

Why isn't TasP already working?

Some more considerations

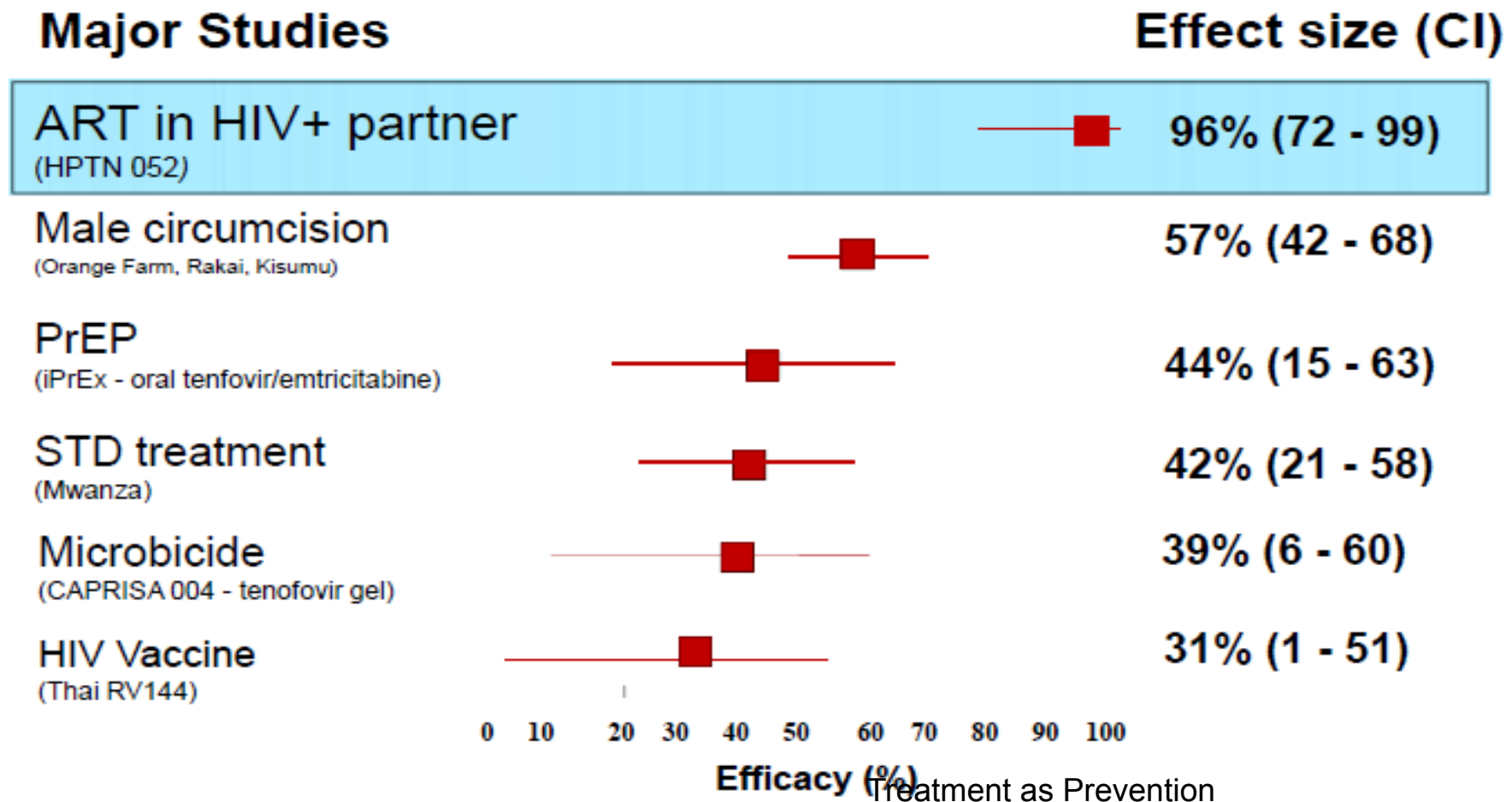
Gus Cairns

Editor, *HIV Treatment Update, Preventing HIV* and www.aidsmap.com



HPTN 052: confidence intervals

Sexual Transmission of HIV (Maximum Observed Benefit)

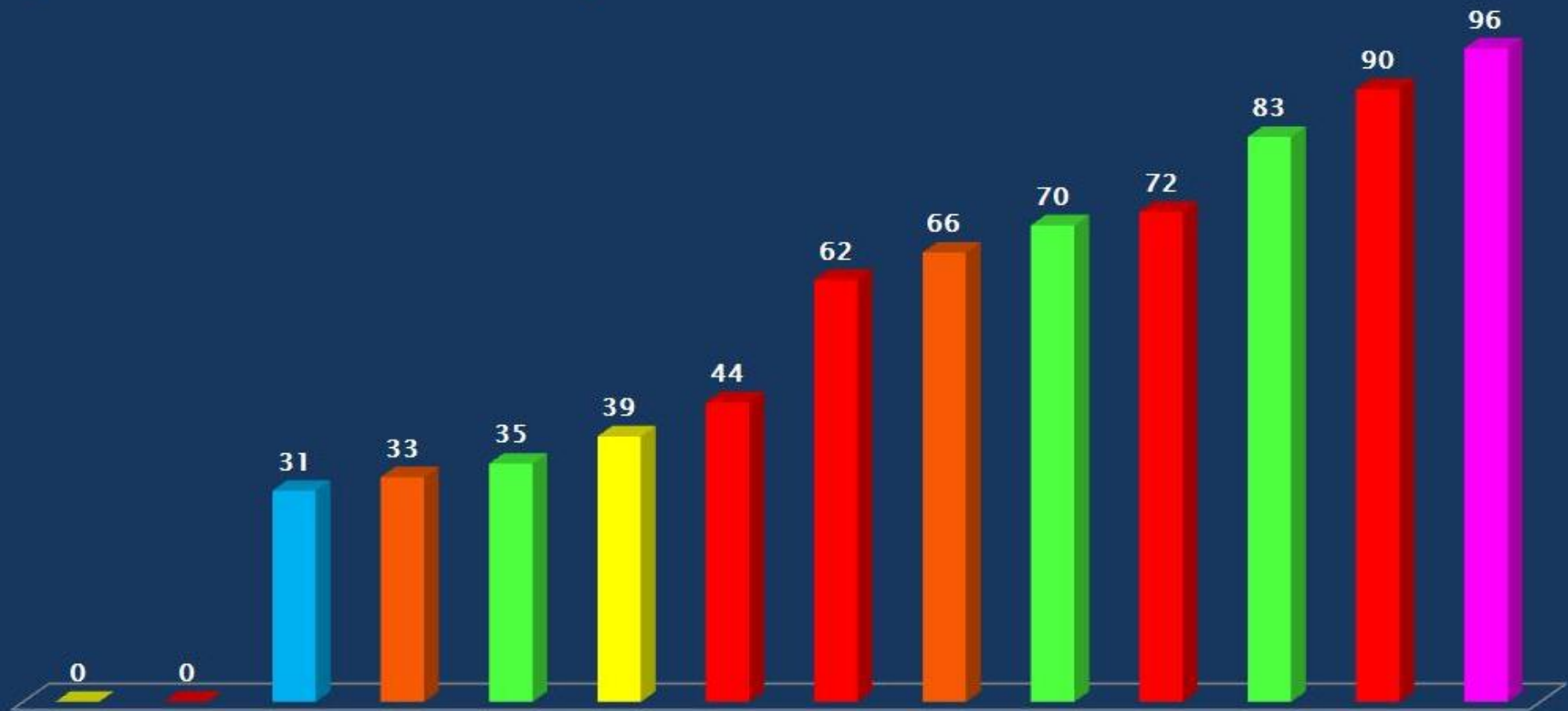


Adapted from Padian et al, 2010; Abdool Karim, 2010; Grant et al, 2010; Cohen et al, 2011

Comparative efficacy of prevention methods

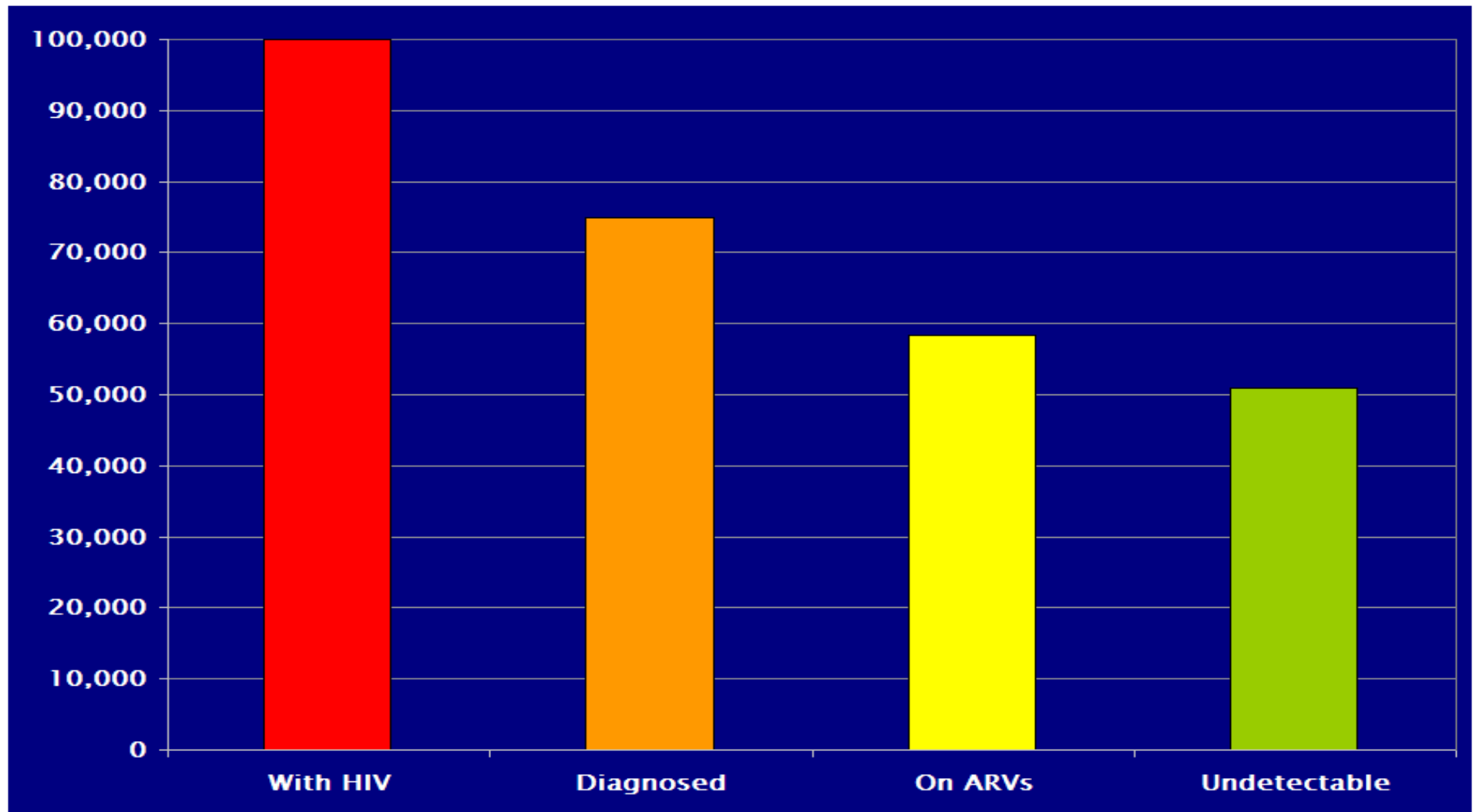
Reduction in HIV infections (unless stated)

- VOICE microbicide
- Male circumcision, women (obs)
- iPrEx PrEP
- 100% condoms in anal sex (3 studies)
- PrEP with >60% adherence (iPrEx)
- FemPrEP and VOICE PrEP
- Behaviour change progs (UAI)
- TDF2 PrEP effectiveness
- Partners PrEP
- HPTN 052
- RV144 HIV vaccine
- Vaginal Microbicide CAPRISA 004
- Male circumcision (3 RCTs)
- 100% condoms (5 meta-analyses)



UK cascade

Data from HPA, SOPHID, UK CHIC



Why isn't it working already?

- Influence of primary infection/high-incidence (already covered)
- Testing policy?
- When-to-start policy?
- Loss to follow-up?
- Behavioural differences?

BHIVA testing recommendations 2008

HIV test should be offered and recommended to all registering with a GP and all general medical hospital admissions, where diagnosed HIV prevalence in local population = **>0.2%**.

HIV testing routinely offered and recommended to:

- All gay men/MSM and female partners; anyone with an HIV+ partner; anyone with symptoms suggesting HIV; anyone diagnosed with an STI; anyone who is or was an IDU; anyone from a country with >1% prevalence or their sexual partners (here or abroad).

Repeat tests should be recommended and offered to

- All who have tested HIV negative but where a possible exposure has occurred within the window period + pregnant women who initially refuse a test
- Men who have sex with men (MSM) and IDUs: **annually**, or more frequently if clinical symptoms are suggestive of seroconversion or ongoing high risk exposure

Testing frequencies

- Proportion of gay men who have tested in last six months:
 - - England 35% (same as Thailand)
 - - France 47%
 - - Lithuania 20% (same as Philippines)
 - Compare:
 - - USA, 53% last 6 months
 - - Australia, last 12 months: 60%
 - - Scotland, last 12 months, 48%

US CDC recently recommended high-risk people test every 3 months

- Is this realistic?

Better targeting? (Ann Sullivan, 2011)

Abstract number	Setting	Number offered testing	Offer rate	Number tested	Uptake	Number newly diagnosed	Positivity per thousand
AB1		3433	62%	2121	62%	4	1.89
	Emergency department						
	Acute care unit	548	40%	348	64%	4	11.49
		884	50%	598	68%	0	-
	Dermatology outpatients						
	One GP surgery	1329	21%	1001	75%	0	-
AB2		1553	40%	1413	91%	2	1.42
	Medical admission unit						
AB3		-	-	984	-	10	10.16
	Medical admissions unit						
AB4	Ten GP surgeries	2478	-	1473	59%	2	1.36
AB5	18 GP surgeries	-	-	2713	62%	19	7.00
AB6		-	-	191	-	4	20.94
a	Community clinics for MSM						
AB6b	Community clinics for African communities	-	-	106	-	2	18.87
AB7		-	-	459	-	4	8.71
	Outreach and community testing for African communities						
AB8		-	-	59	-	0	-
	Postal testing for MSM						

Testing cost

Cost to roll out across UK

Setting	Average cost (Range) per test	Coverage ¹	Number of tests	Total cost (Range)
General medical admissions	£8 (£3-£12)	35%	78,407	£627,256 (£235,221-£940,884)
		75%	168,015	£1,344,120 (£504,045-£2,016,180)
		90%	201,618	£1,612,944 (£604,854-£2,419,416)
Primary Care (including cost of a GP incentive)	£18 (£13-£25)	35%	218,750	£3,937,500 (£2,843,750-£5,468,750)
		75%	468,750	£8,437,500 (£6,093,750-£11,718,750)
		90%	562,500	£10,125,000 (£7,312,500-£14,062,500)
Primary care (excluding cost of GP incentive)	£7.60 (£6-£8)	35%	218,750	£1,662,500 (£1,312,500-£1,750,000)
		75%	468,750	£3,562,500 (£2,812,500-£3,750,000)
		90%	562,500	£4,275,000 (£3,375,000-£4,500,000)

BHIVA treatment recommendations 2012

General recommendation: start if CD4 count is **350 cells/mm³ or less**

In contrast, DHHS (US) and IAS guidelines now recommend **universal treatment on diagnosis**.

Only one cohort study (NA-ACCORD) found benefit in starting at > 500 cells/mm³ and its methods have been questioned. No others have found a mortality benefit for >350 cells/mm³ though they have found some health benefits. No RCT.

START RCT (N=6000) should answer question for >350 cells/mm³ by 2015 but doesn't have a primary endpoint of >500 cells/mm³



BHIVA TasP recommendations

How to balance risk/benefit in these circumstances?

BHIVA's TasP recommendation:

“We recommend the evidence that treatment with ART lowers the risk of transmission is **discussed with all patients**, and an assessment of the current risk of transmission to others is made at the time of this discussion. (GPP)

We recommend following discussion, if a patient with a CD4 count above 350 cell/ μ L wishes to start ART to reduce the risk of transmission to partners, **this decision is respected and ART is started**. (GPP)”

Anecdotally (via LSCG meeting), 5% of patients in London clinics already asking for TasP at CD4s over 350 explicitly for TasP and in some clinics 15%. Has increased since guidelines issued.

Loss to follow-up issue

- LTFU crucial factor in 'cascade': in UK CHIC only 44% classed as in 'consistent engagement' see <http://www.aidsmap.com/page/2553463/>
- May cause underestimate of patients diagnosed/ in care see <http://www.aidsmap.com/page/2600686/>
- Rapid post-test referral essential see <http://www.aidsmap.com/page/1434061/>
- People on treatment less likely to be LTFU than people not on treatment

Behavioural differences US/Europe?

- Cf. Amsterdam and San Francisco studies*
 - Amsterdam: % of men who had UAI
 - 61% 4 years before diagnosis
 - 72% at diagnosis
 - 53% 1 year after diagnosis
 - 61% 4 years after diagnosis
 - SF: no of sdUAI partners in last 3 months
 - 1.8 at diagnosis
 - 0.52 one year after diagnosis
 - 0.14 four years after diagnosis
- SF researchers estimated behaviour change → 92% reduction in HIV transmission

*Heijman RLJ et al. *Changes in sexual behaviour after HIV diagnosis among MSM who seroconverted before and after the introduction of ART.* Eighteenth Conference on Retroviruses and Opportunistic Infections, Boston, [abstract 1034](#), 2011.

*Vallabhaneni S et al. *Seroadaptive tactics adopted by HIV-positive MSM can contribute to profound and sustained reductions in HIV transmission risk following HIV diagnosis.* Eighteenth Conference on Retroviruses and Opportunistic Infections, Boston, [abstract 1038](#), 2011

Questions

- **Should testing be more universalised - or better targeted?**
- **Should we emphasise (very) frequent testing for gay men?**
- **Should we move towards universal treatment on diagnosis, or wait?**
- **Have the BHIVA TasP guidelines got the balance right?**
- **Is loss to follow-up a significant problem in European context?**
- **If so, how do we best address it?**
- **Are behavioural differences an important distinguishing factor?**
- **If so, have we lost focus on old-style HIV prevention work?**