Chronic illness and medication adherence in substance users: challenges and opportunities for research fellows

FIT 2014
Cape Cod, MA

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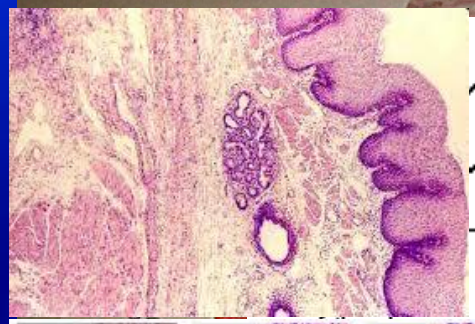
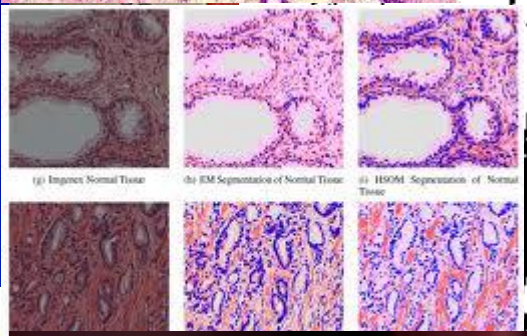
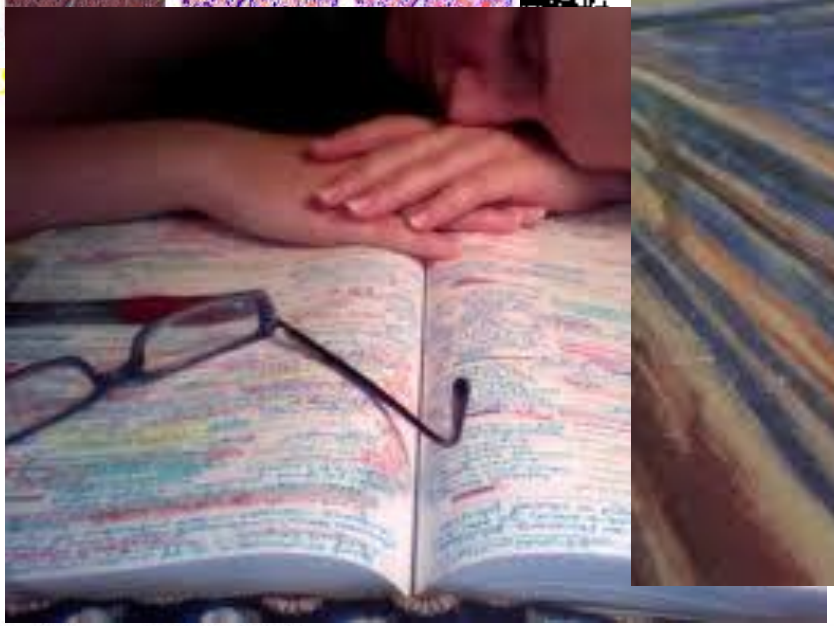
Albert Einstein College of Medicine / Montefiore Medical Center, Bronx, NY


Stepping stones
in a career

1986

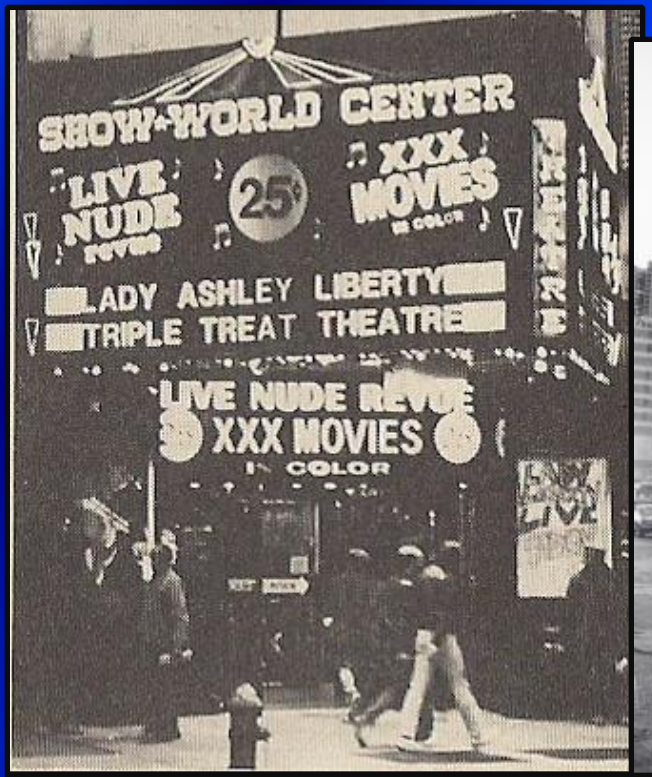


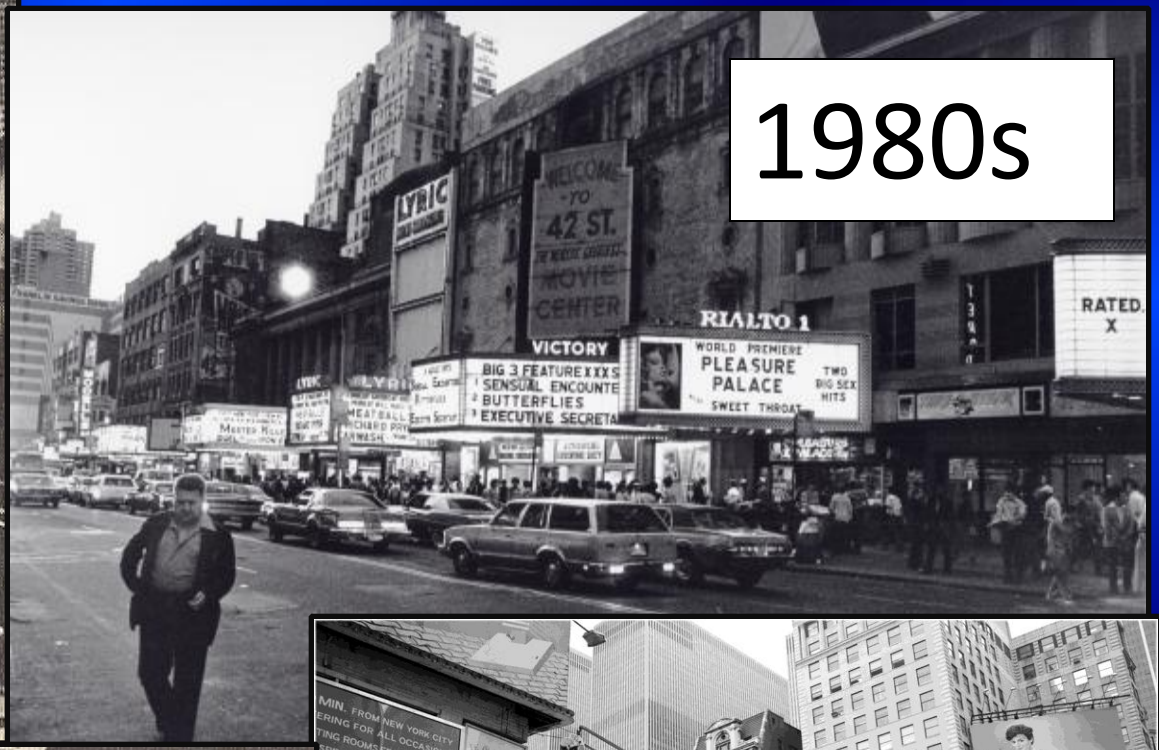




A.J. Hesse, G.E. Duffield adapted from Hastings, M. BMJ 1998;317:1704-1707


Mentorship


SHOW WORLD CENTER
LIVE NUDE REVUE
25¢
XXX MOVIES
IN COLOR
LADY ASHLEY LIBERTY
TRIPLE TREAT THEATRE
LIVE NUDE REVUE
XXX MOVIES
IN COLOR


1980s
WELCOME TO 42 ST.
LYRIC
VICTORY
BIG 3 FEATURE XXXS
SENSUAL ENCOUNTE
BUTTERFLIES
EXECUTIVE SECRETA
RIALTO 1
WORLD PREMIERE
PLEASURE PALACE
SWEET THROAT
TWO BIG SEX HITS
RATED X


FILM 1 PROCESSING
ENTRANCE TO SUBWAY
ARCADE STORES
COSMOS CAMERAS
ELECTRONICS
APPLIANCES
SUPER-FLY
BOUTIQUE
PHOTO I.D CARD


HOWARD JOHNSON'S
COCKTAILS
RESTAURANT
mita
Copiers
JVC
A PAN 400


LG


#DisneyMemories
Disney
Parks

Now


HAIR
PHANTOM


PHANTOM

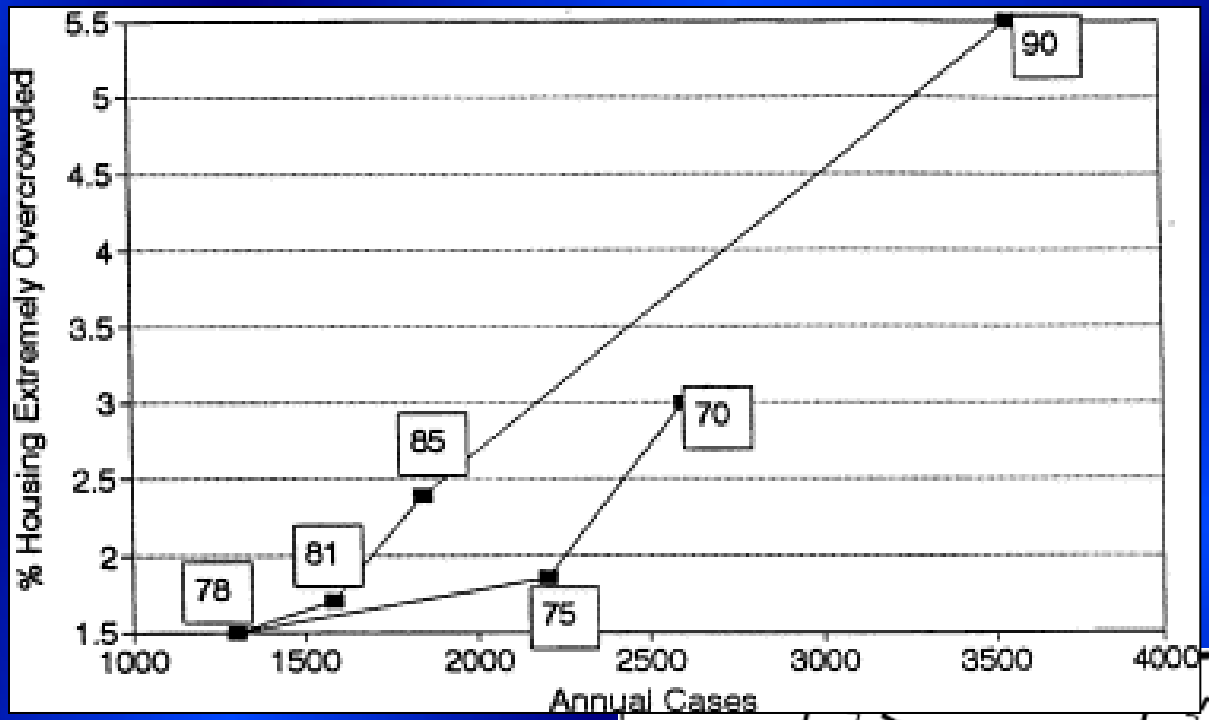

FOREVER
LG

The Impact of New York City's 1975 Fiscal Crisis on the Tuberculosis, HIV, and Homicide Syndemic

- **1978-1992: TB rates in NYC rose *every* year (after a century of decline), leading to 52,000 excess cases**
  - DOH cut TB control program, closing district health centers, chest clinics, and city TB hospital
  - Reduced Medicaid and public housing led to homelessness; shelters and jails were settings for TB transmission
- **1988: 89% of discharges from Harlem Hospital (district with city's highest TB rate) lost to f/u or did not complete TB treatment**
- **HIV/AIDS epidemic coincided with TB resurgence**

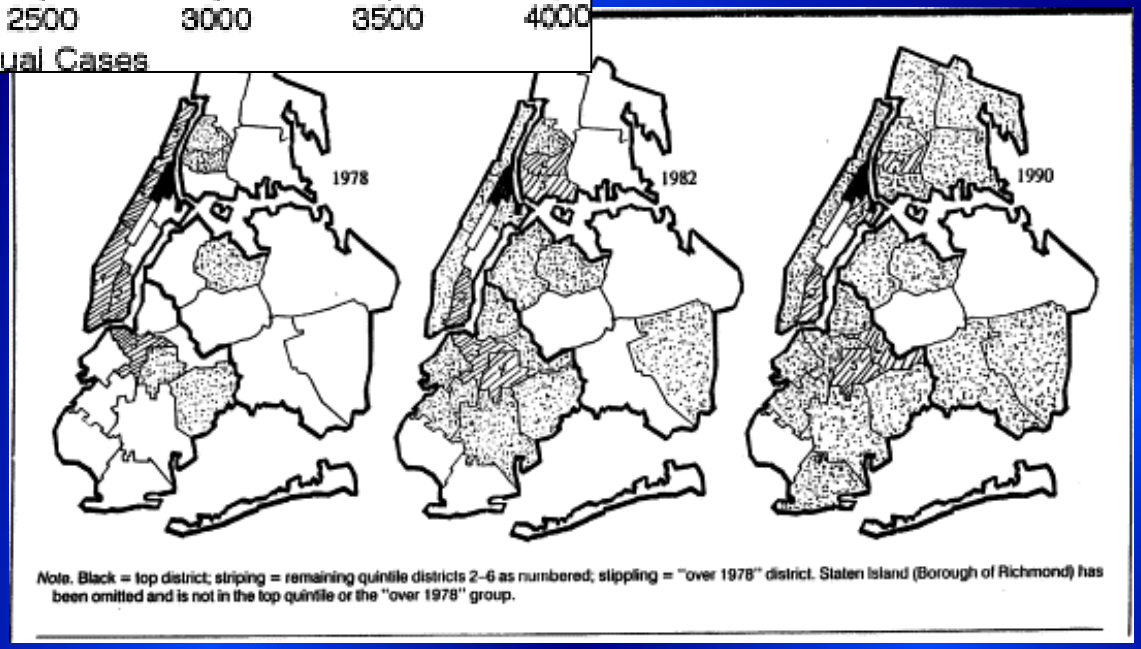
Freudenberg, 2006

TB dynamics in NYC 1970 - 1990



Discriminatory public policies and the NYC TB epidemic 1975–1993

Microbes and Infection
DN Wallace, 2001



Change in TB rates in US cities: 1981-1992

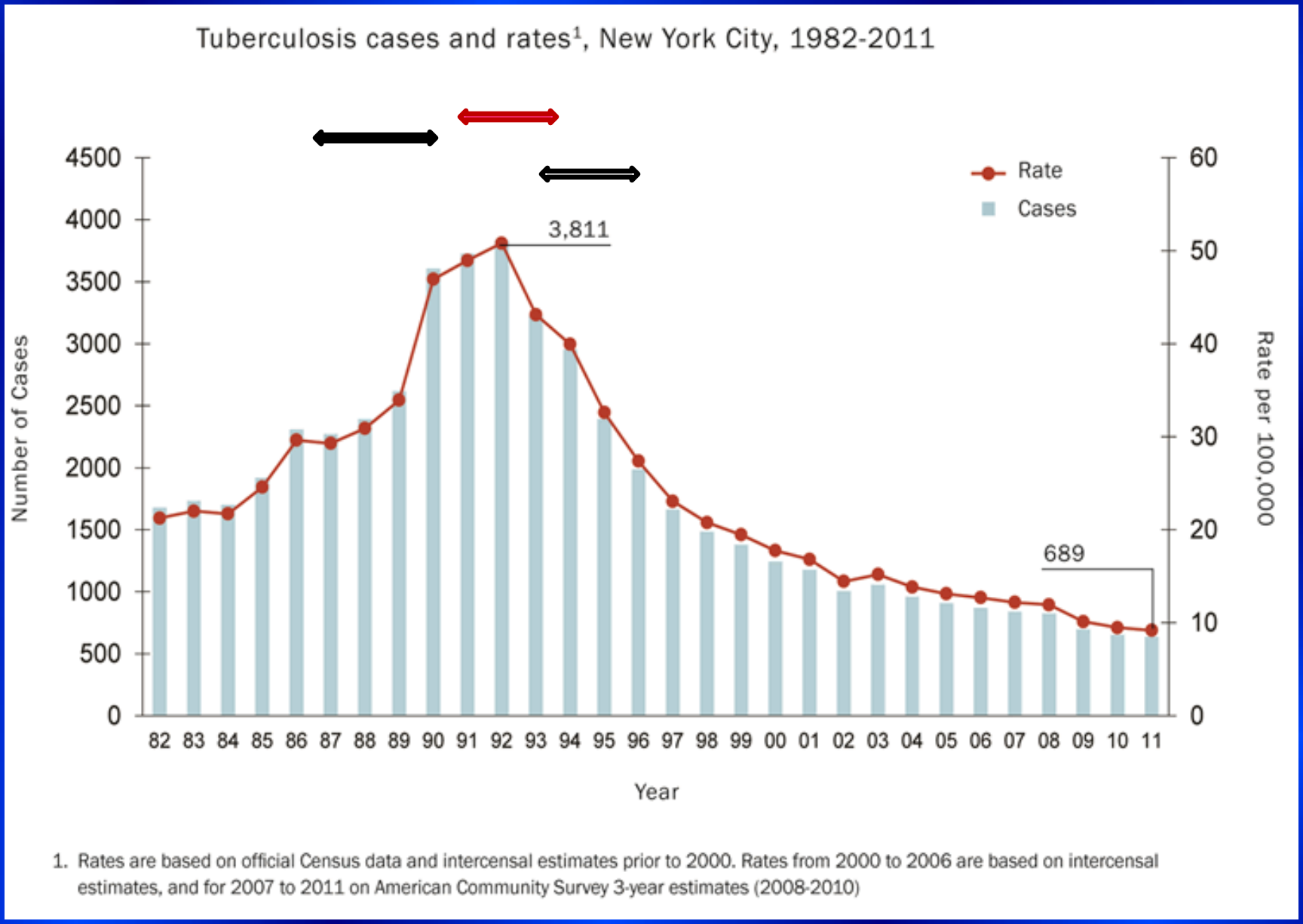
Table 1.—Eleven-Year Trends in the 20 US Cities (Population Over 250 000) With the Highest Incidence of Tuberculosis in 1981*

City	1981 Rate†	1985 Rate†	1992 Rate†	% Change, 1981 Through 1992	% Change, 1985 Through 1992
Miami, Fla	87.0	47.8	47.5	−45.4	−0.6
San Francisco, Calif	56.3	41.6	48.7	−13.5	+17.1
Newark, NJ	40.9	33.7	68.3	+66.9	+102.7
Atlanta, Ga	39.7	47.8	78.2	+96.9	+63.6
Washington, DC	37.9	26.8	24.8	−34.6	−7.5
Baltimore, Md	35.6	24.4	17.2	−51.7	−29.5
Houston, Tex	34.3	26.4	42.4	+23.6	+60.6
Los Angeles, Calif	32.5	23.1	31.1	−4.3	+34.6
Oakland, Calif	32.1	25.1	33.9	+5.6	+35.1
Chicago, Ill	30.7	24.1	28.6	−6.8	+18.7
Tampa, Fla	28.8	33.6	28.7	−0.3	−14.6
Detroit, Mich	28.3	17.0	19.7	−30.4	+15.9
Boston, Mass	27.4	27.0	22.3	−18.6	−17.4
Birmingham, Ala	27.2	16.1	15.1	−44.4	−6.2
Honolulu, Hawaii	27.0	25.6	37.4	+38.5	+46.1
New Orleans, La	24.8	16.7	19.3	−22.2	+15.6
Portland, Ore	23.7	19.0	14.8	−37.6	−22.1
New York, NY	22.4	26.1	52.0	+132.1	+99.2
Long Beach, Calif	22.1	17.5	25.6	+15.8	+46.3
Seattle, Wash	21.9	15.7	17.6	−19.6	+12.1

*Source of data was Centers for Disease Control and Prevention[37] (annual volumes, 1981 through 1992).
†Rate is tuberculosis cases per 100 000 population.

Chaulk, 1995

Rise of TB cases and rates in New York City: 1982 - 2011



1. Rates are based on official Census data and intercensal estimates prior to 2000. Rates from 2000 to 2006 are based on intercensal estimates, and for 2007 to 2011 on American Community Survey 3-year estimates (2008-2010)

Nonadherence in Tuberculosis Treatment: Predictors and Consequences in New York City

Ariel Pablos-Méndez, MD, MPH, Charles A. Knirsch, MD, MPH, R. Graham Barr, MD,
Barron H. Lerner, MD, PhD, *New York, New York*, Thomas R. Frieden, MD, MPH, *Atlanta, Georgia*

The Relationship Between Delayed or Incomplete Treatment and All-Caus Mortality in Patients With Tuberculosis

Ariel Pablos-Méndez, MD, MPH; Timothy R. Sterling, MD; Thomas R. Frieden, MD, MPH

A controlled trial of methadone treatment combined with directly observed isoniazid for tuberculosis prevention in injection drug users

Steven L. Batki [a,*,1], Valerie A. Gruber [b], Julia Moon Bradley [b], Mark Bradley [b], Kevin Delucchi [b]

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The effects of increasing incentives on adherence to tuberculosis directly observed therapy

…r,† P. H. Feldman,‡ D. P. Valentine,§ E. E. Telzak,¶ F. N. Laufer**

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SUMMARY

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OBJECTIVE: A key feature of the TB DOT program was …ts and increase …hesis was that … of incentives …dule of increas-

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RESULTS: Patients who adhered (attending 80% of prescribed DOT visits each month of treatment) and those who did not were similar on seven demographic factors (e.g., age and sex), but were significantly different on clinical and social variables. Previous TB, resistance to rifampin, human immunodeficiency virus infection, psychiatric illness, homelessness, smoking and drug use were related to non-adherence. High adherence was significantly associated with fewer months in treatment ($P < 0.016$). Logistic regression showed that the odds that a patient would adhere to therapy were greater with increased incentives. Odds of adherence were significantly lower with rifampin resistance and psychiatric illness.

CONCLUSION: Increasing incentives is associated with improved adherence to therapy in inner city TB populations.

KEY WORDS: TB; adherence; DOT

INT J TUBERC LUNG DIS 1(5):397–404

Implementation of universal directly observed therapy at a New York City hospital and evaluation of an out-patient directly observed therapy program

N. Salomon, D. C. Perlman, A. Rubenstein, D. Mandelman, F. W. McKinley, S. R. Yancovitz

Department of Medicine, Beth Israel Medical Center, New York, NY, USA

Directly Observed Therapy and Treatment Completion for Tuberculosis in the United States: Is Universal Supervised Therapy Necessary?

MASSACHUSETTS
GENERAL HOSPITAL

MGH
1811


BRONX


SHIVANI


SUNOCO
VIM


QUALITY CHEF
21st CENTURY DENTAL
COSMETIC & ASSOCIATES

THE NEW ENGLAND JOURNAL OF MEDICINE Sept. 28, 1989

SPECIAL ARTICLE

RISK FACTORS FOR HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN INTRAVENOUS DRUG USERS

ELLIE E. SCHOENBAUM, M.D., DIANA HARTEL, M.P.H., PETER A. SELWYN, M.D., M.P.H., ROBERT S. KLEIN, M.D., KATHERINE DAVENNY, M.P.H., MARTHA ROGERS, M.D., CHERYL FEINER, M.P.H., AND GERALD FRIEDLAND, M.D.

Abstract To identify risk factors for human immunodeficiency virus (HIV) infection in intravenous drug users, we undertook a study of the seroprevalence of HIV antibody in 452 persons enrolled in a methadone-treatment program in the Bronx, New York. The seroprevalence of HIV was 39.4 percent overall, 49.1 percent in blacks, 41.8 percent in Hispanics, and 17.2 percent in non-Hispanic whites ($P<0.001$ for all comparisons).

The presence of HIV antibody was associated with the number of injections per month ($P<0.001$), the percentage of injections with used needles ($P<0.001$), the average number of injections with cocaine per month ($P<0.001$), and the percentage of injections with needles that were shared with strangers or acquaintances ($P<0.001$), a practice that was more common among blacks and Hispanics than among whites. The number of heterosexual sex partners who used intravenous drugs was associated with HIV infection in women ($P<0.004$) and was the only risk factor found for users who had not injected drugs after 1982 ($P<0.05$). The presence of HIV antibody was independently associated with being black or Hispanic (adjusted odds ratio, 4.56; 95 percent confidence interval, 2.65 to 8.14), a more recent year of the last injection of drugs (adjusted odds ratio, 1.24; 95 percent confidence interval, 1.13 to 1.35), the percentage of injections of drugs that took place in "shooting galleries" (adjusted odds ratio, 1.49; 95 percent confidence interval, 1.19 to 1.88), having sex partners who used intravenous drugs (adjusted odds ratio 1.24; 95 percent confidence interval, 1.06 to 1.45), and low income (adjusted odds ratio, 1.55; 95 percent confidence interval, 1.10 to 2.17).

We conclude that differences in both the social setting of drug use and behavior related to injection carry different risks for infection with HIV and may explain, in part, the higher seroprevalence of HIV among blacks and Hispanics. In addition, we found that heterosexual activity was an independent risk factor for drug users. (N Engl J Med 1989; 321:874-9.)

HIV/AIDS Timeline 1995 - 2011

1995

Olympic diver Greg Louganis announces he is living with HIV.

1996

FDA approves viral load test, which detects the level of HIV in the body.

Joint United Nations Programme on HIV/AIDS (UNAIDS) begins operations.

1997

Minority AIDS initiative created after African American leaders declare "state of emergency."

HAART, consisting of 3 antiretrovirals, becomes the standard of HIV

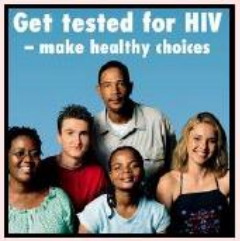
1998

Global AIDS and TB Relief Act authorizes up to $600 million for US global efforts.

Ricky Ray Hemophilia Relief Fund authorizes payments to hemophiliacs infected with HIV through unscreened blood-clotting agents.

2000

Fuzeon, a "last resort" HIV antiretroviral drug that acts as a fusion inhibitor, is introduced to the market.



Nonoxynol-9, a common spermicide agent, is found to actually increase risk of HIV transmission.

2002

Global Fund to Fight AIDS, Tuberculosis, and Malaria is created.

2003

FDA approves first rapid HIV test.

Federal government announces that it would cut funding to states without reliable HIV tracking methods. Many states thereafter require name-based reporting for testing.

2004

In State of the Union address, President Bush announces the President's Emergency Plan for AIDS Relief (PEPFAR), committing $15 billion to combat HIV/AIDS. Provision gives a third of USAID's prevention funding to abstinence programs.

2009

For the first time, South African president Thabo Mbeki offers govt aid for ARV treatment to HIV+ people, following years of denying that HIV was the cause of AIDS.

US releases federal ban on needle exchange.

2010

US releases travel ban on HIV+ individuals.

White House issues first National HIV/AIDS Strategy for United States

President Obama's 2010 federal budget eliminates funding for abstinence-only

2011

June 5, 2011 marks 30 years since the first AIDS case was reported.

Global Prevalence of HIV/AIDS

In 2001: ~29.5 Million

In 2004: ~31 Million

In 2009: ~33.4 Million

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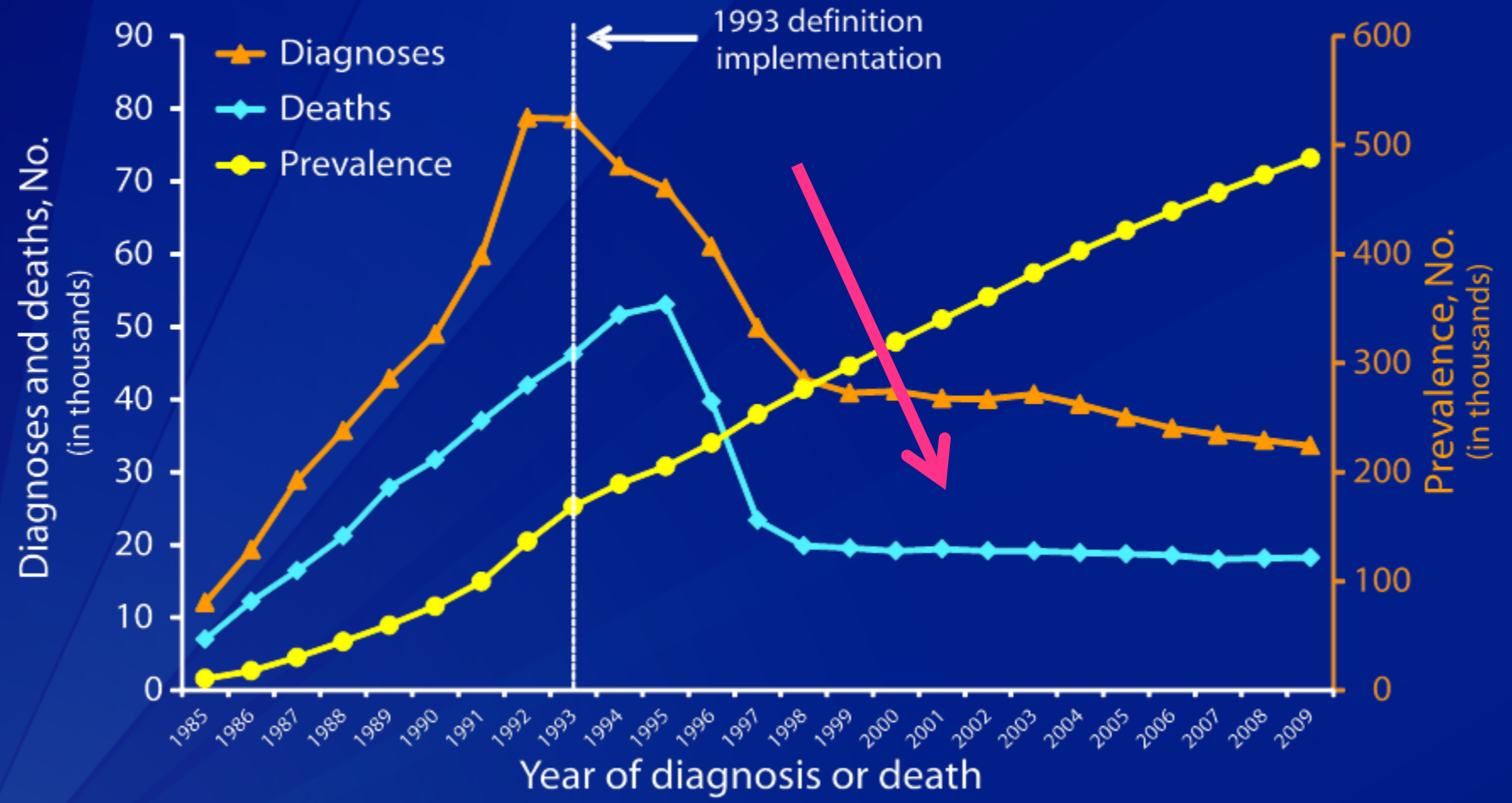
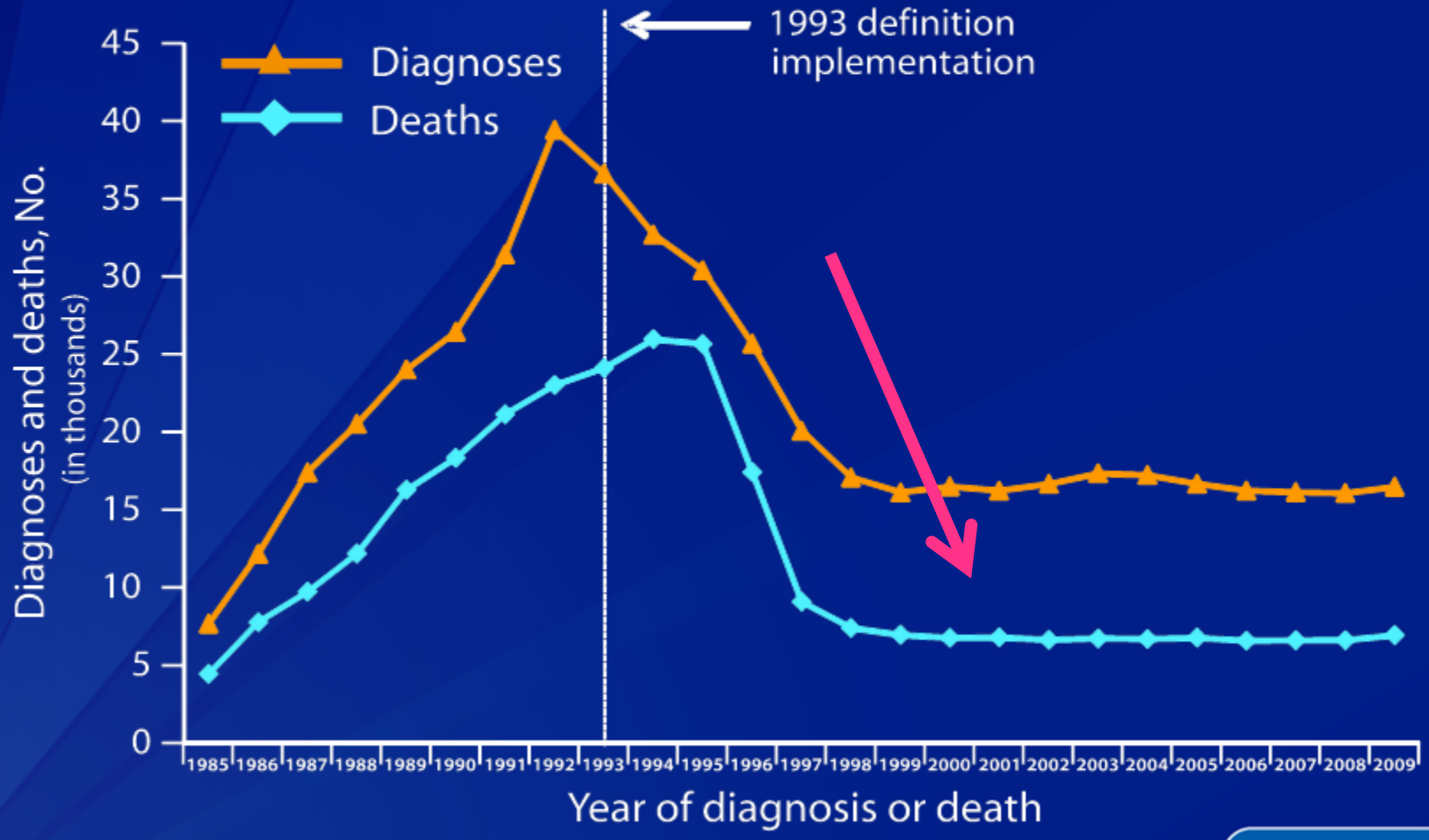
AIDS Diagnoses, Deaths, and Persons Living with AIDS, 1985–2009—United States and 6 U.S. Dependent Areas



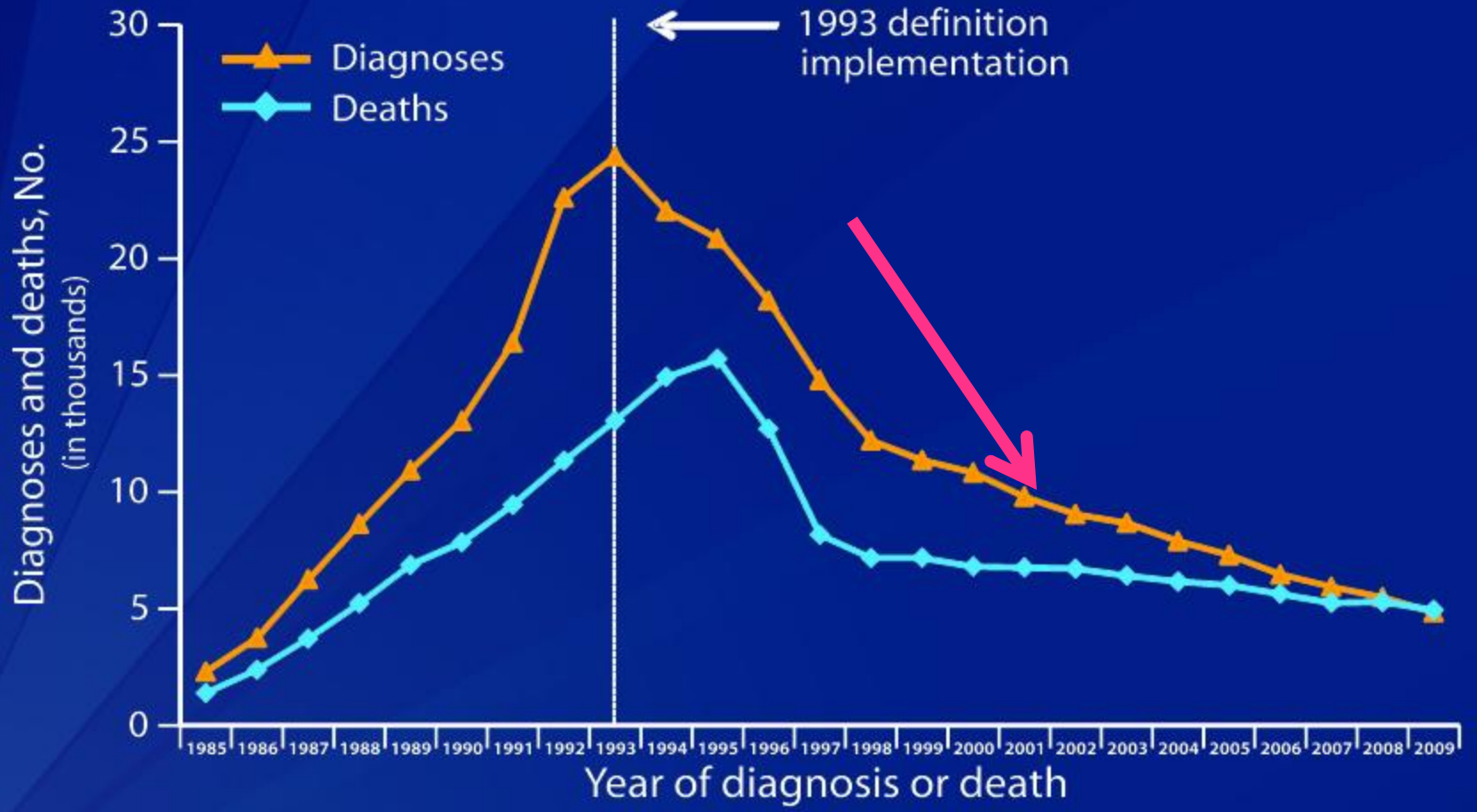
Note. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting. Death may be due to any cause.

AIDS Diagnoses and Deaths of Persons with AIDS, with HIV infection Attributed to Male-to-Male Sexual Contact, 1985–2009—United States and 6 U.S. Dependent Areas



Note. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting. Death may be due to any cause.

AIDS Diagnoses and Deaths of Persons with AIDS, with HIV Infection Attributed to Injection Drug Use, 1985–2009—United States and 6 U.S. Dependent Areas

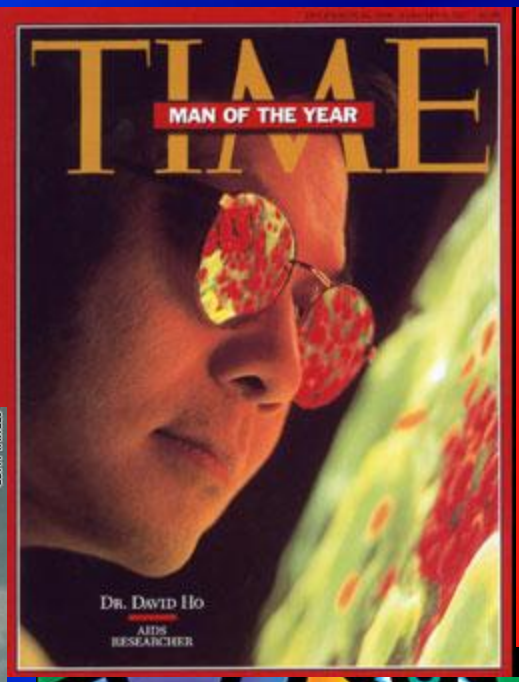


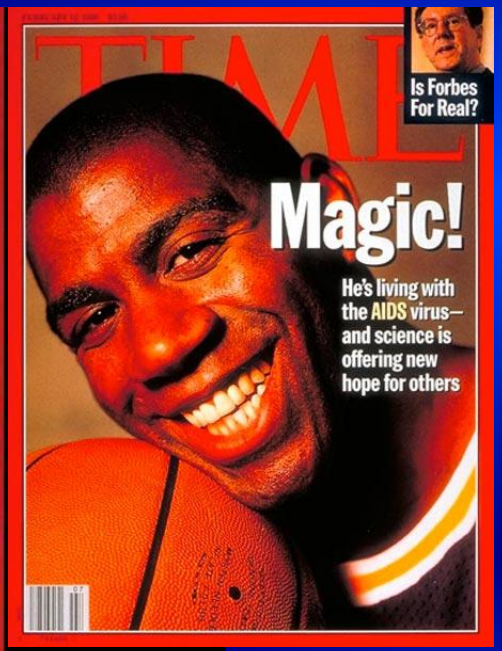
Note. All displayed data have been statistically adjusted to account for reporting delays and missing risk-factor information, but not for incomplete reporting. Death may be due to any cause.

CDC

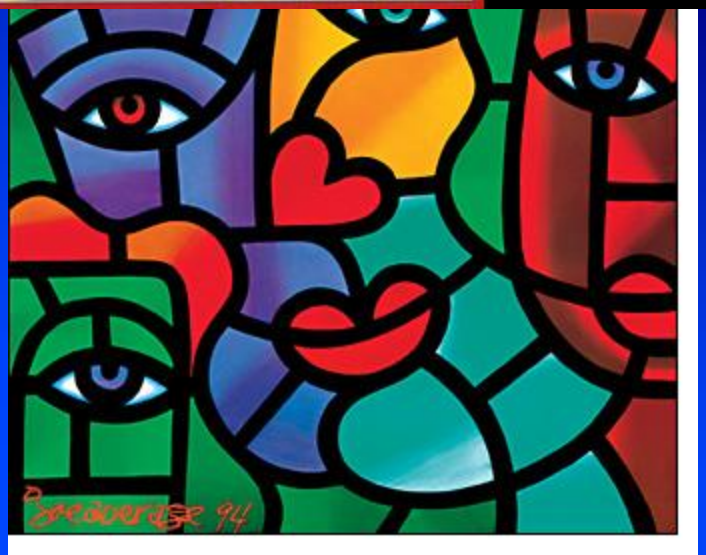
1996


XI International
Conference on AIDS
Vancouver, Canada
July 7–12, 1996

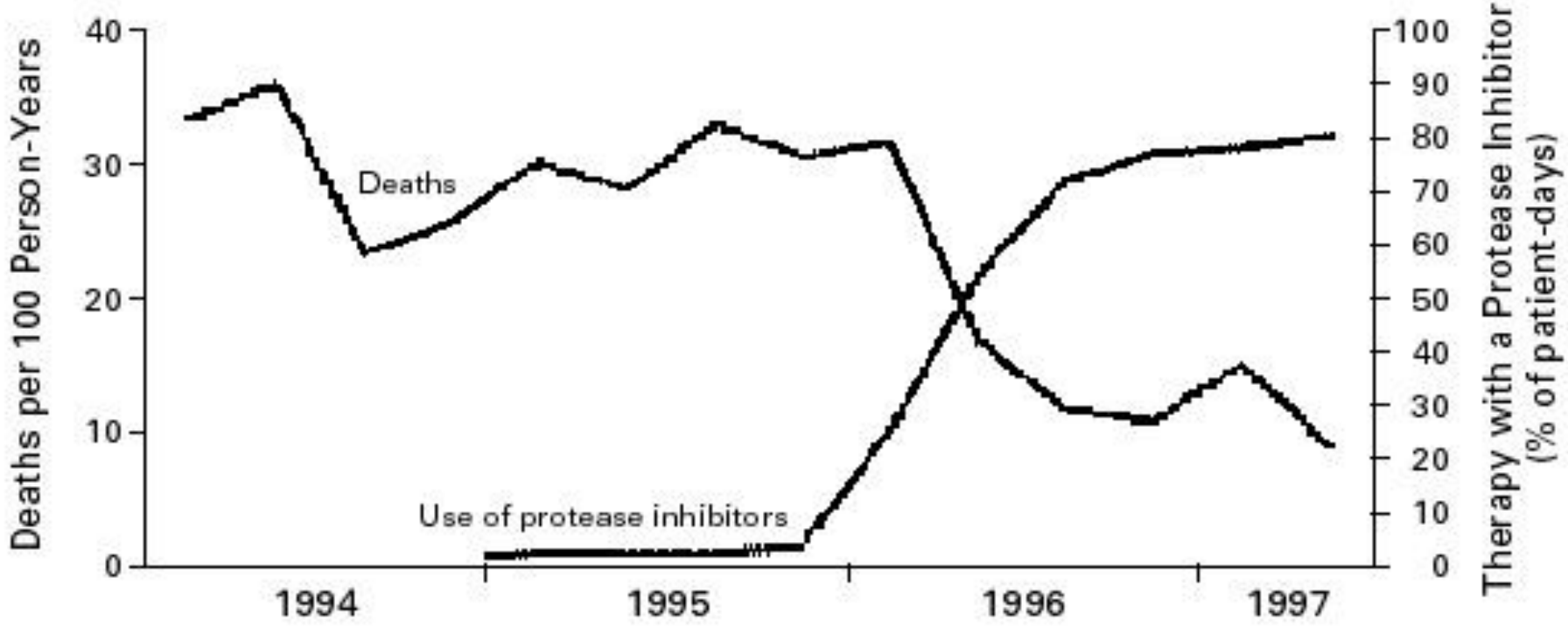

TIME
MAN OF THE YEAR
Dr. David Ho
AIDS
RESEARCHER


TIME
Is Forbes
For Real?
Magic!
He's living with
the AIDS virus–
and science is
offering new
hope for others


GETTY IMAGES



Mortality declines as protease inhibitor therapy use increases, 1994-1997 (CD4 < 100)



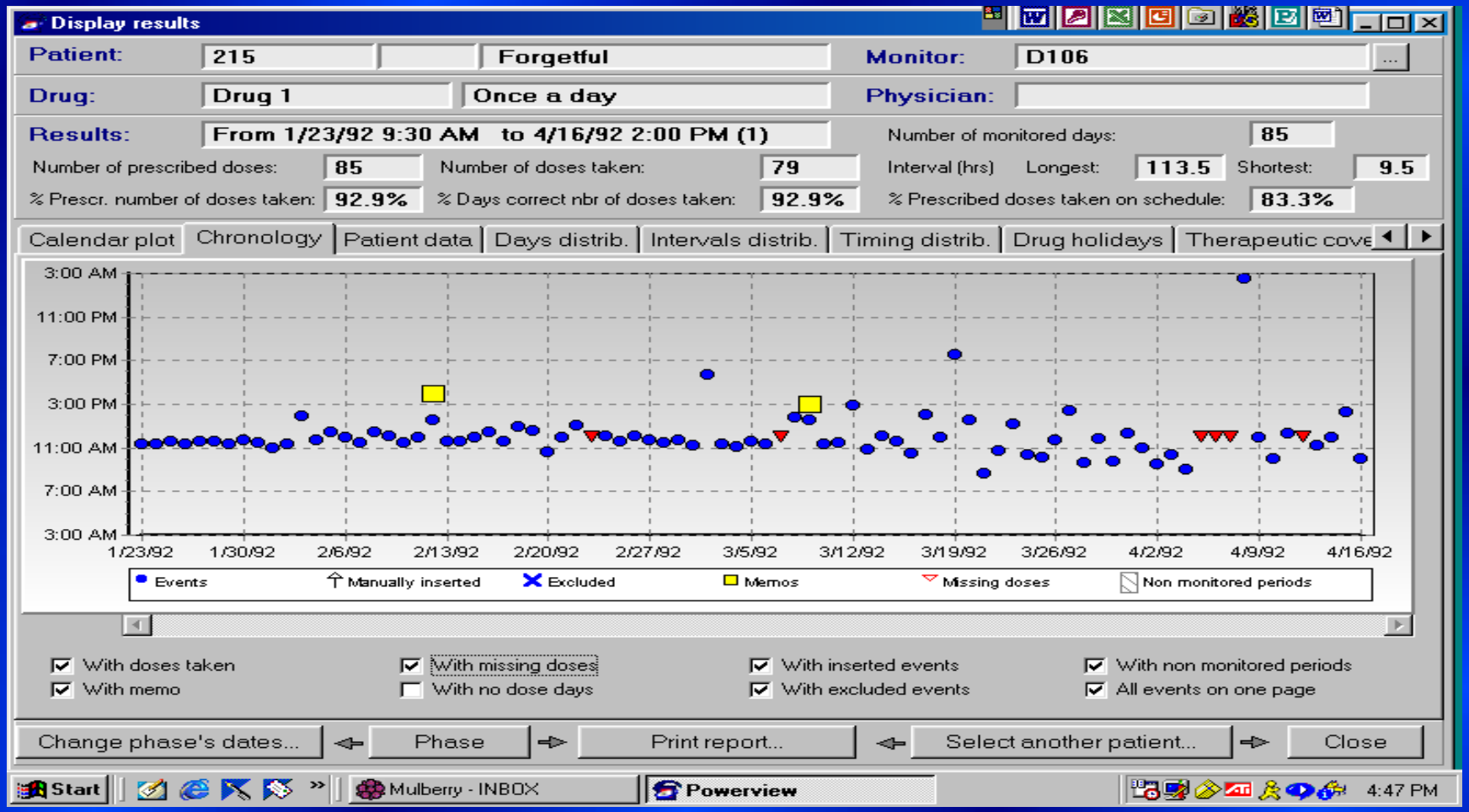
Palella FJ Jr et al. N Engl J Med 1998;338:853-860.

The NEW ENGLAND JOURNAL of MEDICINE

Adherence

Electronic Monitoring (MEMs)

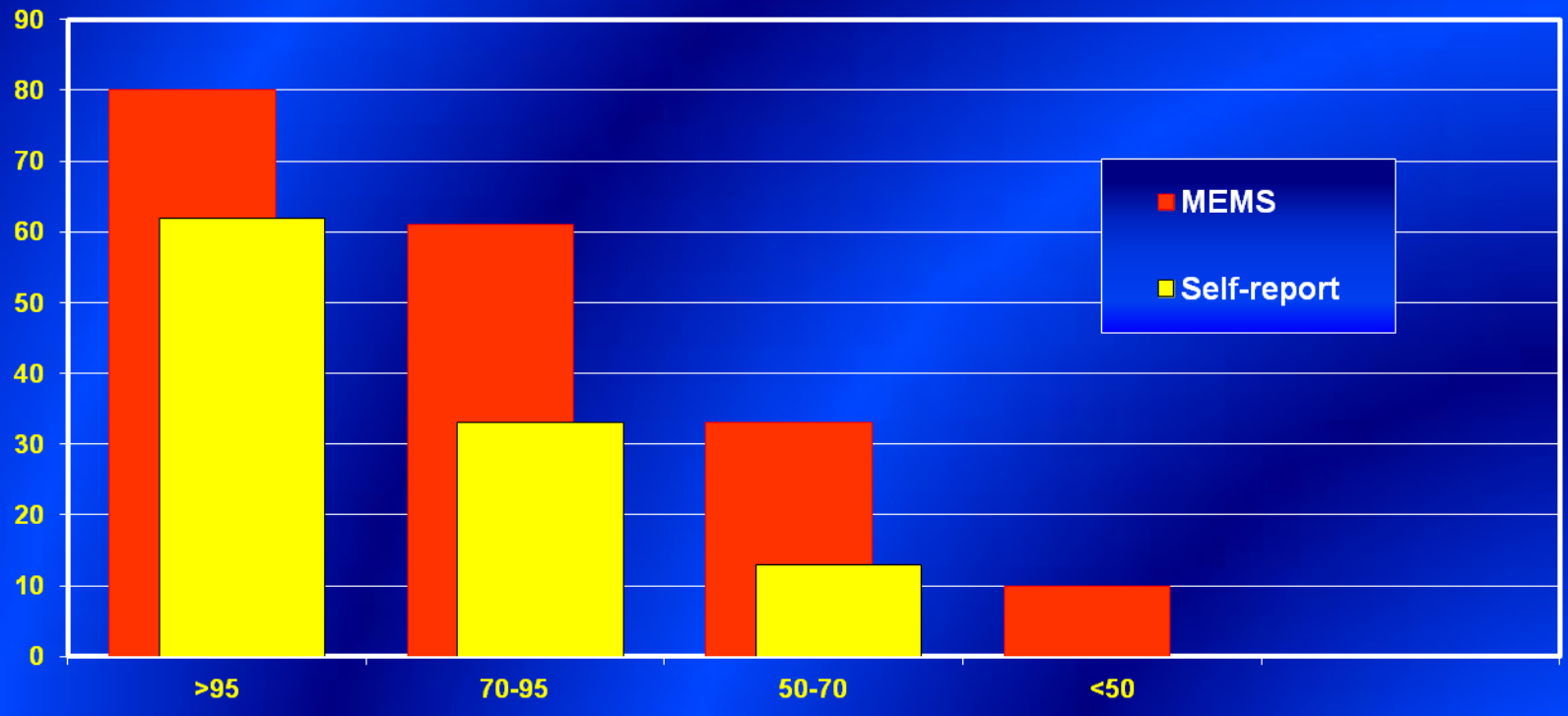
MEMs DATA


Display results
Patient: 215 Forgetful
Monitor: D106
Drug: Drug 1 Once a day
Physician:
Results: From 1/23/92 9:30 AM to 4/16/92 2:00 PM (1)
Number of monitored days: 85
Number of prescribed doses: 85
Number of doses taken: 79
Interval (hrs) Longest: 113.5 Shortest: 9.5
% Prescr. number of doses taken: 92.9%
% Days correct nbr of doses taken: 92.9%
% Prescribed doses taken on schedule: 83.3%
Calendar plot
Chronology
Patient data
Days distrib.
Intervals distrib.
Timing distrib.
Drug holidays
Therapeutic cove
3:00 AM
11:00 PM
7:00 PM
3:00 PM
11:00 AM
7:00 AM
3:00 AM
1/23/92
1/30/92
2/6/92
2/13/92
2/20/92
2/27/92
3/5/92
3/12/92
3/19/92
3/26/92
4/2/92
4/9/92
4/16/92
Events
Manually inserted
Excluded
Memos
Missing doses
Non monitored periods
With doses taken
With memo
With missing doses
With no dose days
With inserted events
With excluded events
With non monitored periods
All events on one page
Change phase's dates...
Phase
Print report...
Select another patient...
Close
Start
Mulberry - INBOX
Powerview
4:47 PM

How do MEMs and self-reported ART adherence compare?

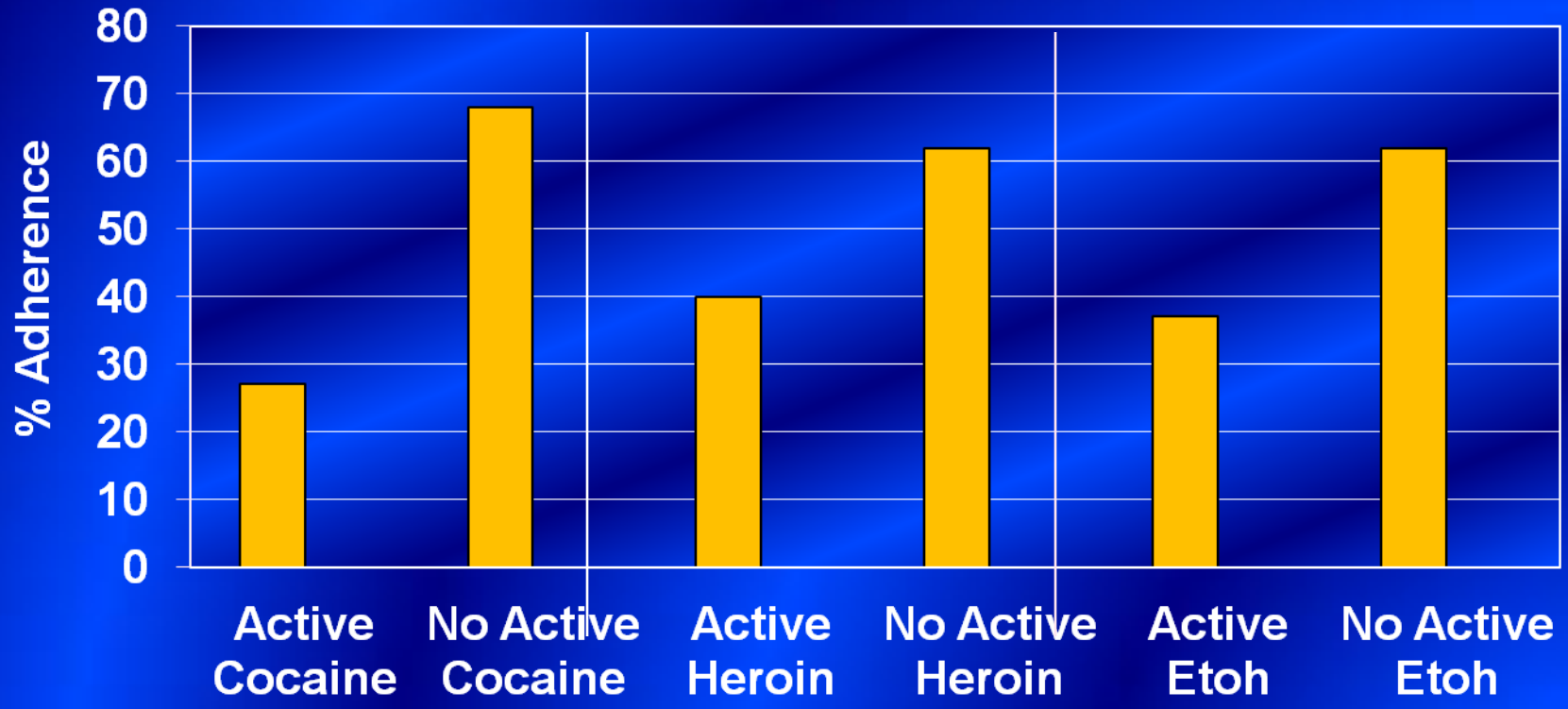
% undetectable viral load

N = 67



Arnsten et al, CID. 2001;33:1417-1423

Higher adherence in substance users without recent use



Arnsten et al, JGIM, May 2002

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Implementation of universal directly observed therapy at a New York City hospital and evaluation of an out-patient directly observed therapy program

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SUMMARY

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erved therapy (DOT) programs in public, private and community facilities in New York City.

OBJECTIVE: A key feature of the TB DOT program was ients and increase othesis was that ue of incentives hedule of increas-

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CONCLUSION: Increasing incentives is associated with improved adherence to therapy in inner city TB populations.

KEY WORDS: TB; adherence; DOT

Directly Observed Therapy and Treatment Completion for Tuberculosis in the United States: Is Universal Supervised Therapy Necessary?

Support for Treatment Adherence Research through Directly Observed Therapy

Specific Aims

To determine in a randomized trial if DOT HAART, provided on-site at a methadone clinic for 24 weeks, is more efficacious than self-administered HAART for:

-increasing adherence

-reducing HIV viral load

To assess durability of HAART DOT 3, 6, and 12 months after DOT discontinuation by comparing outcomes between DOT and self-administered treatment arms

Study arms for 24-week intervention

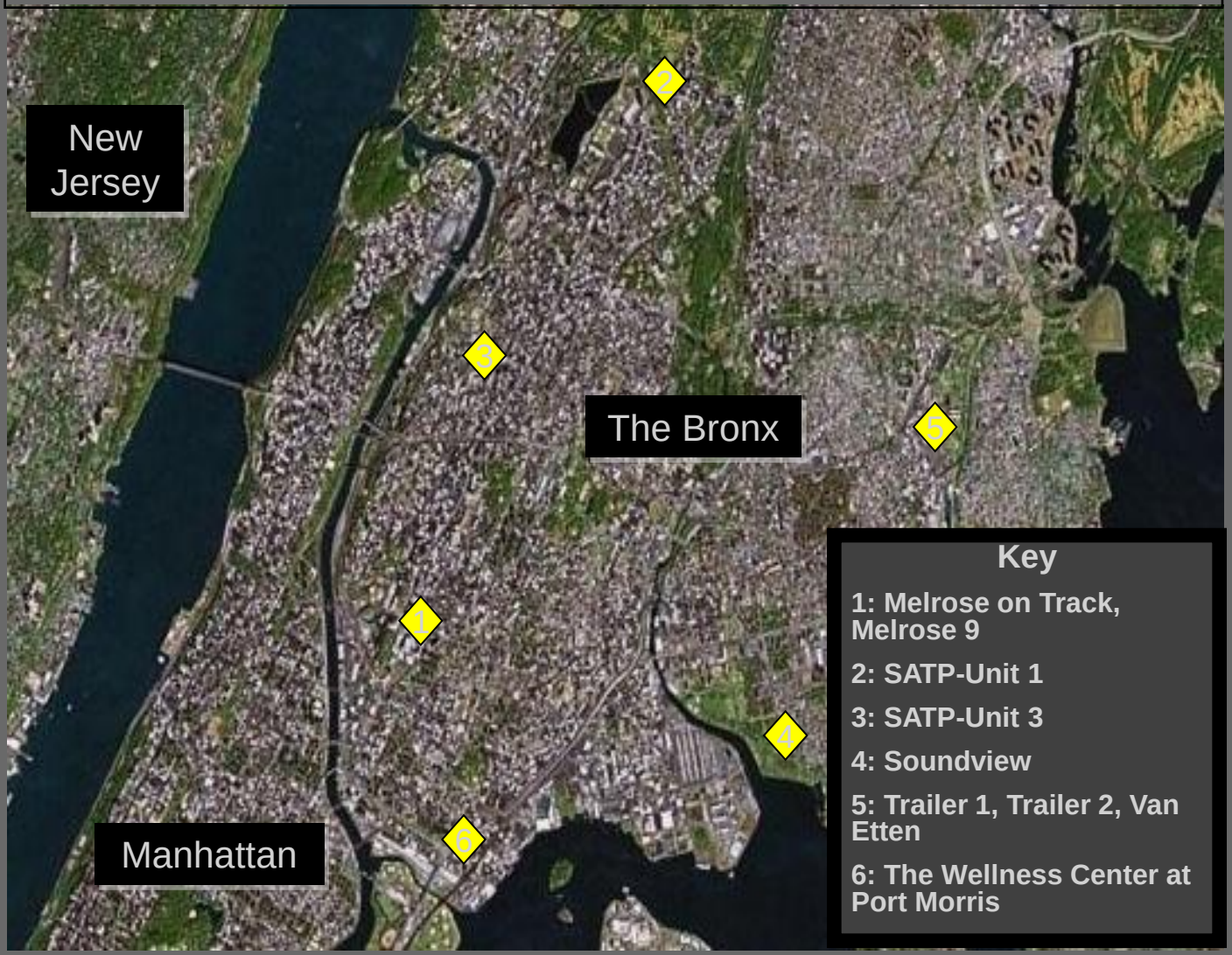
- TAU (Treatment as usual)
  - Adherence support from medical providers and adherence counselors
  - Self-administered antiretrovirals

- DOT (Directly Observed Therapy)
  - Adherence support
  - DOT antiretrovirals, delivered at methadone window 5-6 days/week

Eligibility

- HIV-infected and currently prescribed HAART
- Genotypic susceptibility to prescribed meds
- Methadone pick-up schedule: 5-6 d/week
- Stable methadone dose for 2 weeks
- Receiving HIV medical care from methadone clinic physician, a Montefiore physician , or a physician in a closely affiliated clinic

Clinic Locations



Key

1: Melrose on Track, Melrose 9

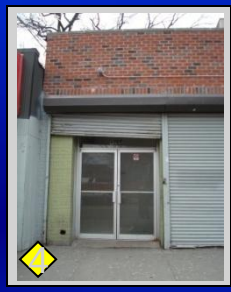
2: SATP-Unit 1

3: SATP-Unit 3

4: Soundview

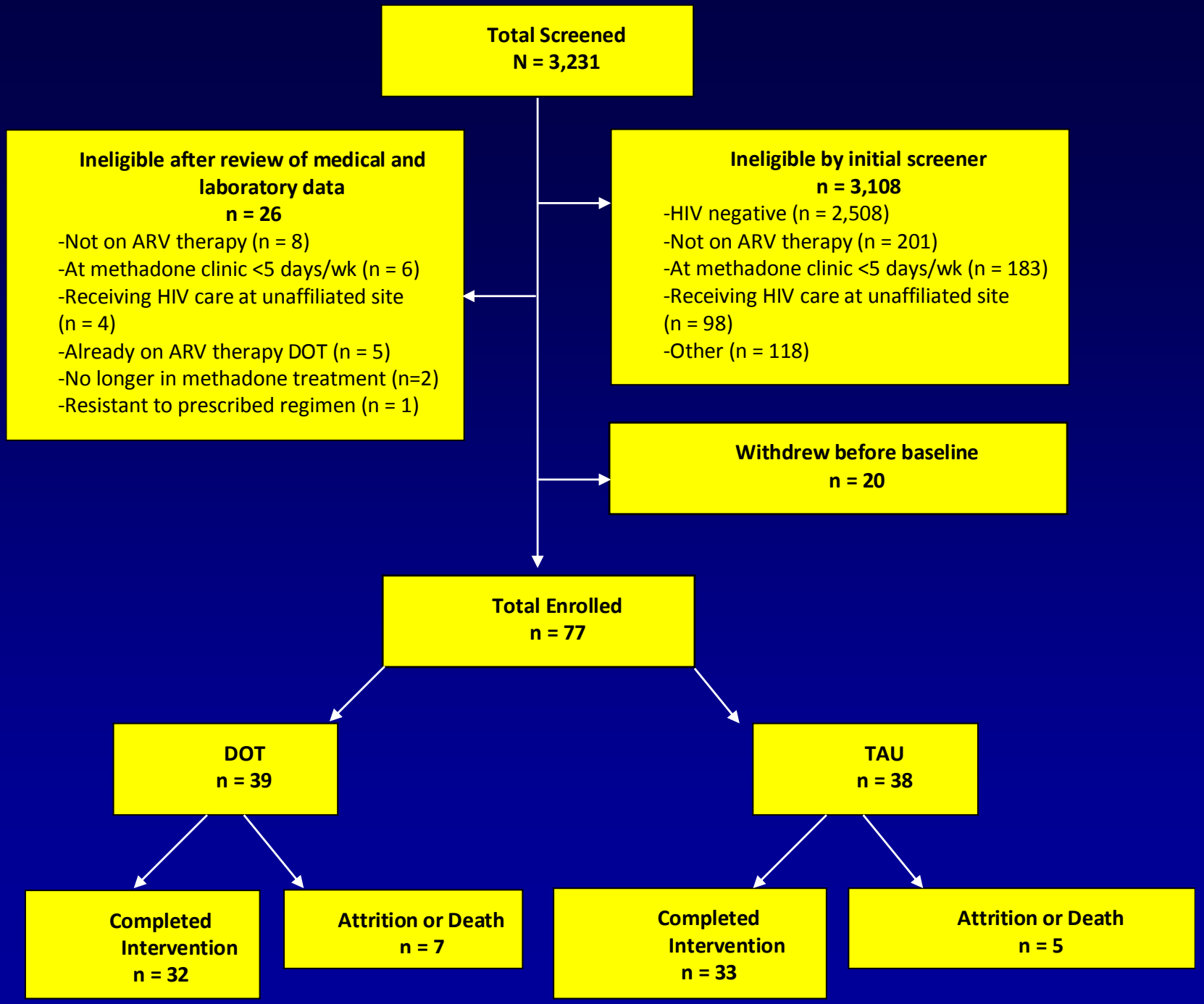
5: Trailer 1, Trailer 2, Van Etten

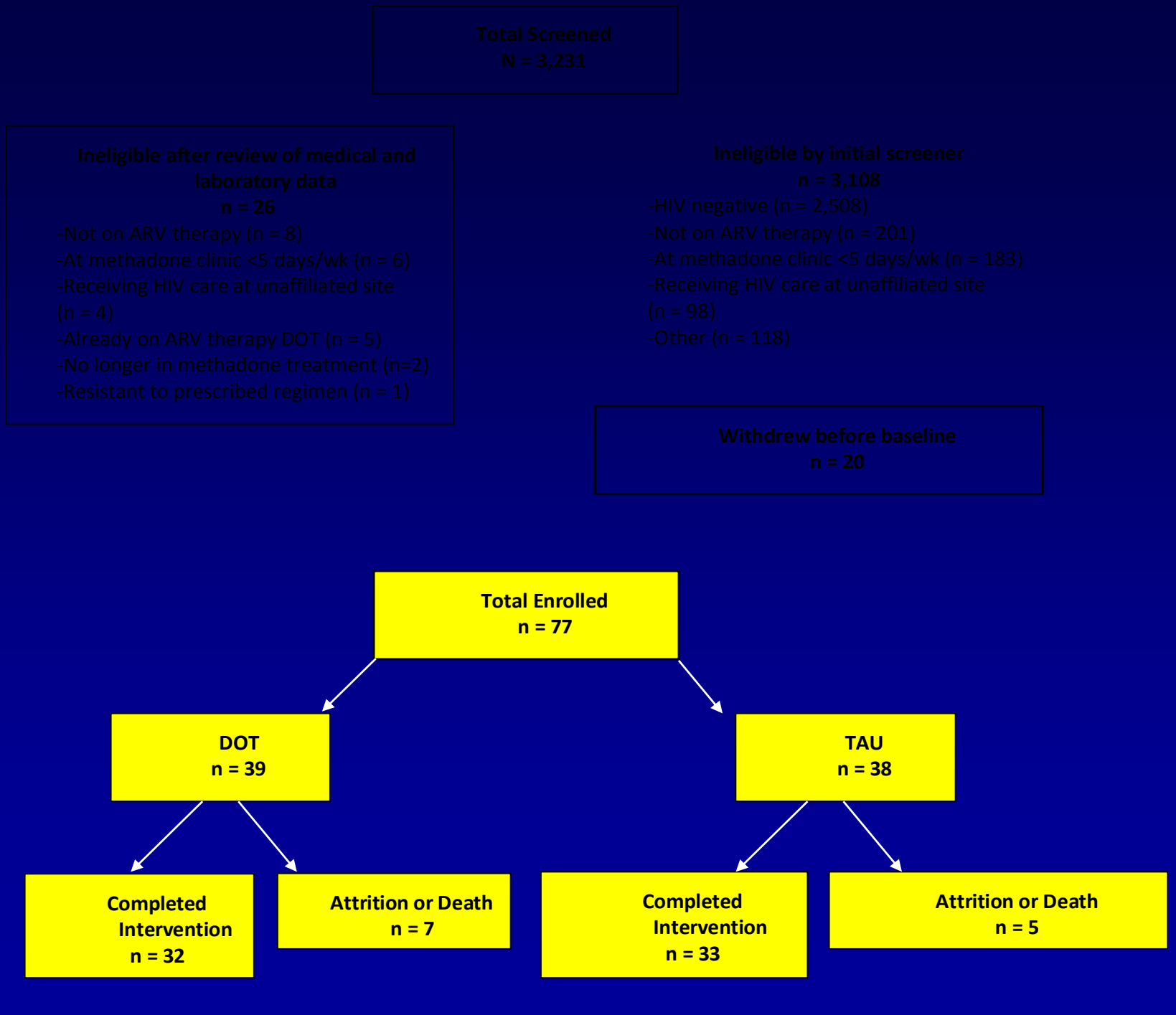
6: The Wellness Center at Port Morris




Hub 1 Methadone Clinic
EXIT

Methadone window


Total Screened
N = 3,231
Ineligible after review of medical and laboratory data
n = 26
-Not on ARV therapy (n = 8)
-At methadone clinic <5 days/wk (n = 6)
-Receiving HIV care at unaffiliated site (n = 4)
-Already on ARV therapy DOT (n = 5)
-No longer in methadone treatment (n=2)
-Resistant to prescribed regimen (n = 1)
Ineligible by initial screener
n = 3,108
-HIV negative (n = 2,508)
-Not on ARV therapy (n = 201)
-At methadone clinic <5 days/wk (n = 183)
-Receiving HIV care at unaffiliated site (n = 98)
-Other (n = 118)
Withdrew before baseline
n = 20
Total Enrolled
n = 77
DOT
n = 39
TAU
n = 38
Completed Intervention
n = 32
Attrition or Death
n = 7
Completed Intervention
n = 33
Attrition or Death
n = 5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DOT
n = 39
TAU
n = 38
Completed Intervention
n = 32
Attrition or Death
n = 7
Completed Intervention
n = 33
Attrition or Death
n = 5

Baseline characteristics (n=77)

	DOT (N = 39) N (%)	TAU (N = 38) N (%)
Age (mean yrs ± SD)	45.3 ± 6.5	48.8 ± 6.9
Race: Black	14 (36)	17 (45)
Hispanic	19 (49)	13 (34)
White	5 (13)	5 (13)
Female	20 (51)	16 (42)
Education (<= HS)	30 (77)	28 (74)
Married/common law	17 (44)	17 (45)

Drug use among study participants

	DOT (N = 39) N (%)	TAU (N = 38) N (%)
Alcohol use ≥2-3x/week (baseline)	7 (18)	7 (19)
Any opiate use	26 (67)	25 (66)
Frequent opiate use (more than 50% urines ++)	9 (23)	11 (29)
Any cocaine use	25 (64)	31 (82)
Frequent cocaine use (more than 50% urines ++)	22 (56)	20 (53)
Number of urine tests	11	12

Specific Aims

To determine in a randomized trial if DOT HAART, provided on-site at a methadone clinic for 24 weeks, is more efficacious than self-administered HAART for:

-increasing adherence

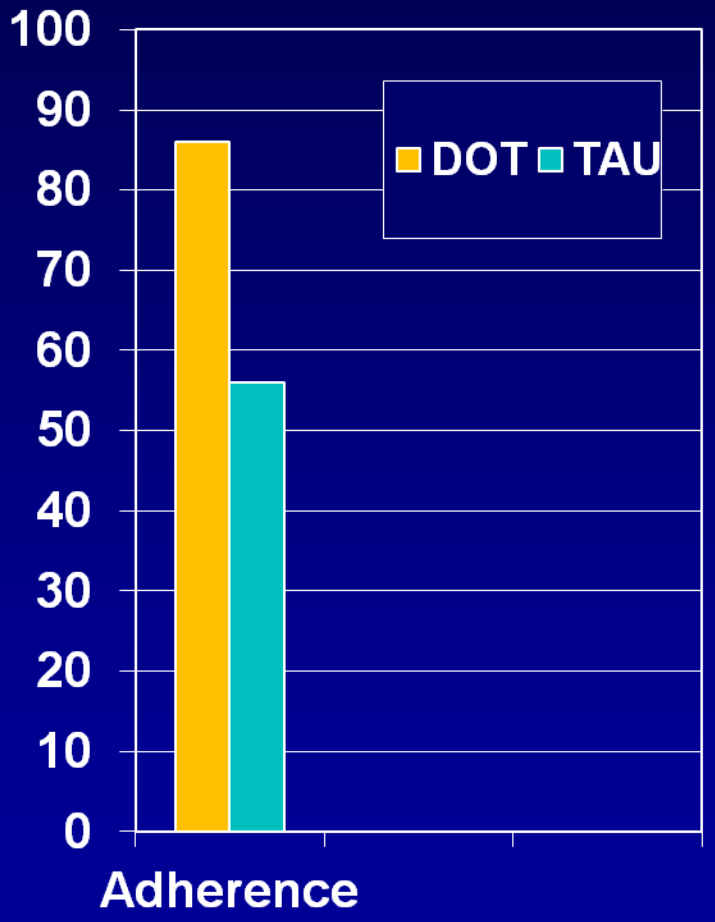
-reducing HIV viral load

To assess durability of HAART DOT 3, 6, and 12 months after DOT discontinuation by comparing outcomes between DOT and self-administered treatment arms

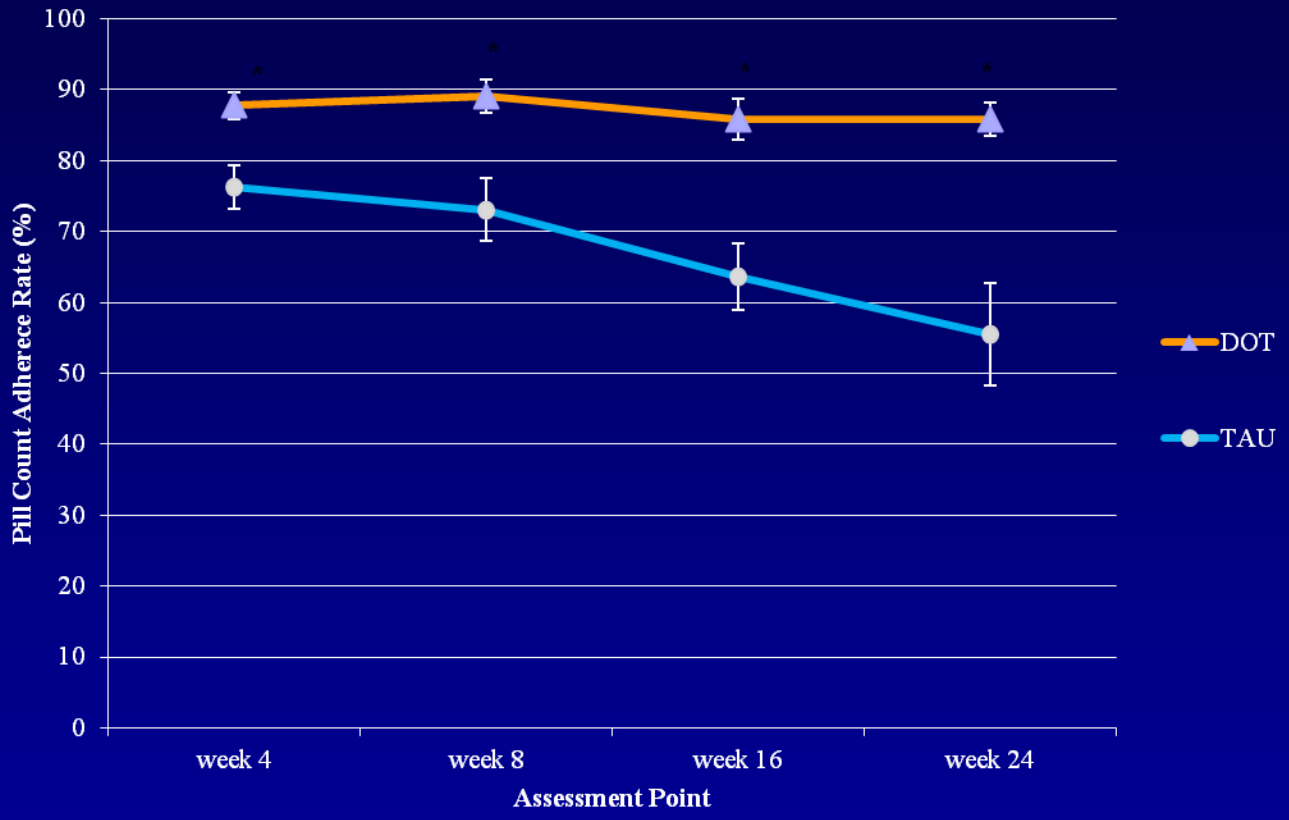
DOT subjects had better adherence

- During 24 weeks, median pill count adherence higher for DOT than TAU subjects

- 86% v. 56%
  $p < 0.001$



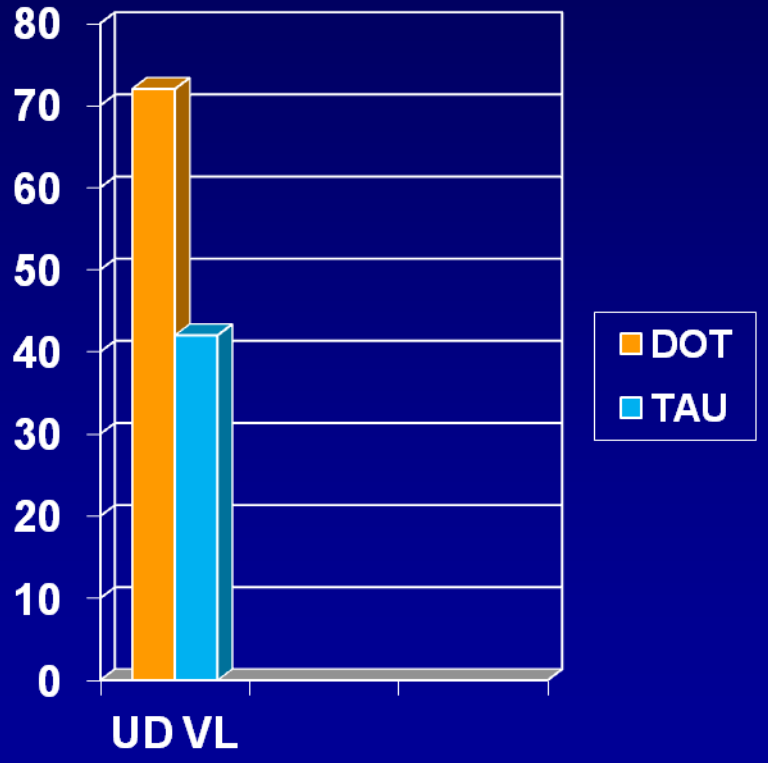
Adherence during intervention



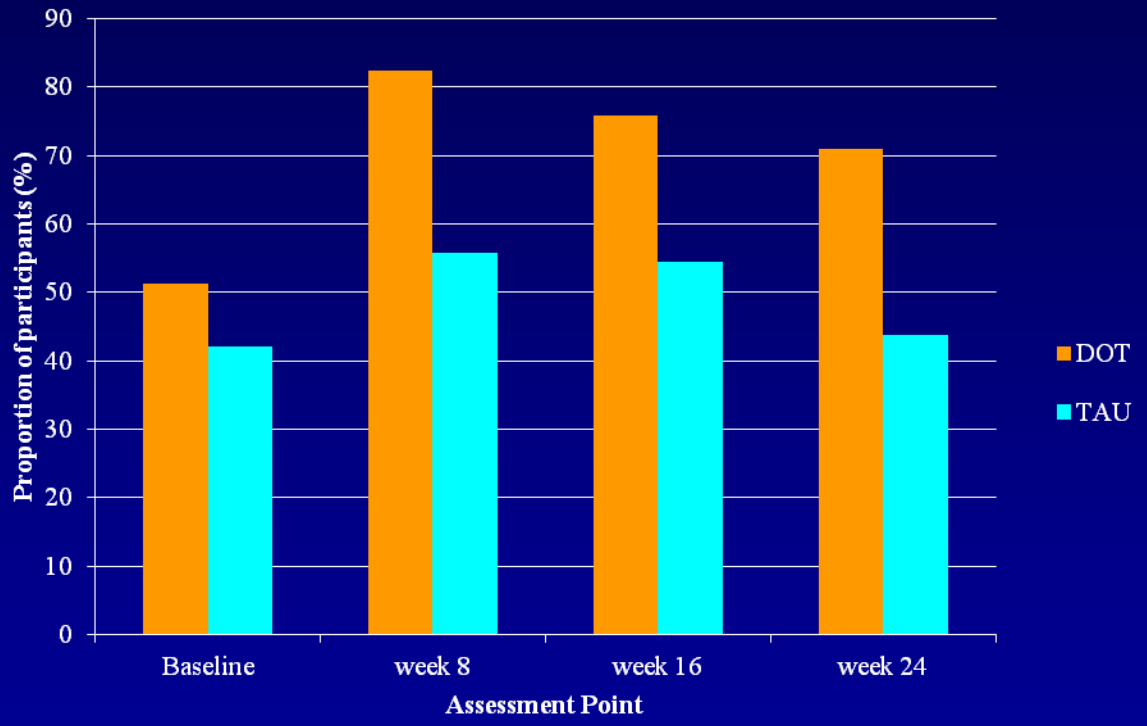
Week	DOT adherence (%)	TAU adherence (%)
Baseline	88	76
Week 8	89	73
Week 16	86	64
Week 24	86	56

DOT subjects more likely to have undetectable viral load

- Adjusting for baseline VL, after 24 weeks, more DOT than TAU participants had undetectable VL (< 75 copies/ml
- 71% v. 44%, p = 0.01
- After 24 weeks, mean VL was lower for DOT than TAU 2.21 v. 2.90 $_{log10}$, p = 0.01
- VL dropped 0.4 $_{log}$ in DOT and increased 0.1 $_{log}$ in TAU.



Viral load during intervention



Week	DOT undetectable (%)	TAU undetectable (%)
Baseline	54	42
Week 8	82	56
Week 16	76	55
Week 24	71	44

Specific Aims

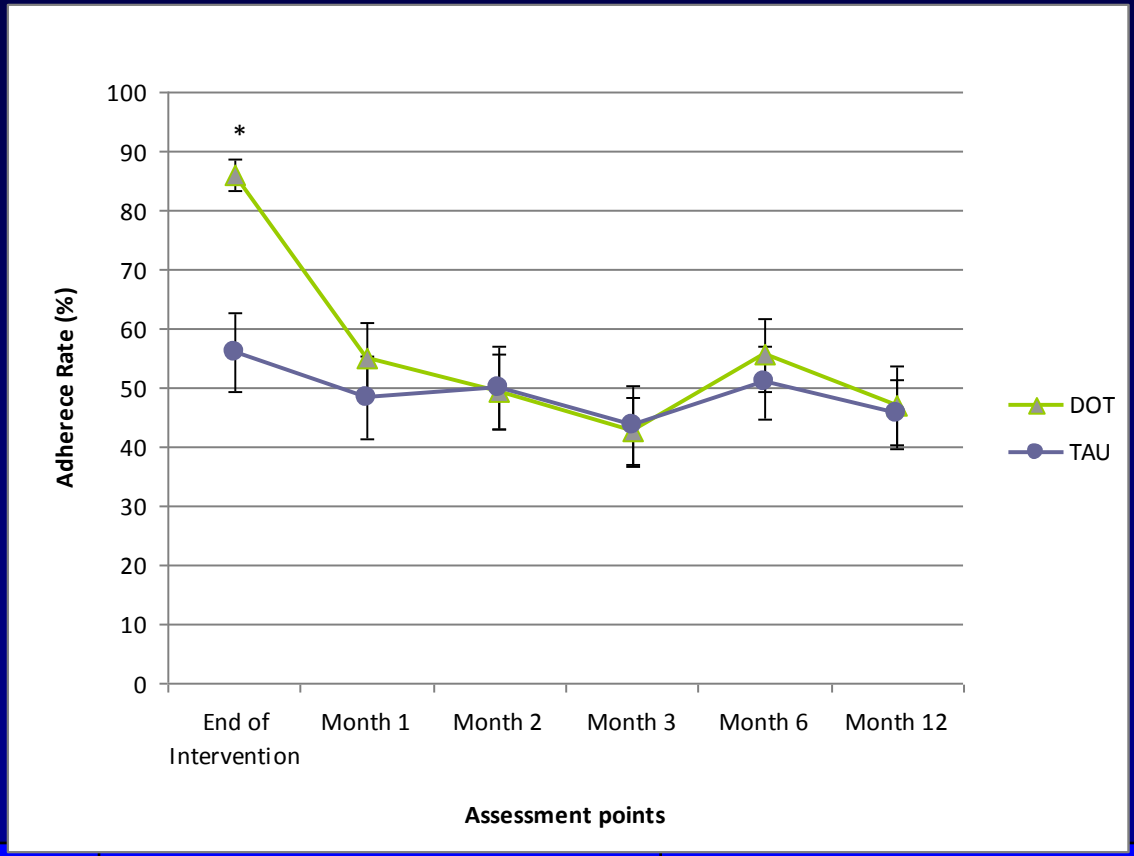
To determine in a randomized trial if DOT HAART, provided on-site at a methadone clinic for 24 weeks, is more efficacious than self-administered HAART for:

-increasing adherence

-reducing HIV viral load

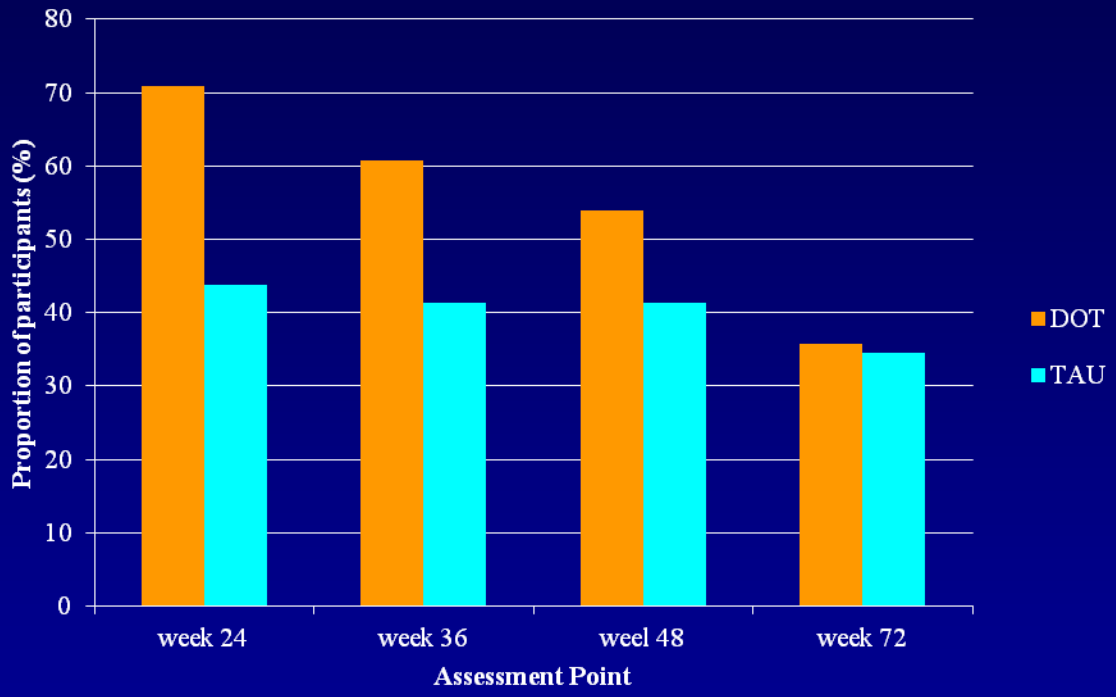
To assess durability of HAART DOT 3, 6, and 12 months after DOT discontinuation by comparing outcomes between DOT and self-administered treatment arms

Adherence post-intervention



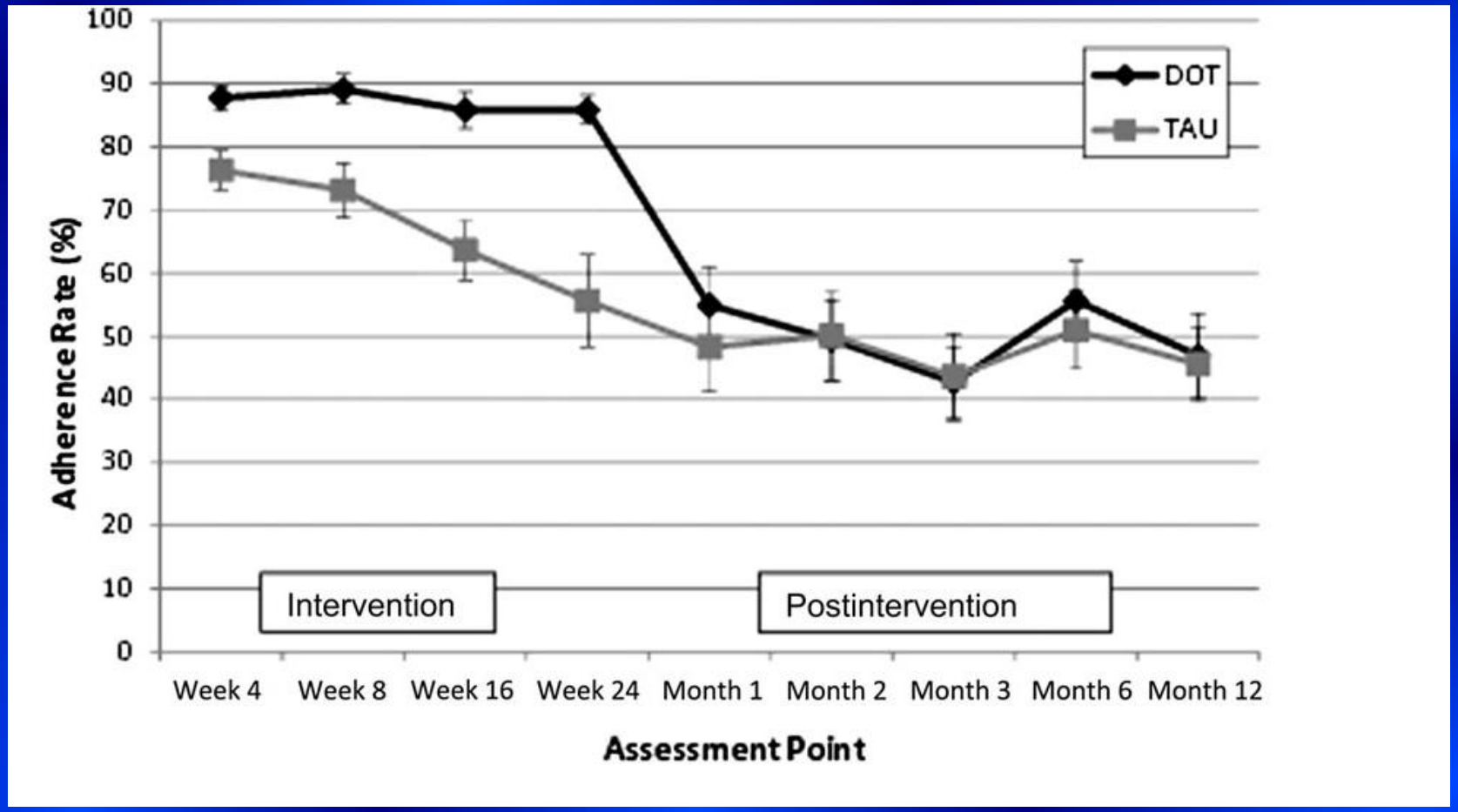
Week	DOT adherence (%)	TAU adherence (%)
Week 24	86	56
Week 36	43	44
Week 48	56	51
Week 72	47	47

Viral load post-intervention



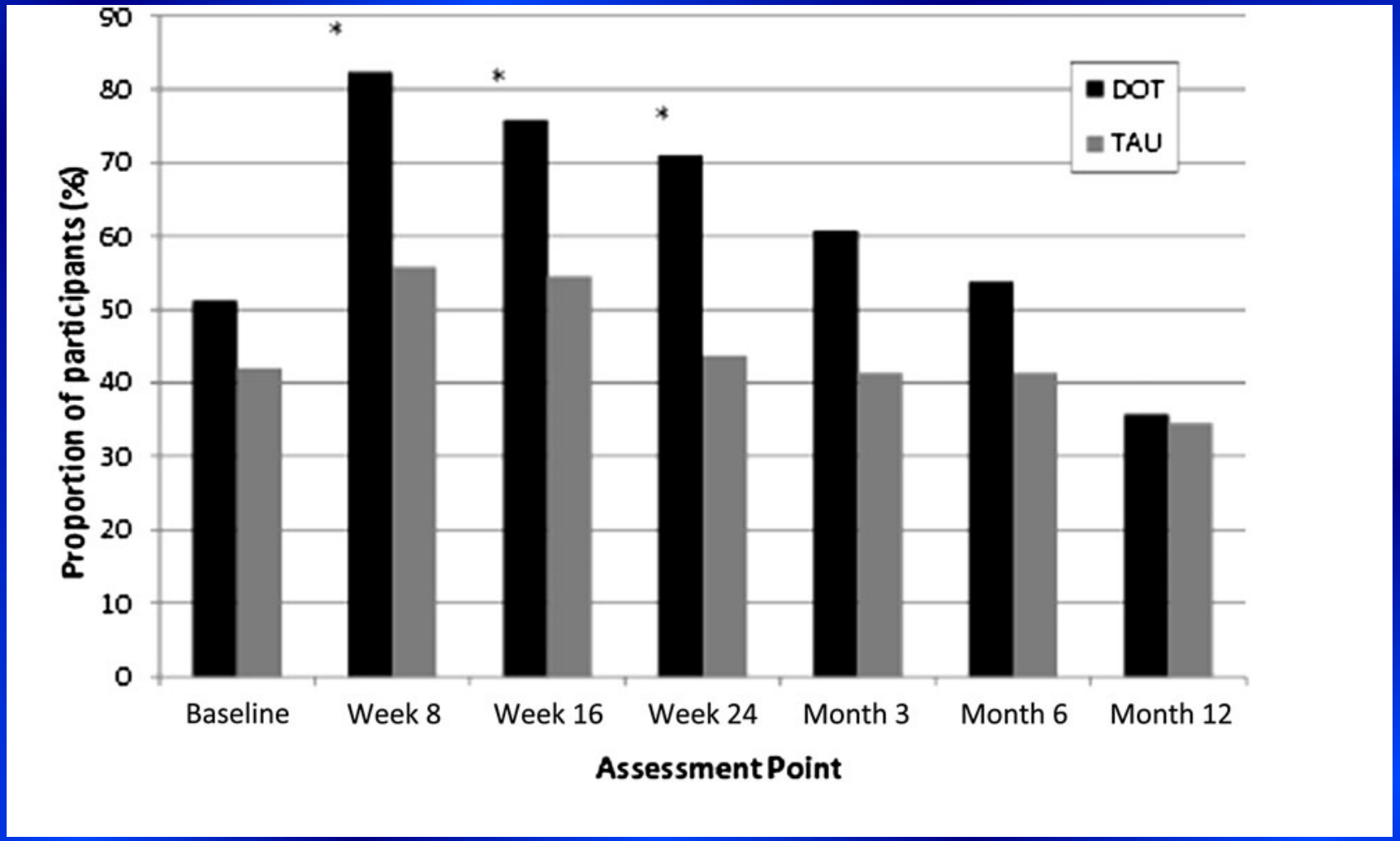
Week	DOT undetectable (%)	TAU undetectable (%)
Week 24	71	44
Week 36	61	41
Week 48	54	41
Week 72	36	34

Adherence during and after intervention



Berg KM, 2010

Viral load during and after intervention



Berg KM, 2010

HIV/AIDS MAJOR ARTICLE

Lack of Sustained Improvement in Adherence or Viral Load Following a Directly Observed Antiretroviral Therapy Intervention

Karina M. Berg,[1,2] Alain H. Litwin,[1,2] Xuan Li,[1] Moonseong Heo,[3] and Julia H. Arnsten[1,2,3]

[1]Department of Medicine, [2]Department of Psychiatry and Behavioral Sciences, and [3]Department of Epidemiology and Population Health, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York

Background. Methadone clinic–based directly observed antiretroviral therapy (DOT) has been shown to be more efficacious for improving adherence and suppressing human immunodeficiency virus (HIV) load than

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Directly observed antiretroviral therapy eliminates adverse effects of active drug use on adherence

Shadi Nahvi[a,b], Alain H. Litwin[a,b], Moonseong Heo[c], Karina M. Berg[a,d], Xuan Li[a], Julia H. Arnsten[a,b,c,*]

[a] Department of Medicine (Division of General Internal Medicine), Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY, United States
[b] Department of Psychiatry and Behavioral Sciences (Division of Substance Abuse), Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY, United States
[c] Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, United States
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AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 26, Number 00, 2010

DOI: 10.1089/aid.2010.0181

Directly Observed Antiretroviral Therapy in Substance Abusers Receiving Methadone Maintenance Therapy Does Not Cause Increased Drug Resistance

James C.M. Brust,[1,2] Alain H. Litwin,[1,3] Karina M. Berg,[1,3] Xuan Li,[1] Moonseong Heo,[4] and Julia H. Arnste

Abstract

Direct observation of antiretroviral t
but whether this affects the develo
conducted a 24-week randomized c
treatment as usual (TAU) among a
new resistance mutations, we identi
either week 8 or week 24. We compa
in the two arms of the trial. Amon
efficacious for improving adherence
HIV viral load at both baseline and
tions not seen at baseline (three in
the TAU arm developed major mut
jects in the DOT arm developed su

AIDS Behav (2012) 16:461–468
DOI 10.1007/s10461-010-9864-z

ORIGINAL PAPER

Comparison of Antiretroviral Adherence Questions

Karina M. Berg · Ira B. Wilson · Xuan Li · Julia H. Arnsten

Published online: 23 December 2010

Abstract Our objective was to compare antiretroviral adherence questions to better understand concordance between measures. Among 53 methadone maintained HIV-infected drug users, we compared five measures, including two single item measures using qualitative Likert-type responses, one measure of percent adherence, one visual analog scale, and one multi-item measure that averaged responses across antiretrovirals. Responses were termed inconsistent if respondents endorsed the highest adherence level on at least one measure but middle levels on others. We examined ceiling effects, concordance, and correlations with VL. Response distributions differed markedly between measures. A ceiling effect was less pronounced for the single-item measures than for the measure that averaged responses for each antiretroviral: the proportion with 100% adherence varied from 22% (single item measure) to 58% (multi-item measure). Overall agreement between measures ranged from fair to good; 49% of participants had inconsistent responses. Though responses correlated with VL, single-item measures had higher cor-

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Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

Rationale, design, and sample characteristics of a randomized controlled trial of directly observed antiretroviral therapy delivered in methadone clinics☆

Karina M. Berg, Jennifer Mouriz, Xuan Li, Elise Duggan, Uri Goldberg, Julia H. Arnsten *

Division of General Internal Medicine, Department of Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467, USA
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Keywords:
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Substance abuse treatment
Antiretroviral therapy

ABSTRACT

Background: Directly observed therapy (DOT) programs for HIV treatment have demonstrated feasibility, acceptability, and improved viral suppression, but few have been rigorously tested. We describe a randomized controlled trial testing the efficacy of an antiretroviral DOT program in methadone maintenance clinics. Our objective was to determine if DOT is more efficacious than self-administered antiretroviral therapy for reducing HIV viral load, improving adherence, and reducing drug resistance among opioid dependent drug users receiving methadone treatment.

Methods: Participants were randomized to treatment as usual (TAU) or antiretroviral DOT for the 24-week intervention. TAU participants received standard adherence counseling, and DOT participants received standard adherence counseling plus directly observed antiretroviral therapy, which was delivered at the same time as they received daily methadone. Assessments occurred at baseline, weekly for 8 weeks, and then monthly for 4 months. Our primary outcomes were between-group changes from baseline to the end of the intervention in: HIV viral load, antiretroviral adherence, and number of viral mutations.

Results: Between June 2004 and August 2007, we screened 3231 methadone-maintained patients and enrolled 77; 39 participants were randomized to DOT and 38 to TAU. 65 completed the 24-week intervention.

Conclusions: Our trial will allow rigorous evaluation of the efficacy of directly observed

Drug and Alcohol Dependence 113 (2011) 192–199

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Drug and Alcohol Dependence

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Directly observed antiretroviral therapy improves adherence and viral load in drug users attending methadone maintenance clinics: A randomized controlled trial☆

Karina M. Berg, Alain Litwin, Xuan Li, Moonseong Heo, Julia H. Arnsten *

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Keywords:
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Medication adherence
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Randomized trial

ABSTRACT

Objective: To determine if directly observed antiretroviral therapy (DOT) is more efficacious than self-administered therapy for improving adherence and reducing HIV viral load (VL) among methadone-maintained opioid users.
Design: Two-group randomized trial.
Setting: Twelve methadone maintenance clinics with on-site HIV care in the Bronx, New York.
Participants: HIV-infected adults prescribed combination antiretroviral therapy.
Main outcomes measures: Between group differences at four assessment points from baseline to week 24 in: (1) antiretroviral adherence measured by pill count, (2) VL, and (3) proportion with undetectable VL (<75 copies/ml).
Results: Between June 2004 and August 2007, we enrolled 77 participants. Adherence in the DOT group was higher than in the control group at all post-baseline assessment points: by week 24 mean DOT adherence was 86% compared to 56% in the control group ($p < 0.0001$). Group differences in mean adherence remained significant after stratifying by baseline VL (detectable versus undetectable). In addition, during the 24-week intervention, the proportion of DOT participants with undetectable VL increased from 51% to 71%.
Conclusions: Among HIV-infected opioid users, antiretroviral DOT administered in methadone clinics was efficacious for improving adherence and decreasing VL, and these improvements were maintained over a 24-week period. DOT should be more widely available to methadone patients.

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Research Fellow, 2004-06
Assistant Professor, 2006-11
Associate Professor (Yale), 2014-

- **Robert Wood Johnson Physician Faculty Scholar award ’06-’09**
- **NIDA/NIMH K23 ’07-’11: Agreement and validity of different adherence self-report measures**

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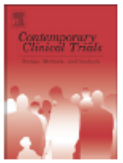

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Keywords Antiretroviral adherence · Self-report · Adherence measurement · HIV · Methadone

Portions of this work were presented at the National Institutes of Mental Health/International Association of Physicians in AIDS Care International Conference on HIV Treatment Adherence, Jersey City, NJ, March 2008 and at the 31st Society of General Internal Medicine Annual Meeting, Pittsburgh, PA, April 2008.

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J. H. Arnsten
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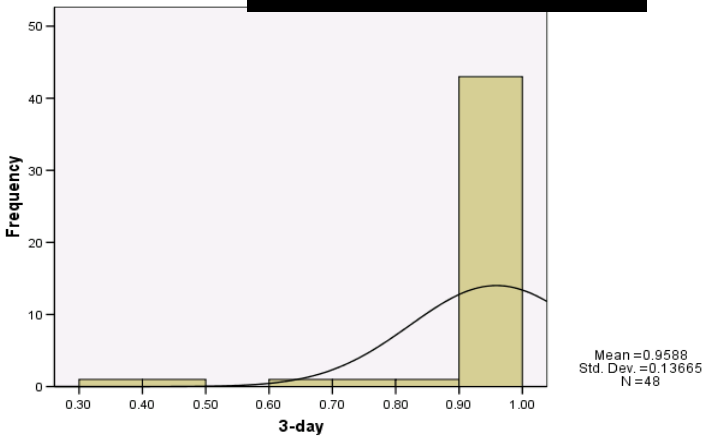
Introduction

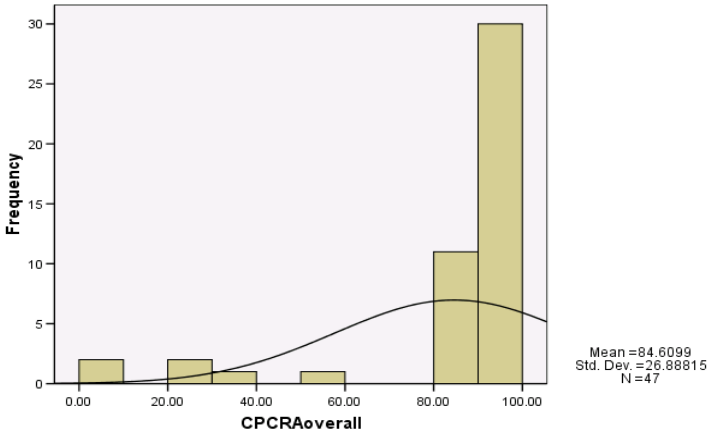
Detecting sub optimal adherence to antiretroviral therapy is critical for HIV providers because adherence-improving interventions have the potential to improve viral response, decrease opportunistic infections, prevent the emergence of drug resistant virus, and improve survival. However, detecting sub optimal adherence in clinical encounters can be challenging. Objective adherence measures, including electronic pill bottle monitors, pill counts, and pharmacy refill records, are considered more accurate than self-report, but are impractical in most clinical settings. Although self-report is vulnerable to numerous biases, associations between self-reported adherence and HIV VL have been well demonstrated [1, 2], including among drug users [3, 4]. However, despite robust evidence supporting the use of self-report to measure adherence, and the surfeit

Self-reported adherence is sensitive to the scale used (Berg et al, 2011)

ACTG



CPCRA



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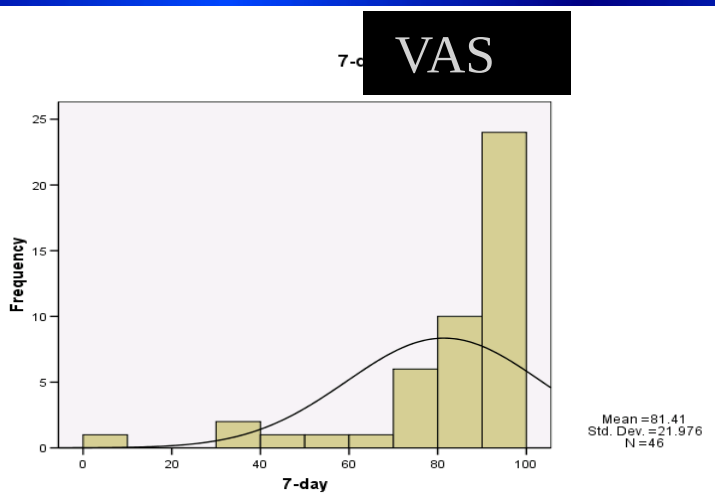
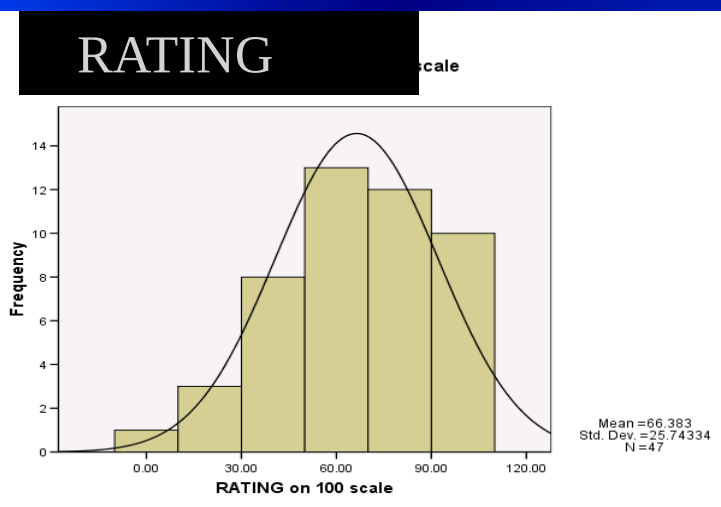


RATING



Shadi Nahvi, MD, MS
Instructor, 2004-2007
Assistant Professor, 2007-

- NIDA K23: RCT of DOT vs. self-administered varenicline for smoking cessation in methadone-maintained substance users
- K12/KL2 (CTSA): Placebo-controlled RCT of varenicline for smoking cessation in methadone maintained substance users

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Directly observed antiretroviral therapy eliminates adverse effects of active drug use on adherence

Shadi Nahvi[a,b], Alain H. Litwin[a,b], Moonseong Heo[c], Karina M. Berg[a,d], Xuan Li[a], Julia H. Arnsten[a,b,c,*]

[a] Department of Medicine (Division of General Internal Medicine), Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY, United States
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[c] Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, United States
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Keywords:
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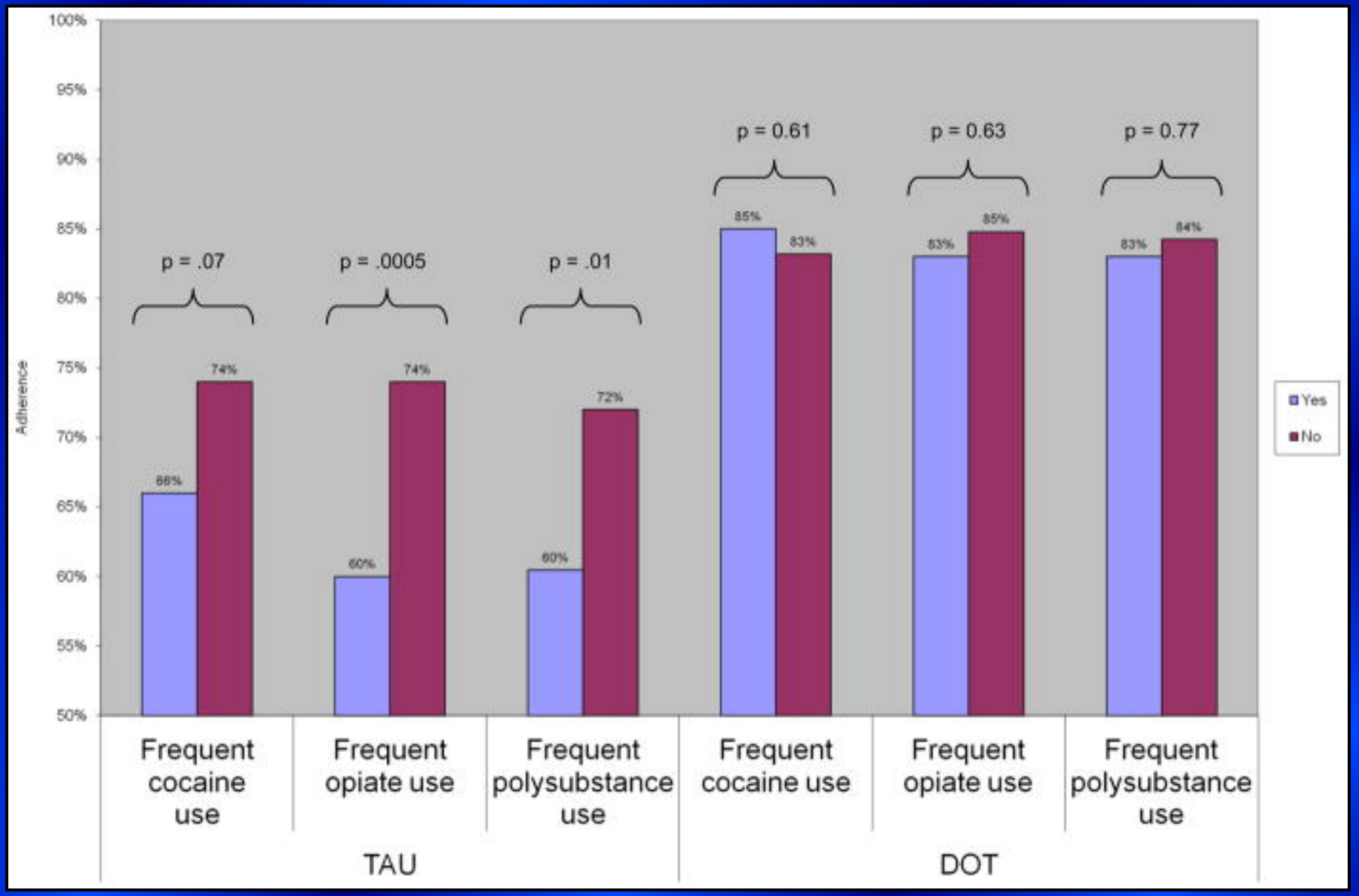
Methadone
Randomized trial
Substance use

ABSTRACT

Background: The impact of adherence enhancing interventions on the relationship between active drug use and adherence is largely unknown.
Methods: We conducted a 24-week randomized controlled trial of antiretroviral directly observed therapy (DOT) vs. treatment as usual (TAU) among HIV-infected methadone patients. Our outcome measure was pill count antiretroviral adherence, and our major independent variables were treatment arm (DOT vs. TAU) and active drug use (opiates, cocaine, or both opiates and cocaine). We defined any drug use as ≥1 positive urine toxicology result, and frequent drug use as ≥50% tested urines positive. We used mixed-effects linear models to evaluate associations between adherence and drug use, and included a treatment arm-by-drug use interaction term to evaluate whether DOT moderates associations between drug use and adherence.
Results: 39 participants were randomized to DOT and 38 to TAU. We observed significant associations between adherence and active drug use, but these were limited to TAU participants. Adherence was worse in TAU participants with any opiate use than in TAU participants without (63% vs. 75%, $p < 0.01$); and worse among those with any polysubstance (both opiate and cocaine) use than without (60% vs. 73%, $p = 0.01$). We also observed significant decreases in adherence among TAU participants with frequent opiate or frequent polysubstance use, compared to no drug use. Among DOT participants, active drug use was not associated with worse adherence.
Conclusions: Active opiate or polysubstance use decreases antiretroviral adherence, but the negative impact of drug use on adherence is eliminated by antiretroviral DOT.


100%
95%
90%
85%
80%
75%
70%
65%
60%
55%
50%
Adherence
p = .07
p = .0005
p = .01
p = 0.61
p = 0.63
p = 0.77
66%
74%
60%
74%
60%
72%
85%
83%
83%
85%
83%
84%
Yes
No
Frequent cocaine use
Frequent opiate use
Frequent polysubstance use
Frequent cocaine use
Frequent opiate use
Frequent polysubstance use
TAU
DOT

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- NIDA K23: Directly observed HCV therapy in methadone clinics
- Robert Wood Johnson Physician Faculty Scholar
- NIDA R03: Evaluating care for HCV by addiction medicine physicians
- NIDA R01: Models of care for HCV-infected drug users

HCV Group Treatment Model

Health Educator / Peer

- Sets up room: coffee, snacks
- Side effect and depression surveys done
- Weights taken
- Group discussion co-facilitated by Health Educator and Peer

Provider

- Conducts semi-private individual visits
- Vitals and focused physical
- Addresses adverse effects and adherence
- Administers peg interferon injections and growth factors as needed
- Answer group questions

Conclude with patient milestones, updates and peer-led meditation

Group Treatment Benefits

For Patients

- Social support is built-in to treatment
- Misconceptions addressed
- Reassurance by concurrent participation of peers
- ↓ fear of side effects: side effects normalized
- Directly administered peg
- Weekly oral meds dispensed
- Support for recovery
- "Upward spiral"

For Providers

- Frequent contact: providers and peers
- Co-management of cohort enhances expertise and confidence
- Multidisciplinary
- Natural mentoring opportunity
- Break from "the usual"

Group Treatment in Action

Thank you for listening