

An Update on the HIV Prevention Landscape: The Role of Combination Prevention

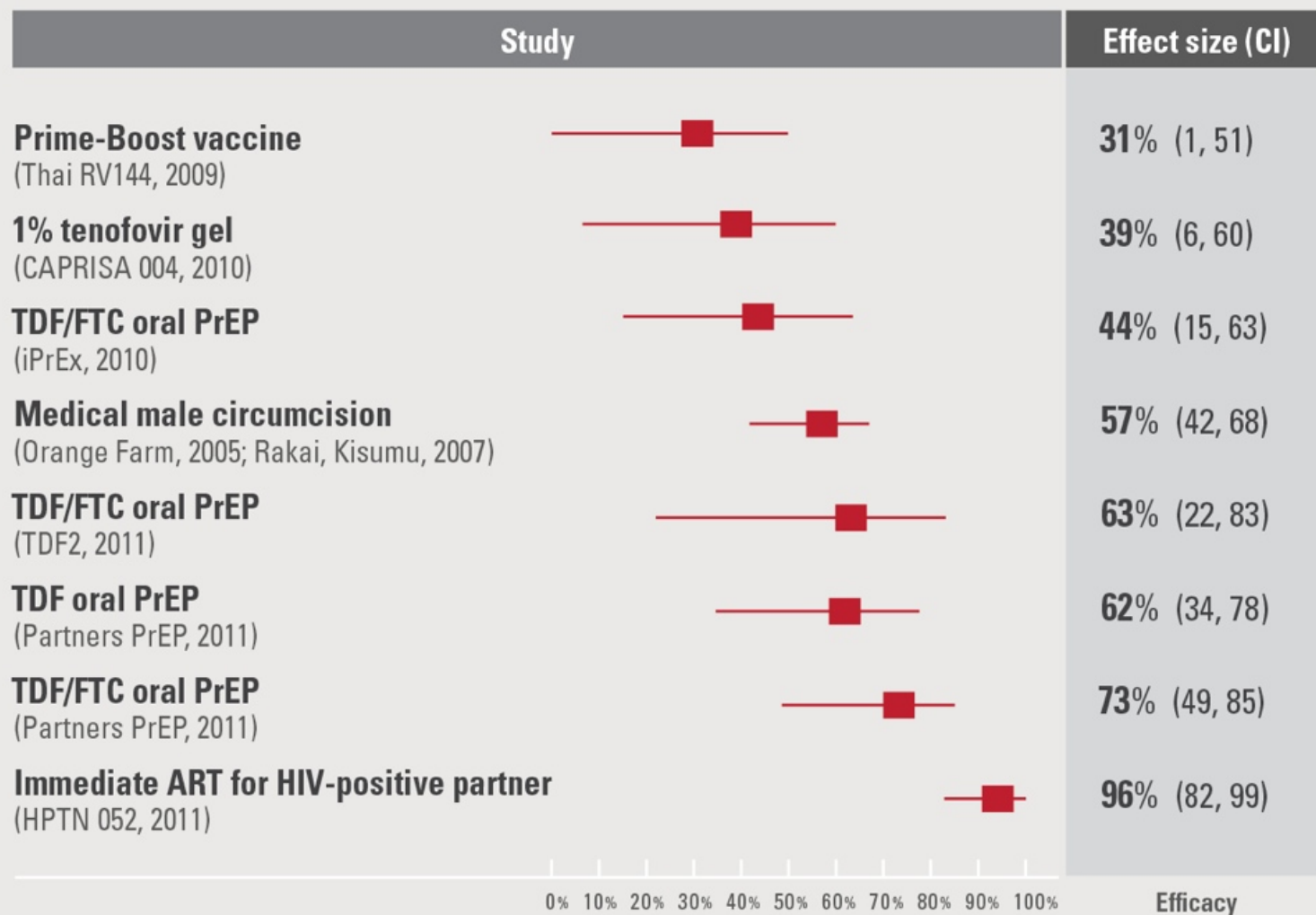
Susan Buchbinder, MD
Bridge HIV, SFDPH; UCSF
MTN Regional Meeting
October 29, 2013

Overview

1. Why combination prevention?
2. Individual prevention components (some highlights)
3. Challenges and the way forward

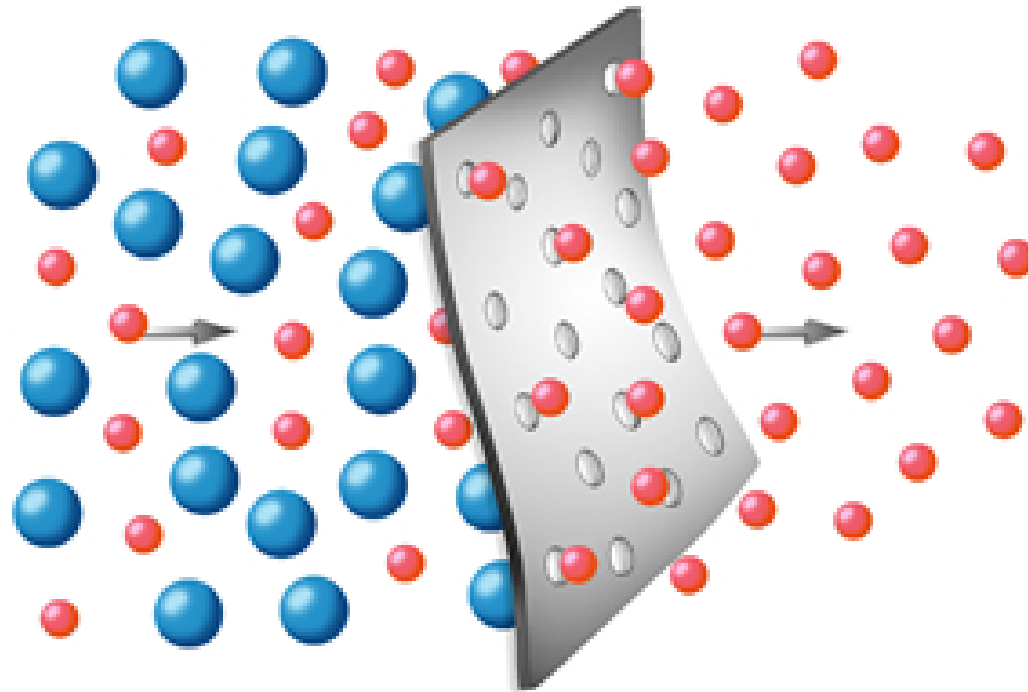
Why combination prevention?

What Works in HIV Prevention – November 2011

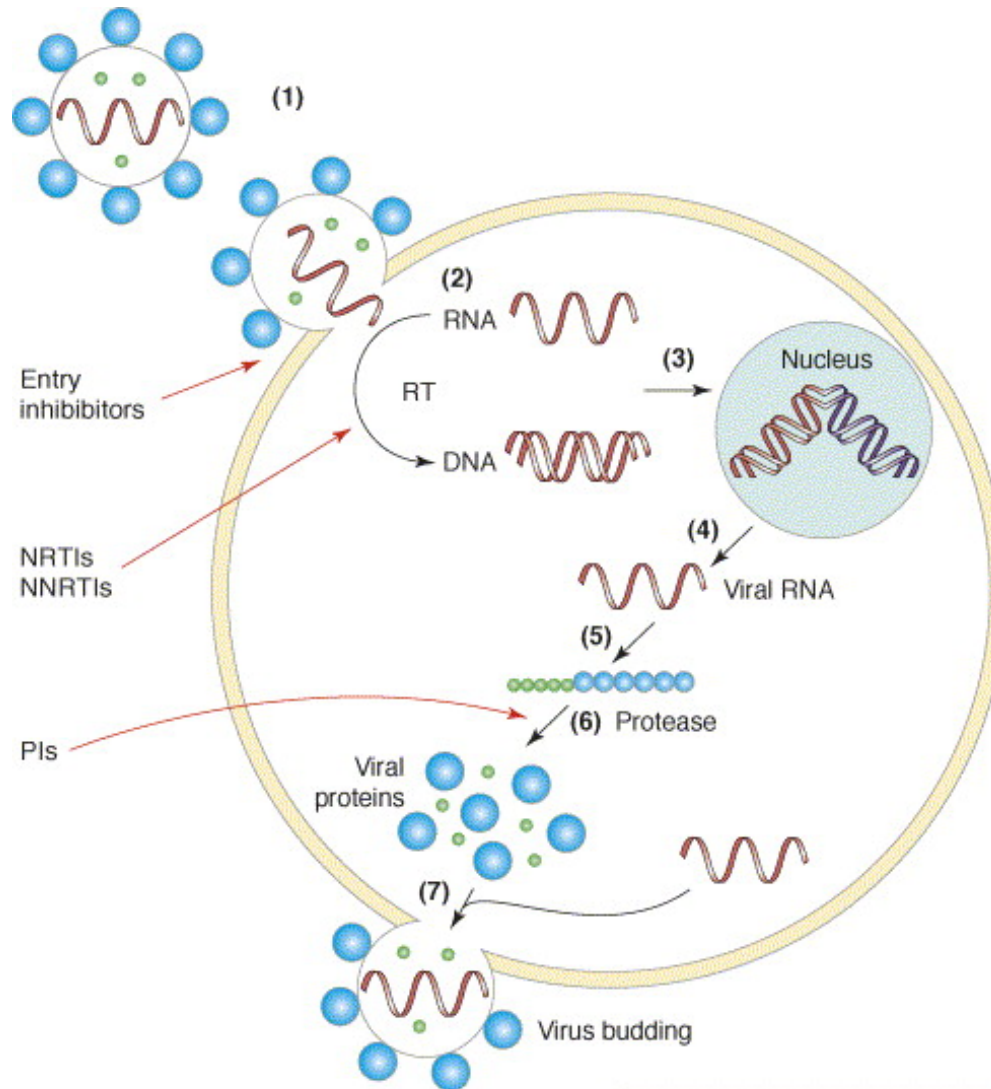


Visit www.avac.org/timeline to find links to the publications and/or presentations associated with each of these findings as well as information on studies that showed flat or insignificant results.

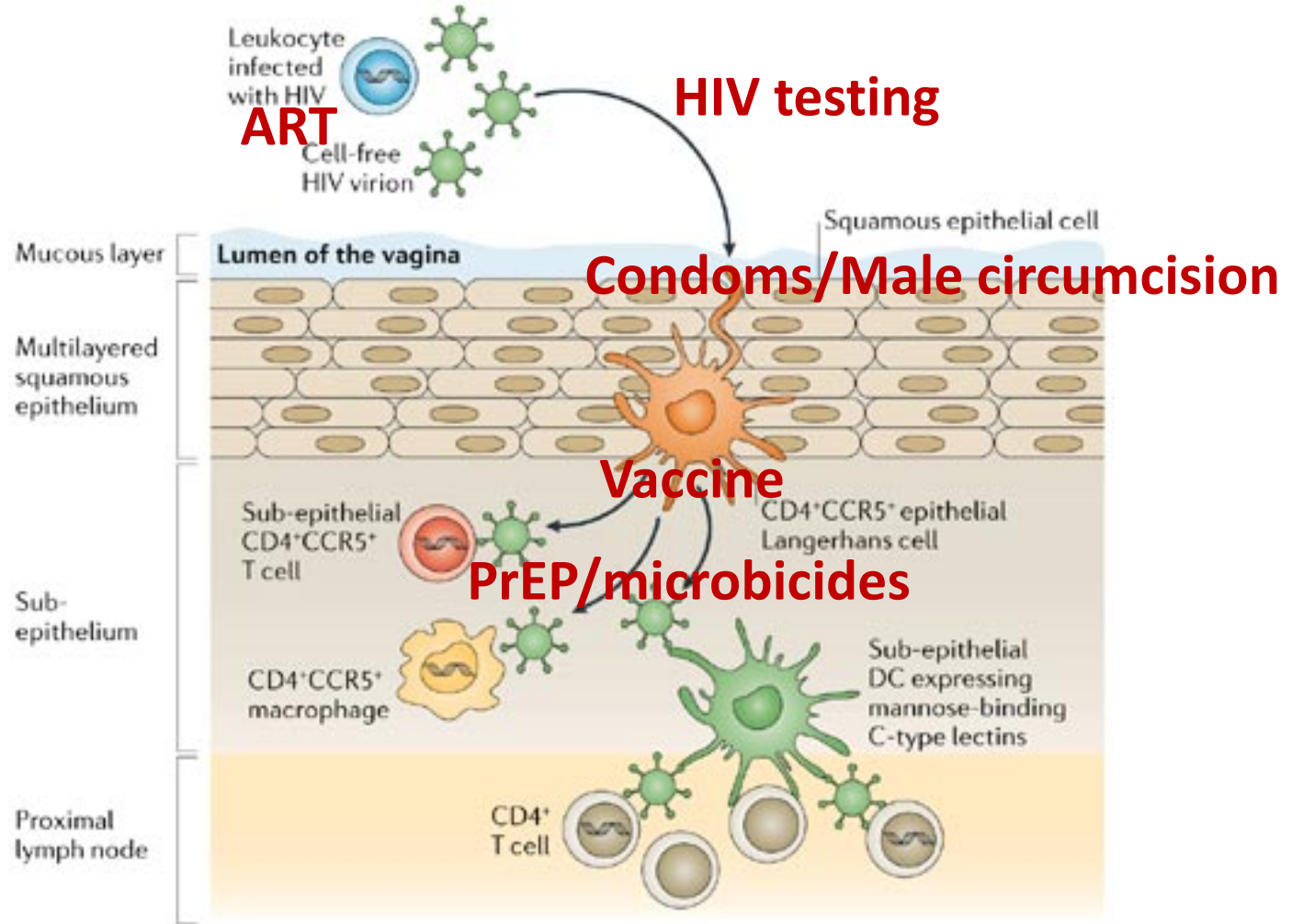
Something for everyone



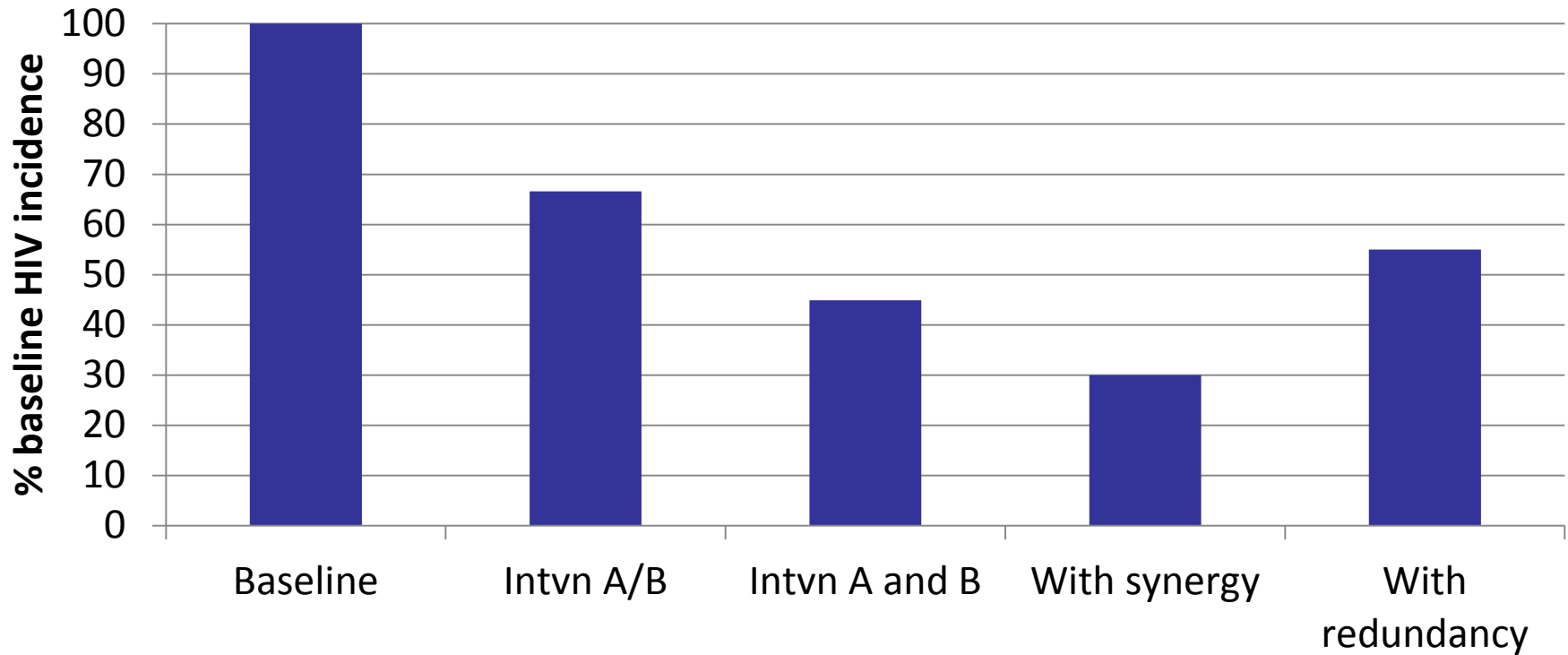
How combination ART works



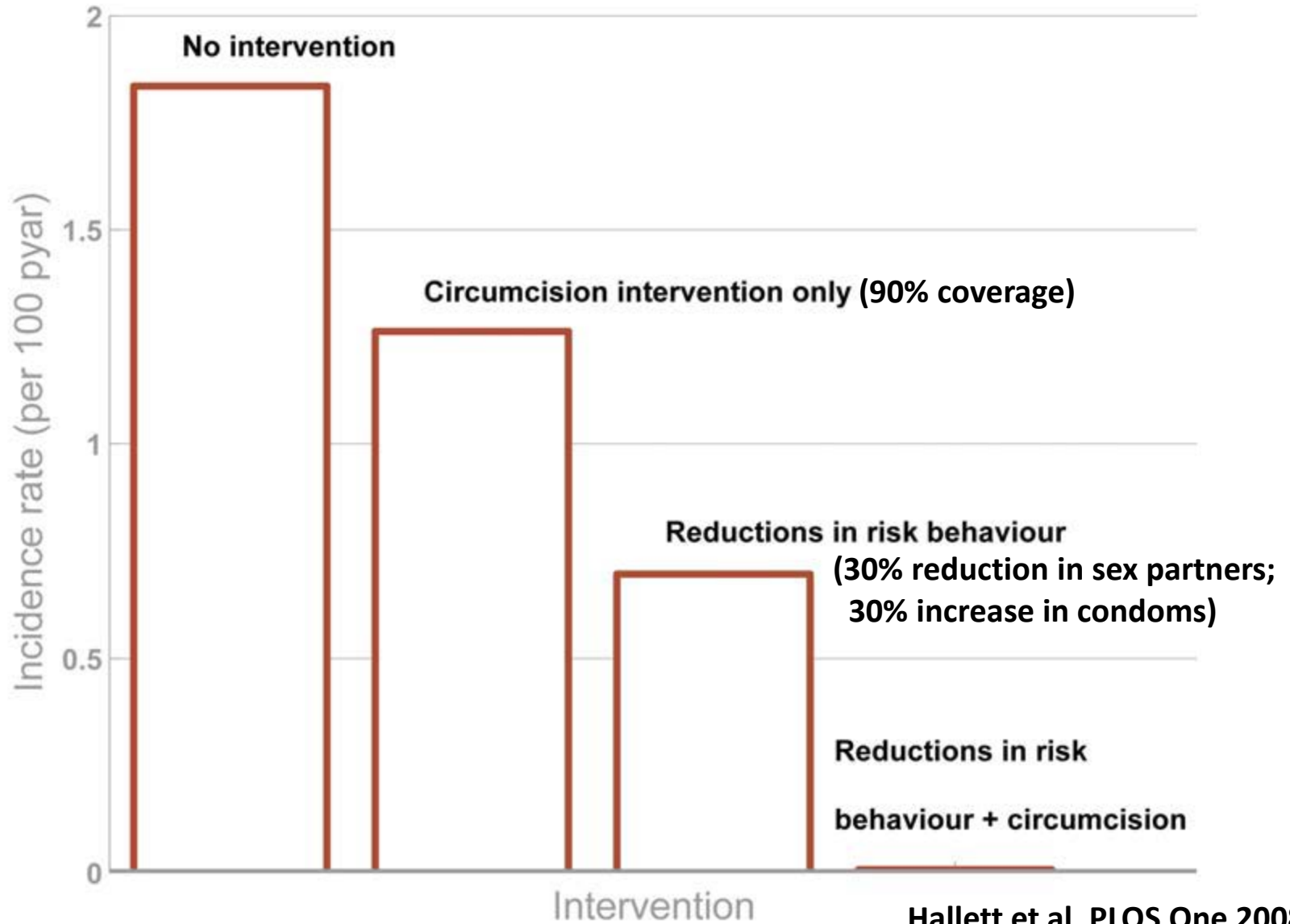
How combination prevention works



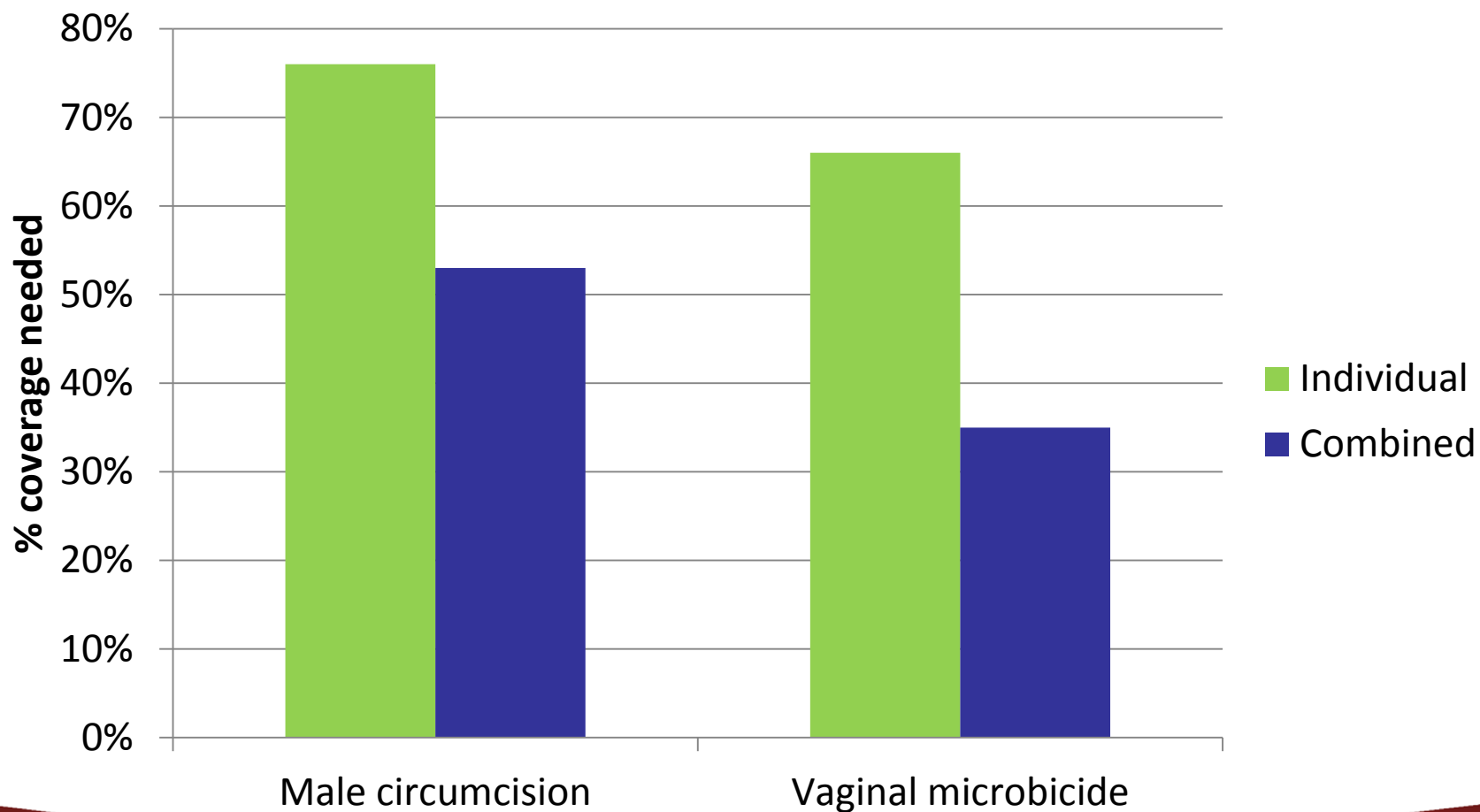
Combining for synergy; but what is synergy?



Synergy with VMMC plus behavior change



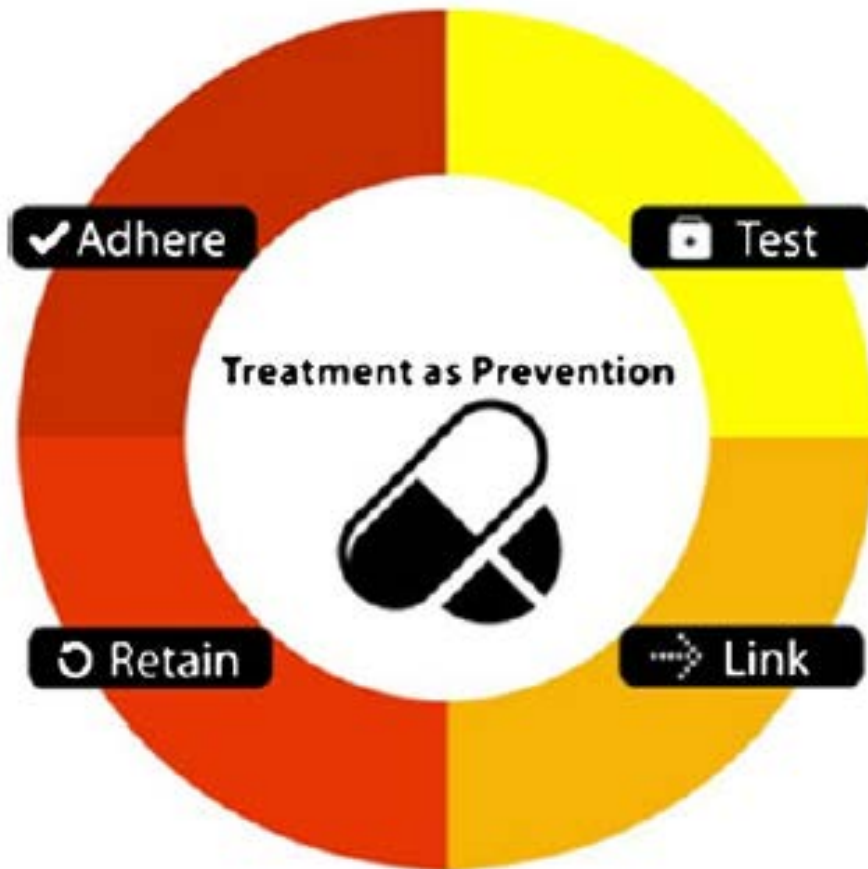
How much coverage is needed for 20% reduction in incidence?



Combination prevention

- **Type of intervention**
 - Biomedical, behavioral, social/structural
- **Level of delivery**
 - Individual, couple, network, community, population
- **HIV status**
 - Positive, negative

All prevention is “combination”



For population impact, need:

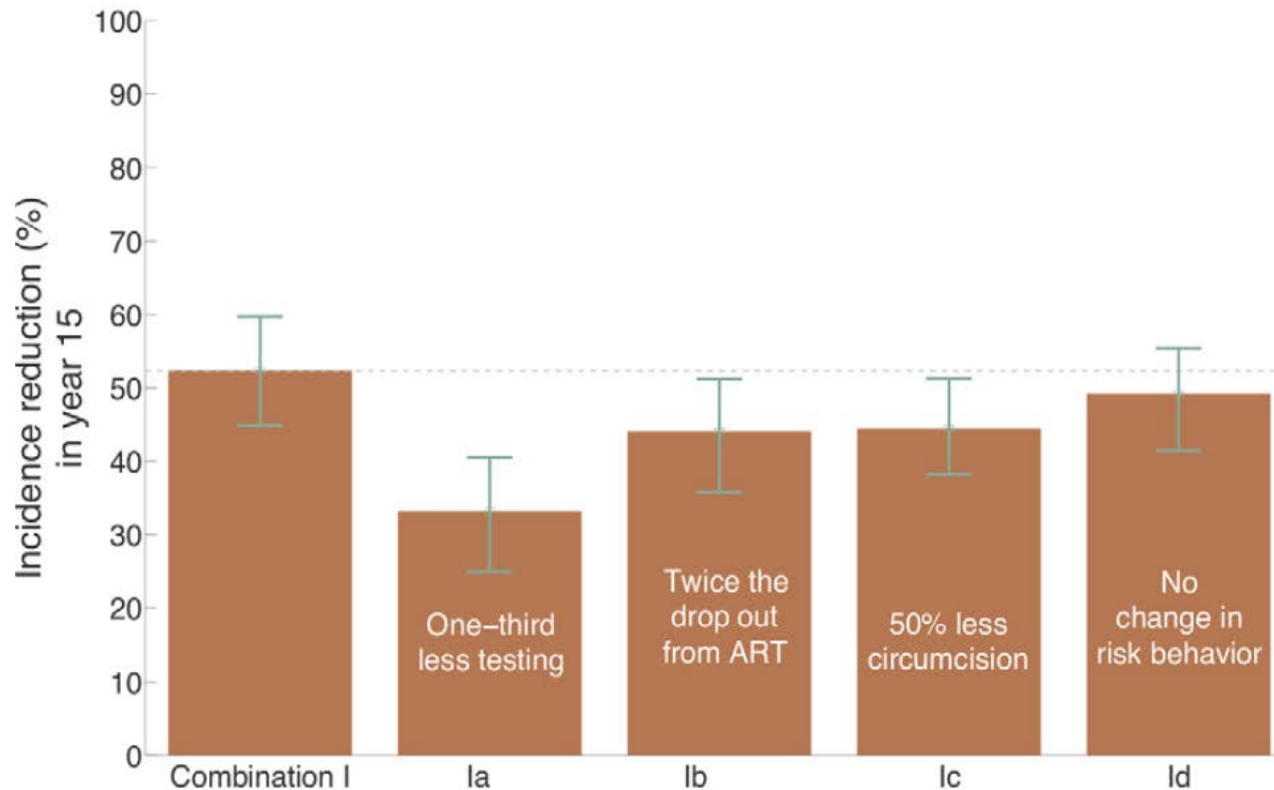
- ✓ Coverage (demand, supply)
- ✓ Adherence
- ✓ Retention
- ✓ Scalable
- ✓ Cost-effective (achievable)
- ✓ Adaptable for different populations

A sample of individual interventions

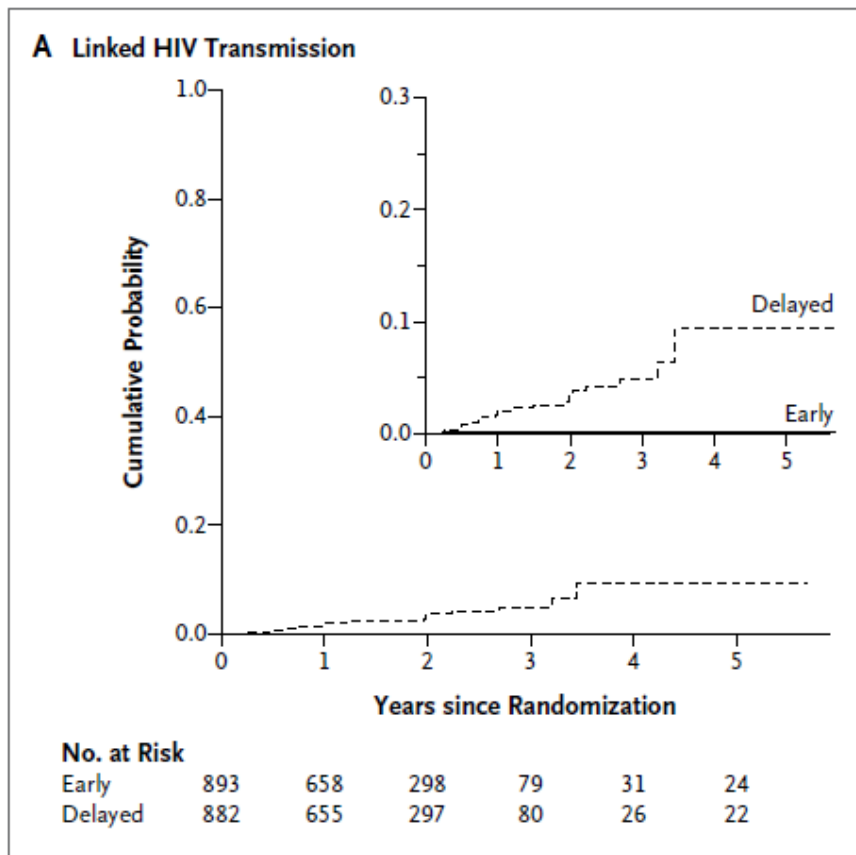
HIV testing

- “Gateway” to other interventions
- Knowing status reduces reported risk for HIV positives only
- In Project Accept (HPTN 043), community mobilized VCT
 - Increased testing (70,000 tests vs. 7600 tests)
 - Non-significant 14% reduction in incidence
- Rapid tests increase results
 - Counseling may not further reduce risk (Metsch JAMA 2013)

Impact of reduced HIV testing coverage



Treatment as Prevention (TasP)



- 96% reduction in HIV transmission when ART started at CD4 350-500 rather than lower
- Doesn't cover 20-35% transmissions outside partnership
- Not known:
 - Effect MSM, IDU
 - Uptake with high CD4 counts
 - Effectiveness in general population (e.g., adherence, retention, STIs)
 - Cost, availability, scale-up

Voluntary medical male circumcision (VMMC)

- **60% reduction in HIV acquisition among HIV- heterosexual men**
 - Protection appears durable and may increase over time
 - Cost-effective, one-time intervention
- **Unclear benefit for**
 - MSM
 - Women (may be largely indirect effects), raising “fairness” questions
- **Scale-up challenging, supply and demand**
 - Dev’t and testing new devices, task shifting

Mixed Oral Pre-Exposure Prophylaxis Results

Study	Population	Product	HIV incidence in placebo	Overall Efficacy	% TDF detected	Efficacy w/drug
iPrEx	MSM, Trans	TDF/FTC	3.9	44%	51%	92%
Partners PrEP	Hetero couples	TDF/FTC TDF	2.0	75% 67%	82%	90%
TDF 2	Young M & W	TDF/FTC	3.1	63%	80%	84%

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Fem-PrEP	Young women	TDF	5.0	None	37%	NA
VOICE	Women	TDF/FTC TDF	5.7	None	30%	NA

Potential reasons for disparate PrEP results

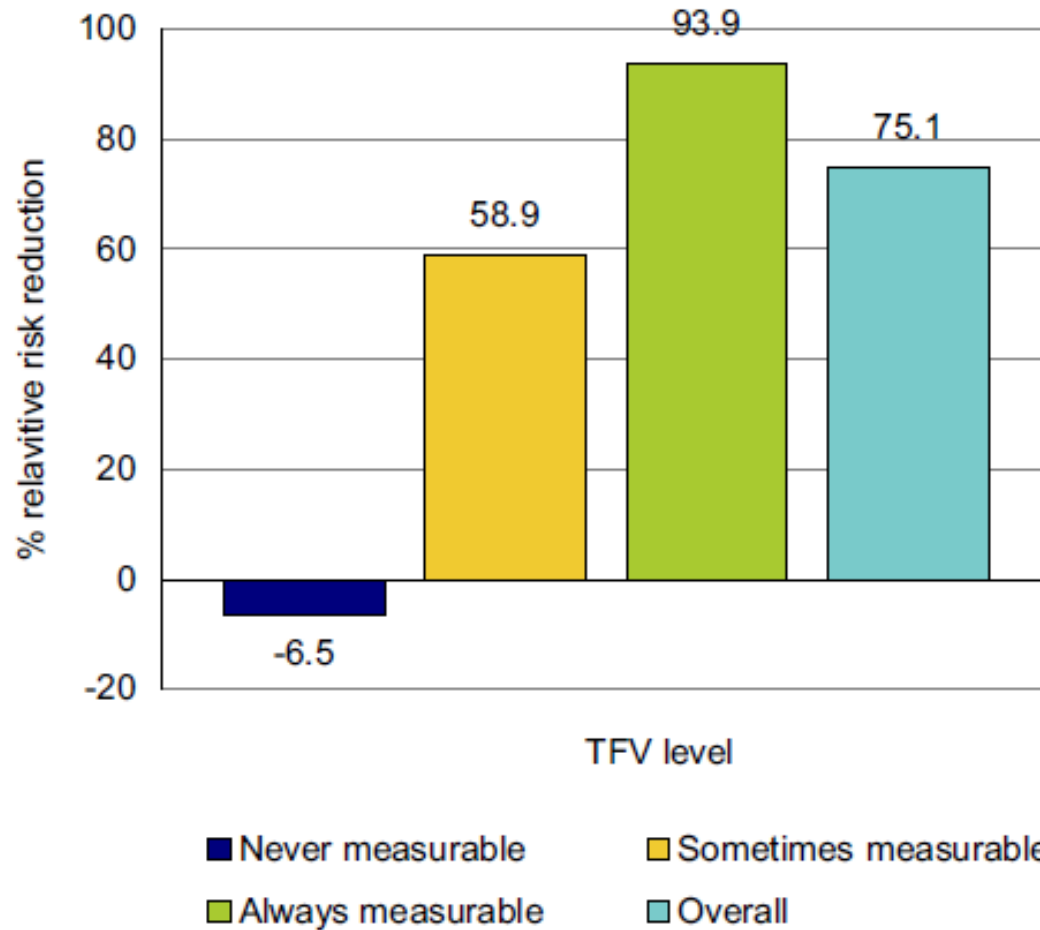
- Adherence, adherence, adherence
 - ✓ Drug levels, relationship to exposure
- High HIV incidence
 - ✓ But subgroup analyses in Partners PrEP, iPrEx didn't find this
- Susceptibility factors (e.g., age, # partners, STI, sexual practices)
- Infectiousness (e.g., ART/VL, STIs)
- Route of acquisition

Challenges and the way forward

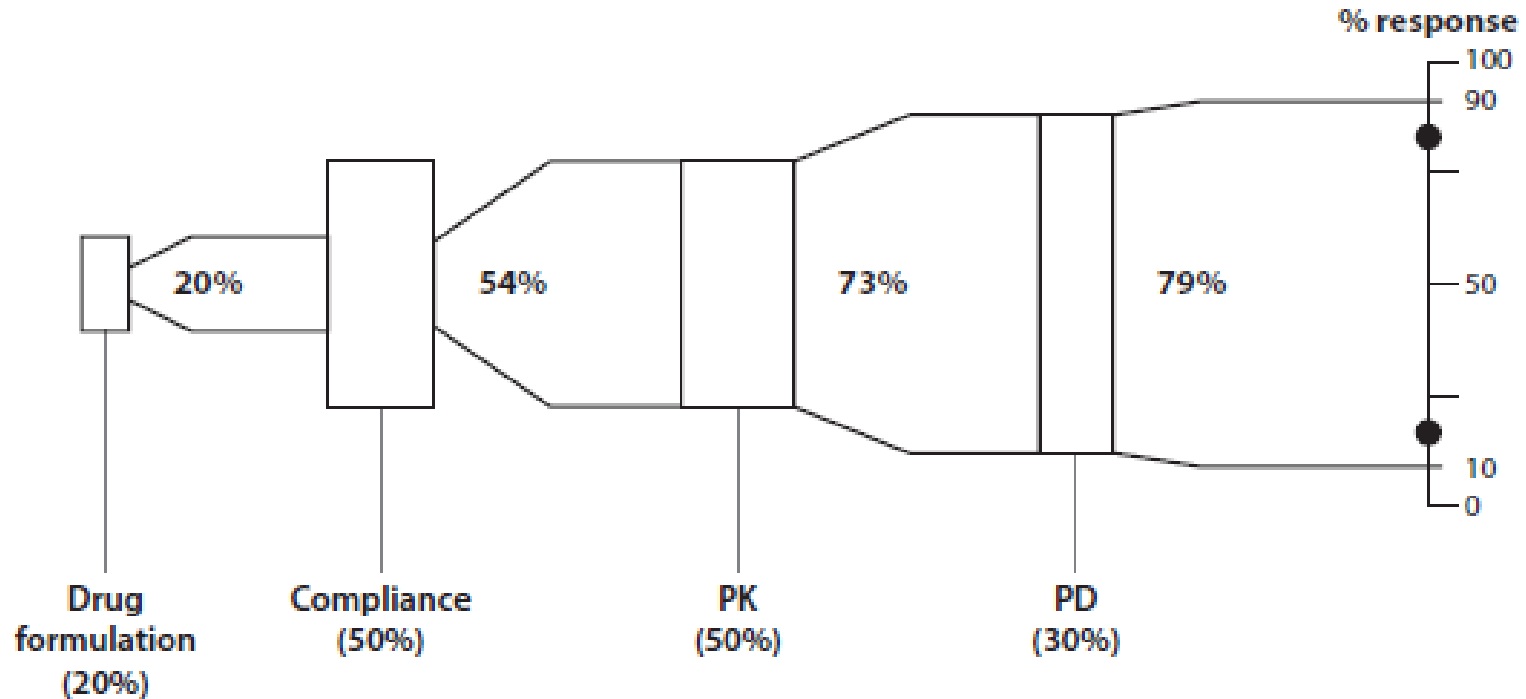
1. Keeping it desirable, deliverable, and scalable



2. Adherence is necessary but not always sufficient for efficacy



Adherence has major effect on variability of response



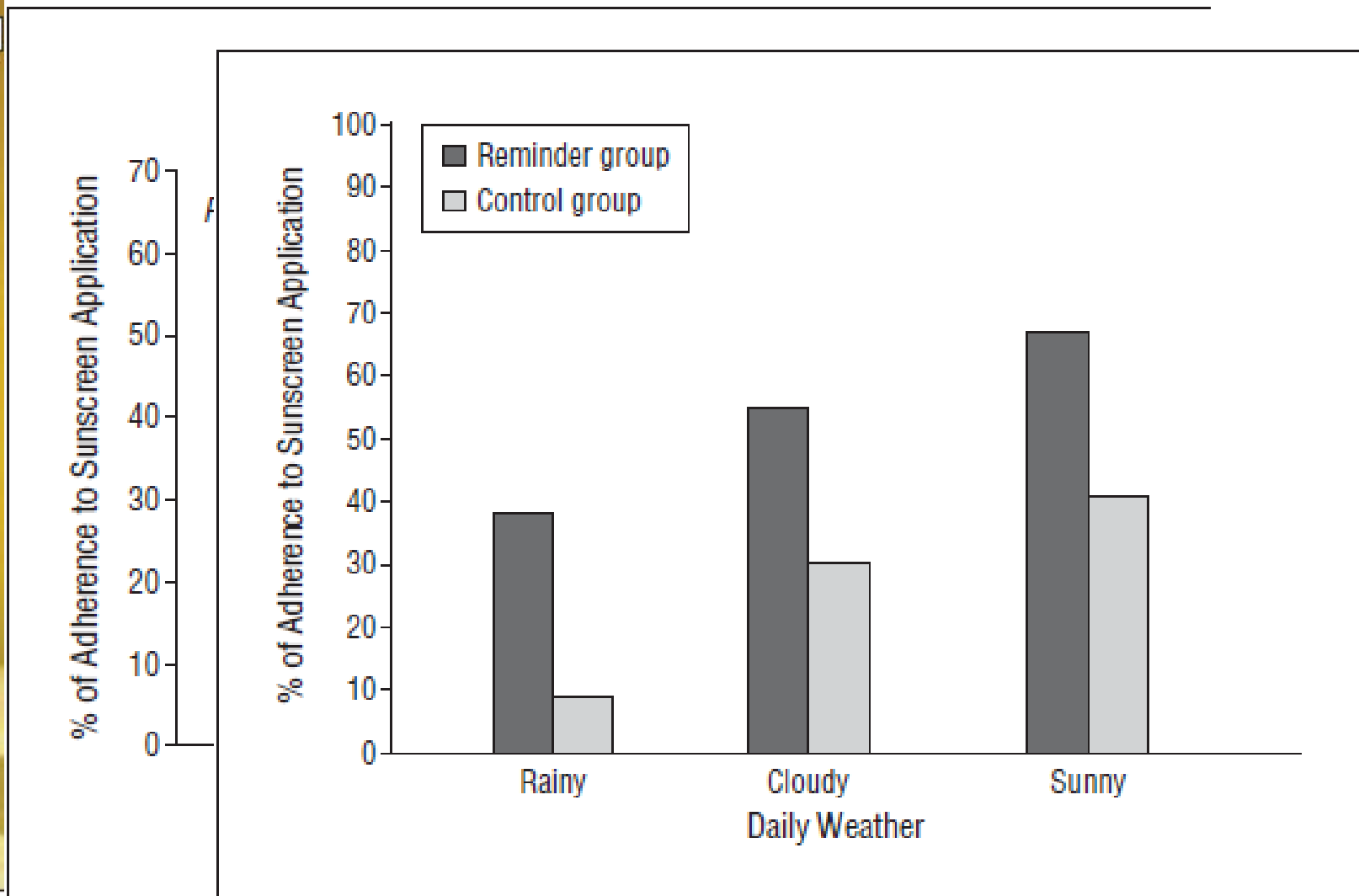
If could reduce variability from PK/PD by 90%, variability only reduced by 1/3

Adherence interventions: scalable and effective

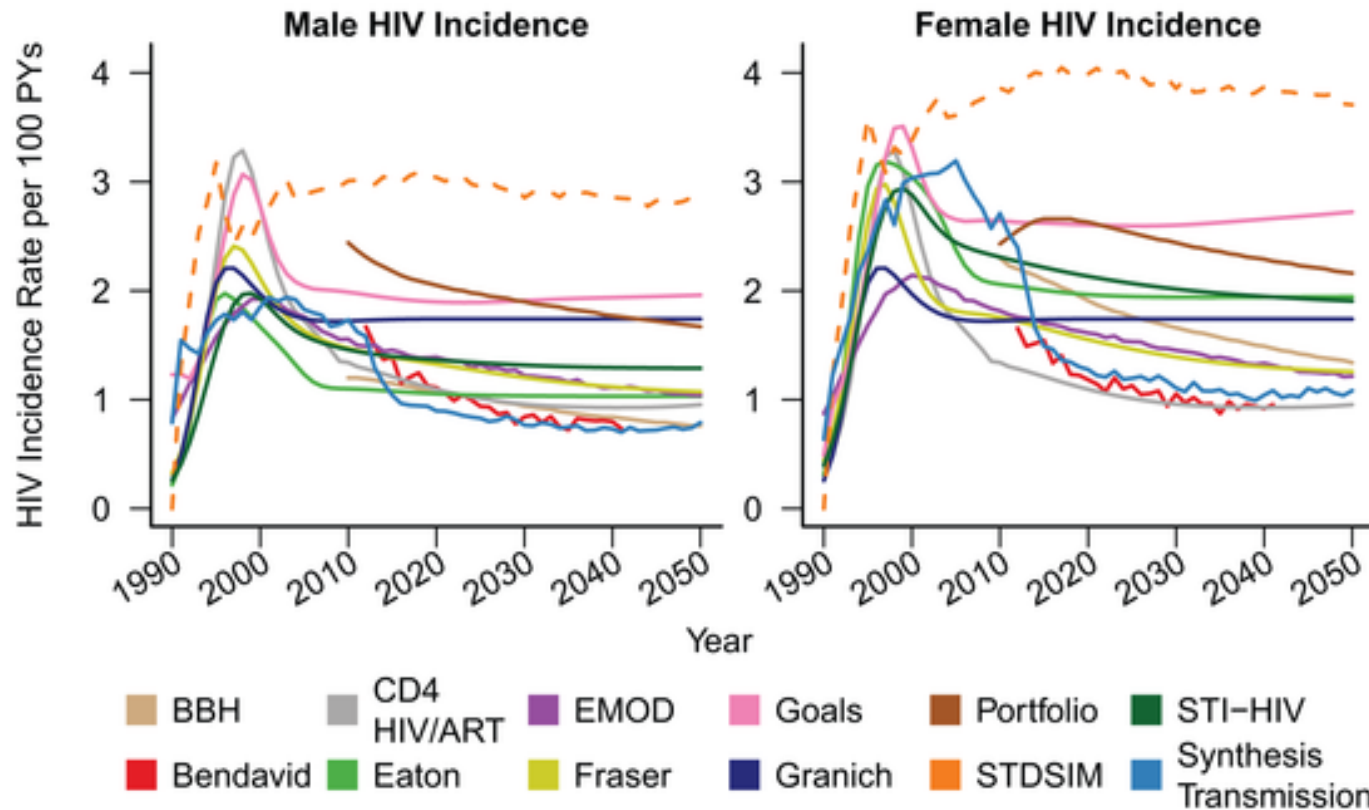
- **Adherence devices**
 - Reminders: pill boxes, alarms, SMS
 - Text messages to triage pts needing help [Lester et al, Lancet 2010]
 - Weekly text to pts initiating ART
 - Improved self-reported adherence and VL suppression
- **Ongoing support**
 - One-on-one counseling deteriorates over time
 - Enlisting partners, families may be effective

SMS Reminders: Sunscreen Example

A

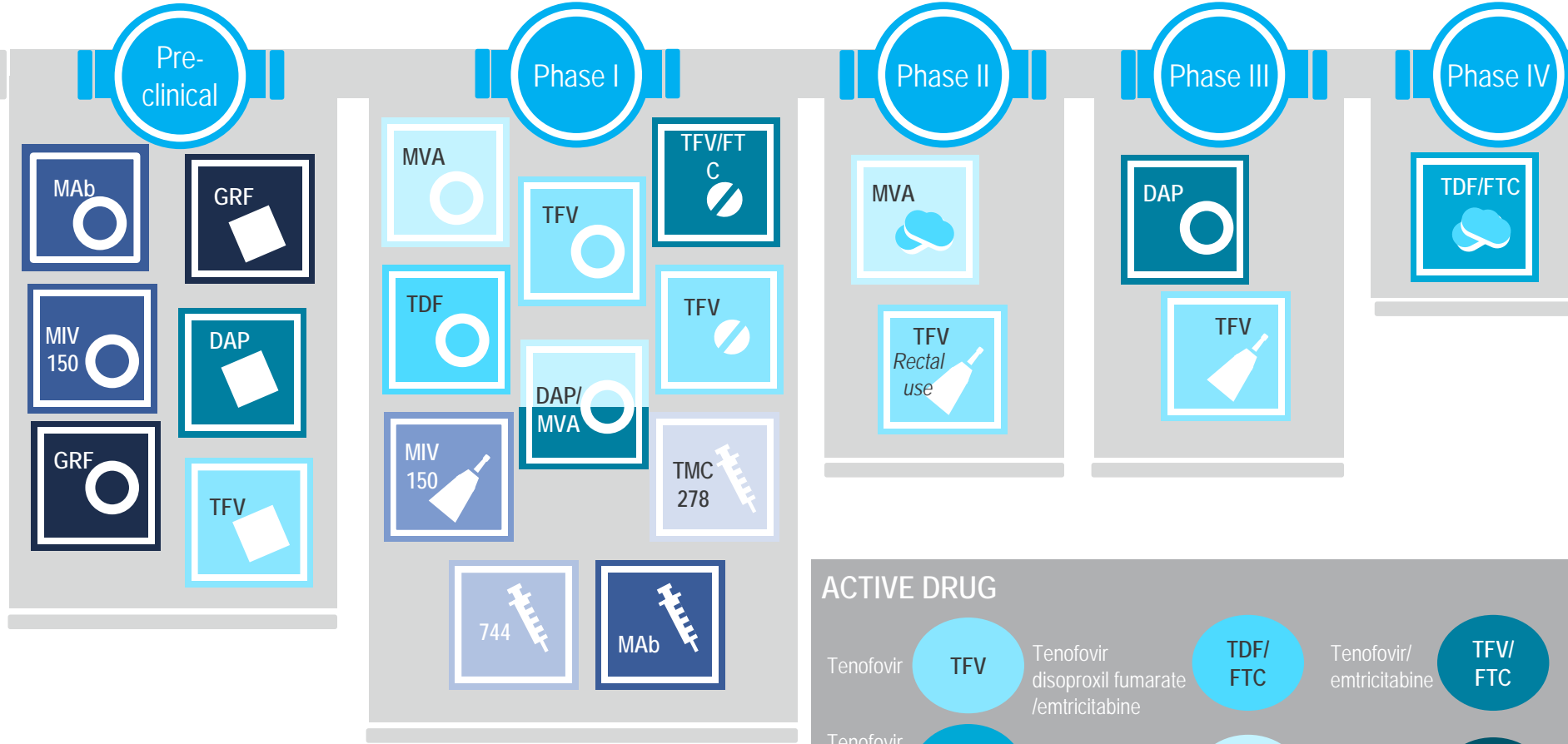


3. Models need input from real world situations



4. Need for a robust product pipeline

AVAC, October 2013



DELIVERY SYSTEM

Vaginal film		Long acting injectable	
Vaginal gel		Vaginal Tablet	
Oral pills		Vaginal ring	

ACTIVE DRUG

Tenofovir		Tenofovir disoproxil fumarate /emtricitabine		Tenofovir/emtricitabine	
Tenofovir disoproxil fumarate		Maraviroc		Dapivirine	
Ripilvirine		Griffithsin		GSK 744	
MIV 150		Monovalent antibody			

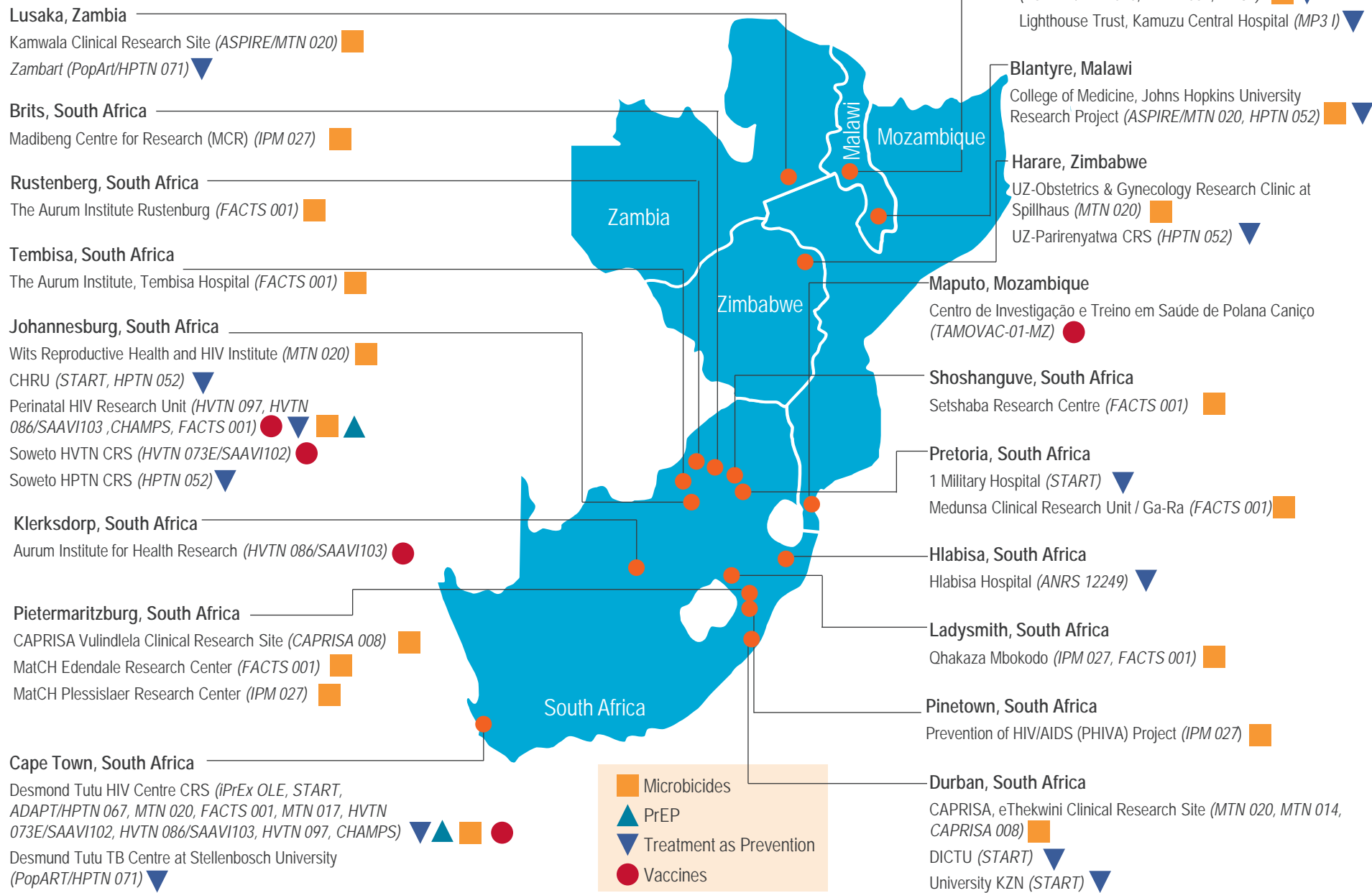
5. Living in a time of constrained resources



"O.K., let's slowly lower in the grant money."

Todd Bearson
Arlington, Mass.

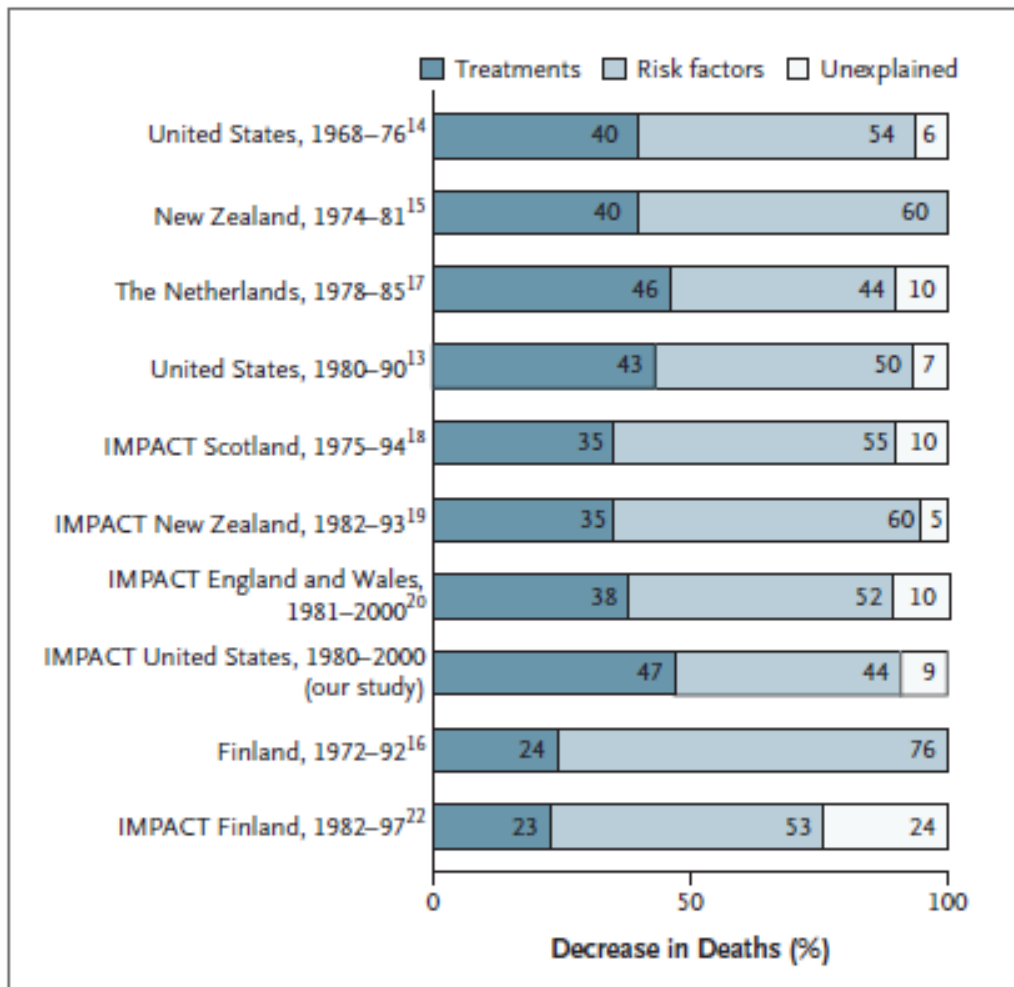
Multiple trials, multiple locations



Maintaining a diversified portfolio

- By population (region, risk group, network structure)
- By stage (individual component, package, scale-up)
- When to “confirm” and when to ask new questions?
- Can “intermediate” endpoints be used? When?

Combination prevention can change outcomes



- Age-adjusted cardiac mortality in the US fell by >40% from 1980-2000
- Approximately half of this reduction from decreased risk factors
- Approximately half from treatment
- Findings similar to other studies

Acknowledgments

Connie Celum

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Albert Liu

Mitchell Warren

Clinical Trials Networks

DAIDS