

"Ending the Epidemic: What has to Change" John G. Bartlett, MD **Professor of Medicine, Emeritus Johns Hopkins University School of Medicine Conflicts of interest: None** 

### **HIV: Current State of the ART**

**Test: Nearly perfect after 3-4 weeks Treatment: 27 ART agents; Virtually all patients can** achieve sustained viral response w/adequate CD4 Guidance: Now clear that all patients should be treated at all CD4 strata everywhere in the world Prevention: Multiple effective methods; ART w/NDV is (96)-100%; PrEP efficacy 44-75% effective Longevity: Average is near normal (71-73 years in large cohorts in US and Europe)

# BUT - US data

- \*About 56,000 new cases/year x 30 years
- \*Average CD4 count at first HIV test is 300-350/mL
- \*About 155,000 (14%) with HIV are unaware of it
- \*PrEP works but greatly underused
- \*Affected community is often poor, disconnected, hard to reach and hard to retain in care
- \*No cure, no vaccine, just lifelong meds

# Lessons from a 20 year experience

Public Health messages - T. Frieden HIV testing- Who, when & what test Lessons from the "Gardner cascade" Retention in care- K. Volpp **PrEP-** implementation failure Expectations from novel, new ART The funding dilemma

#### **T. Frieden, CDCQ Director** NY Times 12/2/15 pg A15 "AIDS Exceptionalism"

Conflict between provider mission (individual health) & public health mission (public protection from infection)

Contact tracing: Model is syphilis, gonorrhea and TB for rigorous contact tracing and testing

CDC recs: MSM- HIV test q 3 mo. Advocacy for condoms, clean needles & named HIV reporting  $\Rightarrow$  health dept for contact tracing (but rarely happens)

#### HIV Epidemiology: US 2003-14 (Freiden T R NEJM 2015: 373: 2281)

Age (yrs.)	No. 2014	% change 2003-14
13-24	8,841 (22%)	+43%
25-34	12,63 (32%)	-12%
35-44	8,011 (20%)	-58%
Risk: MSM	26,612 (67%)	+5.4%
IDU	1,424 (4%)	-73%
Female	6,556 (17%)	-40%

#### COMPOSITE OF HIGHEST PUBLIC HEALTH TARGET TO IDENTFY, TEST AND TREAT

# Young – 13-24 years MSM Anal sex without condom

#### HIV Treatment, Suppression and Transmission (Freiden T NEJM 2015;372:2281)

Category	<b>HIV Infect</b>	Transmissions
ART- HIV suppression	30%	3%
ART - HIV not suppressed	6%	3%
ART -HIV not suppressed	3%	2%
HIV dx,not in care	48%	69%
Undiagnosed	13%	23%

### What's the message here?

#### **Contemporary Data:**

Fastest growing group (10 yr increase of 43%) Young (age 13-24 yrs) MSM **Major source of new infections (69%) HIV** positive infected & not consistently in care The message: Priority for funding & research: Young MSM (test- PrEP or ART); **Known HIV: Adherence & Retention in care** How:

Test- Ab, Ag, RNA; then ART or PrEP Treatment: Volpp plan New ART

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#### **Dynamics of HIV Viremia** (Fiebig EW. AIDS 2003;17:1871)

Stage	Day	RNA	P24Ag	Ab	WB
I	5	+		—	-
Ш	10	+	+	—	-
	14	+	+	+	_
IV	19	+	+	+	_
V	88	+	+	+	$(\mathbf{F})$

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IV	19	+	+	+	
V	88	+	+	+	+

## EARLY ART

Prevent transmission including acute HIV when most contagious (30x)

Reduce HIV reservoir (likely)

Current tests: Never too early, but always too late (for cure)



#### Screening for HIV (Peters, PJ JAMA 2016;315:682)

**TEST:** 1. Screening test: Rapid HIV Ab test- Positive = positive

2. Negative: 4<sup>th</sup> generation HIV Ag/Ab OR HIV quantitative assay (+/- pooled samples to reduce cost)

**TRIAL:** Prospective trial in 7 STD clinics & 4 community clinics

**RESULTS:** N=86,836, MSM-52%)

Acute HIV: N=134	Sensitivity	Specificity	Cost/test
Architech Ag/Ab	80%	99.9%	\$4.23/test
Pooled HIV RNA	98%	100%	\$160.07/test

**CONCLUSION:** Screen with Architech in high prevalence sites

# **HIV Test priorities**

<u>Screening test (low risk):</u> Test: Rapid POC HIV Ab Test Results in EPR Expect low yield -only 14% undetected

<u>Screening test (high risk\*):</u> Regardless of prior neg test + common sense) Test: Rapid POC Ab Test: Neg –reflex to NAT or Architech Ag \*Contact tracing, IDU,MSM(esp young MSM)

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#### **THE CHALLENGE OF HIV CARE** Test → Report for care → Stay in care → ART adherence HIV: 1.2 million – 328,000 (28%): NDV



#### The Continuum of HIV Care – US Gardner EM; CID 2011;52: 793



#### The elephant is the method of analysis

MMWR (60), 2011

HOW BAD ARE STEPS 3-5 OF THE CASCADE?: NA-ACCORD (Samji H PLoS One 2013;8: e81355)

**Cohort:** Canada and US, age >20 yrs, analysis 2000-08; n=22,937; broadly representative (NA-ACCORD data)

**Results:** Life expectancy for 20 yo pt-71.5-73 yrs

**Subset** MSM: 77 yrs; IDU: 49 yrs Entry CD4 < 350: 67 yrs

If only 28% of treated patients have viral control and HIV is fatal why is longevity nearly normal (71-72 yrs)?

**CDC** leader: Problem- changing provider ruled as out of care. Cascade needs to be re-done-2014 Dr. Fauci: Problem is that patients drop out of both care and longevity cohorts so you continually measure those retained in care Drs. R. Moore & S Gange: Dr. Fauci is partly right, but error is minimized by analytic adjustments

#### The Continuum of HIV Sare – US (Bradley H MMWR 2014)63:1113)



MMWR (60), 2011

#### IMPACT OF IMPROVING HIV TESTING, LINKAGE & RETENTION IN CARE (Shah M et al CID 2016;62:220)

"Dynamic transmission model" to compare cost and impact of various interventions intended to improve HIV care continuum

Intervention	Deaths/yr	New cases	Cost/QALY
Testing more	20%	16%	\$84K
Link to care (\$500/yr )	25%	21%	\$66K
Retention in care (\$1,000/yr)	45%	36%	\$33K
Comprehensive package	64%	54%	\$45K

CONCLUSION: Best outcome in mortality, prevention and costeffectiveness is the complete package Retention in Care: Cost-Effective Strategy to Turn the Tide of HIV in the US (Gardner EM CID 2016;62: 230)

More recent CDC data: 30% have NDV (not 18%) New data from M. Shah: First to add cost data Main cost savings: Engagement in care with HIV prevention. Single case saves lifetime cost - \$400K Shah data: Most effective strategy: Retention in care 20 year impact of 50% decrease in "lost to followup": prevent 494,000 new infections & 195,000 deaths at cost of \$33,700/QALY

### Gardner response (2016)

- 1. I think the actual number with NDV is much higher ?60%
- 2. A concern with these analyses is the failure to recognize a 3d category of persons who are in and out of care
- 3. It should not be a "cascade" (which is rigid). It is "continuum"

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HPTN 065: Test, Link to Care Plus Treat (TLC Plus) (W EI-Sadr CROI; 2015)

<u>Trial</u>: 2 Year trial at 39 sites (Bronx and DC sites) randomized for Financial Incentives (FIs) FIs (Gift Cards): Test \$25 Return for evaluation \$100 VL< 400 c/ml: \$70 q3 mo

<u>Results at 2 years</u>: No significant effect for achieving viral suppression

### WHY DID HPTN 065 FAIL?

#### Prof Kevin Volpp Univ Penn:

- Failure to "hover": "Refill, then 5,000 hours of quiet"
- Next generation med incentives: Wireless devices for adherence and ongoing feedback/watching

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### Preventing HIV transmission

Barriers: Condoms etc

#### ART with NDV: (96%)-100%

PrEP: Works in trials, but fails in broad implementation

#### Pre-Exposure Prophylaxis CDC MMWR 2015;63;1291; Mayer K Drugs 2015;75:355

**CDC estimates of indication/need:** 

Population	No.	At risk	Efficacy
MSM	492,000	24.7%	92%
IDU	115,000	18.5%	74%
Hetero	624,000	0.4%	90%

Total who Qualify 1.2 million; No. receiving 0.5-30% CDC Survey 2014-5: 935 HIV providers PrEP Ever: 25%

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#### GSK 1265744 (744)/ Cabotegravir

#### 744: Integrase inhibitor similar to DTG

- <u>Nanotechology form</u>; SC or IM
- T<sup>1</sup>/<sub>2</sub> PO: 40hr; IM/SC nanosusp T1/2: 21-50 days

#### • Dose q 1-3 mo RPV:

#### Nanosuspensions RP+744 q 1-3 mo

• Use: ART or PrEP

• <u>Concerns</u>: #20 needle, IM Injection site ADRs, <u>Drug</u> <u>ADR & Resistance</u>

#### Pharmacokinetics





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A major challenge is separation of individual health and public health which have different goals, leaders, guidelines, meetings and journals. They are paid from different sources on the basis of differing missions & payers. The need for better integration of communication and resources seems obvious.

#### Summary-US

- 1. Test: Need cheap POC NAT test
- Main source of new HIV in US is young MSM & HIV pts out of care: Test & retain
- 3. ART compliance: "Hover"+ support
- 4. "HIV Continuum" needs to be re-thought
- 5. Priorities: Young MSM & HIV+ not in care: PrEP or ART + retention: Communication, coordination and funding
- 6. Utopia: Public health and provider collaboration.

### Global HIV Issues Resource-limited countries

Current data for PEPF	US	
No. living with HIV	36.9 Million	1.2 Million
HIV – Related Deaths	25.3 Million	658,000
HIV Treatment	41%	37%

Unique challenges compared to US: Stigma, lack of medical infrastructure & experience with chronic disease

### **HIV: PEPFAR Data**

<u>Challenges</u>: Stigma, limited experience w/health systems & chronic care, but...

Since 2000- 2014-5:

New HIV infections: decreased 35%

New ped infections: decreased 58%

TB/HIV deaths: decreased 32%

### Thanks

to:

- B. Branson
- A. Fauci
- S. Gange
- E. Gardner
- J. Gallant
- K. Ghanem
- R. Moore
- M. Shah



### **HIV** 2016 **Management** THE NEW YORK COURSE