

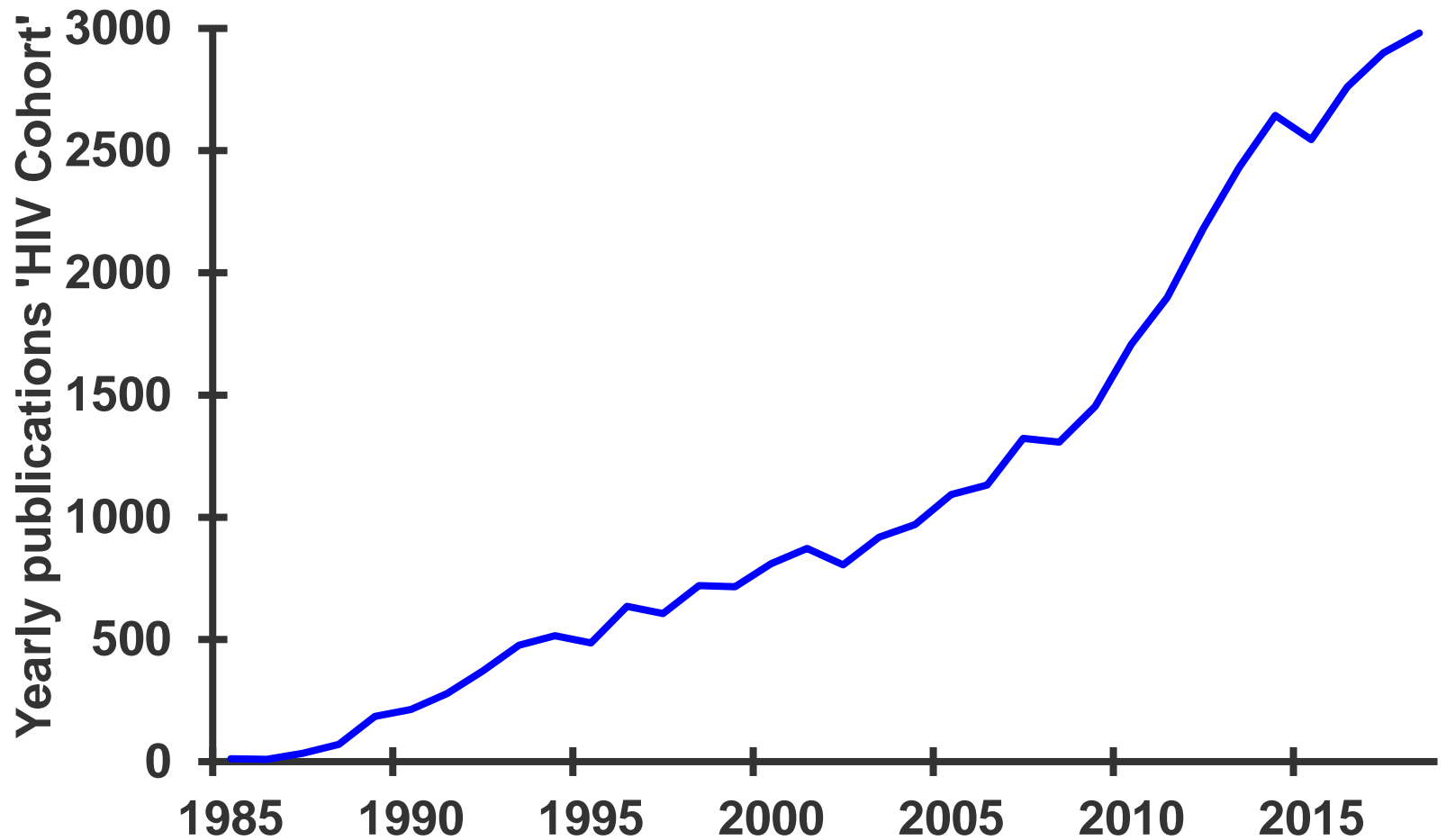


EuroSIDA

What HIV observational cohorts
have brought to the field

Bruno Ledergerber, PhD
University Hospital Zurich
Switzerland

39'000 Publications



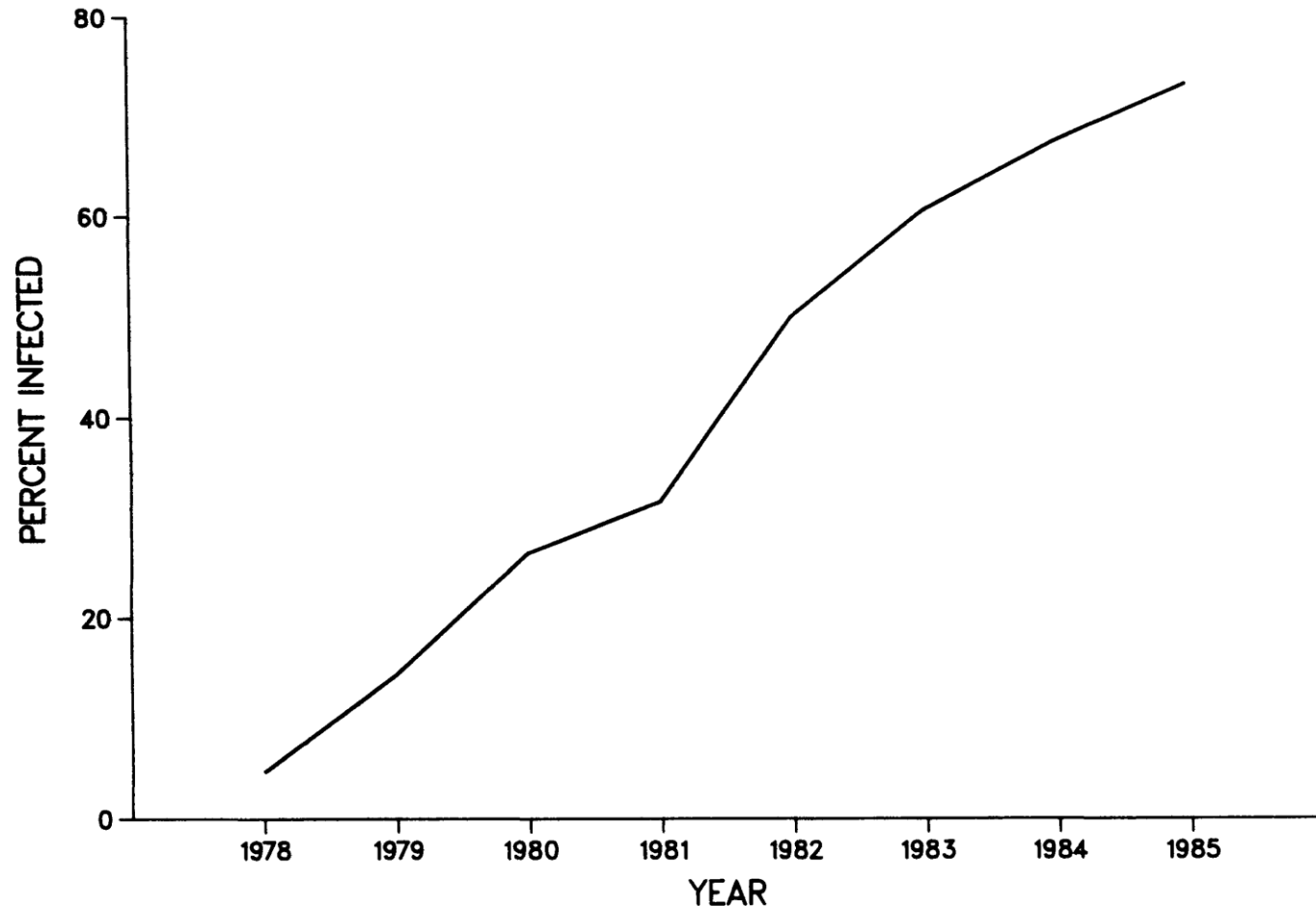
Search term "HIV Cohort" in Web of Science as of October 2019

Which field?

- Medical
 - Persons at risk (Transmission risk)
 - Patients (Clinical course)
 - Health care systems (Disparities)
 - (Basic Science projects based on phenotypes and samples from cohort studies)
- Non-medical
 - Operational
 - Methodological

HTLV-III / LAV epidemic in SF

FIGURE 1. Human T-lymphotropic virus type III/lymphadenopathy-associated virus infections in City Clinic cohort, by year specimen collected — San Francisco, California, 1978-1985



1985 San Francisco Cohort Study

The Lancet · Saturday 14 February 1987

RISK FACTORS FOR SEROCONVERSION TO HUMAN IMMUNODEFICIENCY VIRUS AMONG MALE HOMOSEXUALS

Results from the Multicenter AIDS Cohort Study*

LAWRENCE A. KINGSLEY
RICHARD KASLOW
CHARLES R. RINALDO, JR
KATHERINE DETRE
NANCY ODAKA
MARK VANRADEN

ROGER DETELS
B. FRANK POLK
JOAN CHMIEL
SHERYL F. KELSEY
DAVID OSTROW
BARBARA VISSCHER

Summary 2507 homosexual men who were seronegative for human immunodeficiency virus (HIV) at enrolment were followed for six months to elucidate risk factors for seroconversion to HIV. 95 (3·8%) seroconverted. Of men who did not engage in receptive anal intercourse within six months before baseline and in the six-month follow-up period, only 0·5% (3/646) seroconverted to HIV. By contrast, of men who engaged in

1987 Multicenter AIDS Cohort Study

Annals of Internal Medicine®

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ADVANCE

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ORIGINAL RESEARCH | 1 OCTOBER 1987

Infection with the Human Immunodeficiency Virus: Clinical Manifestations and Their Relationship to Immune Deficiency: A Report from the Multicenter AIDS Cohort Study

RICHARD A. KASLOW, M.D., M.P.H.; JOHN P. PHAIR, M.D.; HEIDI B. FRIEDMAN; DAVID LYTER, M.D.; RACHEL E. SOLOMON, M.H.S.; JAN DUDLEY, M.P.H.; B. FRANK POLK, M.D., M.S.; WILLIAM BLACKWELDER, Ph.D.

1987 Multicenter AIDS Cohort Study

Journal of Acquired Immune Deficiency Syndromes
1:390–395 © 1988 Raven Press, Ltd., New York

Patterns of CD4⁺ Cell Changes After HIV-1 Infection Indicate the Existence of a Codeterminant of AIDS

Roger Detels, Patricia A. English, Janis V. Giorgi, Barbara R. Visscher, John L. Fahey,
Jeremy M. G. Taylor, Janice P. Dudley, Parunag Nishanian, Alvaro Muñoz,
John P. Phair, B. Frank Polk, and Charles R. Rinaldo

*Multicenter AIDS Cohort Study, National Institute of Allergy and Infectious Disease and the National Cancer
Institute, Bethesda, Maryland*

Early-ART Era: First NRTIs

- 1987 Zidovudine (AZT)
- 1991 Didanosine (ddI)
- 1992 Zalcitabine (ddC)
- 1995 Lamivudine (3TC)

Comparison of Long-term Prognosis of Patients With AIDS Treated and Not Treated With Zidovudine

Jens D. Lundgren, MD, DSc; Andrew N. Phillips, PhD; Court Pedersen, MD, DSc; Nathan Clumeck, MD; Jose M. Gatell, MD, PhD; Anne M. Johnson, PhD; Bruno Ledergerber, PhD; Stefano Vella, MD; Jens O. Nielsen, MD, MSc; for the AIDS in Europe Study Group

JAMA. 1994;271:1088-1092

"When initiated after the time of AIDS diagnosis, zidovudine was associated with improved prognosis but for no more than 2 years after starting therapy."

- Protease inhibitors
 - Saquinavir 1995
 - Ritonavir (full dose), Indinavir 1996
- Non-nucleoside reverse transcriptase inhibitors
 - Nevirapin 1997
 - Efavirenz 1998
- Cohorts take over where phase III trials stop
 - Effectiveness on population level (incl. children)
 - Long term tolerability and safety
 - Drug resistance
 - Co-infections
 - Multimorbidity and polypharmacy in aging people
 - Monitoring the HIV epidemic

The New England Journal of Medicine

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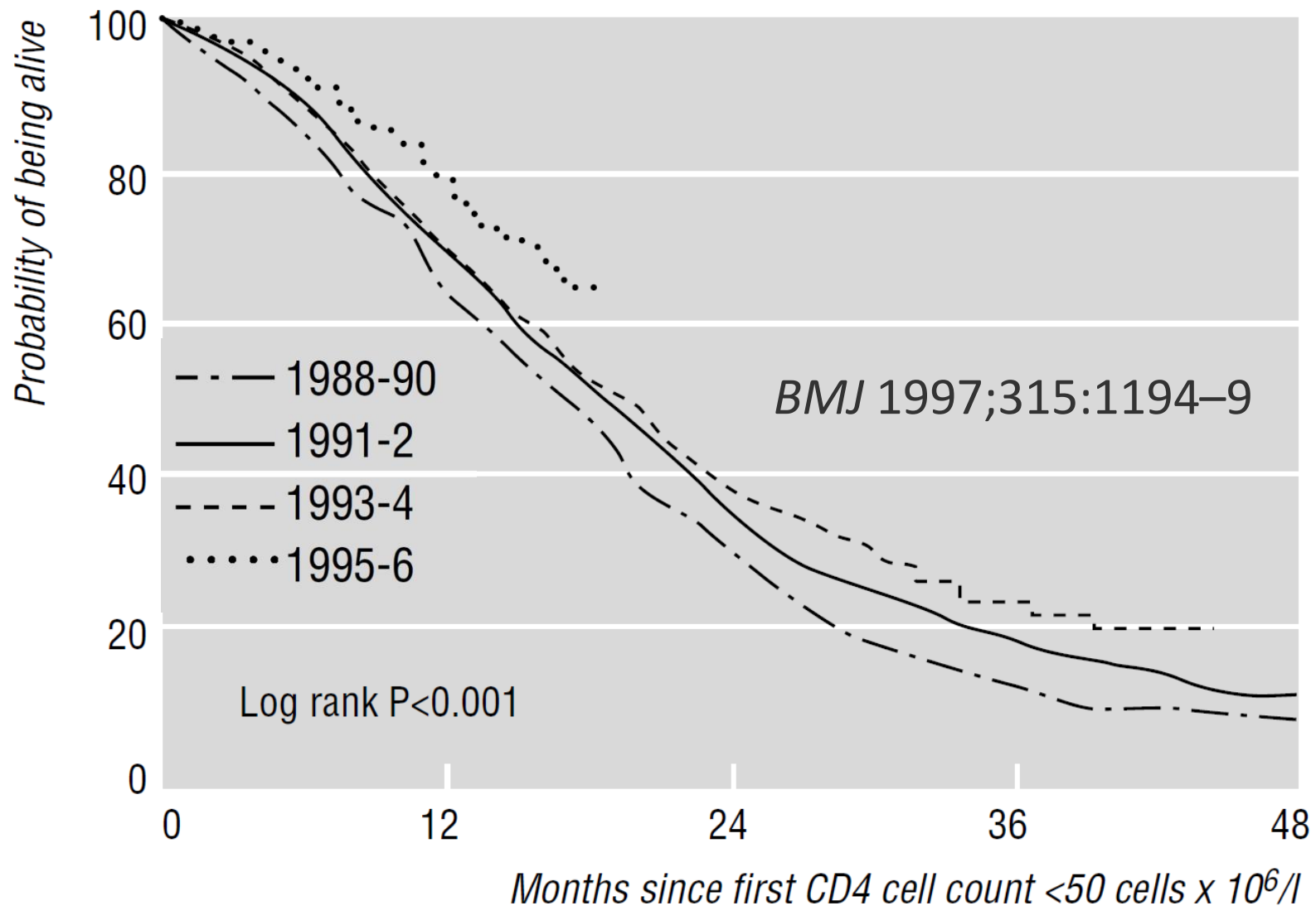


DECLINING MORBIDITY AND MORTALITY AMONG PATIENTS WITH ADVANCED HUMAN IMMUNODEFICIENCY VIRUS INFECTION

FRANK J. PALELLA, JR., M.D., KATHLEEN M. DELANEY, M.S., ANNE C. MOORMAN, B.S.N., M.P.H.,
MARK O. LOVELESS, M.D., JACK FUHRER, M.D., GLEN A. SATTEN, PH.D., DIANE J. ASCHMAN, R.PH., M.S.,
SCOTT D. HOLMBERG, M.D., M.P.H., AND THE HIV OUTPATIENT STUDY INVESTIGATORS*

1998 HIV Outpatient Study (HOPS)

cART/HAART Era: Survival improvement

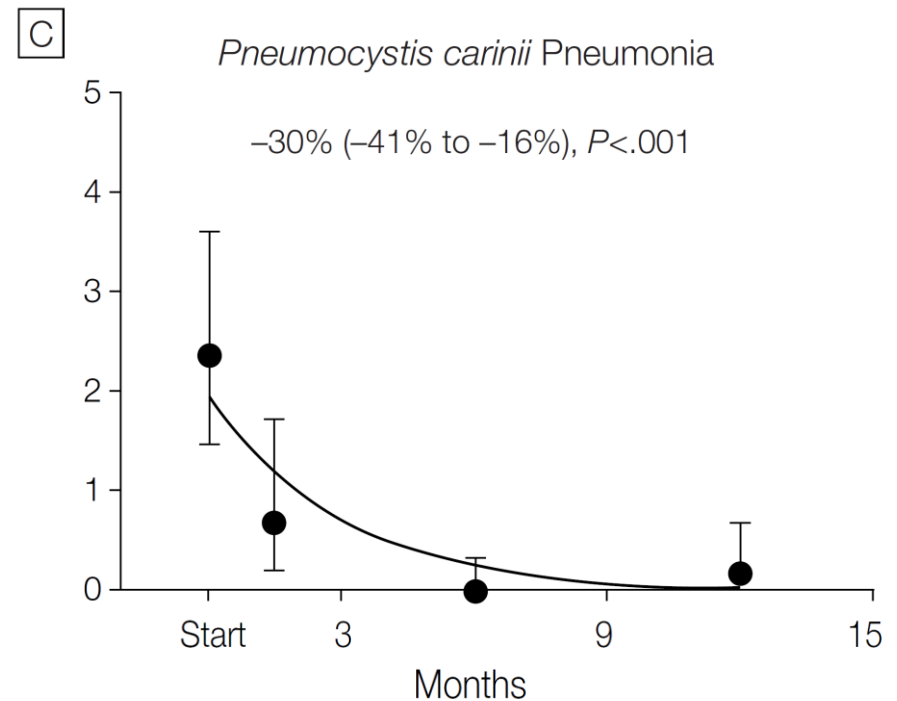
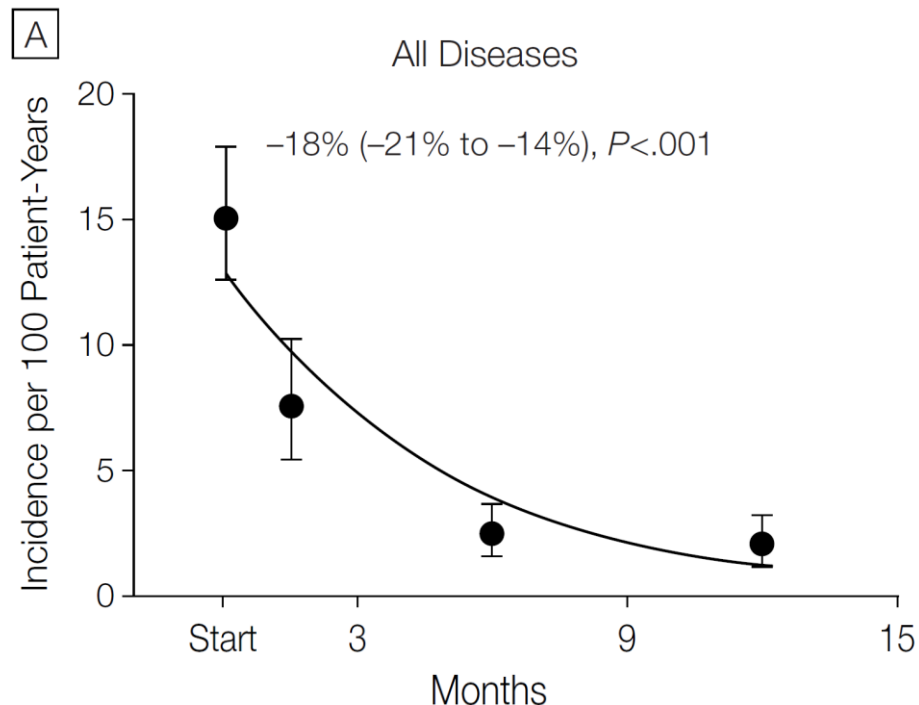


1997 Swiss HIV Cohort Study

AIDS-Related Opportunistic Illnesses Occurring After Initiation of Potent Antiretroviral Therapy

The Swiss HIV Cohort Study

JAMA. 1999;282:2220-2226



1999 Swiss HIV Cohort Study



DISCONTINUATION OF PRIMARY PROPHYLAXIS AGAINST *PNEUMOCYSTIS CARINII* PNEUMONIA IN HIV-1-INFECTED ADULTS TREATED WITH COMBINATION ANTIRETROVIRAL THERAPY

HANSJAKOB FURRER, M.D., MATTHIAS EGGER, M.D., MILOS OPRAVIL, M.D., ENOS BERNASCONI, M.D.,
BERNARD HIRSCHL, M.D., MANUEL BATTEGAY, M.D., AMALIO TELENTI, M.D., PIETRO L. VERNAZZA, M.D.,
MARTIN RICKENBACH, M.D., MARKUS FLEPP, M.D., AND RAFFAELE MALINVERNI, M.D., FOR THE SWISS HIV COHORT STUDY*

N Engl J Med 1999;340:1301-6.

Discontinuation of *Pneumocystis carinii* pneumonia prophylaxis after start of highly active antiretroviral therapy in HIV-1 infection

Gerrit J Weverling, Amanda Mocroft, Bruno Ledergerber, Ole Kirk, Juan Gonz  les-Lahoz, Antonella d'Arminio Monforte,
Rui Proenca, Andrew N Phillips, Jens D Lundgren, Peter Reiss, for the EuroSIDA Study Group*

Lancet 1999; 353: 1293–98

1999: Cohort Collaborations

**Matthias Egger
ART-CC**



**Jens Lundgren
D:A:D**

**30.03.1999 Marbella: 4th International Workshop on HIV
Observational Databases (IWHOD)**

DISCONTINUATION OF SECONDARY PROPHYLAXIS AGAINST *PNEUMOCYSTIS CARINII* PNEUMONIA IN PATIENTS WITH HIV INFECTION WHO HAVE A RESPONSE TO ANTIRETROVIRAL THERAPY

BRUNO LEDERGERBER, PH.D., AMANDA MOCROFT, PH.D., PETER REISS, M.D., HANSJAKOB FURRER, M.D., OLE KIRK, M.D., MARKUS BICKEL, M.D., CATERINA UBERTI-FOPPA, M.D., CHRISTIAN PRADIER, M.D., ANTONELLA D'ARMINIO MONFORTE, M.D., MARGRIET M.E. SCHNEIDER, M.D., AND JENS D. LUNDGREN, M.D., FOR EIGHT EUROPEAN STUDY GROUPS*

N Engl J Med 2001; 344:168-74.

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Recommendations and Reports

1

Guidelines for Preventing Opportunistic Infections Among HIV-Infected Persons — 2002

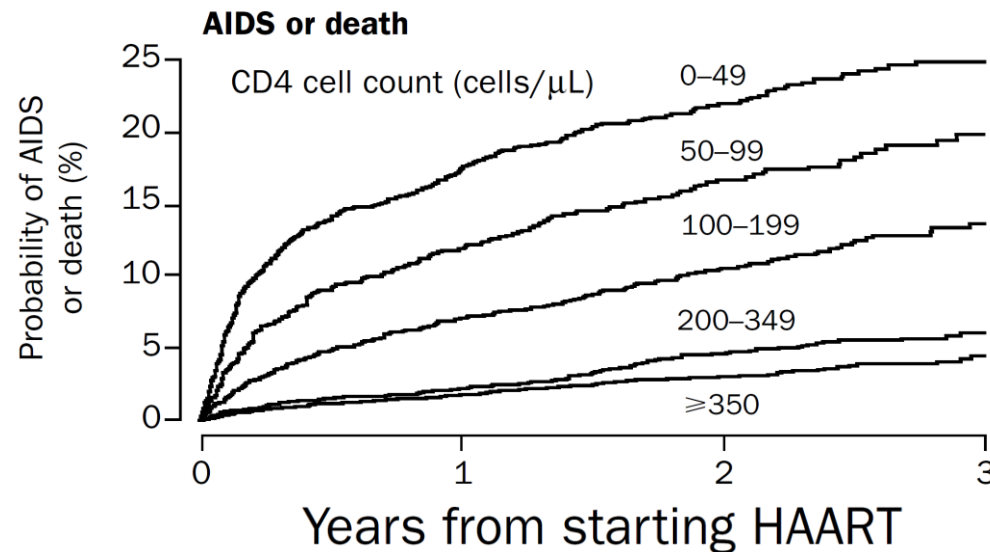
Discontinuing Secondary Prophylaxis (Chronic Maintenance Therapy). Secondary prophylaxis should be discontinued for adult and adolescent patients whose CD4⁺ T lymphocyte cell count has increased from <200 cells/μL to >200 cells/μL for ≥3 months as a result of HAART (BII). Reports from observational studies (37,41,42) and from a randomized trial (39), as well as a combined analysis of eight European cohorts being followed prospectively (43), support this recommendation. In these studies, patients had responded

2001 Collaboration of eight European Cohorts

🕒 Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies

Matthias Egger, Margaret May, Geneviève Chêne, Andrew N Phillips, Bruno Ledergerber, François Dabis, Dominique Costagliola, Antonella D'Arminio Monforte, Frank de Wolf, Peter Reiss, Jens D Lundgren, Amy C Justice, Schlomo Staszewski, Catherine Leport, Robert S Hogg, Caroline A Sabin, M John Gill, Bernd Salzberger, Jonathan A C Sterne, and the ART Cohort Collaboration*

Lancet 2002; 360: 119–29



2002 ART Cohort Collaboration

The NEW ENGLAND JOURNAL of MEDICINE

Combination Antiretroviral Therapy and the Risk of Myocardial Infarction

The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group*

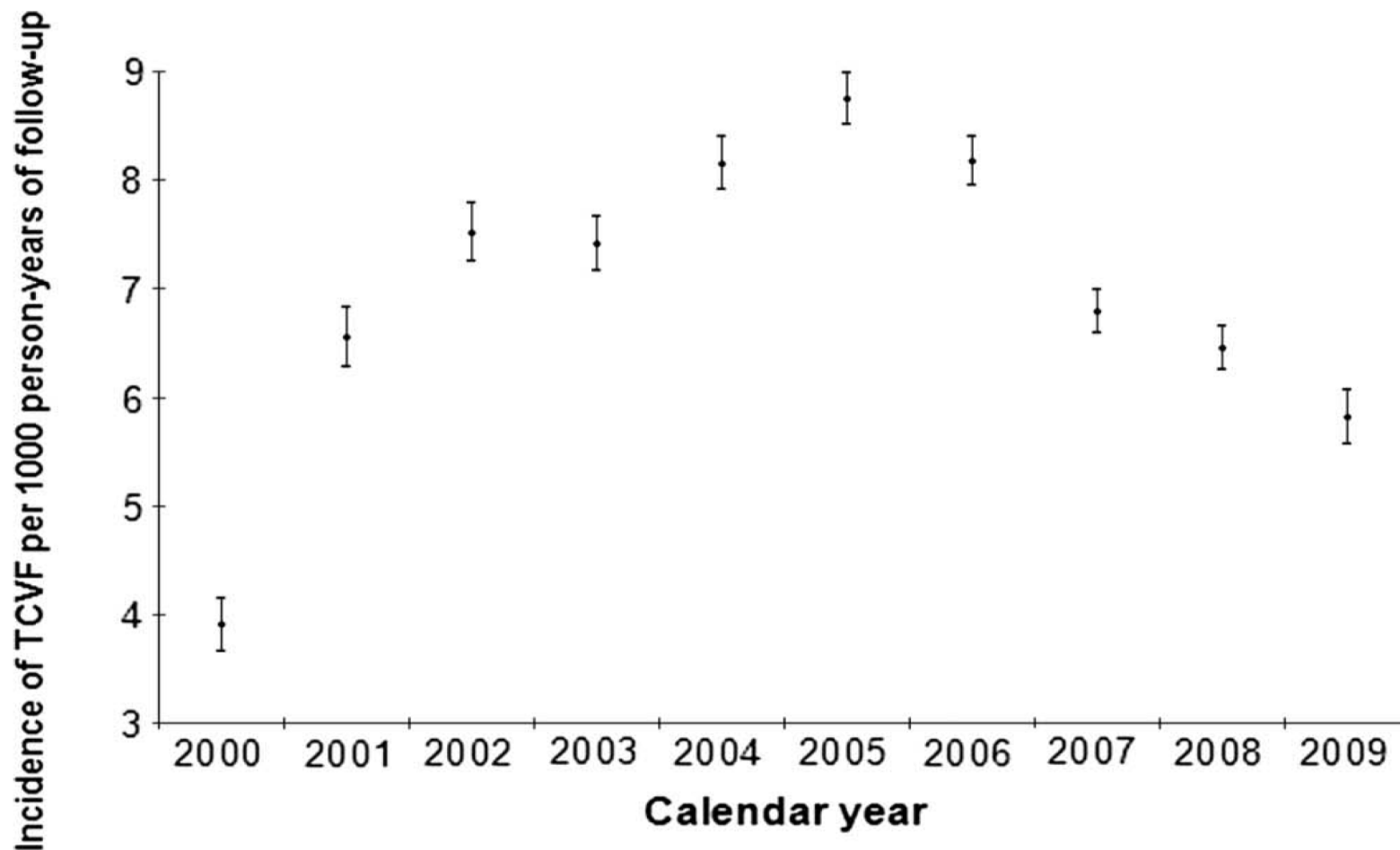
N Engl J Med 2003;349:1993-2003.

Class of Antiretroviral Drugs and the Risk of Myocardial Infarction

The DAD Study Group*

N Engl J Med 2007;356:1723-35.

**2003/2007 Data Collection on Adverse Events
of anti-HIV Drugs (DAD) Study Group**

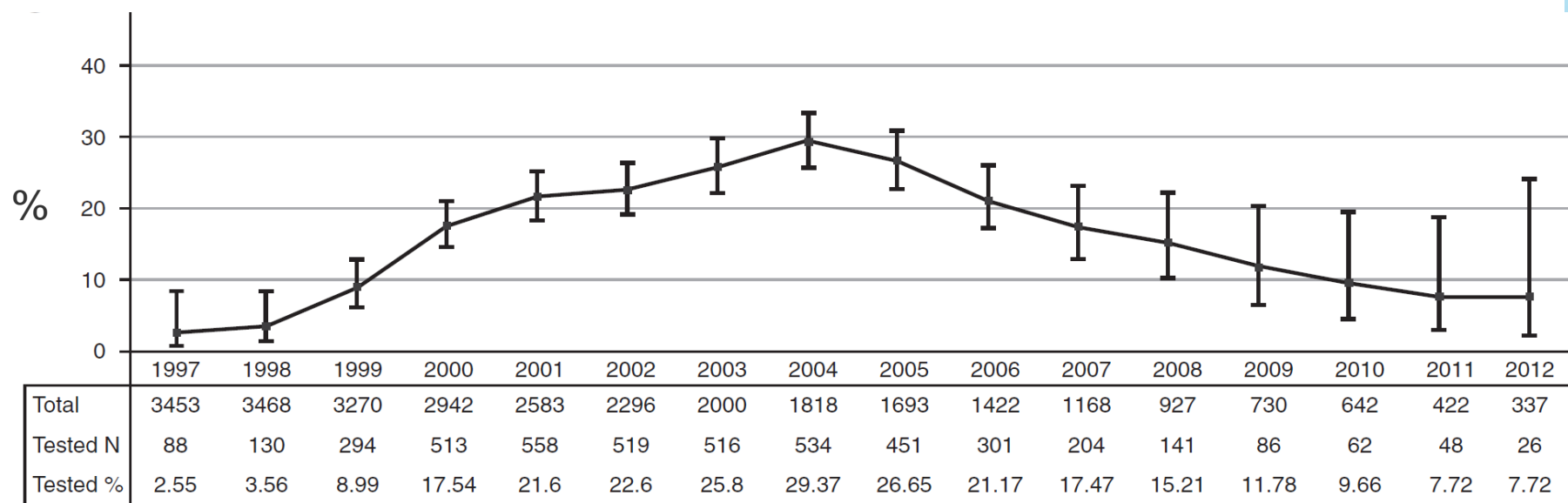


2004/2011/2012 Pursuing Later Treatment Options (PLATO) Collaboration within COHERE

HIV resistance testing and detected drug resistance in Europe

EuroSIDA in EuroCOORD

AIDS 2015, 29:1379–1389



Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study

*The TenoRes Study Group**

Lancet Infect Dis 2016

Methods: The TenoRes collaboration comprises adult HIV treatment cohorts and clinical trials of HIV drug resistance testing in Europe, Latin and North America, sub-Saharan Africa, and Asia.

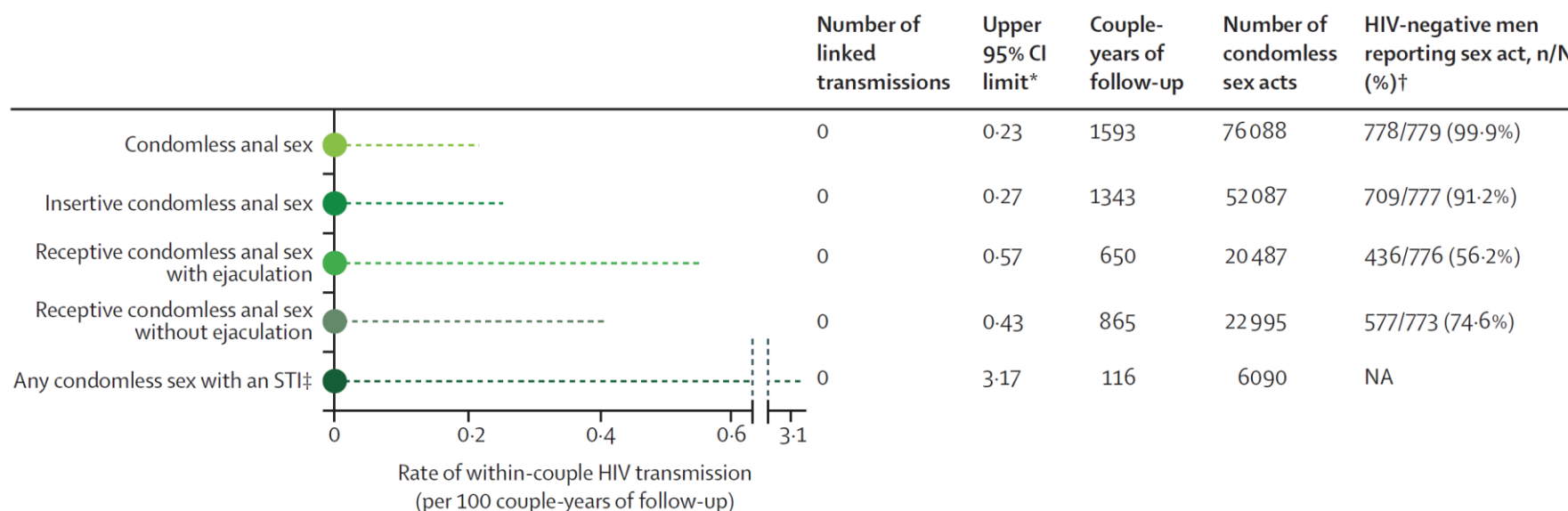
Interpretation: We recorded drug resistance in a high proportion of patients after virological failure on a tenofovir-containing first-line regimen across low-income and middle-income regions.

cART Era: Transmission risk



Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study

Lancet 2019; 393: 2428–38



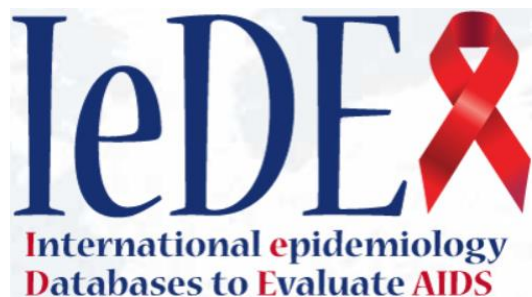
2019 PARTNER Study

Disparities across regions

- Prevention
- Diagnosis
- Treatment
- Outcome

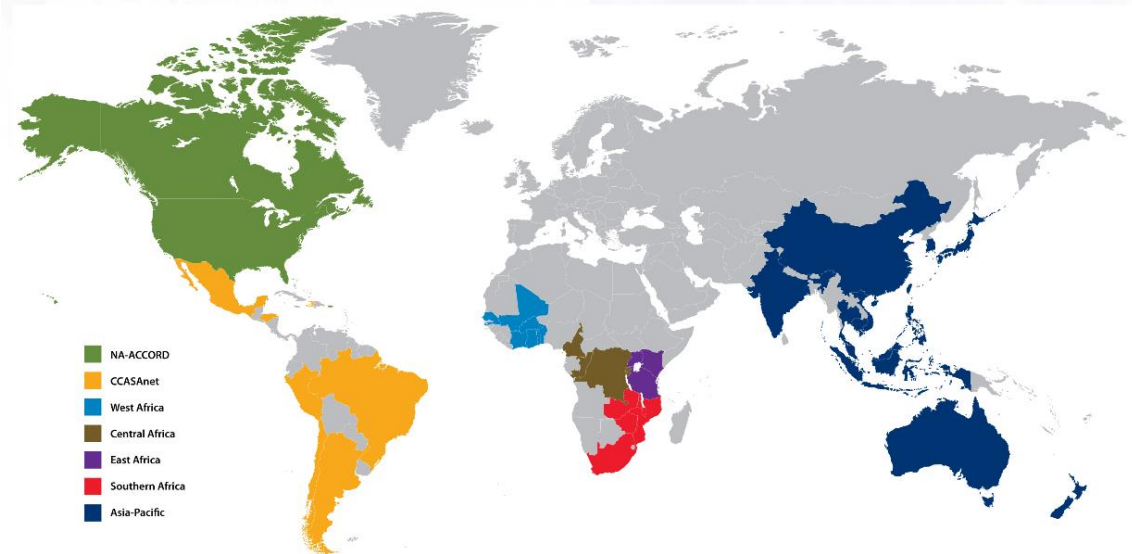
- Variation in antiretroviral treatment coverage and virological suppression among three HIV key populations. AIDS. 2018 Nov 28;32(18):2807-2819.
- Uptake of hepatitis C virus treatment in HIV/hepatitis C virus-coinfected patients across Europe in the era of direct-acting antivirals. AIDS. 2018 Sep 10;32(14):1995-2004.
- Persistent disparities in antiretroviral treatment (ART) coverage and virological suppression across Europe, 2004 to 2015. Euro Surveill. 2018 May;23(21).
- Disparities in HIV clinic care across Europe: findings from the EuroSIDA clinic survey. BMC Infect Dis. 2016 Jul 20;16:335.
- Hepatitis C seroconversions in HIV infection across Europe: which regions and patient groups are affected? Liver Int. 2015 Nov;35(11):2384-91.
- Regional differences in self-reported HIV care and management in the EuroSIDA study. J Int AIDS Soc. 2014 Nov 2;17(4 Suppl 3):19504.
- Regional differences in AIDS and non-AIDS related mortality in HIV-positive individuals across Europe and Argentina. PLoS One. 2012;7(7):e41673.

cART-Era: Benchmarking Global



Since 2006 >200 publications

Regions



- Firmly established collaborations of clinicians, epidemiologists, statisticians and basic scientists brought scientific quality of research to new levels
- Resource for developing and testing of new statistical methods (e.g. Causal models)
- "Big data" to assess the value of bioinformatic approaches (e.g. Machine Learning, AI)
- Stored samples with phenotypes for basic science projects (e.g. GWAS, Proteomics, Metabolomics)

Non-medical: Operational

- Capacity building and standardization of care within and between countries
- Recognition of clinical cohorts as valuable research tools with good return on investment
- Performing successful collaborations
 - Driven by the relevance of the scientific question
 - Largely overcoming rivalry
- Knowledge exchange in a friendly environment of trust





EuroSIDA

All the best for the
next 25 years
Thank You