Commentary: Questioning the HIV-AIDS hypothesis: 30 years of dissent

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A commentary on

Questioning the HIV-AIDS hypothesis: 30 years of dissent by Goodson P. Front Public Health (2014) 2:154. doi: 10.3389/fpubh.2014.00154

A recent Opinion article by Dr. Goodson (1) expresses pseudoscientific views typical of HIV/AIDS denialism (2–13) and ignores the overwhelming evidence that HIV is a causative agent of AIDS, the evidence accumulated during more than 30 years of research.

Fulfilling the Koch’s Postulate 1: HIV is Invariably Epidemiologically Associated with AIDS

Dr. Goodson ignores the fact that Koch’s postulates for viruses have been completely fulfilled in the case of HIV (9, 14, 15).

The overwhelming evidence suggests an invariable epidemiological association of HIV with AIDS. AIDS occurs exclusively in HIV-infected people (16). HIV can be detected in all AIDS patients (17). High levels of HIV in the organism predict progression to AIDS (18–23). Many children born to HIV-infected mothers have developed AIDS and died (24). AIDS-related conditions, such as Pneumocystis pneumonia and disseminated Mycobacterium avium complex disease, have become much more common after the start of the HIV epidemic (25). Death rates are much higher in HIV-seropositive treatment-naive than in seronegative individuals (26–34).

An HIV-triggered decrease in CD4+ T-lymphocyte count is a specific feature of HIV infection, and is extraordinarily rare in the absence of HIV (16, 35–37). The HIV-caused CD4+ T-lymphocyte depletion occurs through at least two mechanisms. (1) Direct killing of infected CD4+ T-lymphocytes. Dr. Goodson seems unfamiliar with the fact that HIV-1, HIV-2, and other representatives of the genus Lentivirus (e.g., Simian immunodeficiency virus), as well as some other retroviruses (e.g., Feline leukemia virus and members of the Avian leukosis virus group), exert a cytopathic effect in infected cells (38). (2) HIV directly kills Th17 CD4+ T-lymphocytes in the intestinal submucosa, triggering the damage of the mucosal integrity, translocation of microbial products from the intestine to the blood and chronic immune activation, resulting in further massive loss of CD4+ T-lymphocytes (39, 40).

Dr. Goodson claims that recreational drug use, clotting factor VIII, or receptive anal intercourse, but not HIV, are causes of AIDS. However, all of these claims have long ago been rejected by overwhelming scientific evidence (16, 35–37, 41–45).

Fulfilling the Koch’s Postulate 2: HIV has been Isolated from Patients at all Stages of the Infection

Contrary to Dr. Goodson’s claims, HIV has been isolated from patients at all stages of HIV infection, including AIDS, and propagated in cell culture (17, 46–54). Various protocols for HIV-1 isolation
(without “contaminants” claimed by Dr. Goodson) have been developed, and each of these protocols can be considered “standard” (55–62). Detailed images of HIV-1 virions, revealing morphology typical of the genus *Lentivirus*, have been obtained using transmission electron microscopy (46–48, 53, 63) and electron cryotomography (64, 65). A combination of immunofluorescent and electron microscopy has allowed visualization of intracellular trafficking of individual HIV-1 particles toward the nucleus of the infected cell (66). The process of cell-to-cell transfer of HIV-1 between T-lymphocytes has been visualized using high-speed three-dimensional video microscopy (67).

**Fulfilling the Koch’s Postulate 3: Accidental HIV Transmission in Humans**

Dr. Goodson ignores several tragic cases of accidental HIV transmission to laboratory workers who worked with purified HIV-1, became infected after a needle-stick or mucosal exposure and developed AIDS-like symptoms. HIV has been isolated from their blood, and DNA sequencing confirmed that the HIV variant isolated was identical to the one they were working with (15, 68–70). Other well-documented cases include HIV transmission from a dentist in the USA to several patients (15, 71), and HIV transmission through blood transfusion to 11 children in the USA (72) and 75 children in the former Soviet Union (73).

In addition, the Koch’s postulates for HIV and another lentivirus, Simian immunodeficiency virus, have been fulfilled in experiments with animal models (15, 74).

**HIV Laboratory Testing**

Three types of assays are used for HIV detection: (1) ELISA – specificity 98.5–99.9% (75–77), (2) Western blot (77), and (3) PCR – specificity 98.3–100% (78–80). The probability that both ELISA and Western blot would give false-positive results is extremely low (<1/140,000) (77). Thus, contrary to Dr. Goodson’s claims, these tests are highly specific for HIV-1. Since the diagnosis is based on the combination of the three tests (77), HIV testing will produce similar conclusions irrespective of the country.

Dr. Goodson misrepresents the study by Rodríguez et al. (81), which has never stated that PCR “is not sufficiently accurate” (1).

**Antiretroviral Therapy**

Contrary to Dr. Goodson’s claims, antiretroviral therapy (ART) has profoundly improved the prognosis for HIV-1-infected patients, suppressing their viral load, restoring CD4⁺ T-lymphocyte count, and reducing the risk of developing AIDS or dying (Figure 1A) (82–104). The success of ART has been determined by its high specificity for HIV-1-encoded proteins (105, 106). Along with therapeutic agents for many other diseases,
ART does have side effects, but these are far outweighed by its benefits (106). New anti-HIV agents should help to mitigate side effects, overcome drug resistance, and ultimately cure HIV infection, e.g., through excising HIV proviral DNA from the chromosome (107–109).

Dr. Goodson misrepresents the study by the ART Cohort Collaboration, which showed that ART is extremely beneficial for HIV-infected patients, but better clinical outcomes are observed when CD4+ T-lymphocyte counts at the start of ART are higher than 200 cells/µl (110). These conclusions have been corroborated by many other studies (111–117) and serve as a background to recommend starting ART early, when the HIV-triggered damage of the immune system is easier to restore (106).

**Detrimental Impact of HIV/AIDS Denialism on Public Health**

P. Duesberg, D. Rasnick, and some other HIV/AIDS denialists served on a controversial advisory panel of the South African president Thabo Mbeki. The policy of the South African government over HIV/AIDS during the period 2000–2005 is considered by a majority of scientists to have resulted in the death of at least 330,000 HIV-infected people (Figure 1B) (9, 12, 118). The Opinion article by Dr. Goodson (1) [as well as earlier published or publicly expressed opinions of P. Duesberg, K. Mullis, and other denialists, none of whom has ever worked with HIV/AIDS (2–5, 7–12)] is similarly harmful for public health, as it disseminates dangerous misinformation about HIV/AIDS that can affect prevention decisions made by uninfected people and treatment decisions made by HIV-infected people. Therefore, the following recommendations should be given to public health workers: (1) to learn and disseminate up-to-date knowledge on HIV/AIDS based on the most recent scientific literature, and (2) to be aware of HIV/AIDS denialism and be able to effectively counteract its detrimental impact on public health.

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**References**

1. Goodson P. Questioning the HIV-AIDS hypothesis: 30 years of dissent. *Front Public Health* (2014) 2:154. doi:10.3389/fpubh.2014.00154
2. Gallo RC. “A single disease with a single cause”, “About causes of disease (and, in particular, why HIV is the cause of AIDS)”. In: Gallo RC, editor. *Virus Hunting. AIDS, Cancer and the Human Retroviruses: A Story of Scientific Discovery*. New York: BasicBooks (1991), p. 127–62, 276–97.
3. Cohen J. The Duesberg phenomenon. *Science* (1994) 266:1642–4. doi:10.1126/science.7992043
4. Abdool Karim Q, Abdool Karim SS, Abimiku A, Abiola N, Adjorlolo-Johnson G, Adler M, et al. The Durban Declaration. *Nature* (2000) 406:15–6. doi:10.1038/35017662
5. Smith TC, Novella SP. HIV denial in the Internet era. *PLoS Med* (2007) 4(8):e256. doi:10.1371/journal.pmed.0040256
6. Specter M. Denialism: How Irrational Thinking Hinders Scientific Progress, Harms the Planet, and Threatens Our Lives. New York, NY: The Penguin Press (2009). 294 p.
7. Kalichman SC. Denying AIDS: Conspiracy Theories, Pseudoscience, and Human Tragedy. New York, NY: Copernicus/Springer (2009). 205 p.
8. Kalichman SC. Commentary on “Questioning the HIV-AIDS hypothesis: 30 years of dissent”. *Front Public Health* (2015) 3:30. doi:10.3389/fpubh.2015.00030
9. Chigwedere P, Essex M. AIDS denialism and public health practice. *AIDS Behav* (2010) 14:237–47. doi:10.1007/s10461-009-9654-7
10. Goertzel T. Conspiracy theories in science. *EMBO Rep* (2010) 11:493–9. doi:10.1038/embob.2010.84
11. Nattrass N. Defending the boundaries of science: AIDS denialism, peer review and the Medical Hypotheses saga. *Social Health Illn* (2011) 33:507–21. doi:10.1111/j.1467-9566.2010.01312.x
12. Nattrass N. The AIDS Conspiracy: Science Fights Back. New York, NY: Columbia University Press (2012). 225 p.
13. Oliver JE, Wood T. Medical conspiracy theories and health behaviors in the United States. *JAMA Intern Med* (2014) 174:817–8. doi:10.1001/jamainternalmed.2014.190
14. Harden VA. Koch’s postulates and the etiology of AIDS: an historical perspective. *Hist Philos Life Sci* (1992) 14:249–69.
15. O’Brien SJ, Goedert JJ. HIV causes AIDS: Koch’s postulates fulfilled. *Curr Opin Immunol* (1996) 8:613–8. doi:10.1016/S0952-7915(96)80075-6
16. Schechter MT, Craib KJ, Gelmon KA, Montaner JS, Le TN, O’Shaughnessy MV. HIV-1 and the etiology of AIDS. *Lancet* (1993) 341:658–9. doi:10.1016/0140-6736(93)90421-C
17. Jackson JB, Kwok SY, Sininsky JH, Hopsicker JS, Sannerud KJ, Rhame FS, et al. Human immunodeficiency virus type 1 detected in all seropositive asymptomatic and asymptomatic individuals. *J Clin Microbiol* (1990) 28:16–9.
18. Cao Y, Qin L, Zhang L, Safrit J, Ho DD. Virologic and immunologic characterization of long-term survivors of human immunodeficiency virus type 1 infection. *N Engl J Med* (1995) 332:201–8. doi:10.1056/NEJM19950126320401
19. Pantaleo G, Menzo S, Vaccarezza M, Graziosi C, Cohen OJ, Demarest JE, et al. Studies in subjects with long-term nonprogressive human immunodeficiency virus infection. *N Engl J Med* (1995) 332:209–16. doi:10.1056/NEJM19950126320402
20. Mellors JW, Muñoz A, Giorgi JV, Margolick JB, Tassoni CJ, Gupta P, et al. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. *Ann Intern Med* (1997) 126:946–54. doi:10.1056/NEJM199706153320403
21. Bailer E, Mackiewicz CE, Reyes-Terán G, Sato A, Stranford SA, Fujimura SH, et al. Virologic and immunological features of long-term human immunodeficiency virus-infected individuals who have remained asymptomatic compared with those who have progressed to acquired immunodeficiency syndrome. *Blood* (1998) 92:3105–14.
22. Palumbo PE, Raskino C, Fiscus S, Pahwa S, Fowler MG, Spector SA, et al. Predictive value of quantitative plasma HIV RNA and CD4+ lymphocyte count in HIV-infected infants and children. *JAMA* (1998) 279:756–61. doi:10.1001/jama.279.10.756
23. Taha TE, Kumwenda NJ, Hoover DR, Biggar RJ, Broadhead RL, Casool S, et al. Association of HIV-1 load and CD4+ lymphocyte count with mortality among untreated African children over one year of age. *AIDS* (2000) 14:453–9. doi:10.1097/00002030-200003100-00021
24. Ades AE, Newell ML, Peckham CS, Giqquinto C, Zucchello F, De Rossi A, et al. Children born to women with HIV-1 infection: natural history and risk of transmission. *European Collaborative Study. Lancet* (1991) 337:253–60. doi:10.1016/0140-6736(91)90866-N
25. Sax PE, Cohen CJ, Kuritzkes DR, Cunha BA, Kbiak DW. Prophylaxis and treatment of opportunistic infections. In: Sax PE, Cohen CJ, Kuritzkes DR, editors. *HIV Essentials*. 7th ed. Burlington, MA: Jones & Bartlett Learning (2014). p. 72–133.
26. Thea DM, St Louis ME, Atido U, Kanjiga K, Kembo B, Matondo M, et al. A prospective study of diarrhea and HIV-1 infection among 429 Zairian infants. *N Engl J Med* (1993) 329:1686–702. doi:10.1056/NEJM199312233290304
27. Ackah AN, Coulibaly D, Digbeu H, Diallo K, Vetter KM, Coulibaly IM, et al. Response to treatment, mortality, and CD4 lymphocyte counts in HIV-infected persons with tuberculosis in Abidjan, Côte d’Ivoire. *Lancet* (1995) 345:607–10. doi:10.1016/S0140-6736(95)90519-7
28. Borgdorf MW, Barongo LR, Klokke AH, Newell JN, Senkoro KP, Velena JP, et al. HIV-1 incidence and HIV-1 associated mortality in a cohort of urban factory workers in Tanzania. *Ganitourin Medica* (1995) 71:212–5.

29. Darby SC, Ewart DW, Giangrande PL, Dolin PJ, Spooner Rj, Rizza CR. Mortality before and after HIV infection in the complete UK population of haemophiliacs. UK Haemophilia Centre Directors’ Organisation. *Nature* (1995) 377:79–82. doi:10.1038/377079a0

30. Leroy V, Mselati P, Lepage P, Batungwanayo J, Hitimanana DG, Taelman H, et al. Four years of natural history of HIV-1 infection in African women: a prospective cohort study in Kugali (Rwanda), 1988–1993. *J Acquir Immune Defic Syndr Hum Retrovir* (1995) 9:415–21. doi:10.1006/jaids.1995.0002–0013

31. Nunn AJ, Mulder DW, Kamali A, Ruberantwari A, Kengeya-Kayondo JF, Whithworth J. Mortality associated with HIV infection over five years in a rural Ugandan population: cohort study. *BMJ* (1997) 315:767–71. doi:10.1136/bmj.315.7111776

32. Spira R, Lepage P, Mselati P, Van De Perre P, Leroy V, Simonon A, et al. Natural history of human immunodeficiency virus type 1 infection in children: a five-year prospective study in Rwanda. Mother-to-Child HIV-1 Transmission Study Group. *Pediatrics* (1999) 104(5):e56. doi:10.1542/peds.104.5.e56

33. Taha TE, Kunwenda NI, Broadhead RL, Hoover DR, Graham SM, Van Der Hoven L, et al. Mortality after the first year of life among human immunodeficiency virus type 1-infected and uninfected children. *Pediatr Infect Dis J* (1999) 18:689–94. doi:10.1097/00006545-199908000-00007

34. Madhi SA, Petersen K, Madhi A, Khosous M, Klugman KP. Increased disease burden and antibiotic resistance of bacteria causing severe community-acquired lower respiratory tract infections in human immunodeficiency virus type 1-infected children. *Clin Infect Dis* (2000) 31:170–7. doi:10.1086/313925

35. Donegan E, Stuart M, Niland JC, Sacks HS, Azen SP, Dietrich SL, et al. Infection with human immunodeficiency virus type 1 (HIV-1) among recipients of antibody-positive blood donations. *Ann Intern Med* (1990) 113:733–9. doi:10.7326/0003-4819-113-10-733

36. Des Jarlais DC, Friedman SR, Marmor M, Mädlvan D, Yancovitz S, Sotheran RJL, et al. CD4 lymphocytopenia among injecting drug users in New York City. *Infection with human immunodeficiency virus type 1 among recipi-ents of blood products and organ donors. J Acquir Immune Defic Syndr Hum Retrovir* (1994) 7:92440–92444.

37. Goedert JJ. Mortality and haemophilia. *J Virol* (1993) 67:1907–13. doi:10.1128/JVI.67.8.1907A-1907B.

38. Goedert JJ. Mortality before and after HIV infection in the complete UK population of haemophiliacs. UK Haemophilia Centre Directors’ Organisation. *Nature* (1995) 377:79–82. doi:10.1038/377079a0

39. Levy JA, Hoffman AD, Kramer SM, Landis JA, Shimabukuro JM, Oshiro LS. Isolation of lymphocytotropic retroviruses from San Francisco patients with AIDS. *Science* (1984) 224:500–3. doi:10.1126/science.6209036

40. Albert J, Gaines H, Sönnerborg A, Nystrom G, Pehrson PO, Chiiodi F, et al. Isolation of human immunodeficiency virus (HIV) from plasma during primary HIV-1 infection. *J Med Virol* (1987) 23:67–73. doi:10.1002/jmv.1890230108

41. Chiiodi F, Albert J, Olausson E, Norkrans G, Hagberg L, Sonnnerborg A, et al. Isolation frequency of human immunodeficiency virus type 1 in spinal cords of acquired immunodeficiency syndrome patients with myelopathy: expression and replication in macrophages. *Proc Natl Acad Sci U S A* (1989) 86:3337–41. doi:10.1073/pnas.86.9.3337

42. Brown BK, Darden JM, Tovanabutra S, Oblander T, Frost J, Sanders-Buell E, et al. Biological and genetic characterization of a panel of 60 human immunodeficiency virus type 1 isolates, representing clades A, B, C, D, CRF01_AE, and CRF02_AG, for the development and assessment of candidate vaccines. *J Virol* (2005) 79:6089–101. doi:10.1128/JVI.79.6089-6101.2005

43. Gorantla S, Che M, Gendelman HE. Isolation, propagation, and HIV-1 infec-tion of monocyte-derived macrophages and recovery of virus from brain and cerebrospinal fluid. *Methods Mol Biol* (2005) 304:35–48. doi:10.1007/1-59259-907-9:035

44. Gorry PR, Sonza S, Kedziorska K, Crowe SM. Isolation of human immunodefi-ciency virus type 1 from peripheral blood monocytes. *Methods Mol Biol* (2005) 304:25–33. doi:10.1007/1-59259-907-9:025

45. Kessling AA. Isolation of human immunodeficiency virus type 1 from semen and vaginal fluids. *Methods Mol Biol* (2005) 304:71–86. doi:10.1007/1-59259-907-9:071

46. Schuitemaker H, Kootstra NA. Isolation, propagation, and titration of human immunodeficiency virus type 1 from peripheral blood of infected individuals. *Methods Mol Biol* (2005) 304:17–24. doi:10.1007/1-59259-907-9:017

47. Tamalet C. Isolation and quantification of HIV from lymph nodes. *Methods Mol Biol* (2005) 304:87–94. doi:10.1007/1-59259-907-9:087

48. Ott DE. Purification of HIV-1 virions by subtilisin digestion or CD45 immunoaffinity depletion for biochemical studies. *Methods Mol Biol* (2009) 485:15–25. doi:10.1007/978-1-59747-170-2_3

49. Karetinov A, Suomalainen T. Tethered virions are intermediates in the assembly and release of HIV-1 particles. *Urology* (2010) 70:289–95. doi:10.1016/j.urologi.2010.08.020

50. Dispinesi S, Saba E, Vicenzi E, Kootstra NA, Schuitemaker H, Scarletti G. HIV-1 isolation from infected peripheral blood mononuclear cells. *Methods Mol Biol* (2014) 1087:187–96. doi:10.1007/978-1-62703-670-2_15

51. Achilli G, Barbartini G, Cattaneo E, Cechini A, Concia E, De Rocco L, et al. AIDS nosography. In: Rondanelli EG, editor. *AIDS: Clinical and Laboratory Atlas. Pavia: Edizione Medico-Scientifica*. (1989). p. 10–40.

52. Schur FK, Hagen W, Rumlová M, Ruml T, Müller B, Krausslich HG, et al. Structure of the immature HIV-1 capsid in intact virus particles at 8 Å resolution. *Nature* (2015) 517:505–8. doi:10.1038/nature13838

53. Woodward CL, Cheng SN, Jensen GJ. Electron cryotomography studies of maturing HIV-1 particles reveal the assembly pathway of the viral core. *J Virol* (2015) 89:1267–77. doi:10.1128/JVI.02997-14

54. McDonald D, Vodicka MA, Lucero G, Svitkina TM, Borisy GG, Emerman M, et al. Visualization of the intracellular behavior of HIV in living cells. *J Cell Biol* (2002) 159:441–52. doi:10.1083/jcb.200203150

55. Hübner W, McNerney GP, Chen P, Dale BM, Gordon RE, Chuang FY, et al. Quantitative 3D video microscopy of HIV transfer across T cell virological synapses. *Science* (2009) 323:1743–7. doi:10.1126/science.1167525
86. Cameron DW, Heath-Chiozzi M, Danner S, Cohen C, Kravick S, Mauritser C, et al. Randomised placebo-controlled trial of ritonavir in advanced HIV disease. The Advanced HIV Disease Ritonavir Study Group. Lancet (1998) 351:543–9. doi:10.1016/S0140-6736(97)60416-5

87. Detels R, Muñoz A, McFarlane G, Kingsley LA, Margolick JB, Giorgi J, et al. Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration. Multicenter AIDS Cohort Study Investigators. JAMA (1998) 280:1497–503. doi:10.1001/jama.280.17.1497

88. Marschner IC, Collier AC, Cooms RW, D'Aquila RT, DeGruttola V, Fischel MA, et al. Use of changes in plasma levels of human immunodeficiency virus type 1 RNA to assess the clinical benefit of antiretroviral therapy. J Infect Dis (1998) 177:40–7. doi:10.1086/513823

89. Mocroft A, Vella S, Benfield TL, Chiesi A, Miller V, Gargalianos P, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. Lancet (1998) 352:1725–30. doi:10.1016/S0140-6736(98)03021-2

90. Montaner JS, DeMasi R, Hill AM. The effects of lamivudine treatment on HIV-1 disease progression are highly correlated with plasma HIV-1 RNA and CD4 cell count. AIDS (1998) 12:E23–8. doi:10.1097/00002030-199805000-00003

91. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med (1996) 335:853–60. doi:10.1056/NEJM199608033351502

92. Hogg RS, Yip B, Kulky C, Crabbe KJ, O'Shaughnessy MV, Schechter MT, et al. Improved survival among HIV-infected patients after initiation of triple-drug antiretroviral regimens. CMAJ (1999) 160:659–65.

93. Ledergerber B, Egger M, Opravil M, Telen T, Härschel B, Battogtokh M, et al. Clinical progression and virological failure on highly active antiretroviral therapy in HIV-1 patients: a prospective cohort study. Swiss HIV Cohort Study. Lancet (1999) 353:863–8. doi:10.1016/S0140-6736(99)01122-8

94. McNagnath AD, Hanson DL, Jones JL, Dworkin MS, Ward JW. Effects of antiretroviral therapy and opportunistic illness primary chemoprophylaxis on survival after AIDS diagnosis. Adult/Adolescent Spectrum of Disease Group. AIDS (1999) 13:1687–95. doi:10.1097/00002030-199909010-00012

95. Vittinghoff E, Scheer S, O'Malley P, Colfax G, Holmberg SD, Buchbinder SP. Combination antiretroviral therapy and recent declines in AIDS incidence and mortality. J Infect Dis (1999) 179:717–20. doi:10.1086/314623

96. Porter K. Survival after introduction of HAART in people with known duration of HIV-1 infection. The CASCADE Collaboration. Concreted Action on Seroconversion to AIDS and Death in Europe. Lancet (2000) 355:1158–9. doi:10.1016/S0140-6736(00)02069-9

97. de Martino M, Tovo PA, Balducci M, Galli L, Gabiano C, Rezza G, et al. Reduction in mortality with availability of antiretroviral therapy for children with perinatal HIV-1 infection. Italian Register for HIV Infection in Children and the Italian National AIDS Registry. JAMA (2000) 284:190–7. doi:10.1001/jama.284.2.190

98. Kaplan JE, Hanson D, Dworkin MS, Frederick T, Bertolli J, Lindeng ML, et al. Epidemiology of human immunodeficiency virus-associated opportunistic infections in the United States in the era of highly active antiretroviral therapy. Clin Infect Dis (2000) 30(Suppl 1):S5–14. doi:10.1086/313843

99. Mocroft A, Katlama C, Johnson AM, Pradier C, Antunes F, Mulcahy F, et al. AIDS across Europe, 1994-98: the EuroSIDA study. Lancet (2000) 356:291–6. doi:10.1016/S0140-6736(00)02504-6

100. Schwartz SK, Hsu LC, Vittinghoff E, Katz MH. Impact of protease inhibitors and other antiretroviral treatments on acquired immunodeficiency syndrome survival in San Francisco, California, 1987–1996. Am J Epidemiol (2000) 152:178–85. doi:10.1093/aje/152.2.178

101. Schneider MR, Gange SJ, Williams CM, Anastos K, Greenblatt RM, Kingsley L, et al. Patterns of the hazard of death after AIDS through the evolution of antiretroviral therapy: 1984-2004. AIDS (2005) 19:2009–18. doi:10.1097/00002030-200511010-00020

102. Holkmann Olsen C, Mocroft A, Kirk O, Vella S, Blaxhult A, Clumeneck N, et al. Interruption of combination antiretroviral therapy and risk of clinical disease progression to AIDS or death. HIV Med (2007) 8:96–104. doi:10.1111/j.1468-1293.2007.00436.x

103. Torian L, Chen M, Hall HL. Centers for Disease Control and Prevention (CDC). HIV surveillance – United States, 1981-2008. MMWR Mortal Wkly Rep (2011) 60:689–93.
104. Lima VD, Lourenço L, Yip R, Hogg RS, Phillips P, Montaner JS. Trends in AIDS incidence and AIDS-related mortality in British Columbia between 1981 and 2013. Lancet HIV (2015) 2(3):e92–7. doi:10.1016/S2352-3018(15)00017-X

105. Arts EJ, Hazuda DJ. HIV-1 antiretroviral drug therapy. Cold Spring Harb Perspect Med (2012) 2(4):a007161. doi:10.1101/cshperspect.a007161

106. Sax PE, Cohen CJ, Kuritzkes DR, Cunha BA, Kubiak DW. Treatment of HIV infection. In: Sax PE, Cohen CJ, Kuritzkes DR, editors. HIV Essentials. 7th ed. Burlington, MA: Jones & Bartlett Learning (2014). p. 19–54.

107. Hoxie JA, June CH. Novel cell and gene therapies for HIV. Cold Spring Harb Perspect Med (2012) 2(10):a007179. doi:10.1101/cshperspect.a007179

108. Hu W, Kaminski R, Yang F, Zhang Y, Cosentino L, Li F, et al. RNA-directed gene editing specifically eradicates latent and prevents new HIV-1 infection. Proc Natl Acad Sci U S A (2014) 111:11461–6. doi:10.1073/pnas.1405186111

109. Le Grice SE. Targeting the HIV RNA genome: high-hanging fruit only needs a longer ladder. Curr Top Microbiol Immunol (2015) 389:147–69. doi:10.1007/82_2015_434

110. May MT, Sterne JA, Costagliola D, Sabin CA, Phillips AN, Justice AC, et al. HIV treatment response and prognosis in Europe and North America in the first decade of highly active antiretroviral therapy: a collaborative analysis. Lancet (2006) 368:451–8. doi:10.1016/S0140-6736(06)69152-6

111. Egger M, May M, Chêne G, Phillips AN, Ledergerber B, Dabis F, et al. Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies. Lancet (2002) 360:119–29. doi:10.1016/S0140-6736(02)09411-4

112. Antiretroviral Therapy Cohort Collaboration. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. Lancet (2008) 372:293–9. doi:10.1016/S0140-6736(08)61113-7

113. Antiretroviral Therapy Cohort Collaboration; Zwahlen M, Harris R, May M, Hogg R, Costagliola D, et al. Mortality of HIV-infected patients starting potent antiretroviral therapy: comparison with the general population in nine industrialized countries. Int J Epidemiol (2009) 38:1624–33. doi:10.1093/ije/dyp306

114. HIV-CAUSAL Collaboration; Ray M, Logan R, Sterne JA, Hernández-Diaz S, Robins JM, et al. The effect of combined antiretroviral therapy on the overall mortality of HIV-infected individuals. AIDS (2010) 24:123–37. doi:10.1097/QAD.0b013e3283324283

115. Opportunistic Infections Project Team of the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in EuroCoord; Young J, Pschogios M, Meyer L, Ayari S, Grabar S, et al. CD4 cell count and the risk of AIDS or death in HIV-Infected adults on combination antiretroviral therapy with a suppressed viral load: a longitudinal cohort study from COHERE. PLoS Med (2012) 9(3):e1001194. doi:10.1371/journal.pmed.1001194

116. May MT, Ingle SM, Costagliola D, Justice AC, de Wolf F, Cavassini M, et al. Cohort profile: antiretroviral therapy cohort collaboration (ART-CC). Int J Epidemiol (2014) 43:691–702. doi:10.1093/ije/dyt010

117. Zhu H, Napravnik S, Eron JJ, Cole SR, Ma Y, Wohl DA, et al. Decreasing excess mortality of HIV-infected patients initiating antiretroviral therapy: comparison with mortality in general population in China, 2003-2009. J Acquir Immune Defic Syndr (2013) 63(5):e150–7. doi:10.1097/QAI.0b013e3182948d82

118. Chigwedere P, Seage GR III, Gruskin S, Lee TH, Essex M. Estimating the lost benefits of antiretroviral drug use in South Africa. J Acquir Immune Defic Syndr (2008) 49:410–5. doi:10.1097/QAI.0b013e31818a6cd5

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