# “Antiretroviral therapy for HIV patients: The Basics”

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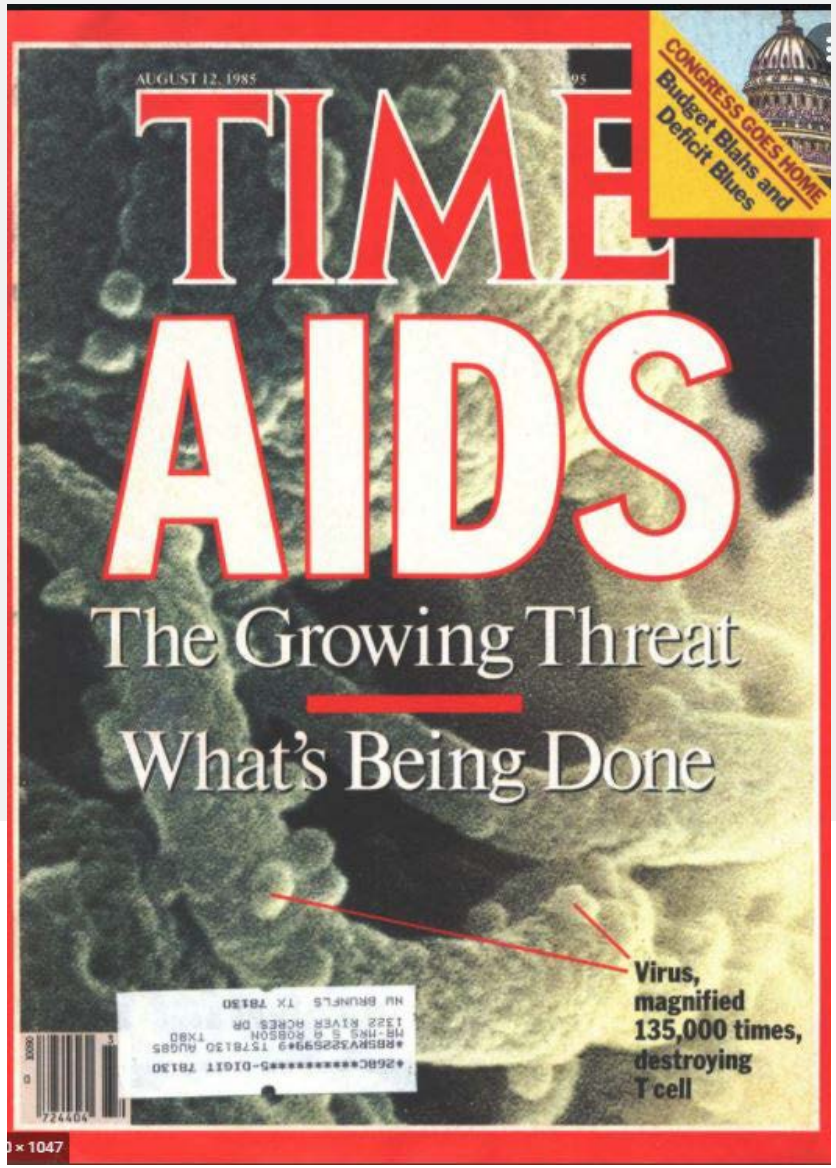


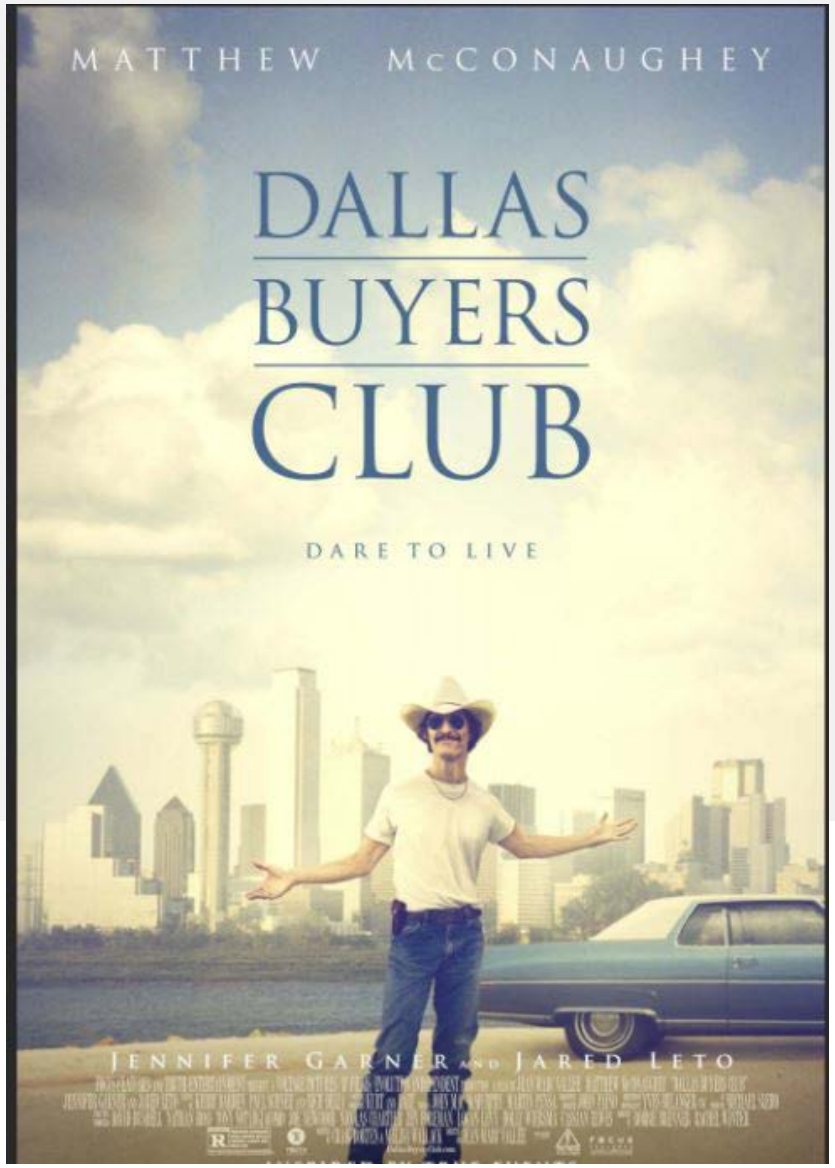


# Historical Perspective

# e New York Times

**Late Edition**

New York: Today and tonight, cloudy, breezy, occasional light snow. High 38-45, low 31-37. Tomorrow, decreasing clouds, breezy. High 48-52. Yesterday: High 48, low 35. Details on page 33.

Times NEW YORK, SATURDAY, MARCH 21, 1987 50 cents beyond 75 miles from New York City, except on Long Island. 30 CENTS


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# SENATE SETS STAGE FOR REAGAN CLASH OVER HIGHWAY BILL

## Finishes Work on $87 Billion Measure — White House Reaffirms Vow of Veto

By LINDA GREENHOUSE
Special to The New York Times

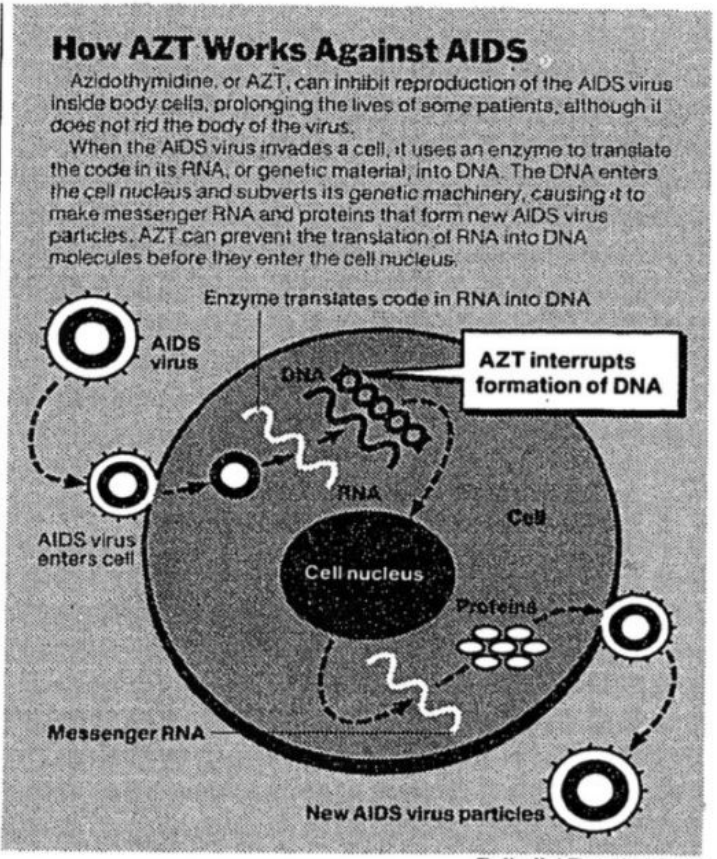
WASHINGTON, March 20 — The Senate set the stage today for a major battle with the White House by sending President Reagan a highway bill that he has promised to veto despite its bipartisan popularity in both houses of Congress.

The final part of the bill, an amendment permitting states to raise the speed limit to 65 miles an hour on rural sections of the Interstate highway system, passed by a vote of 60 to 21. The highway bill itself, which would authorize highway and mass transit programs costing up to $87.9 billion over the next five years, passed the Senate Thursday night, 79 to 17.

The bill, the product of a House-Senate conference that resolved a year-long stalemate, passed the House Wednesday by a vote of 407 to 17.

### Override of Veto in Doubt

There is little doubt that the House would override a veto. But members of both parties said a veto could be sustained in the Senate, despite the com-




The New York Times/March 21, 1987

# U.S. APPROVES DRUG TO PROLONG LIVES OF AIDS PATIENTS

## CURE STILL NOT ACHIEVED

## Distribution Will Be Limited Because of Short Supply and Fear of Side Effect

By IRVIN MOLOTSKY
Special to The New York Times

WASHINGTON, March 20 — The first drug proved to prolong the lives of AIDS patients was given Federal approval today. Both Government and drug company officials emphasized, however, that the drug was not a cure for the fatal disorder of the immune system, which has struck 33,000 Americans.

The drug is azidothymidine, or AZT, an antiviral drug made by the Burroughs Wellcome Company under the brand name Retrovir. Its approval, which means it can be prescribed by doctors, had been expected since January, when the company made its presentation before the Food and Drug Administration.

Even before today's approval, the drug had been made available to more than 5,000 patients in clinical tests and in a special program to many of the

# *American Express and 2 Brokers*

# Objectives

Upon completion of this activity, the participants should be able to:

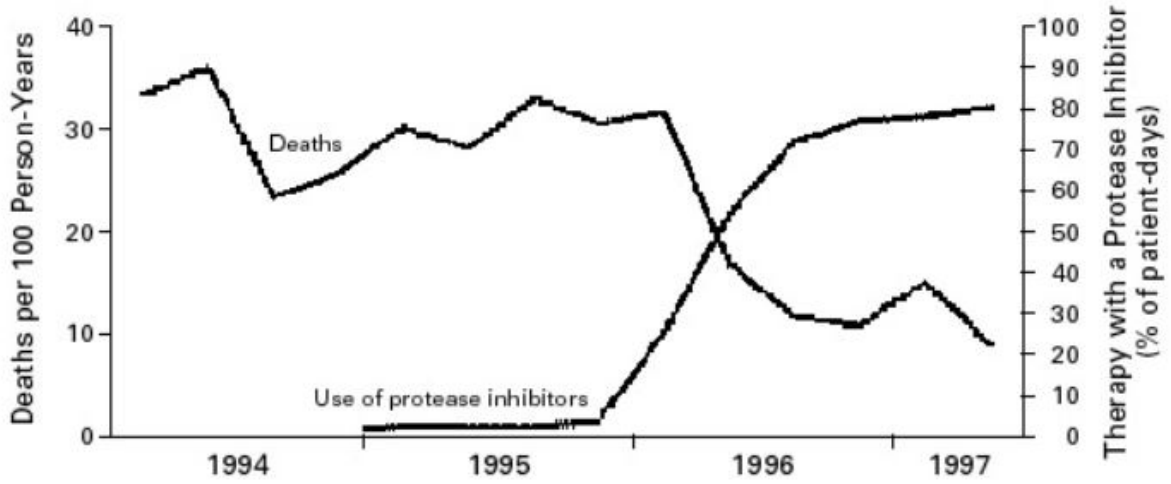
- Goals of HIV Therapy
- The Drug Classes
- When do we initiate Antiretroviral Therapy
- Selection of Antiretroviral Therapy
- Long-Term Benefits of Anti-Retroviral Therapy
  - Reduction in Morbidity and Mortality

# Goals of HIV Therapy

- Reduce morbidity and mortality
  - Since 2004, AIDS related deaths have decreased by 64% (UNAIDS)
- Reduction of opportunistic infections
  - Provided patient is on appropriate HIV therapy
  - Compliance
- Increase CD4 (Helper T-cells), decrease HIV RNA (viral load)

# Declining Morbidity and Mortality among Patients with Advanced Human Immunodeficiency Virus Infection

Mortality and Frequency of Use of Combination Antiretroviral Therapy Including a Protease Inhibitor among HIV-Infected Patients with Fewer than 100 CD4+ Cells per Cubic Millimeter, According to Calendar Quarter, from January 1994 through June 1997.

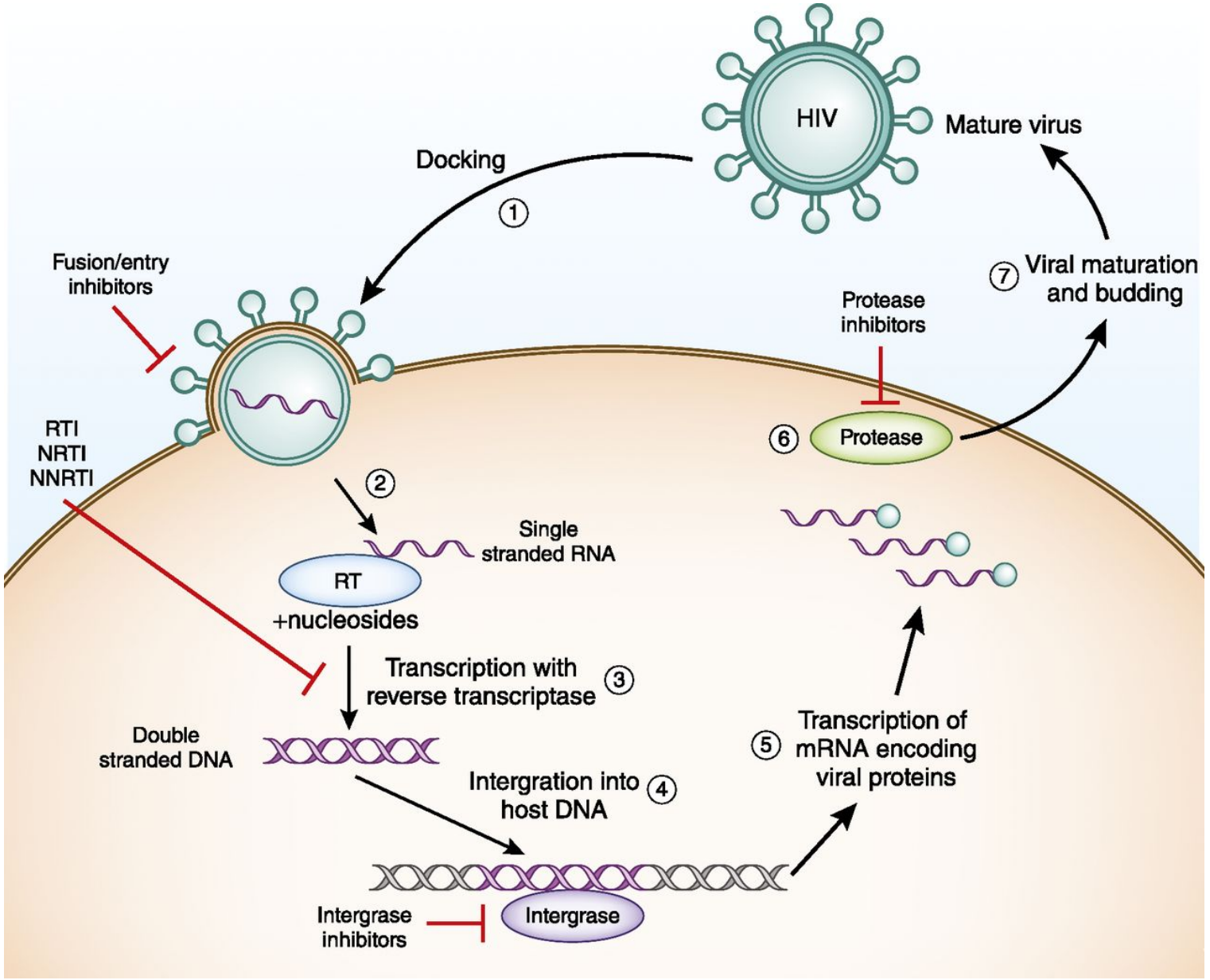



Palella et al, N Engl J Med 1998; 338:853-860

# The HIV Drug Classes

- There are 5 drug classes and over 30 medications available
  - Four antiretroviral drug classes used in initial regimens
    - Nucleoside (and nucleotide) reverse transcriptase inhibitors (NRTIs)
    - Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
    - Protease inhibitors (PIs)
    - Integrase strand transfer inhibitors (INSTIs)

## Targeting HIV-1.




**Mohamed G. Atta et al. CJASN 2019;14:435-444**

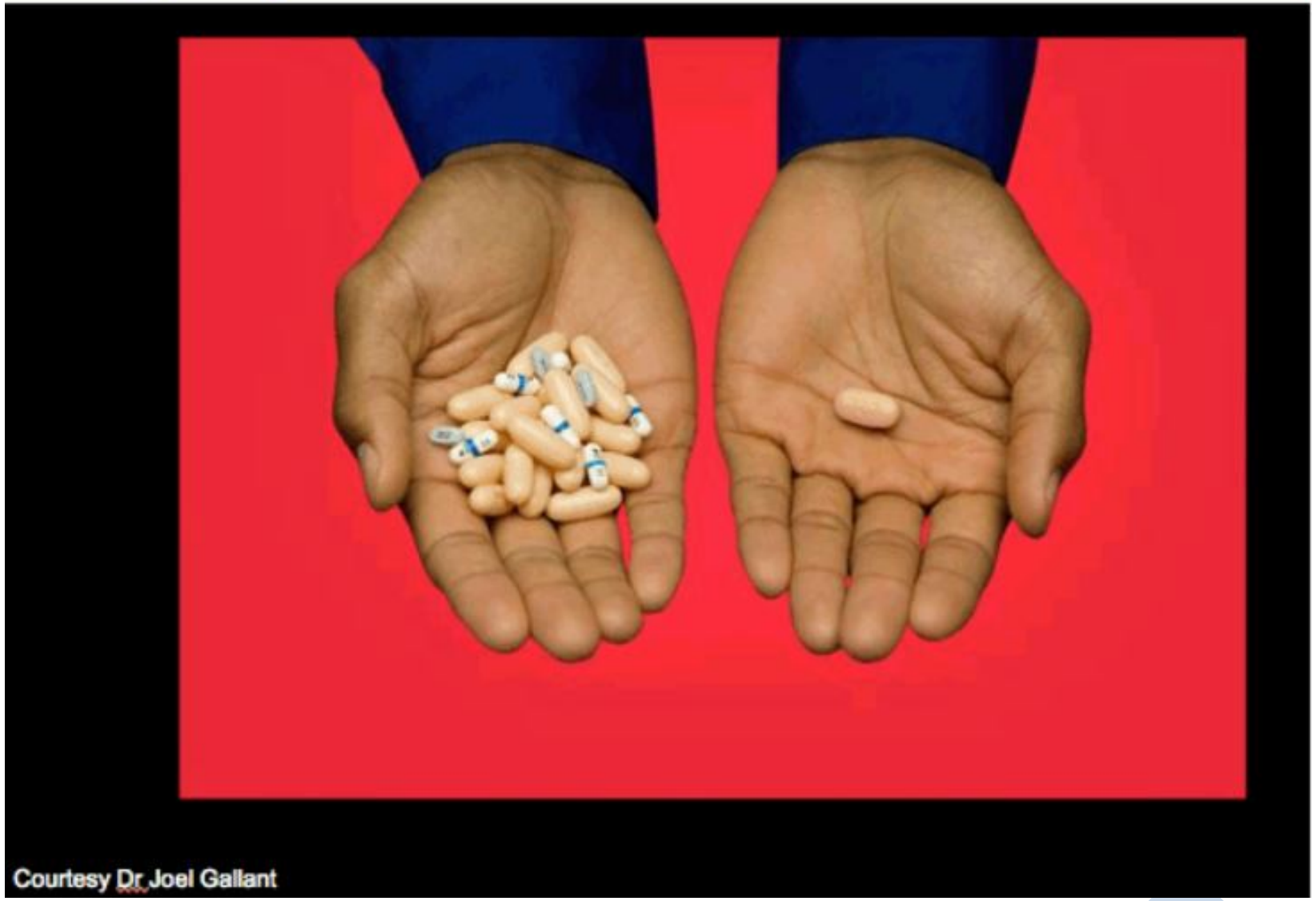


CJASN
Clinical Journal of the American Society of Nephrology

# Initiation of Anti-Retroviral Therapy (ART)

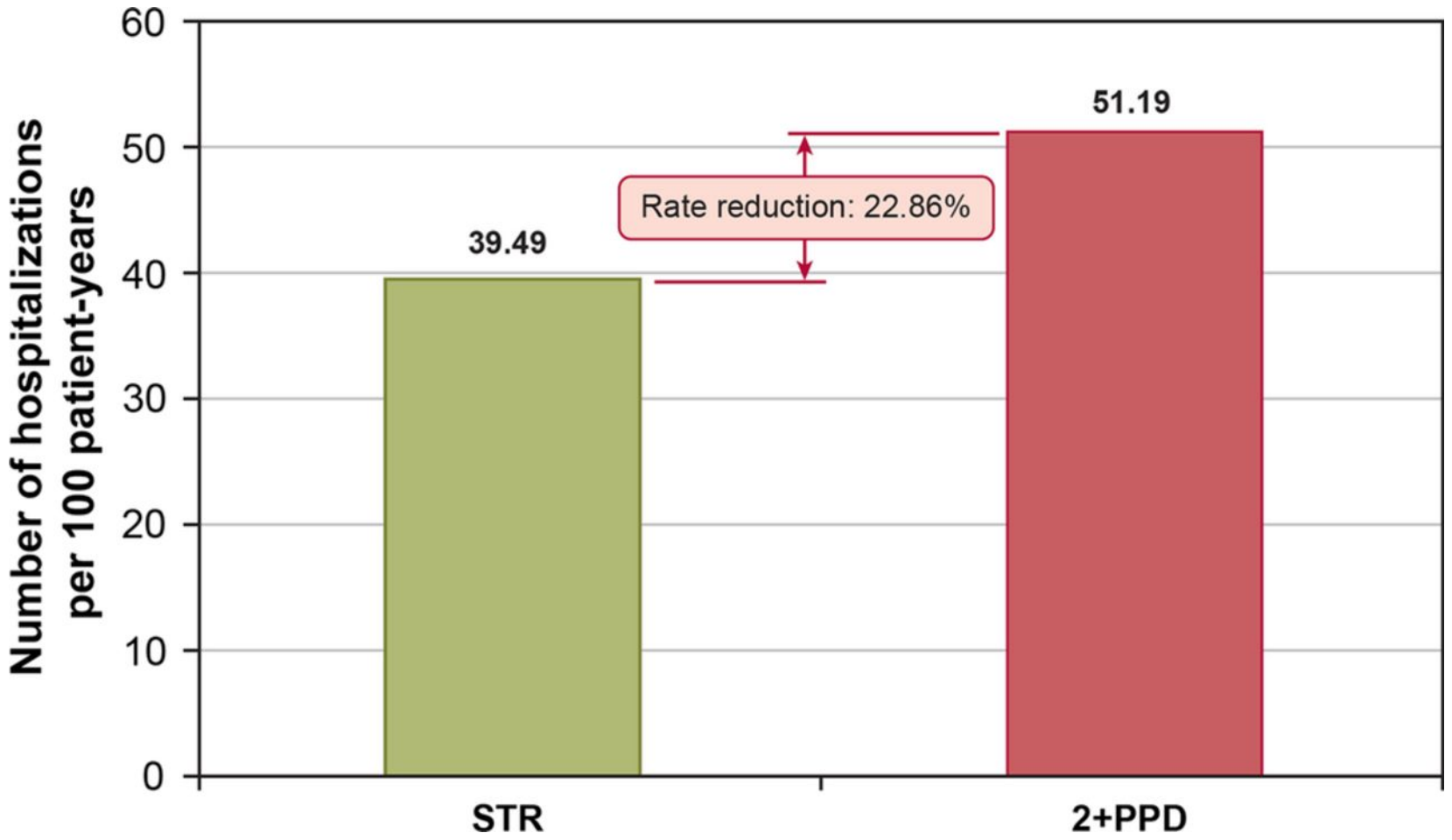
- Initially there was a "hit hard and hit early" approach to treatment
  - all patients should be treated with combination therapy as soon as possible **(N Engl J Med. 1995;333(7):450.)**
  - Some providers, however, withheld therapy in patients with relatively preserved CD4 due to toxicity and complexity of early ART.
  - Lack of clinical evidence proving a benefit of therapy for those with normal CD4 counts.

# 1997-2013: The long Road to QD ART Regimen, Patient Convenience and Adherence



Courtesy Dr Joel Gallant

**Adjusted rate of hospitalisations per 100 patient-years, by cohort.**

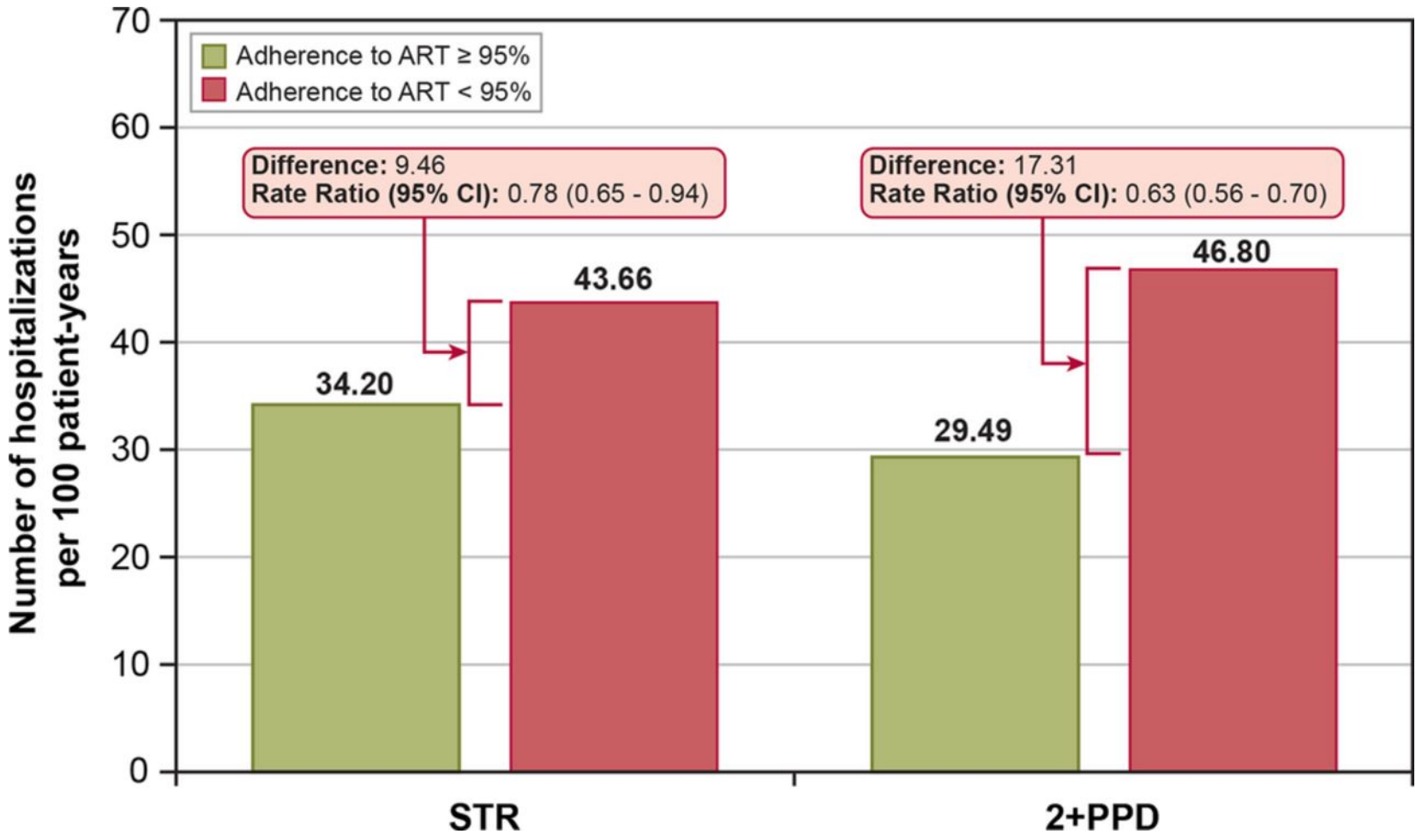



Calvin J Cohen et al. BMJ Open 2013;3:e003028



BMJ Open

**Hospitalisations per 100 patient-years, by cohort and adherence.**




Calvin J Cohen et al. BMJ Open 2013;3:e003028



BMJ Open

# Initiation of Anti-Retroviral Therapy (Today)

- Benefit of ART for individuals with HIV, regardless of CD4 count or the presence of symptoms, was suggested by a large cohort study
  - Described reduced mortality among those who received ART when the CD4 count was >500 cells/microL compared with starting treatment below this threshold. **(Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med. 2009)**

ORIGINAL ARTICLE

# Effect of Early versus Deferred Antiretroviral Therapy for HIV on Survival

Mari M. Kitahata, M.D., M.P.H., Stephen J. Gange, Ph.D., Alison G. Abraham, Ph.D., Barry Merriman, M.A., Michael S. Saag, M.D., Amy C. Justice, M.D., Ph.D., Robert S. Hogg, Ph.D., Steven G. Deeks, M.D., Joseph J. Eron, M.D., John T. Brooks, M.D., Sean B. Rourke, Ph.D., M. John Gill, M.B., Ch.B., et al., for the NA-ACCORD Investigators*

BACKGROUND: The optimal time for the initiation of antiretroviral therapy for asymptomatic patients with human immunodeficiency virus (HIV) infection is uncertain.

METHODS: Total of 17,517 asymptomatic patients with HIV infection in the United States and Canada who received medical care during the period from 1996 through 2005. None of the patients had undergone previous antiretroviral therapy. In each group, patients stratified according to the CD4+ count (351 to 500 cells per cubic millimeter or>500 cells per cubic millimeter) at the initiation of antiretroviral therapy.

RESULTS: In the first analysis, which involved 8362 patients, 2084 (25%) initiated therapy at a CD4+ count of 351 to 500 cells per cubic millimeter, and 6278 (75%) deferred therapy. After adjustment for calendar year, cohort of patients, and demographic and clinical characteristics, among patients in the deferred-therapy group there was an increase in the risk of death of 69%, as compared with that in the early-therapy group (relative risk in the deferred-therapy group, 1.69; 95% confidence interval [CI], 1.26 to 2.26; P<0.001).
In the second analysis involving 9155 patients, 2220 (24%) initiated therapy at a CD4+ count of more than 500 cells per cubic millimeter and 6935 (76%) deferred therapy. Among patients in the deferred-therapy group, there was an increase in the risk of death of 94% (relative risk, 1.94; 95% CI, 1.37 to 2.79; P<0.001).

CONCLUSIONS: The early initiation of antiretroviral therapy before the CD4+ count fell below two prespecified thresholds significantly improved survival, as compared with deferred therapy.

# Selection of Anti-Retroviral Therapy

- Initiate ART irrespective of CD4 count and detectable viremia
- Treatments are based on upon high barrier of resistance (for example, a NRTI based regimen with INSTI)
- Labs such as chemistry, CBC, liver panel monitored closely while on HAART in addition to CD4 and HIV RNA by PCR
  - We check HIV genotype and HLAB5701 (abacavir hypersensitivity) in all patients at time of initiation of ART

# Long-Term Benefits of Anti-Retroviral Therapy

- Effective ART results in sustained suppression of HIV RNA.
  - Leads to improvements in cellular immunity (eg, CD4 count) and a subsequent reduction in AIDS-related morbidity and mortality.
  - Suppression in HIV RNA can also result in a reduction in HIV immune activation (eg, proinflammatory cytokines, chronic inflammation, and T-cell activation)
    - Otherwise leads to end-organ damage (eg, coronary artery disease, liver and kidney disease, malignancy, neurologic disease)

***Shorter survival in advanced human immunodeficiency virus type 1 infection is more closely associated with T lymphocyte activation than with plasma virus burden or virus chemokine coreceptor usage.* J Infect Dis. 1999;179(4):859.**

# Conclusion

- ART has evolved over time thanks to reduction of pill burden and studies demonstrating benefit in early initiation of ART irrespective of CD4
  - Viral suppression has led to reduced HIV transmission
  - Early initiation of ART has led to reduction in HIV immune activation leading to reduced mortality in patients with co-morbidities such as cardiovascular disease, HIV associated-nephropathy, malignancies (HIV and non-HIV), hepatitis B &C, tuberculosis, and diabetes.
  - Reduction in opportunistic infections

# Take Home Message:

# Early initiation of HIV therapy improves survival!

# Thank you!