ARVs through 30 years

Eileen Nixon

University Hospitals Sussex

Conflict of Interest

I have received speaker fees from Viiv for presenting on the Model of HIV Nursing Care.

Speakers are required by the Federation of the Royal Colleges of Physicians to disclose conflicts of interest at the beginning of their presentation, with sufficient time for the information to be read by the audience. They should disclose financial relationships with manufacturers of any commercial product and/or providers of commercial services used on or produced for patients relating to the 36 months prior to the event. These include speaker fees, research grants, fees for other educational activities such as training of health professionals and consultation fees. Where a speaker owns shares or stocks directly in a company producing products or services for healthcare this should also be declared. Finally, other conflicts of interest including expert functions in health care or healthcare guidance processes should be declared (eg if the professional is a member of a health board). The Federation considers it good practice to also make speakers' disclosures available in digital format(s) relating to the educational event.

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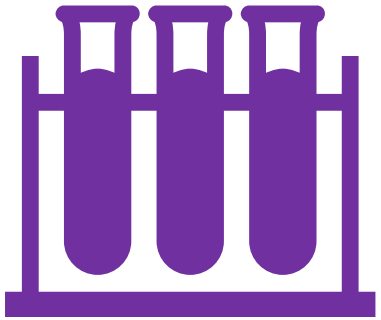
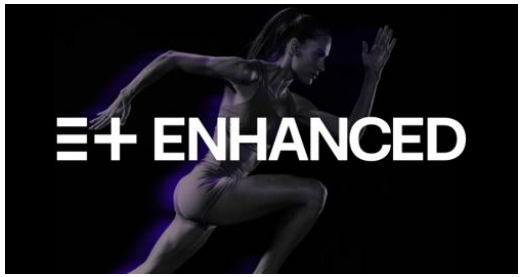


Then and Now

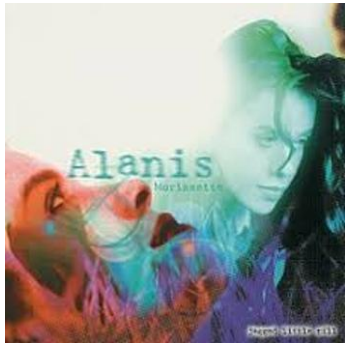
Dance Crazes 1996 and 2026

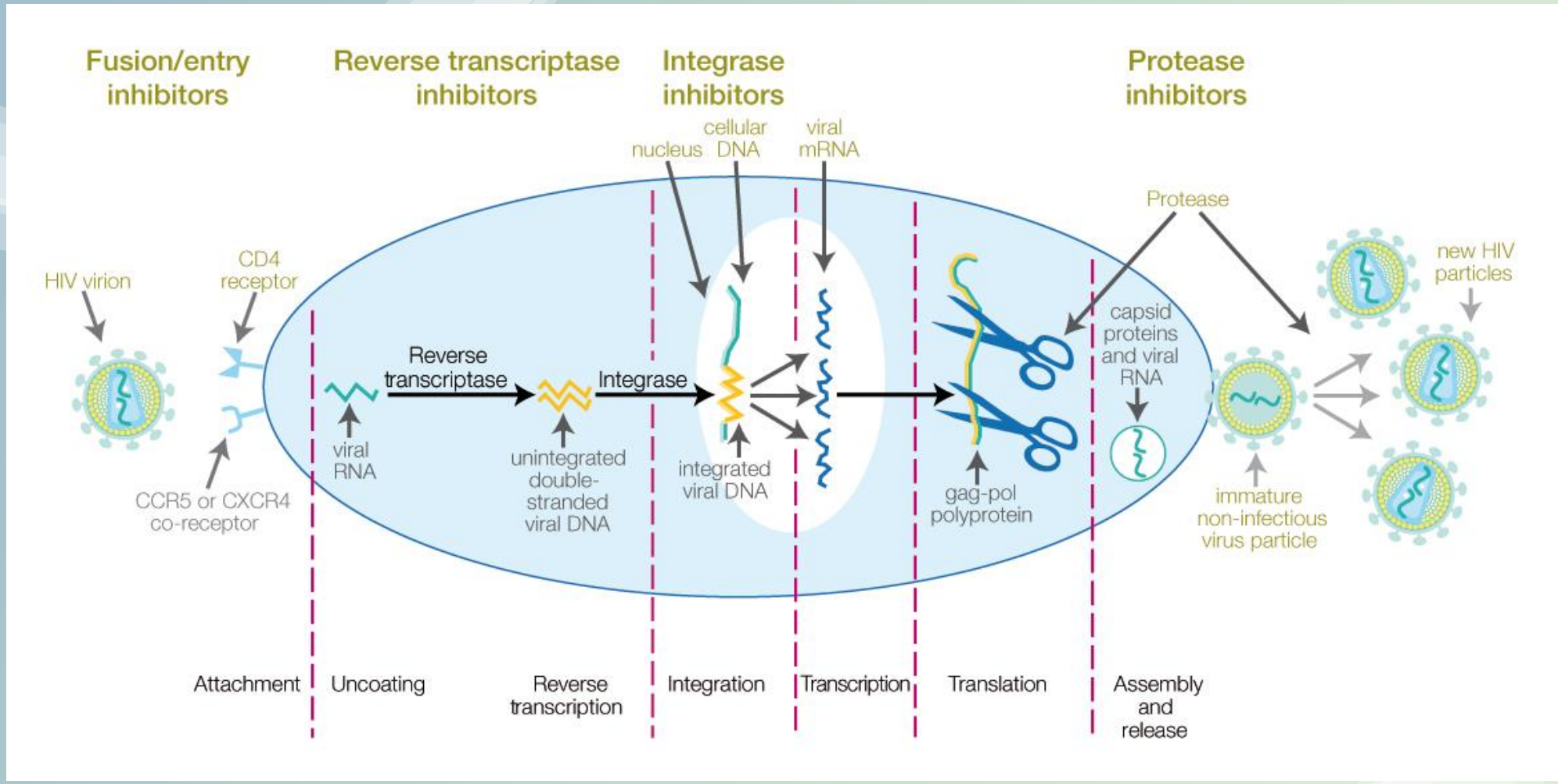
Sport 1996 and 2026

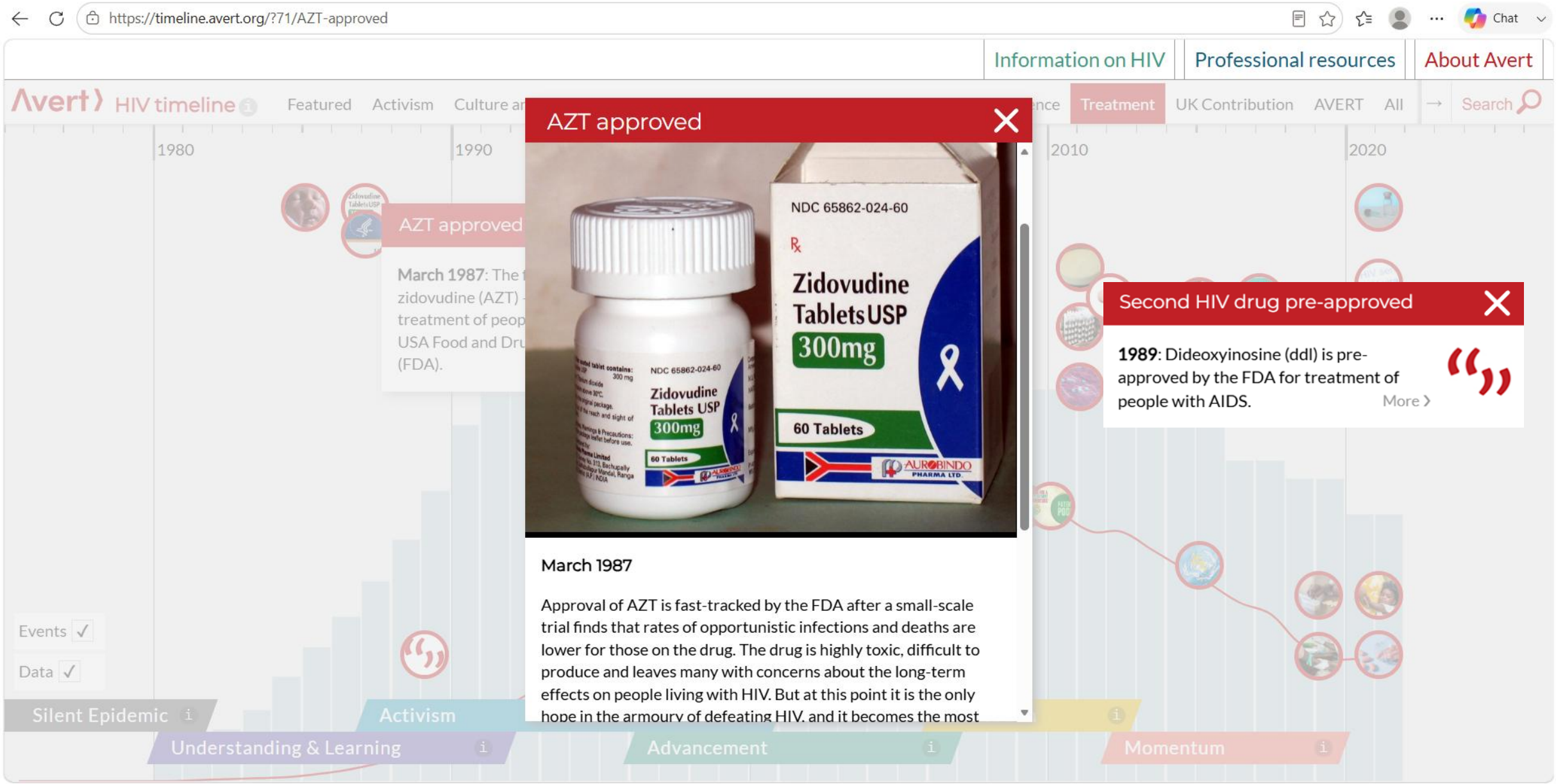
Atlanta 1996



Grammy’s 1996 and 2026




Fusion/entry inhibitors
Reverse transcriptase inhibitors
Integrase inhibitors
Protease inhibitors
cellular nucleus DNA
viral mRNA
Protease
HIV virion
CD4 receptor
CCR5 or CXCR4 co-receptor
Reverse transcriptase
Integrase
viral RNA
unintegrated double-stranded viral DNA
integrated viral DNA
gag-pol polyprotein
capsid proteins and viral RNA
new HIV particles
immature non-infectious virus particle
Attachment
Uncoating
Reverse transcription
Integration
Transcription
Translation
Assembly and release



Yarchoan, R Lietzau, JA and Nguyen, BY · et al. 1994. Meng, TC · Fischl, MA · Boota, AM · et al. 1992. Ann Intern Med. 1992; 116(1):13-20. Derbyshire. Delta Co-ordinating Committee. 1996. Lancet. Volume 348, Issue 9023p283-291August 03, 1996

1996-2006

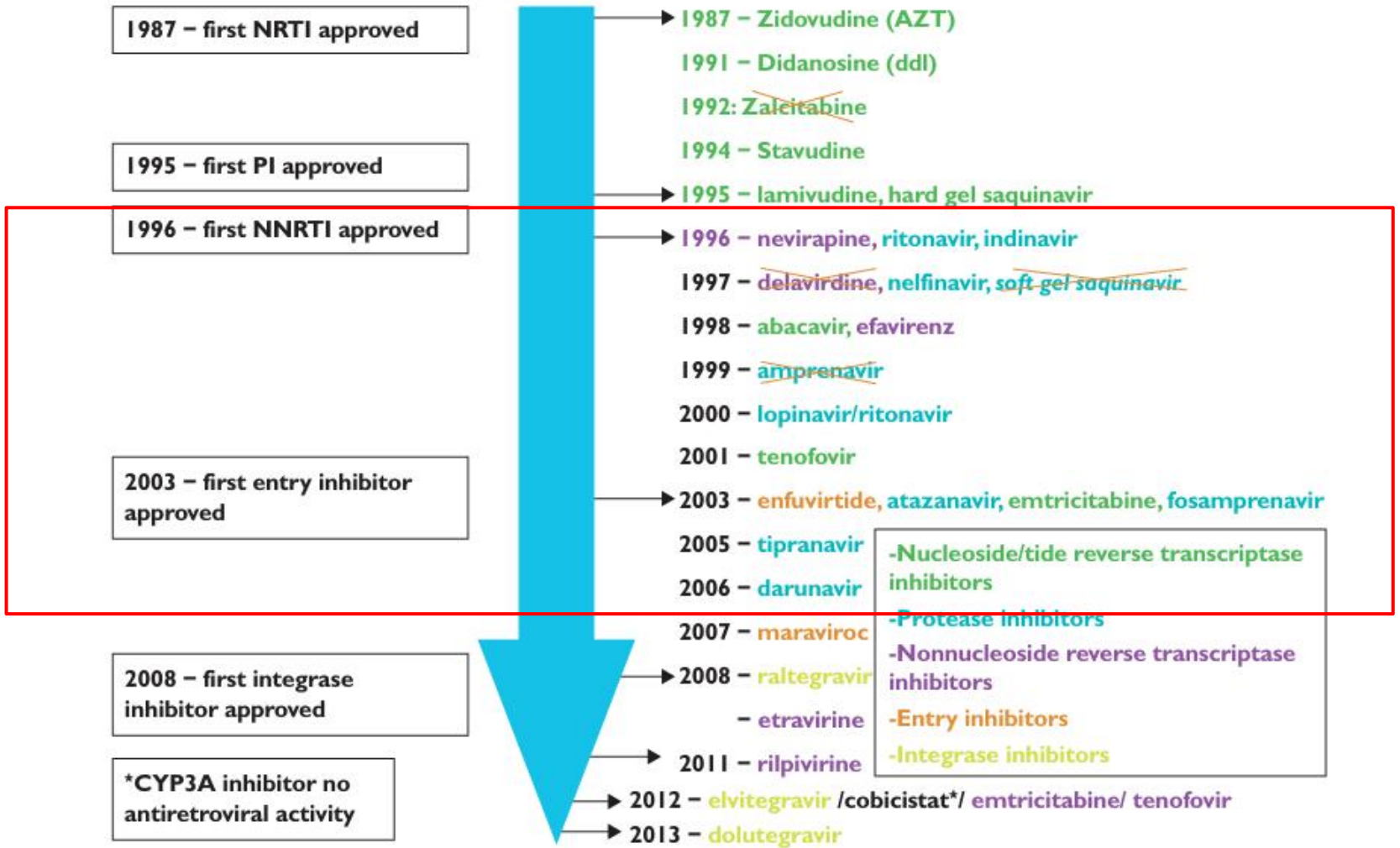


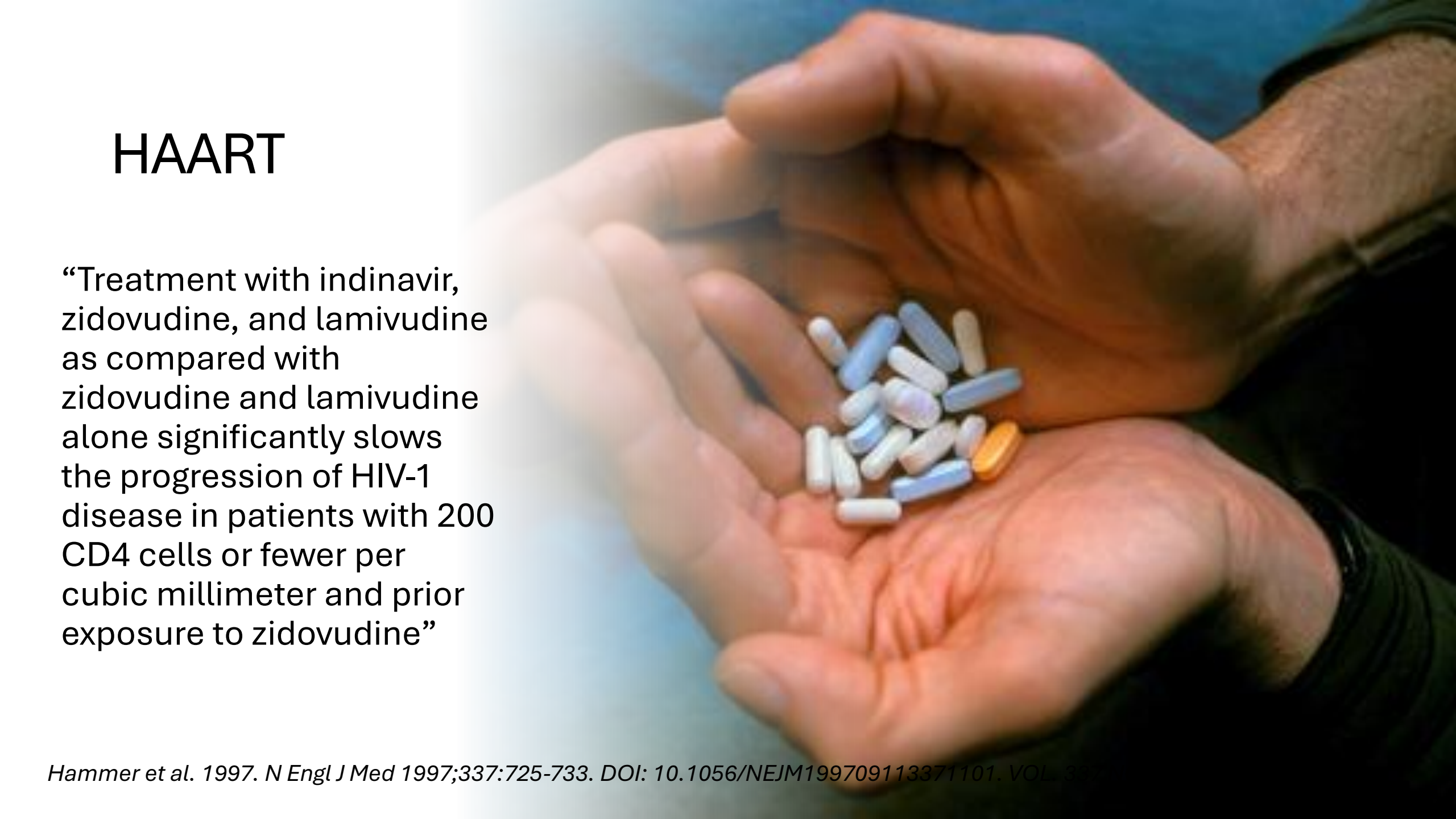
Figure 1

Time lines of antiretroviral development. The time course of development of >25 drugs across five different classes over the last 27 years is highlighted according to the US Food and Drug Administration (FDA) approval date. Those that are no longer in use or available are illustrated with an 'X' through them

Tseng et al. British Journal of Clinical Pharmacology. 2015 Feb;79(2):182-94. doi: 10.1111/bcp.12403.

HAART

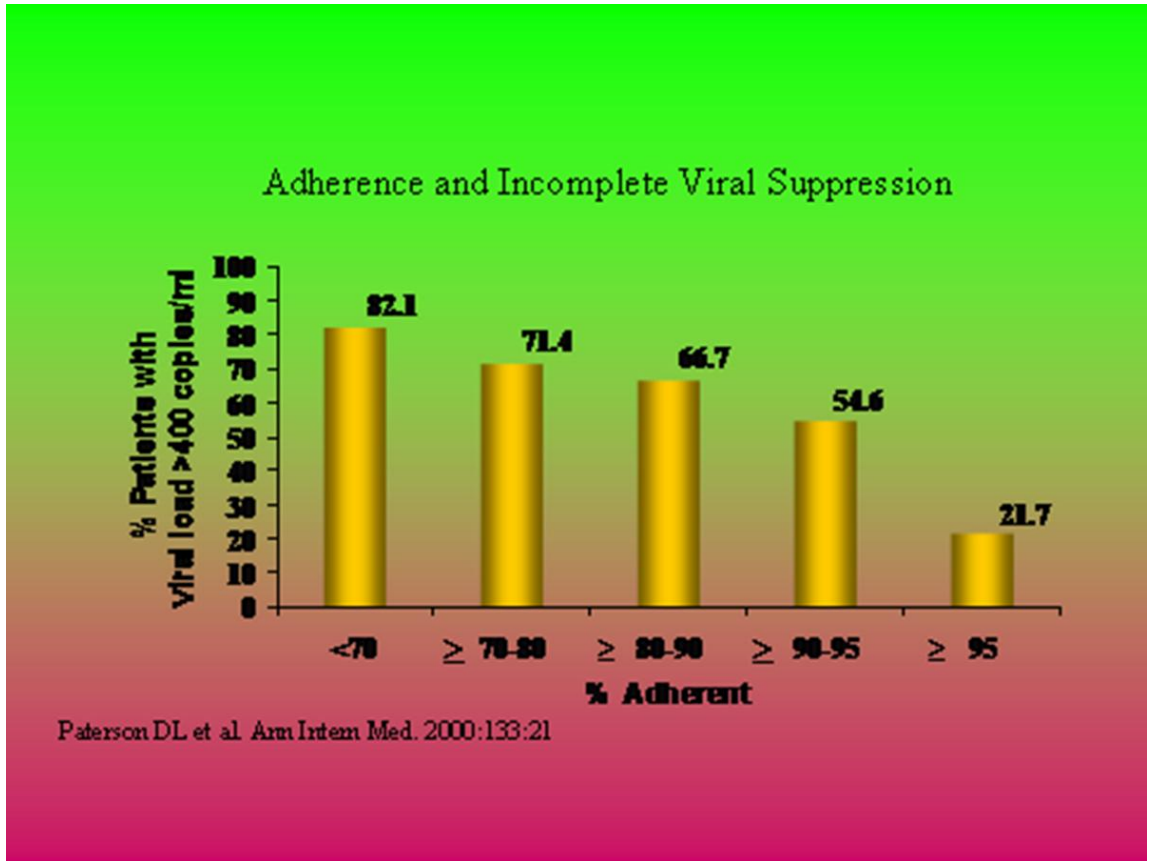
“Treatment with indinavir, zidovudine, and lamivudine as compared with zidovudine and lamivudine alone significantly slows the progression of HIV-1 disease in patients with 200 CD4 cells or fewer per cubic millimeter and prior exposure to zidovudine”



Hammer et al. 1997. N Engl J Med 1997;337:725-733. DOI: 10.1056/NEJM199709113371101. VOL. 337


Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
NAUSEA
AZT Zidovudine ZDV
FATIGUE
ANAEMIA
HEADACHE
MUSCLE PAIN
D4T Stavudine Zerit Stag
PERIPHERAL NEUROPATHY
LACTIC ACIDOSIS
PANCREATITIS
3TC Lamivudine
ddC Zalcitabine
ddI Didanosine Videx
PERIPHERAL NEUROPATHY
DIARRHOEA
LACTIC ACIDOSIS
PANCREATITIS
ABDOMINAL PAIN
ABC Abacavir Ziagen
DIZZINESS
Rash
FEVER
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
FATIGUE
Efavirenz EFV Stocrin
PSYCHOSIS
RASH
DEPRESSION
Nevirapine NVP
LIVER TOXICITY
HEPATITIS
RASH
STEVENS-JOHNSON SYNDROME
FEVER
Delavirdine DLV
ALL ANTIRETROVIRALS
Abdominal pain
SHORT TERM NAUSEA Vomiting
Vomiting
Dizziness
Rash
Protease Inhibitors
Saquinivir SQV
DIARRHOEA
Indinovir IDV
Nelfinivir NFL Viracept
Lopinavir + Ritonivir LPV+RTV Crixivan
DIARRHOEA
HEPATITIS
RITONAUIR RTV
TDF Tenofovir
KIDNEY FAILURE
d4T+3TC+NVP
Stavudine + Lamivudine + Nevirapine
Trimune Nevilas
FEVER
ABC+3TC+AZT
Abacavir + Lamivudine + Zidovudine
3TC+AZT+NVP
Lamivudine + Zidovudine
Duovir-N

Adherence Support



Introduction of CNS roles and CNS clinics[2,3]

Adherence clinics[1]

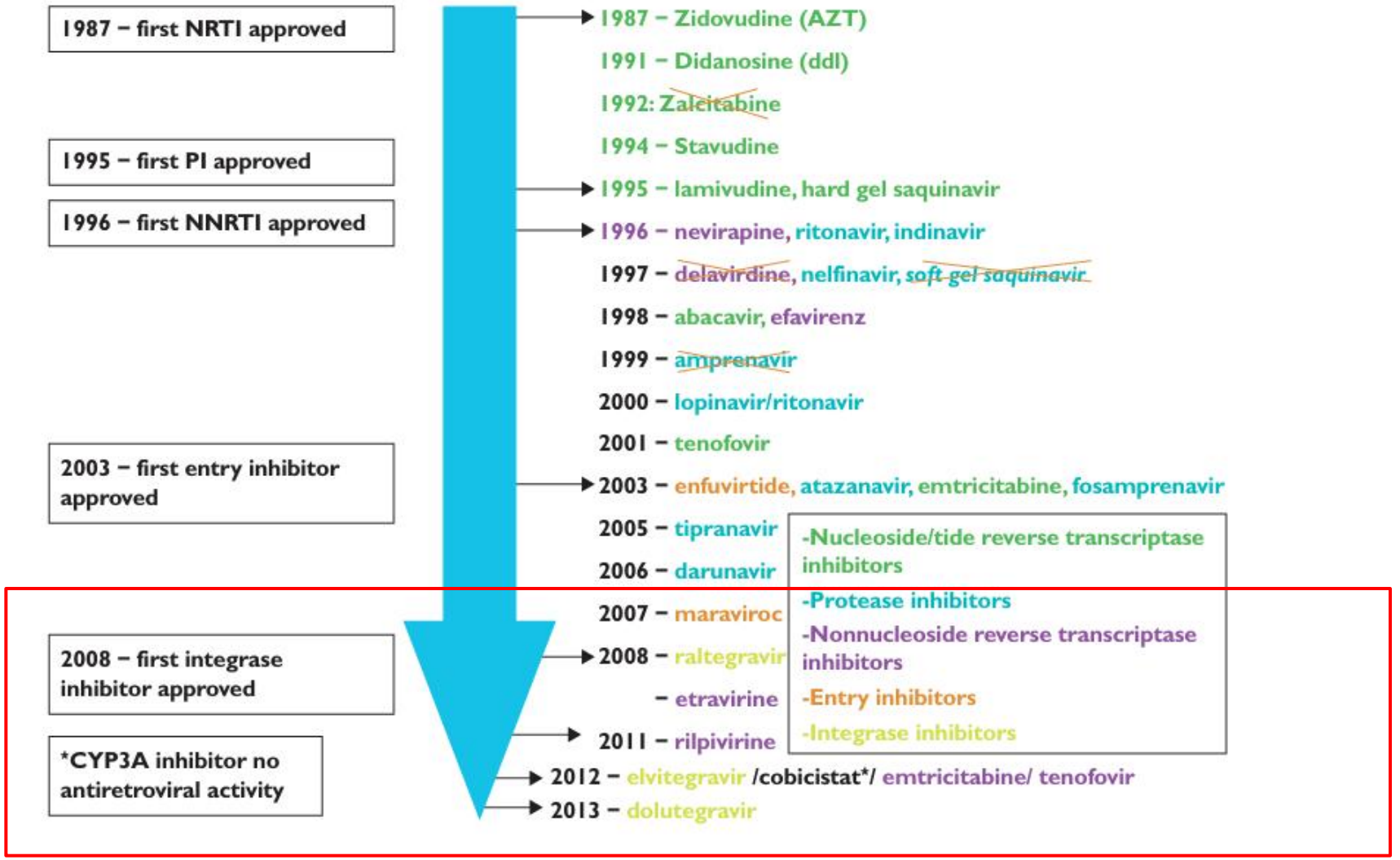
Pill reminders

Medication charts

Dosette boxes

[1]. Poppa et al 2004. HIV Medicine. Jul:5 Suppl 2:46-60. doi: 10.1111/j.1468-1293.2004.00215.x. [2]. Griffiths et al. 2006. https://doi.org/10.1080/09540120500101807. [3]. Griffiths et al 2007. https://doi.org/10.1111/j.1365-2648.2007.04248.

2006-2016



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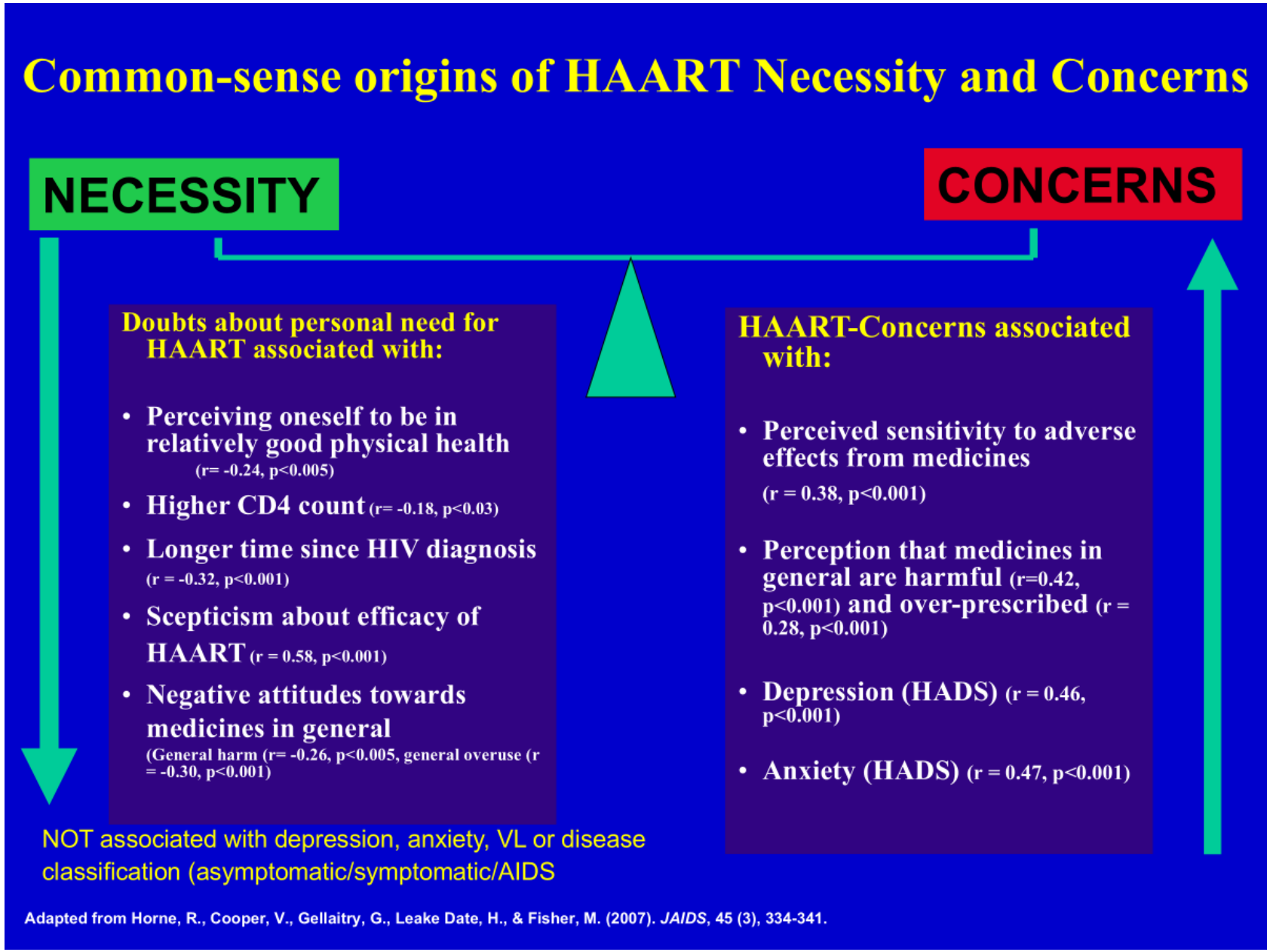
Adherence



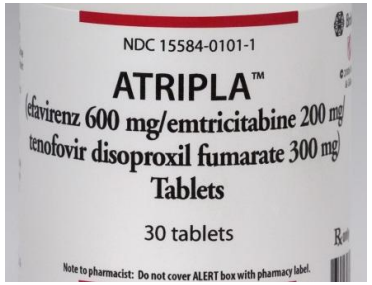
SMART Study group. 2006. DOI: 10.1056/NEJMoa062360. VOL. 355 NO. 22.

Fixed Dose Combinations and Single dose regimens

1997

2004

2004



2006

2011

2012

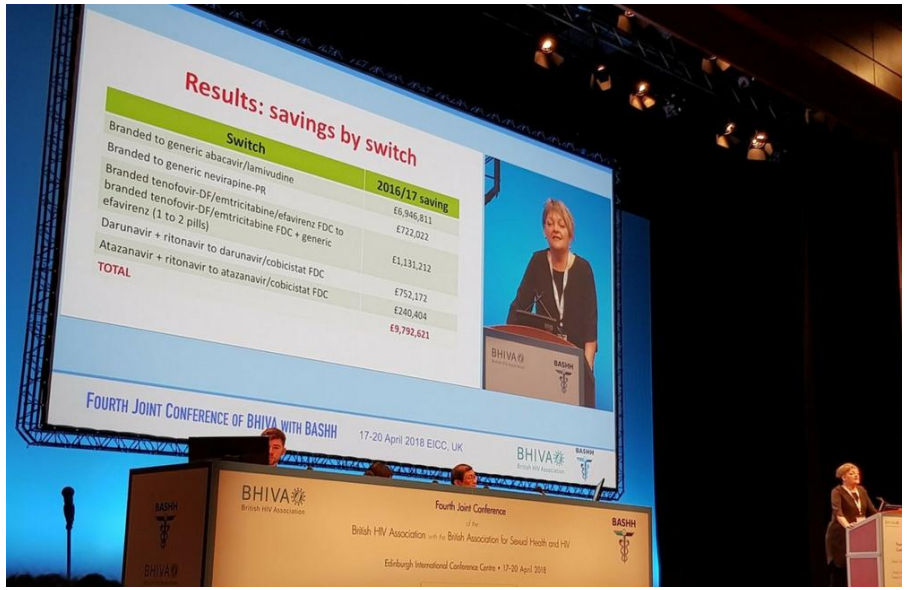
2014

Parienti et al. 2009. https://doi.org/10.1086/596482

Generics

Table 1: Generic antiretroviral drugs in the UK

Drug	UK Patent Expiry	Comments
AZT (zidovudine)	2009	Although no longer widely used or recommended, generic AZT is already used in the UK.
saquinavir	January 2011	No UK generic available – very low usage.
3TC (lamvudine)	February 2011	Two generics available for 150mg and 300mg strengths from 1 July 2012. London contract prices from 1 August 2012.
d4T (stavudine)	May 2011	No UK generic available – very low usage.
indinavir	November 2012	No UK generic available – almost no usage.
nevirapine	December 2012	At least two generics for the 200 mg formulation expected from **mid-2013**. Unclear on availability of 400 mg prolonged release formulation.
AZT + 3TC	May 2013	At least one generic version of Combivir will be available.
efavirenz	November 2013	Generic products will be available as there is significant usage.
ritonavir	2013/14	Will impact on the cost of all protease inhibitor/ritonavir combinations.
abacavir	2016	Has implications for the combined abacavir/3TC (Kivexa). Generic versions of the combined formulation should be available.
lopinavir/ ritonavir	2016	Lopinavir/r (Kaletra) is no longer widely recommended or used but generic versions are already produced for use outside the UK. Heat-stable Kaletra and ritonavir may have a longer patent.



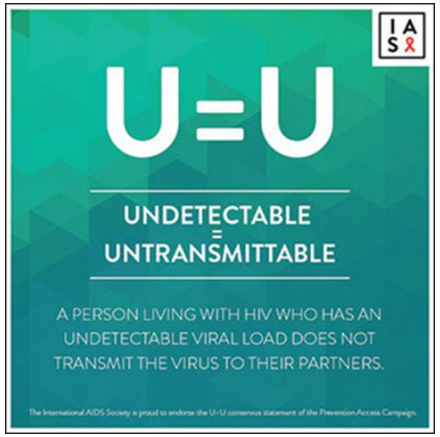
£ 7,000,000, 000

projected savings by 2033 from generic switches

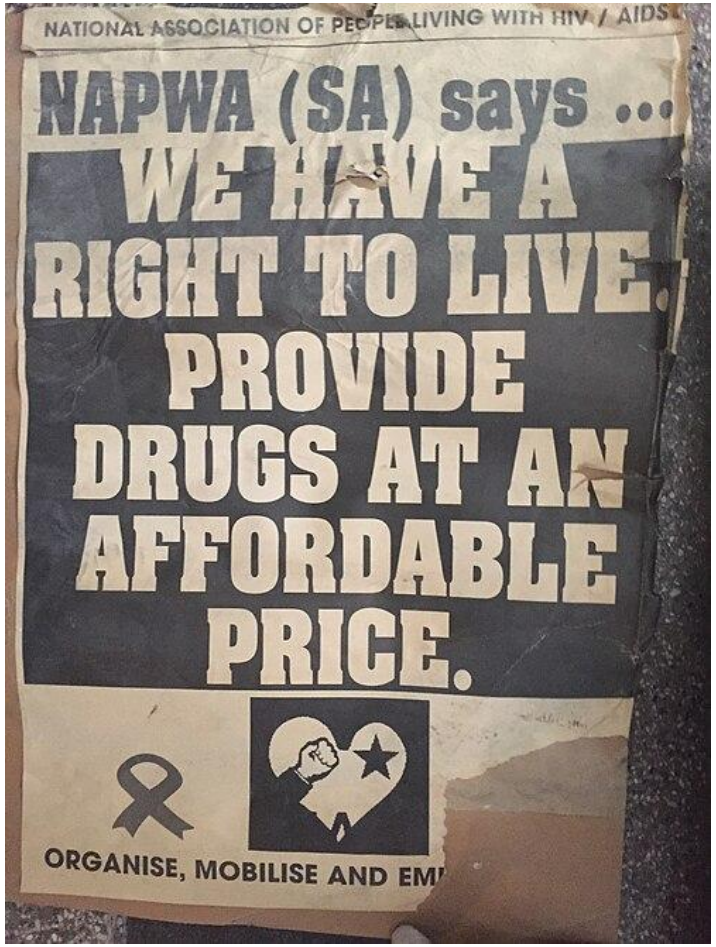
Simon Collins. 2014. https://i-base.info/generic-arvs-in-the-uk/. Peabody, R. 2018. https://www.aidsmap.com/news/apr-2018/nhs-england-saved-ps10-million-switching-generic-anti-hiv-drugs-2016. Waters L et al. Was the pain worth the gain? Antiretroviral savings from the 'Improving value' project and generics use in England. Clinical Medicine, 19: 76, March 2019. Ong KJ et al. HIV Medicine, 2019 Jul;20(6):377-391. doi: 10.1111/hiv.12725. Epub 2019 Apr 29.

Milestone studies on ARVs and transmission

- Vernazza P et al. 2008. Swiss Statement: Evidence review on transmission when <40
- Cohen MS et al for the HPTN 052 Study Team. 2011: No transmission in undetectable arm – high condom usage
- Rodger AJ et al for the PARTNER study group. 2016: No transmission in undetectable arm with condomless sex.
- The INSIGHT START Study Group 2015: Start ARVs at CD4 count of 500



Activism and Advocacy



2016-2026

And so it goes on .....

- Arrival of Tenofovir Alafenamide (TAF) in 2015
  - Descovy
  - Odefsey
  - Genvoya
  - Biktarvy
- Two drug oral regimes for switching in virological supression
  - Juluca - dolutegravir-rilpivirine
  - Dovato – dolutegravir and lamivudine
- Monoclonal antibody: ibalizumab (Trogarzo)
- Attachment inhibitor- Fostemsavir

Cabotegravir and Rilpivirine launched 2021

Patient:

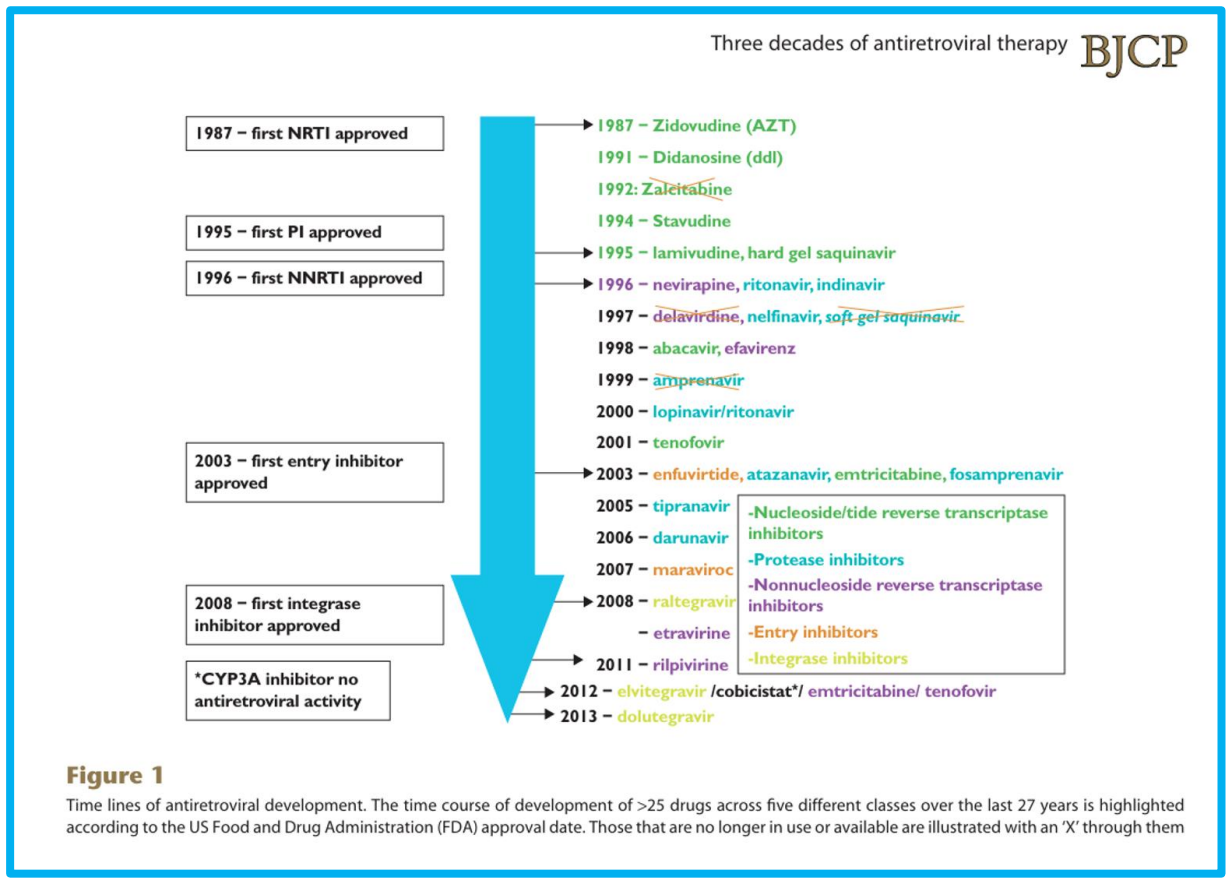
- Freedom from daily pills
- Less concerns about pills being discovered
- Increased clinic visits

Service delivery:

- 97% delivered within 7 day window
- 0.7% virological failure
- 6% withdrew.

Limited data in pregnancy

Akinwunmi B et al. Sexually Transmitted Infections, 97: 566-573, 2021. Garris et al. 2024. Plos One. https://doi.org/10.1371/journal.pone.0309588. Panton, l. 2024. British Journal of Nursing https://doi.org/10.12968/bjon.2024.0146
Ring et al. 2024. HIV Medicine. DOI: 10.1111/hiv.13679



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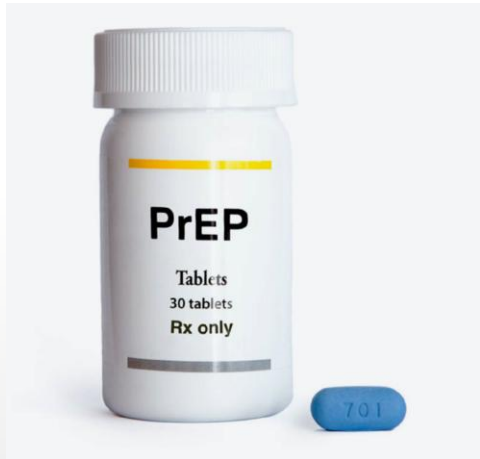
Optimal adherence in the era of modern antiretroviral therapy

- While some studies indicate >95% is no longer essential, the consensus remains to aim for 95%

- There are also additional factors affecting adherence today
  - Poverty
  - Mental health
  - Soclal isolation
  - Substance use
  - Duration on treatment
  - HIV Stigma persists!

Byrd et al. 2019. Journal of Acquired Immune Deficiency Syndrome. 82 (3): 245-251. Maggiolo et al. 2022. Journal of IAPAC. Nov 2022.

i want PrEP now .co.uk



It is the role of the HIV nurse to deliver the highest quality of care by addressing any adherence issues and providing the best treatment options, enabling people to live healthy fulfilling lives

Well done to everyone involved in getting us to this point.

What a fantastic achievement!