

Gary Reiter 1955-
2003



Andy Kaplan
1959-2006



Rob Malow
1953-2013

(My) Turning Points in HIV Treatment Adherence Research

David Bangsberg, MD, MPH

Director
Massachusetts General Hospital Center for Global Health

Professor
Harvard Medical School

Professor
Harvard School of Public Health

Visiting Professor
Mbarara University of Science and Technology



SUCCEED WE MUST

My Turning Points

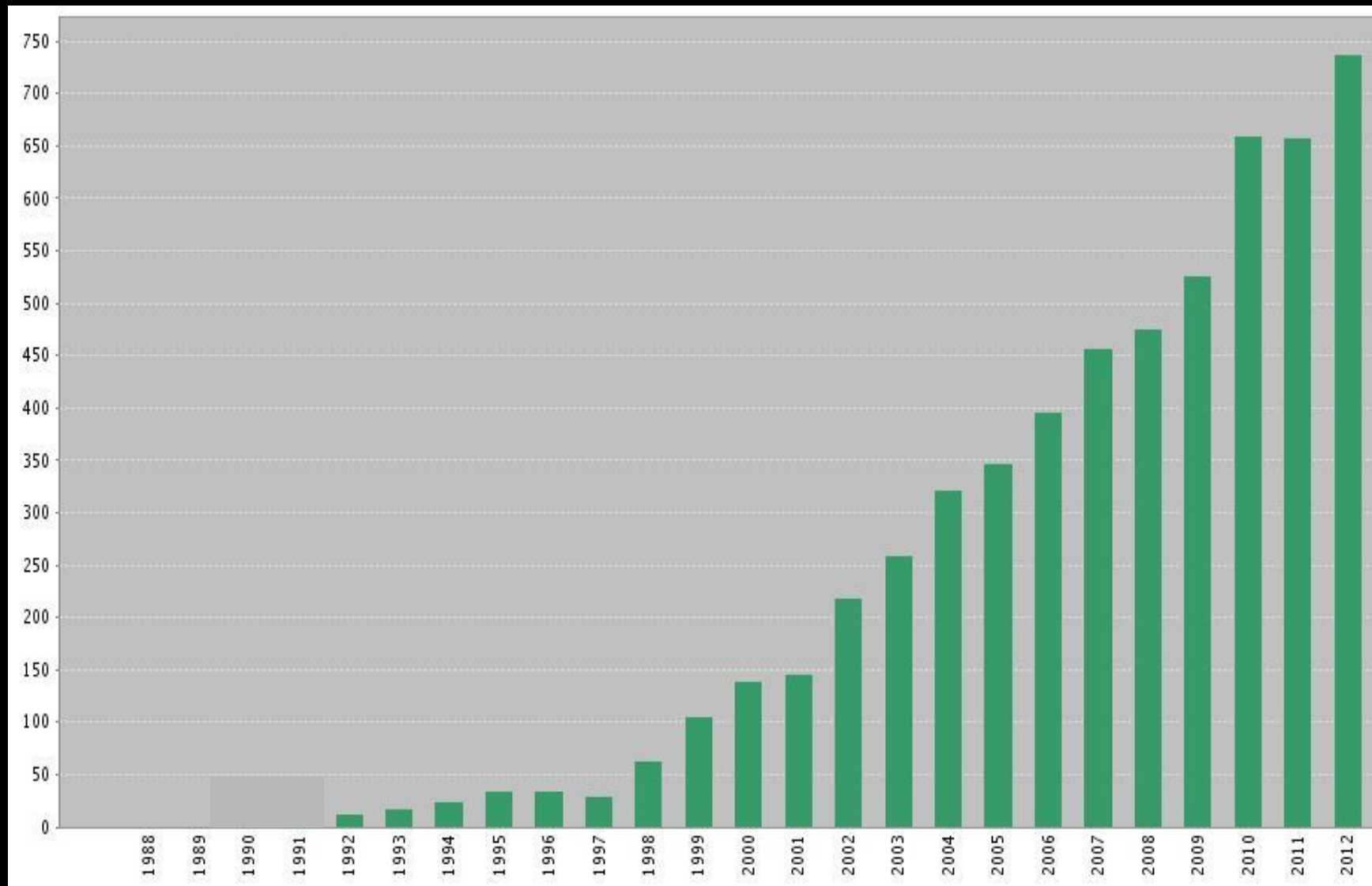
“ 1992 Missed the first ART adherence study for over 10 years

Samet et al AJM May 1992

Compliance With Zidovudine Therapy in Patients Infected With Human Immunodeficiency Virus, Type 1: A Cross-Sectional Study in a Municipal Hospital Clinic*

JEFFREY H. SAMET, M.D., HOWARD LIBMAN, M.D., KATHLEEN A. SIEGER, R.N., M.P.H.,
RAJEEV K. DHAWAN, Ph.D., JOHN CHEN, M.D., ABBY H. SHIEVITZ, M.D.,
REBECCA DEWEES-DJUNK, R.N., SUZETTE LEVYNSON, M.P.H.,
DONALD KUFE, M.D., DONALD E. CRAVEN, M.D., Boston, Massachusetts

ART Adherence Publications by Year



My Turning Points

- “ 1992 Missed the first ART adherence study for over 10 years
- “ 1995 Back to basics



"In sum, a well designed study and important contribution to the field of nosocomial transmission of TB, but I strongly recommend that the author find an editor whose first language is English."

Anonymous reviewer



“He or she is right. Your prose is tortured. Let’s start with a simple sentence and progress toward a comprehensible paragraph.”

Andrew Moss, PhD



My Turning Points

- “ 1992 Missed the first ART adherence study for over 10 years
- “ 1995 Back to basics
- “ 1996 Hope and fear

Hope



Fear

THE NEW YORK TIMES NEW YORK SUNDAY, MARCH 2, 1997

Doctors Withhold H.I.V. Pill Regimen From Some

Failure to Follow Rigid Schedule Could Hurt Others, They Fear

By DEBORAH SONTAG
and LYNDIA RICHARDSON

Tyeisha Ross, an 18-year-old who has H.I.V., is street smart but childishly innocent. She does not understand the full import of the virus that she carries, believing that it requires only a "minor adjustment" in her everyday life. So she often misses doctor's appointments and fails to take medications.

Through her Medicaid coverage, Ms. Ross, who lives in the Bronx, can afford the costly new drugs that might halt her progress toward AIDS. But her doctor will not prescribe them to her. She does not think that Ms. Ross can handle a complex, drug-taking regimen, in which missing doses could have serious consequences, making her virus resistant to future treatment.

"I don't trust her ability to stick to a schedule," said Dr. Jeanne Carey, a physician at Beth Israel Medical Center's H.I.V. clinic in Manhattan.

With the early successes of drug cocktails built on a new class of drugs called protease inhibitors, national concern has focused on whether their high cost puts them out of the reach of many AIDS patients. But in New York State, which has the most comprehensive drug assistance program in the nation, everyone is covered for the new AIDS drugs.

But not everyone can get them. And cost is not the deciding factor; doctors are. Since the exacting regi-



Michelle V. Agins/The New York Times

Eddie Ramos, a counselor to the homeless, says some H.I.V.-infected addicts cannot keep to the pattern of pill-taking he follows himself.

Patient Compliance and Drug Failure in Protease Inhibitor Monotherapy

Geertrui F. Vanhove, MD, PhD; Jonathan M. Schapiro, MD; Mark A. Winters, MSc; Thomas C. Merigan, MD; Terrence F. Blaschke, MD

JAMA. 1996;276(24):1955-1956.

ation and recommendations for change from the highest levels of academic medicine.

Linda P. Fried, MD, MPH
 Clair A. Francmano, MD
 Susan M. MacDonald, MD
 Elizabeth M. Wagner, PhD
 Wilma B. Bue, PhD
 Emma J. Stokes, PhD
 Mary M. Newman, MD
 John D. Stobo, MD
 Johns Hopkins University School of Medicine
 Baltimore, Md

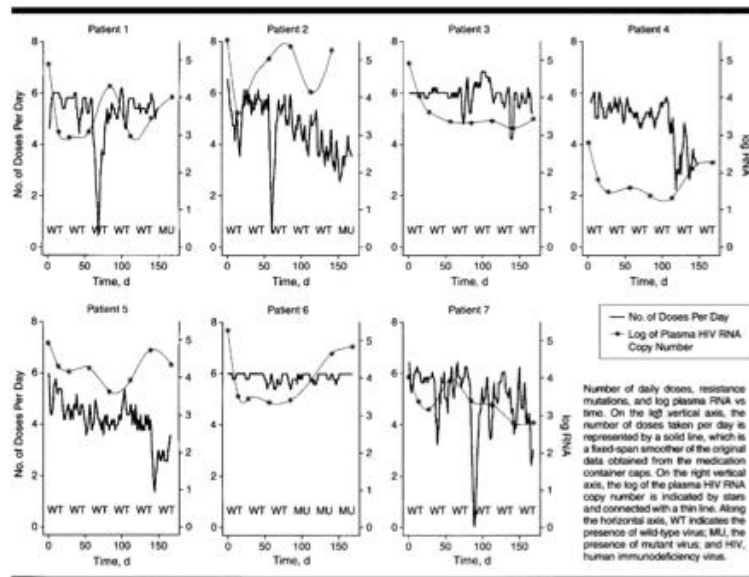
Patient Compliance and Drug Failure in Protease Inhibitor Monotherapy

To the Editor.—We conducted a 2-dose study of saquinavir in which 40 human immunodeficiency virus type 1 (HIV-1)-positive patients received either three or six 200-mg capsules of saquinavir (Roche Products, Welwyn, United Kingdom) 6 times daily (total dose, 3600 mg/d or 7200 mg/d).¹ Analysis of an early cohort of patients enrolled in the study demonstrated that the duration of the response as measured by HIV-1 plasma RNA copy number varied widely within the 2 groups. This variation was not accounted for by the development of resistant mutations alone.

To investigate whether decreased patient compliance with this intensive regimen could explain the observed variation

in viral responses, we monitored drug-taking behavior in the remaining patients on their enrollment into the high-dose group for the initial 24 weeks of therapy using medication container closures or caps that record the precise date and time of the opening and closing of the container on a microchip in the cap; the data are later downloaded and analyzed. Plasma samples were assayed for HIV-1 plasma RNA copy number (by polymerase chain reaction assay) and mutations on a monthly basis.²

The actual number of medication doses taken per day together with log plasma RNA copy number vs time and the presence or absence of mutated virus are shown in the Figure. Patients 1 and 2 were initially compliant and their viral load decreased promptly. When they took a true drug holiday (defined as a period of 3 or more days of taking very little or no medication), plasma HIV RNA levels increased in close proximity to the holiday. Shortly after these patients began taking their medication regularly again, plasma HIV RNA levels decreased. The second increase in plasma RNA levels toward the end of the study, despite good compliance, might be explained at least in part by the development of a mutation between weeks 20 and 24. Patients 3, 4, and 5 were also compliant in the beginning of the study, and their viral loads decreased. When, toward the end of the study, compliance decreased in 2 of these 3 patients (patients 4 and 5), plasma RNA levels increased subsequently. These patients developed no mutations before 24 weeks. Patient 6 developed a mutation that may have been the cause of the subsequent increase in plasma



Patient Compliance and Drug Failure in Protease Inhibitor Monotherapy

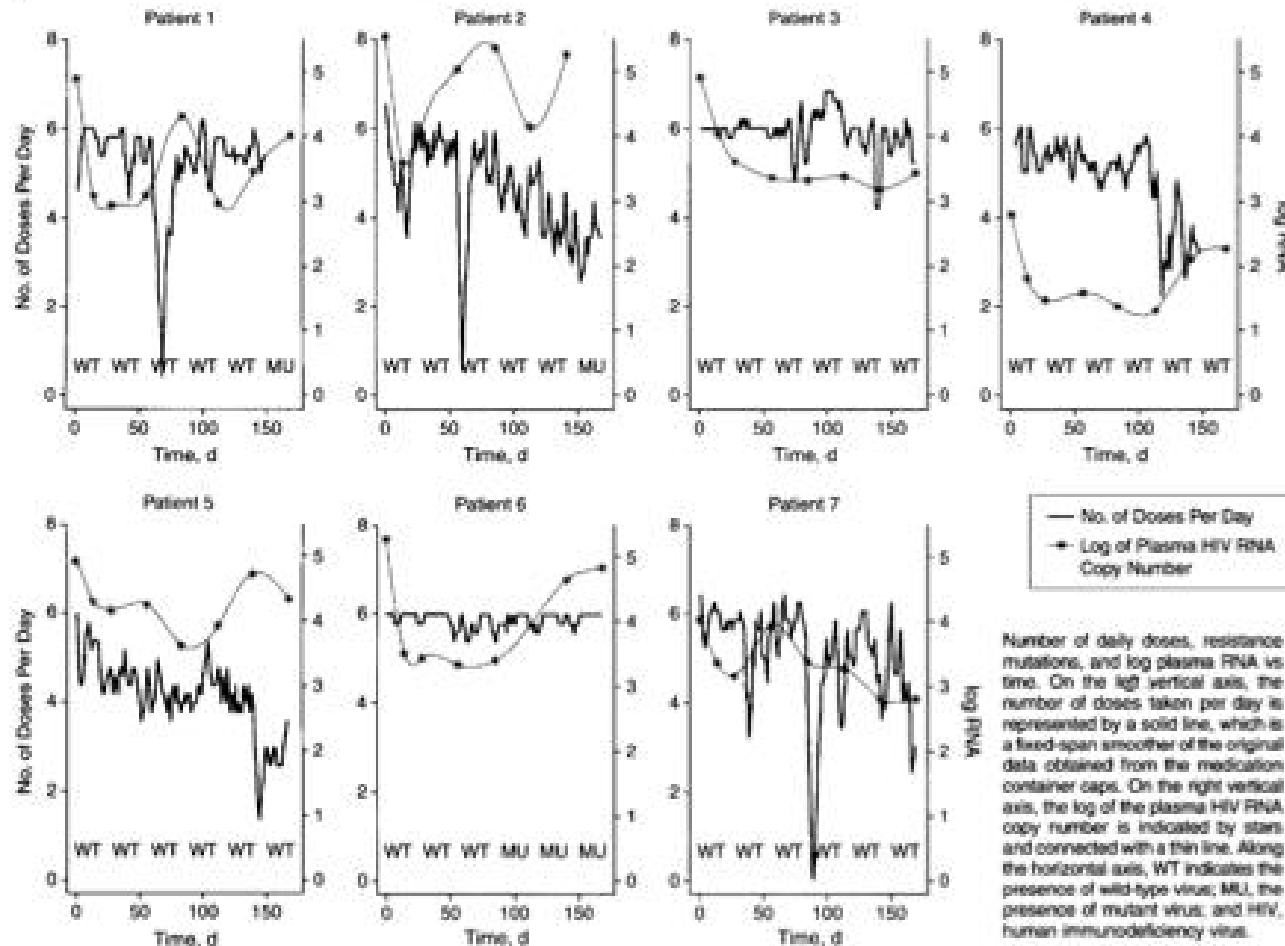
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- “ 1999-2000 The 95% rule

1999: Adherence and Viral Suppression

Antiviral Therapy 4: 157-161

Percentage of adherence correlates with the risk of protease inhibitor (PI) treatment failure in HIV-infected patients

Jose L. Casado^{1*}, Raquel Sabido², Maria J. Perez-Elias¹, Antonio Antela¹, Jesús Oliva¹, Fernando Dronda¹, Blanca Mejía² and Jesús Fortún¹

The value of patient-reported adherence to antiretroviral therapy in predicting virologic and immunologic response

Richard H. Haubrich^{a,b}, Susan J. Little^a, Judith S. Currier^d, Donald N. Forthal^c, Carol A. Kemper^e, Gildon N. Beall^f, Debra Johnson^d, Michael P. Dubé^d, Jimmy Y. Hwang^{a,b}, J. Allen McCutchan^a and the California Collaborative Treatment Group*

JARTS: Journal of Acquired Immune Deficiency Syndromes
22:156-161, 1999. Copyright Williams & Wilkins, Inc., Philadelphia

Disease Progression, Adherence, and Response to Protease Inhibitor Therapy for HIV Infection in an Urban Veterans Affairs Medical Center

*Kevin Maher, [§]N. Klimas, ^{||}M. A. Fletcher, [§]V. Cohen, [§]C. M. Maggio, [§]J. Triplett, [§]R. Valenzuela, and [†]G. Dickinson

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 15, Number 18, 1999, pp. 1631-1638
Mary Ann Liebert, Inc.

Incidence and Predictors of Virologic Failure of Antiretroviral Triple-Drug Therapy in a Community-Based Cohort

DANIEL PARIS, BRUNO LEDERGERBER, RAINER WEBER, JOSEF JOST, MARKUS FLEPP, MILOŠ OPRAVIL, CHRISTIAN RUEF, and STEFAN ZIMMERLI

2000: Objectives Measures Cement the Relationship

Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population

David R. Bangsberg^{ab}, Frederick M. Hecht^{tb}, Edwin D. Charlebois^a,
Andrew R. Zolopa^f, Mark Holodniy^{fg}, Lewis Sheiner^c,
Joshua D. Bamberger^h, Margaret A. Chesney^d and Andrew Moss^e

ARTICLE

Adherence to Protease Inhibitor Therapy and Outcomes in Patients with HIV Infection

David L. Paterson, MB, BS, FRACP; Susan Swindells, MD; Jeffrey Mohr, MSW; Michelle Brester, RN; Emanuel N. Vergis, MD; Cheryl Squier, RN; Marilyn M. Wagener, MPH; and Nina Singh, MD

MAJOR ARTICLE HIV/AIDS

Antiretroviral Therapy Adherence and Viral Suppression in HIV-Infected Drug Users: Comparison of Self-Report and Electronic Monitoring

Julia H. Arnsten,^{1,2} Penelope A. Demas,¹ Homayoon Farzadegan,⁴ Richard W. Grant,¹ Marc N. Gourevitch,^{1,2} Chee-Jen Chang,^{1,4} Donna Buono,¹ Haftan Eckholdt,⁵ Andrea A. Howard,^{1,2} and Ellie E. Schoenbaum^{1,2}

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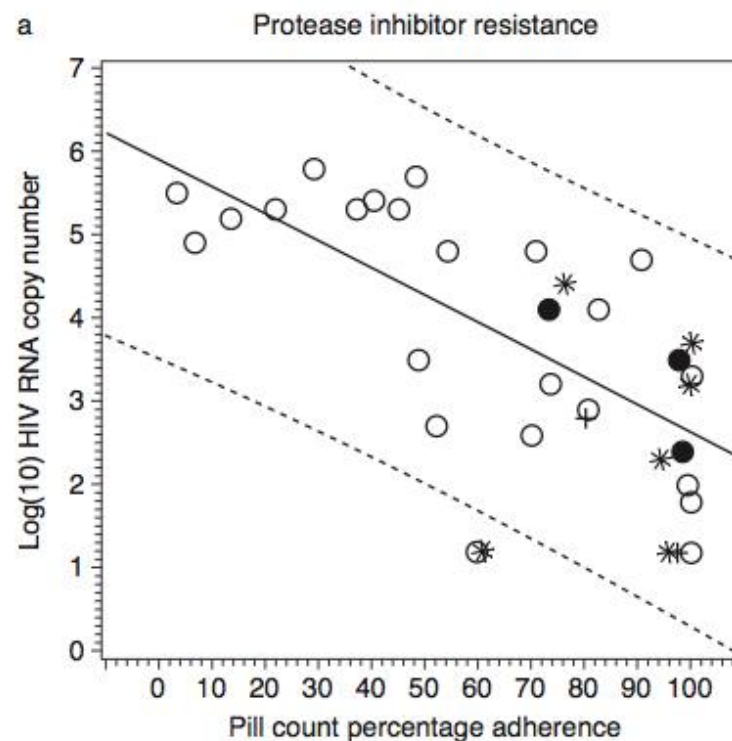


Fig. 2. Drug resistance by adherence and viral suppression.

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MAJOR ARTICLE HIV/AIDS

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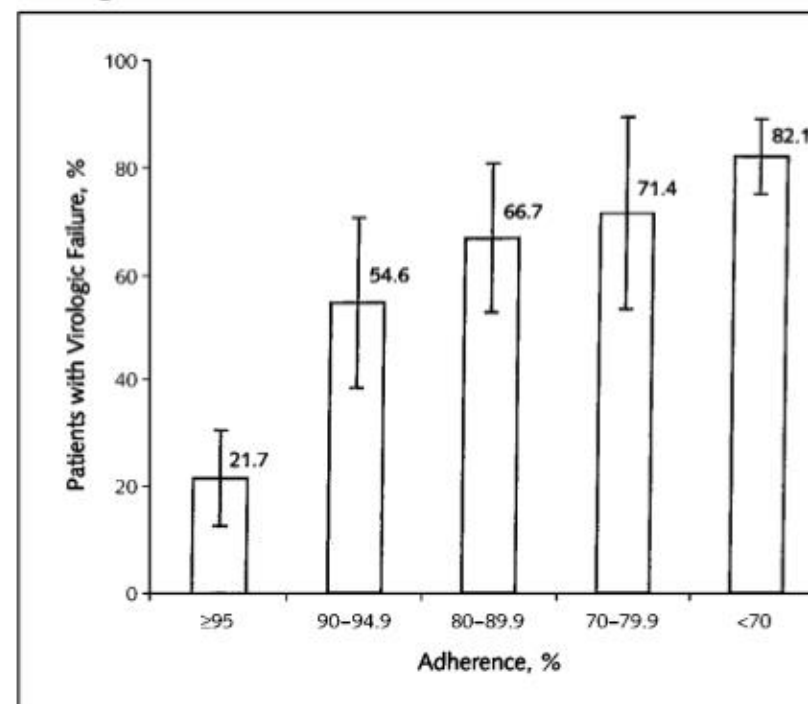
Adherence to protease inhibitors and the development of drug resistance

David R. Bangsberg^{ab}, Frederic D. O'Garra^c,
Andrew R. Zolopa^f, Margaret A. Fischl^g,
Joshua D. Bamberger^h, Margot A. Fischlⁱ

Adherence with HIV

David L. Paterson,
Cheryl Squier, RN;

Figure 1. Adherence to antiretroviral therapy and virologic failure.



The degree of adherence was significantly associated with risk for virologic failure ($P < 0.001$). Adherence of 95% or greater was associated with the lowest incidence of virologic failure.

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MAJOR ARTICLE HIV/AIDS

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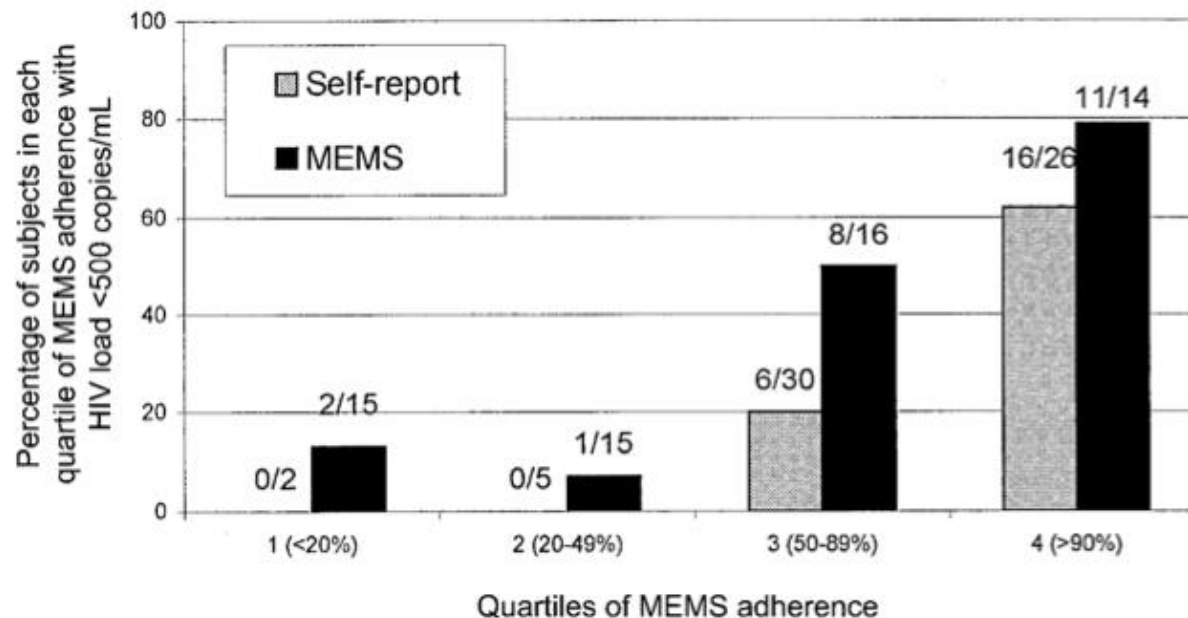


Figure 1. Subjects were categorized by quartile of electronic monitoring (MEMS) adherence: (1) <20%, (2) 20%–49%, (3) 50%–89%, and (4) ≥90%. Among the 22 subjects with a virus load of <500 copies/mL, the number and percentage in each quartile by both MEMS and self-reported adherence are indicated.

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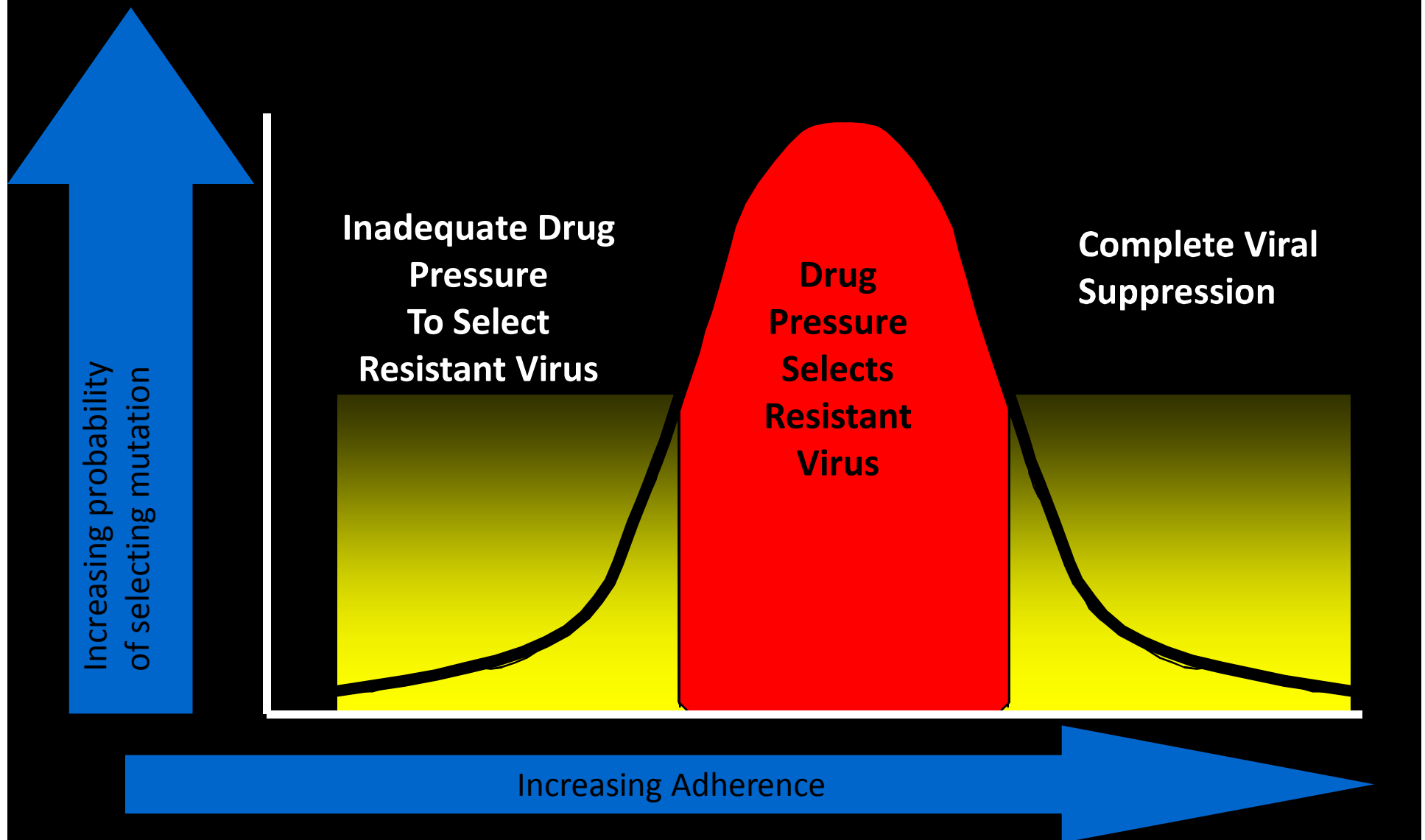
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Bell-shaped Adherence and Resistance Curve



Resistance is Complicated

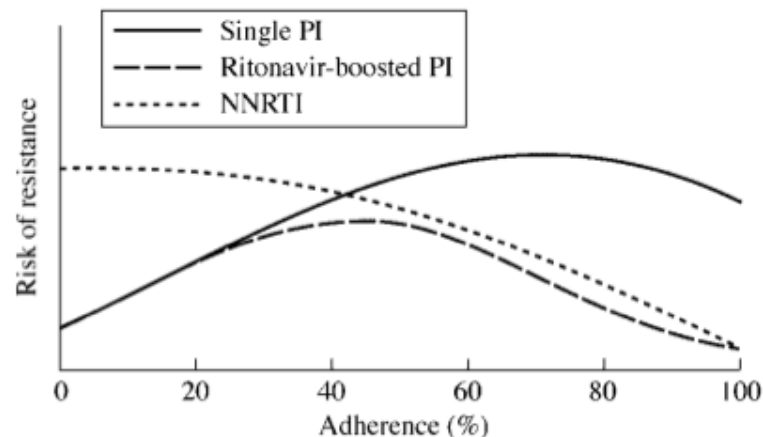
Advance Access published March 24, 2004



Journal of Antimicrobial Chemotherapy
DOI: 10.1093/jac/dkh162

Paradoxes of adherence and drug resistance to HIV antiretroviral therapy

David R. Bangsberg^{1,2*}, Andrew R. Moss³ and Steven G. Deeks²



Bangsberg DR, Kroetz DL, Deeks SG. Adherence-resistance relationships to combination HIV antiretroviral therapy. *Curr HIV/AIDS Rep.* 2007 May;4(2):65-72. Review. PubMed PMID: 17547827.

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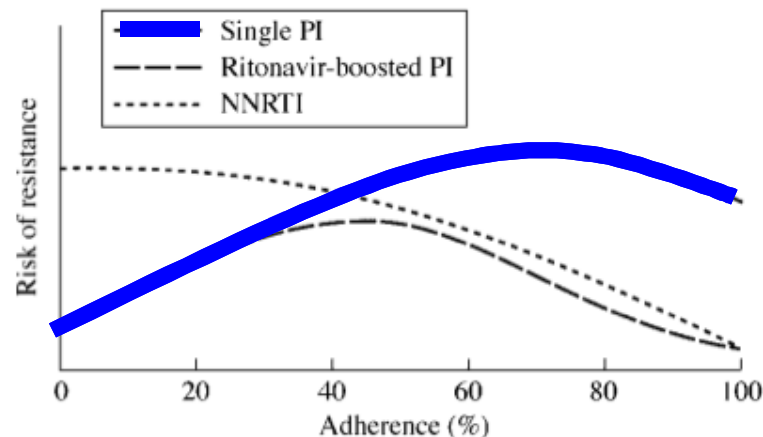
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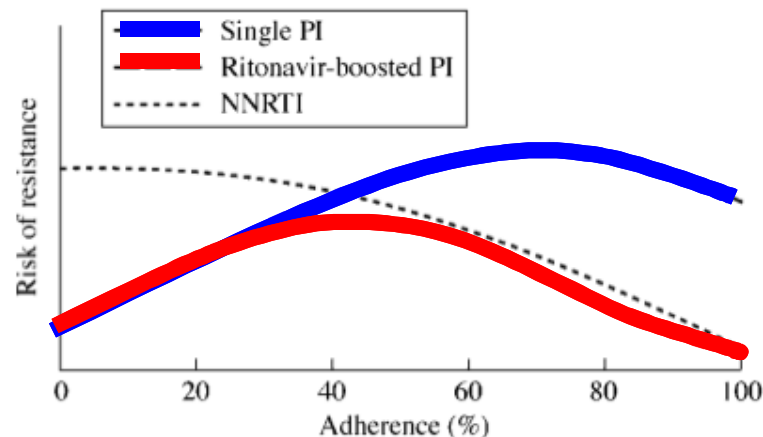
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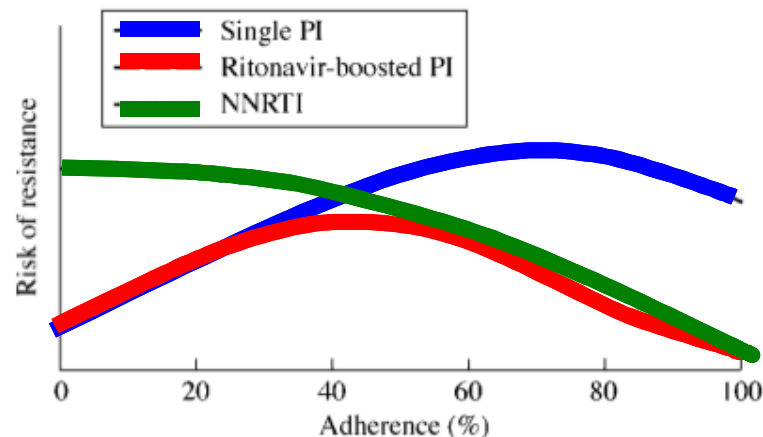
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Paradoxes of adherence and drug resistance to HIV antiretroviral therapy

David R. Bangsberg^{1,2*}, Andrew R. Moss³ and Steven G. Deeks²

Effect of Adherence to HAART on Virologic Outcome and on the Selection of Resistance-Confering Mutations in NNRTI- or PI-Treated Patients

Franco Maggiolo,^{1,2} Monica Airolidi,^{1,2} Hendrik Daniël Kleinloog,^{1,2} Annapaola Callegaro,³ Veronica Ravasio,^{1,2} Claudio Arici,¹ Enrico Bombana,¹ and Fredy Suter¹

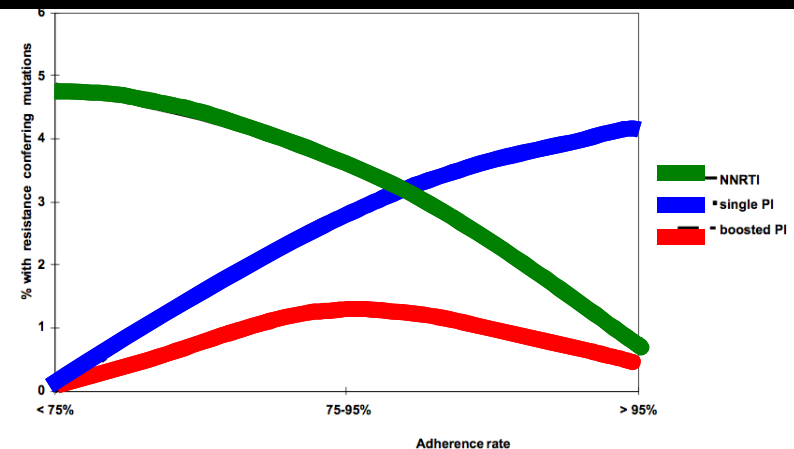
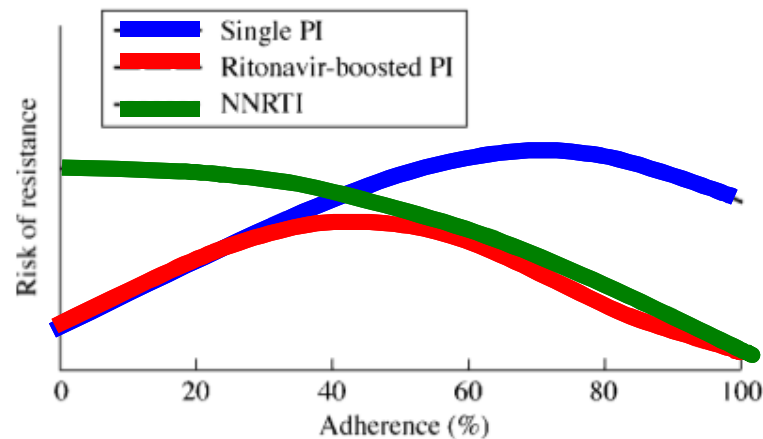


Figure 4. Adherence rate and risk of selecting for resistance-inducing viral mutations. Rate of rebound adjusted analysis. NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor.

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- “ 2004 Doom and gloom

[In sub-Saharan Africa]....the potential short term gains from reducing individual morbidity and mortality may be far outweighed by the potential for the long term spread of drug resistance.... In Africa, a higher proportion of patients are likely to fall into the category of potential poor adherers unless resource intensive adherence programmes are available.

Antiretroviral therapy in Africa

Warren Stevens, Steve Kaye, Tumani Corrah

BMJ 2004;328:280-282

Continued on Page A15

Continued on Page A16

Africans Outdo U.S. Patients In Following AIDS Therapy

By DONALD G. McNEIL Jr.

Contradicting long-held prejudices that have clouded the campaign to bring AIDS drugs to millions of peo-

in Europe are resistant to at least one drug.

For Africa, the issue is particular-

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Adherence to Antiretroviral Therapy in Sub-Saharan Africa and North America A Meta-analysis

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Jean B. Nachega, MD, MPH

Iain Buchan, MD, FFPH

James Orbinski, MD, MA

Amir Attaran, DPhil, LLB

Sonal Singh, MD

Beth Rachlis, BSc

Ping Wu, MBBS, MSc

Curtis Cooper, MD, MSc

Lehana Thabane, PhD, MSc

Kumanan Wilson, MD, MSc

Gordon H. Guyatt, MD, MSc

David R. Bangsberg, MD, MPH

Context Adherence to antiretroviral therapy is a powerful predictor of survival for individuals living with human immunodeficiency virus (HIV) and AIDS. Concerns about incomplete adherence among patients living in poverty have been an important consideration in expanding the access to antiretroviral therapy in sub-Saharan Africa.

Objective To evaluate estimates of antiretroviral therapy adherence in sub-Saharan Africa and North America.

Data Sources Eleven electronic databases were searched along with major conference abstract databases (inclusion dates: inception of database up until April 18, 2006) for all English-language articles and abstracts; and researchers and treatment advocacy groups were contacted.

Study Selection and Data Abstraction To best reflect the general population, studies of mixed populations in both North America and Africa were selected. Studies evaluating specific populations such as men only, homeless individuals, or drug users, were excluded. The data were abstracted in duplicate on study adherence outcomes, thresholds used to determine adherence, and characteristics of the populations. A random-effects meta-analysis was performed in which heterogeneity was examined using multivariable random-effects logistic regression. A sensitivity analysis was performed us-

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Annals of Internal Medicine

ARTICLE

Adherence to Nonnucleoside Reverse Transcriptase Inhibitor–Based HIV Therapy and Virologic Outcomes

Jean B. Nachega, MD, MPH; Michael Hislop, MSc; David W. Dowdy, ScM; Richard E. Chaisson, MD; Leon Regensberg, MBChB; and Gary Maartens, MBChB

EPIDEMIOLOGY AND SOCIAL SCIENCE

Adherence to Highly Active Antiretroviral Therapy Assessed by Pharmacy Claims Predicts Survival in HIV-Infected South African Adults

Jean B. Nachega, MD, MPH, Michael Hislop, MSc,† David W. Dowdy, ScM,‡ Melanie Lo, MHS,*
Saad B. Omer, MBBS, MPH,* Leon Regensberg, MBChB, MRCP,† Richard E. Chaisson, MD,§
and Gary Maartens, MBChB, FCP||*

Africans Outdo U.S. Patients In Following AIDS Therapy

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that have
bring ALL

Adherence to Antiretroviral Therapy in Sub-Saharan Africa and North America A Meta-analysis

Edward J. Mills, PhD, MSc
Jean B. Nachega, MD, MPH
Iain Buchan, MD, FFPH
James Orbinski, MD, MA
Amir Attaran, DPhil, LLB
Sonal Singh, MD
Beth Rachlis, BSc
Ping Wu, MBBS, MSc
Curtis Cooper, MD, MSc
Lehana Thabane, PhD, MSc
Kumanan Wilson, MD, MSc
Gordon H. Guyatt, MD, MSc
David R. Bangsberg, MD, MPH

Context Adherence to antiretroviral therapy is a powerful predictor of survival for individuals living with human immunodeficiency virus (HIV) and AIDS. Concerns about incomplete adherence among patients living in poverty have been an important consideration in expanding the access to antiretroviral therapy in sub-Saharan Africa.

Annals of Internal Medicine

ARTICLE

Adherence to Nonnucleoside Reverse Transcriptase Inhibitor–Based HIV Therapy and Virologic Outcomes

Jean B. Nachega, MD, MPH; Michael Hislop, MSc; David W. Dowdy, ScM; Richard E. Chaisson, MD; Leon Regensberg, MBChB; and Gary Maartens, MBChB

EPIDEMIOLOGY AND SOCIAL SCIENCE

Adherence to Highly Active Antiretroviral Therapy Assessed by Pharmacy Claims Predicts Survival in HIV-Infected South African Adults

Jean B. Nachega, MD, MPH,* Michael Hislop, MSc,† David W. Dowdy, ScM,‡ Melanie Lo, MHS,*
Saad B. Omer, MBBS, MPH,* Leon Regensberg, MBChB, MRCP,† Richard E. Chaisson, MD,§
and Gary Maartens, MBChB, FCP||

OPEN ACCESS Freely available online

PLOS MEDICINE

Explaining Adherence Success in Sub-Saharan Africa: An Ethnographic Study

Norma C. Ware^{1*}, John Idoko², Sylvia Kaaya³, Irene Andia Biraro⁴, Monique A. Wyatt¹, Oche Agbaji²,
Guerino Chalamilla^{5,6}, David R. Bangsberg^{1,7,8}

My Turning Points

- “ 1992 Missed the first ART adherence study for over 10 years
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- “ 1999-2000 The 95% rule
- “ 2003 More than one flavor of resistance
- “ 2004 Doom and gloom
- “ 2008 Letting go of 95% rule

Letting go of “The 95% rule”

BRIEF REPORT HIV/AIDS

Less Than 95% Adherence to Nonnucleoside Reverse-Transcriptase Inhibitor Therapy Can Lead to Viral Suppression

David R. Bangsberg

Current goals of 95% adherence are based on a cutoff level of 400 copies/mL [1], an analysis that directly compares viral suppression at 400 copies/mL using objective measures of adherence is needed to assess whether the goal of >95% adherence is still critical for virologic success with more potent therapy.

Methods. Participants were identified from the Research

RAPID COMMUNICATION

HIV-Infected Patients Receiving Lopinavir/Ritonavir-Based Antiretroviral Therapy Achieve High Rates of Virologic Suppression Despite Adherence Rates Less Than 95%

Jonathan Shuter, MD,*† Julie A. Sarlo, PA,* Tina J. Kanmaz, PharmD,‡
Richard A. Rode, PhD,§ and Barry S. Zingman, MD*†||

CONCISE COMMUNICATION

A single tablet regimen is associated with higher adherence and viral suppression than multiple tablet regimens in HIV+ homeless and marginally housed people

David R. Bangsberg^a, Kathleen Ragland^b, Alex Monk^b
and Steven G. Deeks^b

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- “ 2004 Doom and gloom
- “ 2008 Letting go of 95% rule
- “ 2007-2012 Dynamic adherence-VL and patterns matter

Dynamic Adherence-VL Relationships

OPEN ACCESS Freely available online



The Risk of Virologic Failure Decreases with Duration of HIV Suppression, at Greater than 50% Adherence to Antiretroviral Therapy

Michael Rosenblum¹, Steven G. Deeks¹, Mark van der Laan², David R. Bangsberg^{3*}

Published in final edited form as:

J Acquir Immune Defic Syndr. 2010 December 1; 55(4): 460–465. doi:10.1097/QAI.0b013e3181f2ac87.

Risk of Viral Failure Declines with Duration of Suppression on HAART, Irrespective of Adherence Level

Viviane D. Lima^{1,2}, David R. Bangsberg³, P. Richard Harrigan^{1,2}, Steven G. Deeks⁴, Benita Yip¹, Robert S. Hogg^{1,5}, and Julio S.G. Montaner^{1,2}

Increased duration of viral suppression is associated with lower viral rebound rates in patients with previous treatment failures

Andrew A. Benzie^a, Loveleen K. Bansil^b, Caroline A. Sabin^b, Simon Portsmouth^a, Teresa Hill^a, Margaret Johnson^c, Richard Gilson^b, Philippa Easterbrook^d, Brian Gazzard^e, Martin Fisher^f, Chloe Orkin^g, David Dunn^h, Valerie Delpechⁱ, Graham P. Taylor^a, John C. Walsh^a, and Andrew N. Phillips^b on behalf of the United Kingdom Collaborative HIV Cohort (CHIC) Study

Patterns Matter

Treatment interruptions predict resistance in HIV-positive individuals purchasing fixed-dose combination antiretroviral therapy in Kampala, Uganda

Jessica H. Oyugi^a, Jayne Byakika-Tusiime^b, Kathleen Ragland^d, Oliver Laeyendecker^e, Roy Mugerwa^b, Cissy Kityo^c, Peter Mugenyi^c, Thomas C. Quinn^e and David R. Bangsberg^{d,f}

OPEN ACCESS Freely available online



Not All Missed Doses Are the Same: Sustained NNRTI Treatment Interruptions Predict HIV Rebound at Low-to-Moderate Adherence Levels

Jean-Jacques Parienti^{1,2*}, Moupali Das-Douglas³, Véronique Massari², David Guzman⁵, Steven G. Deeks³, Renaud Verdon¹, David R. Bangsberg⁴

Patterns of antiretroviral therapy adherence and impact on HIV RNA among patients in North America

Becky L. Genberg^a, Ira B. Wilson^a, David R. Bangsberg^b, Julia Arnsten^c, Kathy Goggin^d, Robert H. Remien^e, Jane Simoni^f, Robert Gross^g, Nancy Reynolds^h, Marc Rosen^h, Honghu Liuⁱ,
for the MACH14 Investigators

My Turning Points

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- “ 2007-2012 Dynamic adherence-VL and patterns matter
- “ 2000-2008 Remembering what we forgot

Remembering What We Forgot

AIDS CARE (2000), VOL. 12, NO. 3, pp. 255-266



Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG Adherence Instruments

M. A. CHESNEY,¹ J. R. ICKOVICS,² D. B. CHAMBERS,¹
A. L. GIFFORD,³ J. NEIDIG,⁴ B. ZWICKL,⁵ A. W. WU,⁶
PATIENT CARE COMMITTEE & ADHERENCE WORKING
GROUP OF THE OUTCOMES COMMITTEE OF THE ADULT
AIDS CLINICAL T

Measuring Adherence to Antiretroviral Therapy in a Diverse Population Using a Visual Analogue Scale

Thomas P. Giordano, MD,¹ David Guzman, MS,² Richard Clark, MPH,⁴
Edwin D. Charlebois, MPH, PhD,² and David R. Bangsberg, MD, MPH^{2,3}

AIDS PATIENT CARE and STDs
Volume 22, Number 9, 2008
© Mary Ann Liebert, Inc.
DOI: 10.1089/apc.2007.0229

Diagnostic Value of Different Adherence Measures Using Electronic Monitoring and Virologic Failure as Reference Standards

Ann E. Deschamps, M.S.N.,¹
Herman Bobb

AIDS Behav (2008) 12:96-94
DOI 10.1007/s10461-007-9261-4

ORIGINAL PAPER

Optimal Recall Period and Response Task for Self-Reported HIV Medication Adherence

Minyi Lu · Steven A. Safren · Paul R. Skolnik ·
William H. Rogers · William Coady · Helene Hardy ·
Ira B. Wilson

Remembering What We Forgot

AIDS CARE (2000), VOL. 12, NO. 3, pp. 255-266



Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG Adherence
Ir

JGIM

BRIEF REPORTS

Adherence to Antiretroviral Therapy Assessed by Unannounced Pill Counts Conducted by Telephone

Seth C. Kalichman, PhD¹, Christina M. Amaral, BA², Heidi Stearns, BA², Denise White, BA², Jody Flanagan, BA², Howard Pope, BS², Chauncey Cherry, MPH², Demetria Cain, MPH², Lisa Eaton, BA², and Moira O. Kalichman, MSW²

Diagnostic Value of Different Adherence Measures
Using Electronic Monitoring and Virologic Failure as
Reference Standards

Ann E. Deschamps, M.S.N.,¹
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AIDS Behav (2008) 12:96-94
DOI 10.1007/s10461-007-9261-4

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- “ 2007-2012 Adherence-VL is dynamic and patterns matter
- “ 2000-2008 Remembering what we forgot
- “ 2007-2011 Adherence is more than pill taking

Adherence is More than Pill Taking “The Cascade”

REVIEW ARTICLE HIV/AIDS

The Spectrum of Engagement in HIV Care and its Relevance to Test-and-Treat Strategies for Prevention of HIV Infection

Edward M. Gardner,^{1,2} Margaret P. McLees,^{1,2} John F. Steiner,² Carlos del Rio,^{4,5} and William J. Burman^{1,2}

OPEN ACCESS  Freely available online

PLOS MEDICINE

Retention in HIV Care between Testing and Treatment in Sub-Saharan Africa: A Systematic Review

Sydney Rosen^{1,2*}, Matthew P. Fox^{1,2,3}

Adherence is More than Pill Taking “The Cascade”

MAJOR ARTICLE HIV/AIDS

Retention in Care: A Challenge to Survival with HIV Infection

Thomas P. Giordano,^{1,2} Allen L. Gifford,^{3,4,5} A. Clinton White, Jr.,^{1,2} Maria E. Suarez-Almazor,^{1,2,*} Linda Rabeneck,⁷
Christine Hartman,^{1,7} Lisa I. Backus,⁶ Larry A. Mole,⁶ and Robert O. Morgan^{1,2}

REVIEW ARTICLE HIV/AIDS

The Spectrum of Engagement in HIV Care and its Relevance to Test-and-Treat Strategies for Prevention of HIV Infection

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PLOS MEDICINE

Retention in HIV Care between Testing and Treatment in Sub-Saharan Africa: A Systematic Review

Sydney Rosen^{1,2,*}, Matthew P. Fox^{1,2,3}

Hasan Baryahikiwa “The Ascertainer” Employed by Elvin Geng in Mbarara Uganda



Sampling Based Approach

- “ Not all loss is bad (Geng, Plos One 2011)
- “ Disengagement is overestimated (Geng, Plos One 2011)
- “ Mortality is underestimated (Geng Jama 2008)
- “ Death between appts more common than death after missed appts (Geng, JAIDS 2010; Geng AJE 2012)
- “ Corrects mistaken risk factors (Geng, Trop Med Int Health 2010)
- “ Disengagement is erosion of a social bond between patient and clinic in face of structural barriers (Ware PLoS Med 2013)

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- “ 2000-2008 Remembering what we forgot
- “ 2007-2011 Adherence is more than pill taking
- “ 2000-2013 Interventions work – but for whom and how long?

Adherence Interventions Work

J AIDS Journal of Acquired Immune Deficiency Syndromes
25:221-228 © 2000 Lippincott Williams & Wilkins, Inc., Philadelphia

Prospective Randomized Two-Arm Controlled Study To Determine the Efficacy of a Specific Intervention To Improve Long-Term Adherence to Highly Active Antiretroviral Therapy

*Albert Tuldrà, *Carmina R. Fumaz, *Ma José Ferrer, †Ramon Bayés, *Albert Arnó, *Montserrat Balagué, *Anna Bonjoch, *Antoni Jou, *Eugènia Negredo, *Roger Paredes, *Lidia Ruiz, *Joan Romeu, *Guillem Sirera, *Cristina Tural, ‡David Burger, and *Bonaventura Clotet

Review - Antiretroviral Adherence Interventions Volume 11 Issue 6 November/December 2003

1

Review

Antiretroviral Adherence Interventions: A Review of Current Literature and Ongoing Studies

Jane M. Simoni, PhD, Pamela A. Frick, PharmD, MPH, David W. Pantalone, AB, Barbara J. Turner, MD, MEd

CLINICAL SCIENCE

Efficacy of Antiretroviral Therapy Adherence Interventions

A Research Synthesis of Trials, 1996 to 2004

K. Rivet Amico, PhD,* Jennifer J. Harman, PhD,*† and Blair T. Johnson, PhD*‡

Strategies for Promoting Adherence to Antiretroviral Therapy: A Review of the Literature

Jane M. Simoni, PhD, K. Rivet Amico, PhD, Cynthia R. Pearson, PhD, and Robert Malow, PhD

Slide 50

1

READ summary to quote several interventions

David Bangsberg, 5/20/2013

Adherence Interventions Can Be Delivered by Telephone

CLINICAL SCIENCE

Telephone Support to Improve Antiretroviral Medication Adherence

A Multi:

Nancy R. Reynolds, PhD, M
Judith L. Neidig, PhD,^{||} I
and Gregory K. Robbins,*

Brief Behavioral Self-Regulation Counseling for HIV Treatment Adherence Delivered by Cell Phone: An Initial Test of Concept Trial

Seth C. Kalichman, Ph.D., Moira O. Kalich
Connie Swetzes, L.P.N., Christina M. Amaral, E
Tamar Grebler, B.A., a

Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders

Cristian Pop-Eleches^{a,b,*}, Harsha Thirumurthy^{c,d,*},
James P. Habyarimana^{e,*}, Joshua G. Zivin^f, Markus P. Goldstein^g,
Damien de Walque^g, Leslie Ma
Sylvester Kimaiyo^j, John Sidl
David R. Bar



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, E
Joshua Kimani, Marta Ackers, Francis A Plummer

ORIGINAL INVESTIGATION

Managed Problem Solving for Antiretroviral Therapy Adherence

A Randomized Trial

Robert Gross, MD, MSCE; Scarlett L. Bellamy, ScD; Jennifer Chapman, MPH;
Xiaoyan Han, MS; Jacqueline O'Duor, MSW; Steven C. Palmer, PhD;
Peter S. Houts, PhD; James C. Coyne, PhD; Brian L. Strom, MD, MPH

OPEN ACCESS Freely available online

PLOS ONE

The Cameroon Mobile Phone SMS (CAMPS) Trial: A Randomized Trial of Text Messaging versus Usual Care for Adherence to Antiretroviral Therapy

Lawrence Mbuagbaw^{1,2*}, Lehana Thabane^{2,3}, Pierre Ongolo-Zogo¹, Richard T. Lester^{4,5}, Edward J. Mills⁶,
Marek Smieja^{2,7}, Lisa Dolovich⁸, Charles Kouanfack⁹

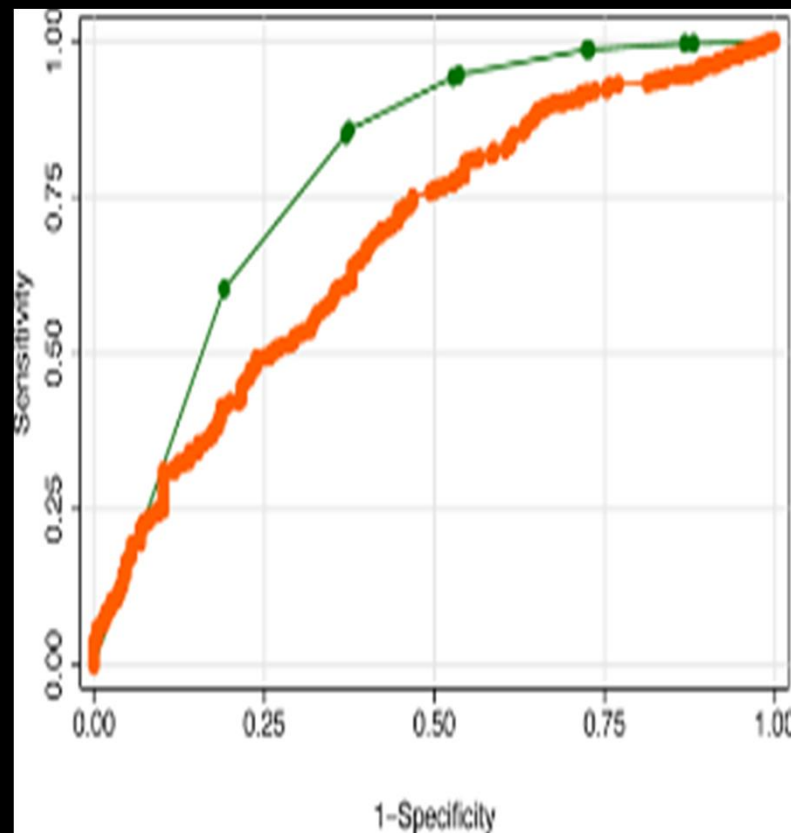
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- “ 2008 Adherence behavior to diagnose treatment failure

Adherence Behavior to Diagnose Treatment Failure

Pharmacy Refill Adherence Compared with CD4 Count Changes for Monitoring HIV-Infected Adults on Antiretroviral Therapy

Gregory P. Bisson^{1,2*}, Robert Gross^{1,2}, Scarlett Bellamy², Jesse Chittams², Michael Hislop³, Leon Regensberg³, Ian Frank¹, Gary Maartens⁴, Jean B. Nachega^{4,5,6*}

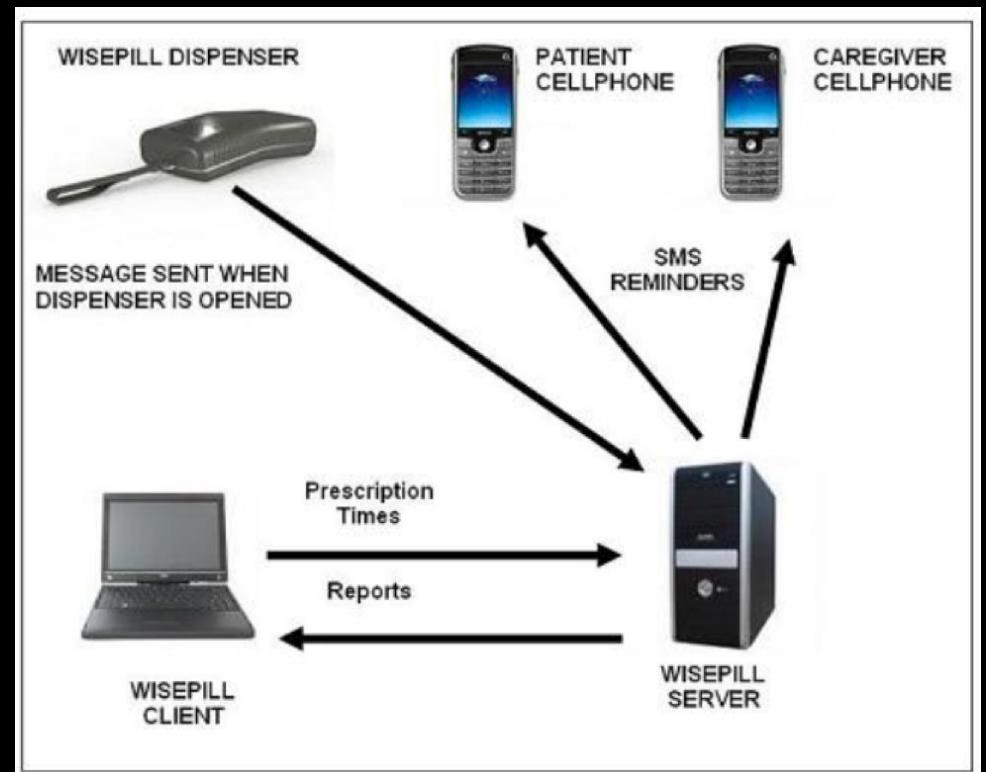
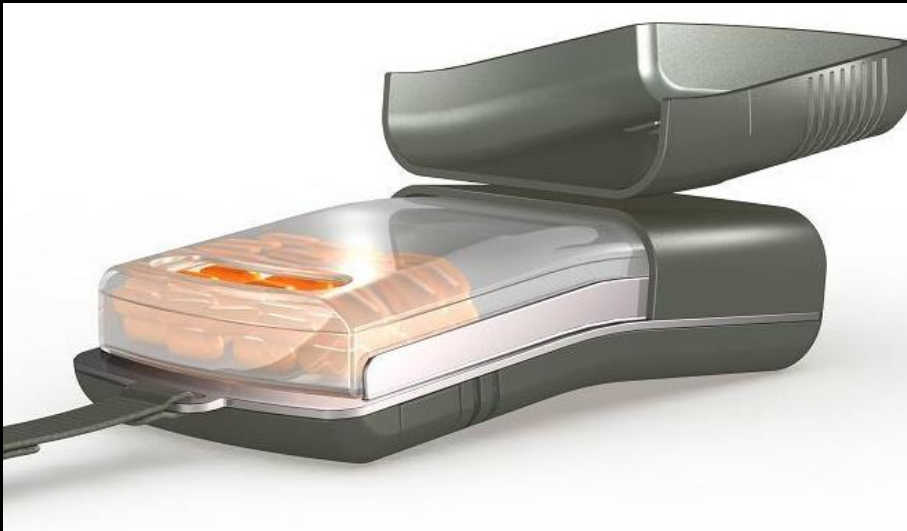


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- “ 2000-2013 Interventions work – but for whom and how long?
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- “ 2010 Doing it in real time

Real-time Adherence Monitoring

Haberer et al AIDS and Behavior 2010



Real-time Adherence Monitoring

Haberer et al AIDS and Behavior 2010

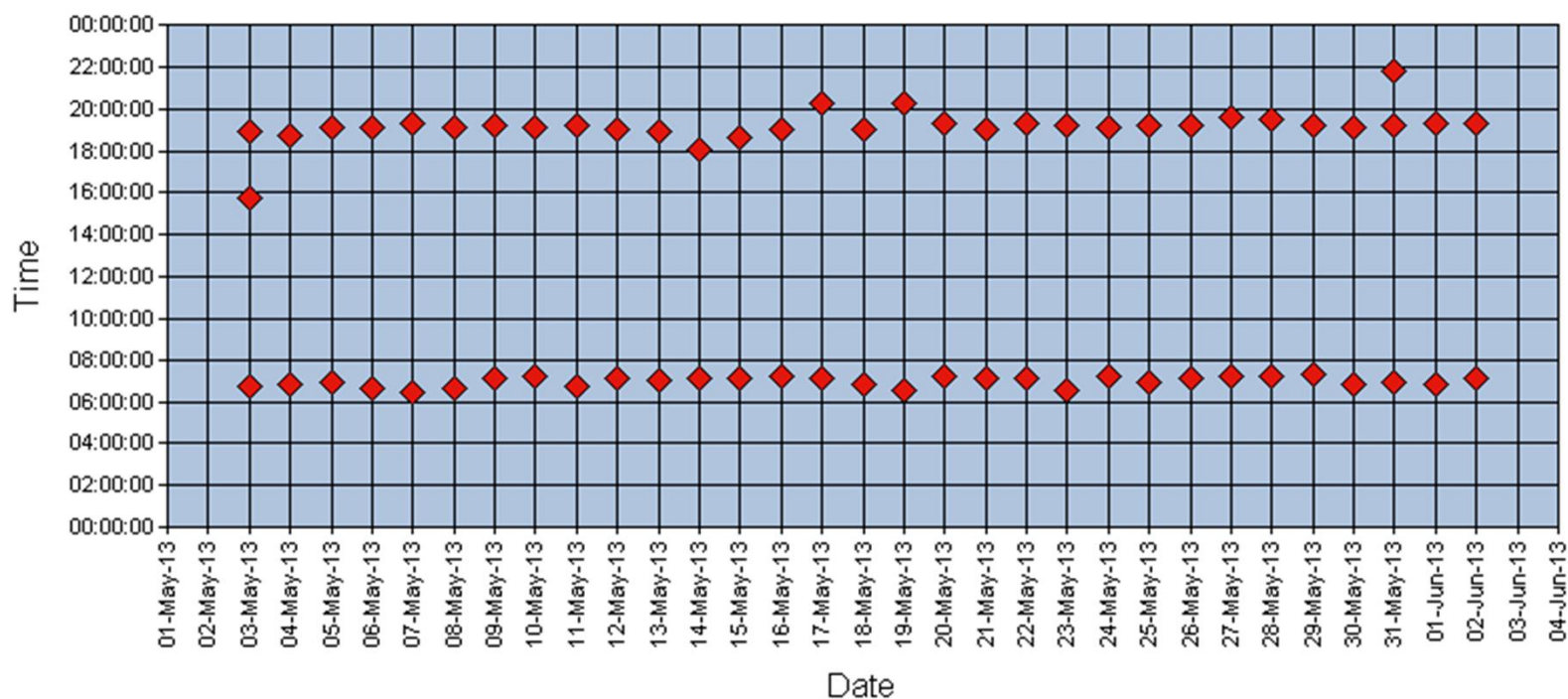


Real-time Adherence Monitoring

Haberer et al AIDS and Behavior 2010



Adherence Dot Chart



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- “ 2008 Adherence behavior to diagnose treatment failure
- “ 2010 Doing it in real time
- “ 2012 Adherence to prevention

ART is Prevention

The NEW ENGLAND JOURNAL *of* MEDICINE

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AUGUST 11, 2011

VOL. 365 NO. 6

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D.,
Mina C. Hosseinipour, M.D., Nagalingeswaran Kumarasamy, M.B., B.S., James G. Hakim, M.D.,
Johnstone Kumwenda, F.R.C.P., Beatriz Grinsztejn, M.D., Jose H.S. Pilotto, M.D., Sheela V. Godbole, M.D.,
Sanjay Mehendale, M.D., Suwat Charialertsak, M.D., Breno R. Santos, M.D., Kenneth H. Mayer, M.D.,
Irving F. Hoffman, P.A., Susan H. Eshleman, M.D., Estelle Piwowar-Manning, M.T., Lei Wang, Ph.D.,
Joseph Makhema, F.R.C.P., Lisa A. Mills, M.D., Guy de Bruyn, M.B., B.Ch., Ian Sanne, M.B., B.Ch.,
Joseph Eron, M.D., Joel Gallant, M.D., Diane Havlir, M.D., Susan Swindells, M.B., B.S., Heather Ribaudo, Ph.D.,
Vanessa Elharrar, M.D., David Burns, M.D., Taha E. Taha, M.B., B.S., Karin Nielsen-Saines, M.D.,
David Celentano, Sc.D., Max Essex, D.V.M., and Thomas R. Fleming, Ph.D., for the HPTN 052 Study Team*

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David Celentano, Sc.D., Max Essex, D.V.M., and Thomas R. Fleming, Ph.D., for the HPTN 052 Study Team*

BRIEF REPORT: CLINICAL SCIENCE

Higher Baseline CD4 Cell Count Predicts Treatment Interruptions and Persistent Viremia in Patients Initiating ARVs in Rural Uganda

Susan A. Adakun, MD, Mark J. Siedner, MD, MPH,† Conrad Muzoora, MD,*
Jessica E. Haberer, MD, MS,‡ Alexander C. Tsai, MD,§ Peter W. Hunt, MD,|| Jeff N. Martin, MD, MPH,¶
and David R. Bangsberg, MD, MPH*†#*

PrEP Adherence

RESEARCH ARTICLES

CORRECTED 29 JULY 2011; SEE LAST

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim,^{1,2*} Salim S. Abdool Karim,^{1,2,3*} Janet A. Frohlich,¹ Anneke C. Grobler,¹ Cheryl Baxter,¹ Leila E. Mansoor,¹ Ayesha B. M. Kharsany,¹ Sengeziwe Sibeko,¹ Koleka P. Misana,¹ Zaheen Omar,¹ Tanuja N. Gengiah,¹ Silvia Maarschalk,¹ Natasha Arulappan,¹ Mukelisiwe Mlotshwa,¹ Lynn Morris,⁴ Douglas Taylor,² on behalf of the CAPRISA 004 Trial Group†

The NEW ENGLAND JOURNAL of MEDICINE

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DECEMBER 30, 2010

VOL. 363 NO. 27

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdílea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana

Michael C. Thigpen, M.D., Poloko M. Kebaabetswe, Ph.D., M.P.H., Lynn A. Paxton, M.D., M.P.H., Dawn K. Smith, M.D., M.P.H., Charles E. Rose, Ph.D., Tebogo M. Segolodi, M.Sc., Faith L. Henderson, M.P.H., Sonal R. Pathak, M.P.H., Fatma A. Soud, Ph.D., Kata L. Chillag, Ph.D., Rodreck Mutanhaurwa, M.B., Ch.B., Lovemore Ian Chirwa, M.B., Ch.B., M.Phil., Michael Kasonde, M.B., Ch.B., Daniel Abebe, M.D., Evans Buliva, M.B., Ch.B., Roman J. Gvetadze, M.D., M.S.P.H., Sandra Johnson, M.A., Thom Sukalac, Vasavi T. Thomas, M.P.H., R.Ph., Clyde Hart, Ph.D., Jeffrey A. Johnson, Ph.D., C. Kevin Malotte, Dr.P.H., Craig W. Hendrix, M.D., and John T. Brooks, M.D., for the TDF2 Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 2, 2012

VOL. 367 NO. 5

Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women

J.M. Baeten, D. Donnell, P. Ndase, N.R. Mugo, J.D. Campbell, J. Wangisi, J.W. Tappero, E.A. Bukusi, C.R. Cohen, E. Katabira, A. Ronald, E. Tumwesigye, E. Were, K.H. Fife, J. Kiarie, C. Farquhar, G. John-Stewart, A. Kania, J. Odoyo, A. Mucunguzi, E. Nakku-Joloba, R. Twesigye, K. Ngure, C. Apaka, H. Tamoo, F. Gabona, A. Mujugira, D. Panteleeff, K.K. Thomas, L. Kidoguchi, M. Krows, J. Revall, S. Morrison, H. Haugen, M. Emmanuel-Ogier, L. Ondrejcek, R.W. Coombs, L. Frenkel, C. Hendrix, N.N. Bumpus, D. Bangsberg, J.E. Haberer, W.S. Stevens, J.R. Lingappa, and C. Celum, for the Partners PrEP Study Team*



CONTACT: Lisa Rossi
+1-412-916-3315 (mobile) or
+27-(0)73-323-4087 (through 7 March)
rossil@upmc.edu



FOR IMMEDIATE RELEASE

Daily HIV prevention approaches didn't work for African women in the VOICE Study

Truvada found not an effective strategy in this population

Young, single women were least likely to use tablets or gel, and more likely to get infected at very high rates

ATLANTA, March 4, 2013 – Results of a major HIV prevention trial suggest that daily use of a product – whether a vaginal gel or an oral tablet – does not appear to be the right approach for preventing HIV in young, unmarried African women.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preexposure Prophylaxis for HIV Infection among African Women

Lut Van Damme, M.D., Amy Corneli, Ph.D., Khatija Ahmed, M.Med., Kawango Agot, Ph.D., Johan Lombaard, M.B., Ch.B., Saidi Kapiga, M.D., Mookho Malahleha, M.B., Ch.B., Fredrick Owino, M.B., Ch.B., Rachel Manongi, M.D., Jacob Onyango, M.A., Lucky Temu, M.D., Modie Constance Monedi, Adv.Dip.Mid., Paul Mak'Oketch, B.Pharm., Mankalimeng Makanda, M.B., Ch.B., Ilse Reblin, B.Soc.Sc., Shumani Elsie Makatu, M.A., Lisa Saylor, B.A., Haddie Kiernan, B.S.N., Stella Kirkendale, M.P.H., Christina Wong, Ph.D., Robert Grant, M.D., Angela Kashuba, Pharm.D., Kavita Nanda, M.D., Justin Mandala, M.D., Katrien Franssen, M.S., Jennifer Deese, M.P.H., Tania Crucitti, Ph.D., Timothy D. Mastro, M.D., and Douglas Taylor, Ph.D., for the FEM-PrEP Study Group*

PrEP Adherence

RESEARCH ARTICLES

CORRECTED 29 JULY 2011; SEE LAST

Effectiveness and Safety of Tenofovir Gel

The NEW ENGLAND
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CLINICAL SCIENCE

What's Love Got to Do With It? Explaining Adherence to Oral Antiretroviral Pre-Exposure Prophylaxis for HIV-Serodiscordant Couples

Norma C. Ware, PhD, Monique A. Wyatt,* Jessica E. Haberer, MD, MS,† Jared M. Baeten, MD, PhD,‡ Alexander Kintu, MD,§ Christina Psaros, PhD,|| Steven Safren, PhD,|| Elioda Tumwesigye, MD,§ Connie L. Celum, MD, MPH,‡¶ and David R. Bangsberg, MD, MPH†**

ORIGINAL ARTICLE

Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana

Michael C. Thigpen, M.D., Poloko M. Kebaabetswe, Ph.D., M.P.H.,
Lynn A. Paxton, M.D., M.P.H., Dawn K. Smith, M.D., M.P.H.,
Charles E. Rose, Ph.D., Tebogo M. Segolodi, M.Sc., Faith L. Henderson, M.P.H.,
Sonal R. Pathak, M.P.H., Fatma A. Soud, Ph.D., Kata L. Chillag, Ph.D.,
Rodreck Mutanhaurwa, M.B., Ch.B., Lovemore Ian Chirwa, M.B., Ch.B., M.Phil.,
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Roman J. Gvetadze, M.D., M.S.P.H., Sandra Johnson, M.A., Thom Sukalac,
Vasavi T. Thomas, M.P.H., R.Ph., Clyde Hart, Ph.D., Jeffrey A. Johnson, Ph.D.,
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for the TDF2 Study Group*

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What's Love Got to Do With It?



Courtesy of Fran Priddy IAVI

Conclusions

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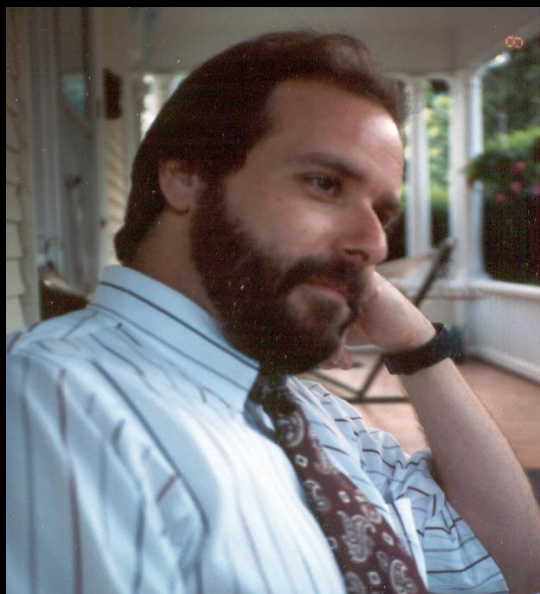
Conclusions

- “ How will we keep up w/o Rob's listserve?
- “ Strong and data-less opinions about marginalized groups are low hanging fruit.
- “ Are we measuring the right thing in the right way at the right time?
- “ We should not Invest hundreds of millions of dollars to test drug efficacy *before* investing hundreds of thousands of dollars to understand whether people will take it.

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