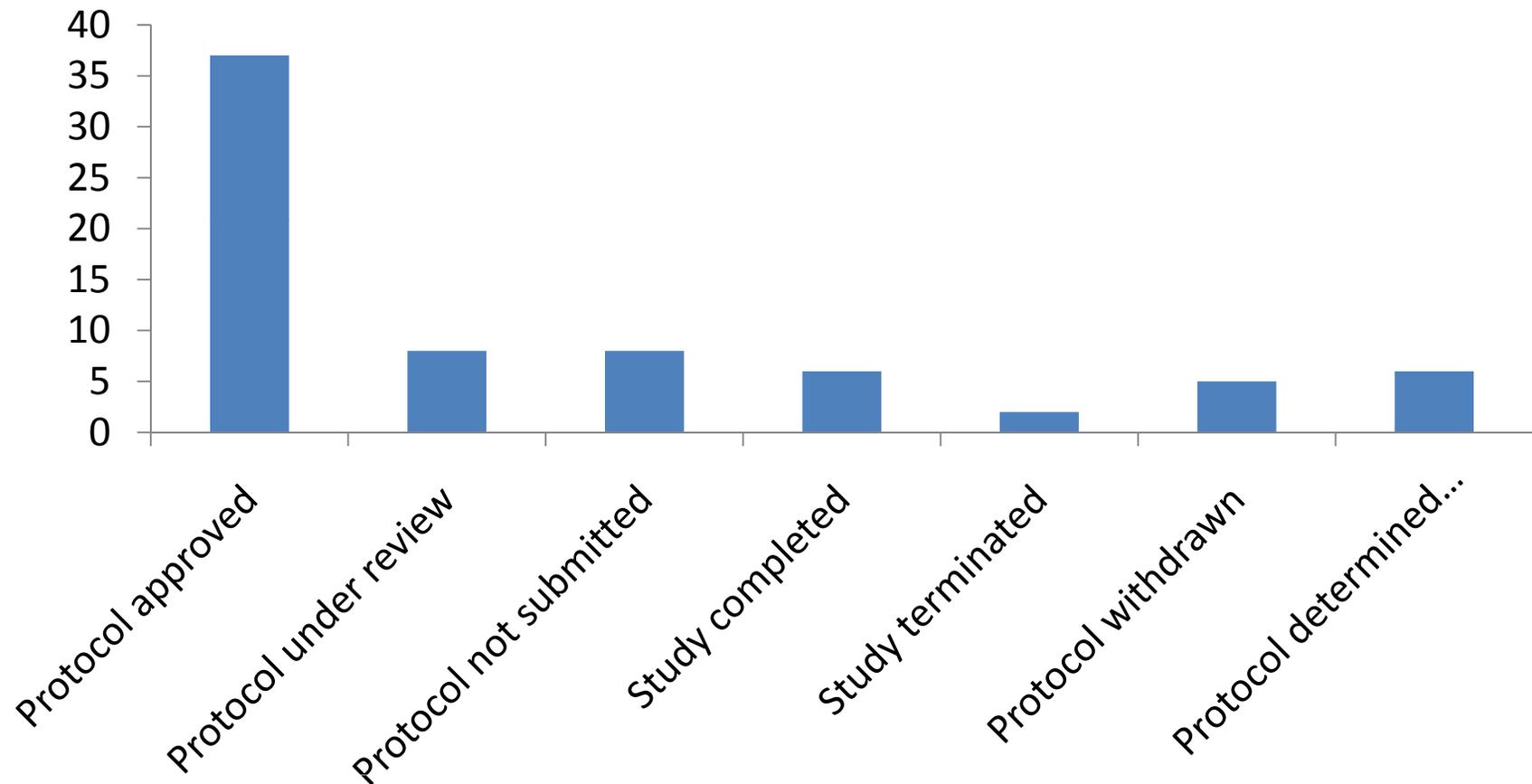


OTHER: Cervical cancer screening, food supplementation, opportunistic infection, Prevention, human resources for health , STI prevalence, blood safety, training,



Status of approved CART PHE concepts

2006-2010 (n=72)





Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WeTel Kenya1): a randomised trial



Richard T Lester, Paul Ritvo, Edward J Mills, Antony Kariri, Sarah Karanja, Michael H Chung, William Jack, James Habyarimana, Mohsen Sadatsafavi, Mehdi Najafzadeh, Carlo A Marra, Benson Estambale, Elizabeth Ngugi, T Blake Ball, Lehana Thabane, Lawrence J Gelmon, Joshua Kimani, Marta Ackers, Francis A Plummer

Summary

Background Mobile (cell) phone communication has been suggested as a method to improve delivery of health services. However, data on the effects of mobile health technology on patient outcomes in resource-limited settings are limited. We aimed to assess whether mobile phone communication between health-care workers and patients starting antiretroviral therapy in Kenya improved drug adherence and suppression of plasma HIV-1 RNA load.

Methods WeTel Kenya1 was a multisite randomised clinical trial of HIV-infected adults initiating antiretroviral therapy (ART) in three clinics in Kenya. Patients were randomised (1:1) by simple randomisation with a random number generating program to a mobile phone short message service (SMS) intervention or standard care. Patients in the intervention group received weekly SMS messages from a clinic nurse and were required to respond within 48 h. Randomisation, laboratory assays, and analyses were done by investigators masked to treatment allocation; however, study participants and clinic staff were not masked to treatment. Primary outcomes were self-reported ART adherence (>95% of prescribed doses in the past 30 days at both 6 and 12 month follow-up visits) and plasma HIV-1 viral RNA load suppression (<400 copies per mL) at 12 months. The primary analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, NCT00830622.

Findings Between May, 2007, and October, 2008, we randomly assigned 538 participants to the SMS intervention (n=273) or to standard care (n=265). Adherence to ART was reported in 168 of 273 patients receiving the SMS intervention compared with 132 of 265 in the control group (relative risk [RR] for non-adherence 0.81, 95% CI 0.69–0.94; p=0.006). Suppressed viral loads were reported in 156 of 273 patients in the SMS group and 128 of 265 in the control group, (RR for virologic failure 0.84, 95% CI 0.71–0.99; p=0.04). The number needed to treat (NNT) to achieve greater than 95% adherence was nine (95% CI 5.0–29.5) and the NNT to achieve viral load suppression was 11 (5.8–227.3).

Interpretation Patients who received SMS support had significantly improved ART adherence and rates of viral suppression compared with the control individuals. Mobile phones might be effective tools to improve patient outcome in resource-limited settings.

Funding US President's Emergency Plan for AIDS Relief.

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See Online/Comment
DOI:10.1016/S0140-6736(10)62046-6

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Strengths

- Closely linked with program delivery
- Component of broader strategic-information framework
- Strong in-country partner involvement
- Geographical diversity
- Broad range of subject areas



Challenges

- Difficulty of conducting research within programmatic initiative
- Research partners with varying levels of research experience
- Lag time for protocol development and clearance
- Oversight/monitoring
- Need to promote publication and dissemination of results