The Arc of Science:
What It Asks of Us

Edwina Wright

Australasian Sexual and Reproductive Health Oration

Australasian Sexual and Reproductive Health Conference

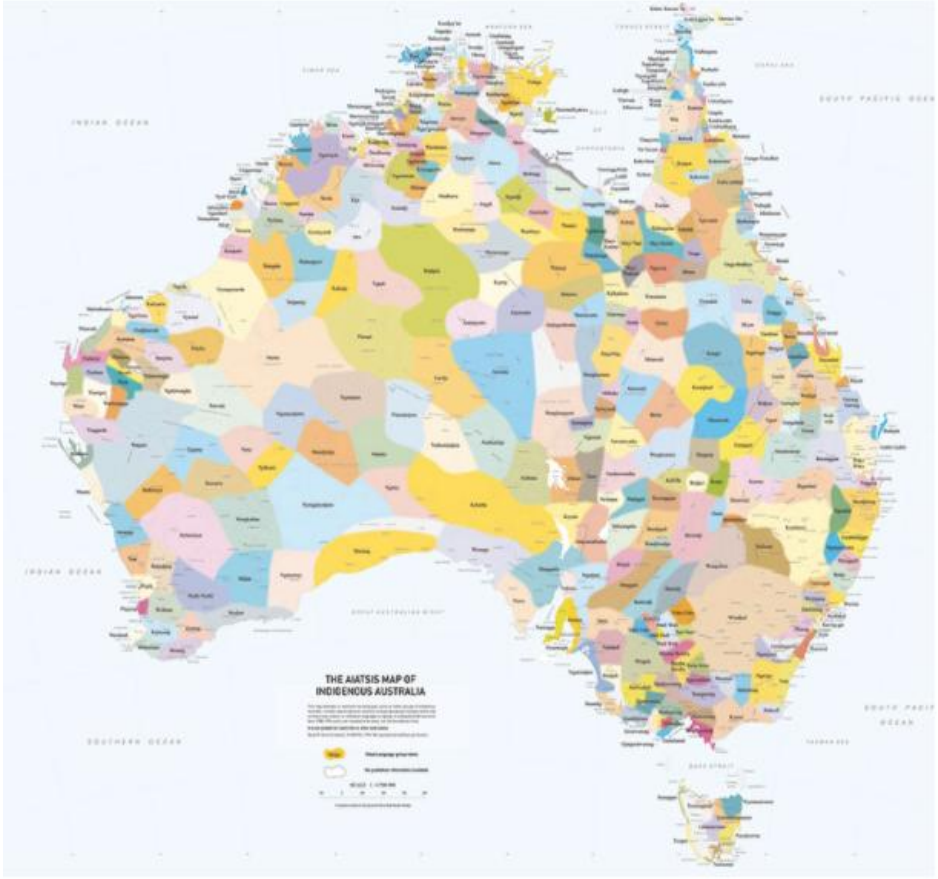
Adelaide, 2025

Burnet Institute
Medical Research. Practical Action.

Doherty Institute

MONASH University

TheAlfred



This map attempts to represent the language, social or nation groups of Aboriginal Australia. It shows only the general locations of larger groupings of people which may include clans, dialects or individual languages in a group. It used published resources from 1988-1994 and is not intended to be exact, nor the boundaries fixed. It is not suitable for native title or other land claims. David R Horton (creator), © Aboriginal Studies Press, AIATSIS, 1996. No reproduction without permission. To purchase a print version visit: www.aiatsis.ashop.com.au/

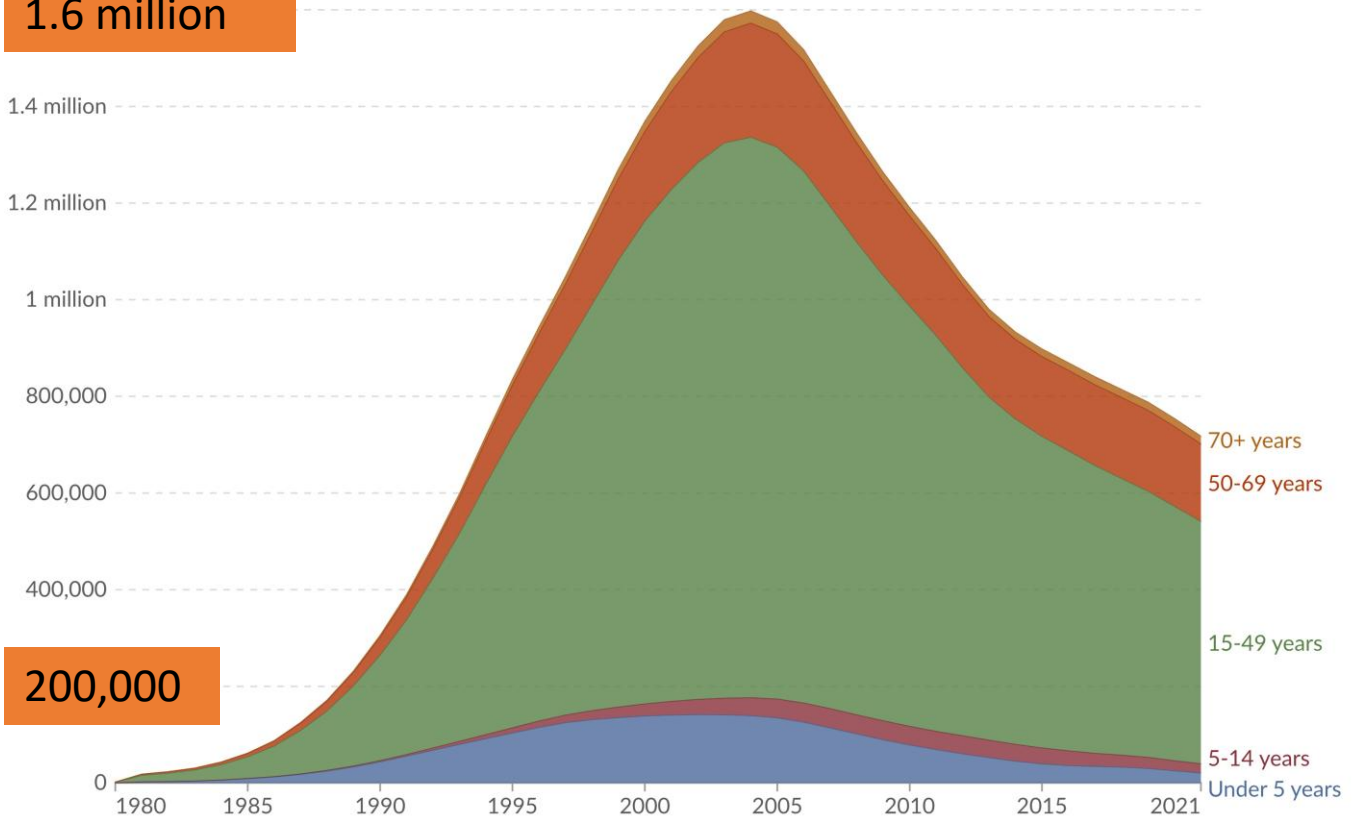
Conflicts of Interest

- **During the past 4 years the following companies have paid monies to my institution:**
  - **Gilead Sciences:** educational events, advisory board, commemorative World AIDS Day event
  - **ViiV Healthcare:** unrestricted research funding, an educational event and work on a compassionate access scheme

HIV/AIDS Deaths by age, World

Our World in Data

1.6 million



1980

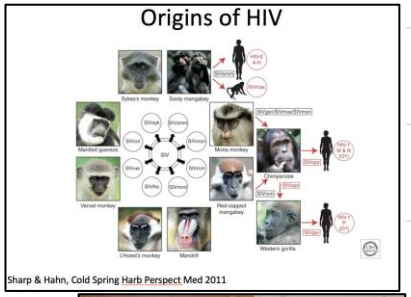
2021

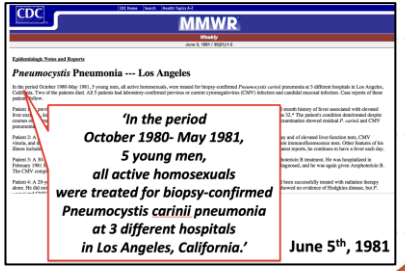
Data source: IHME, Global Burden of Disease (2024)

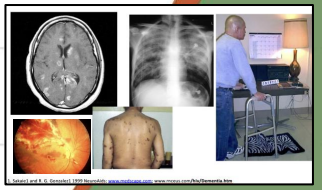
OurWorldinData.org/hiv-aids | CC BY

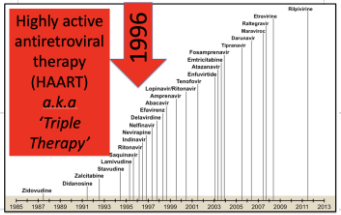
https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

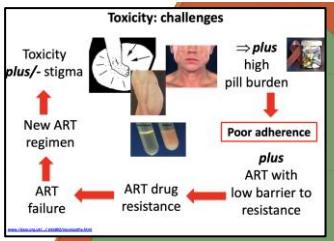
HIV/AIDS Deaths by age, World

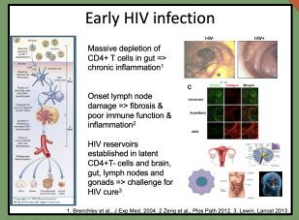


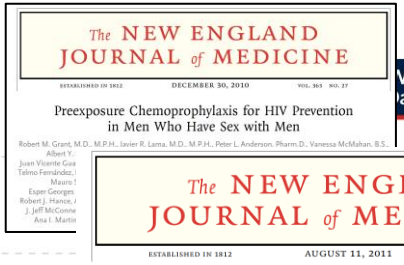








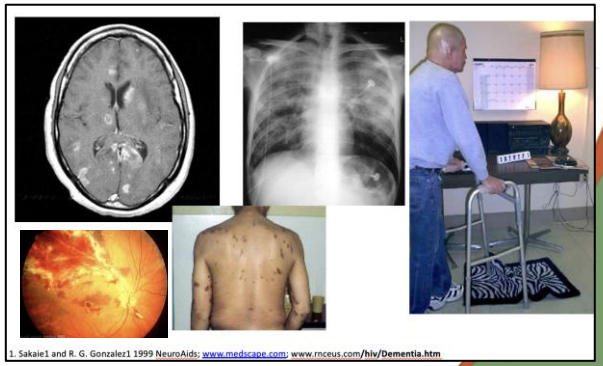




https://ourworldindata.org/hiv-aids from https://www.healthdata.org/ https://wspartners.bbc.com/. Grant et al, NEJM 2010; INSIGHT Group NEJM 2015; Roger et al, Lancet 2019; Bavinton et al, Lancet HIV 2018

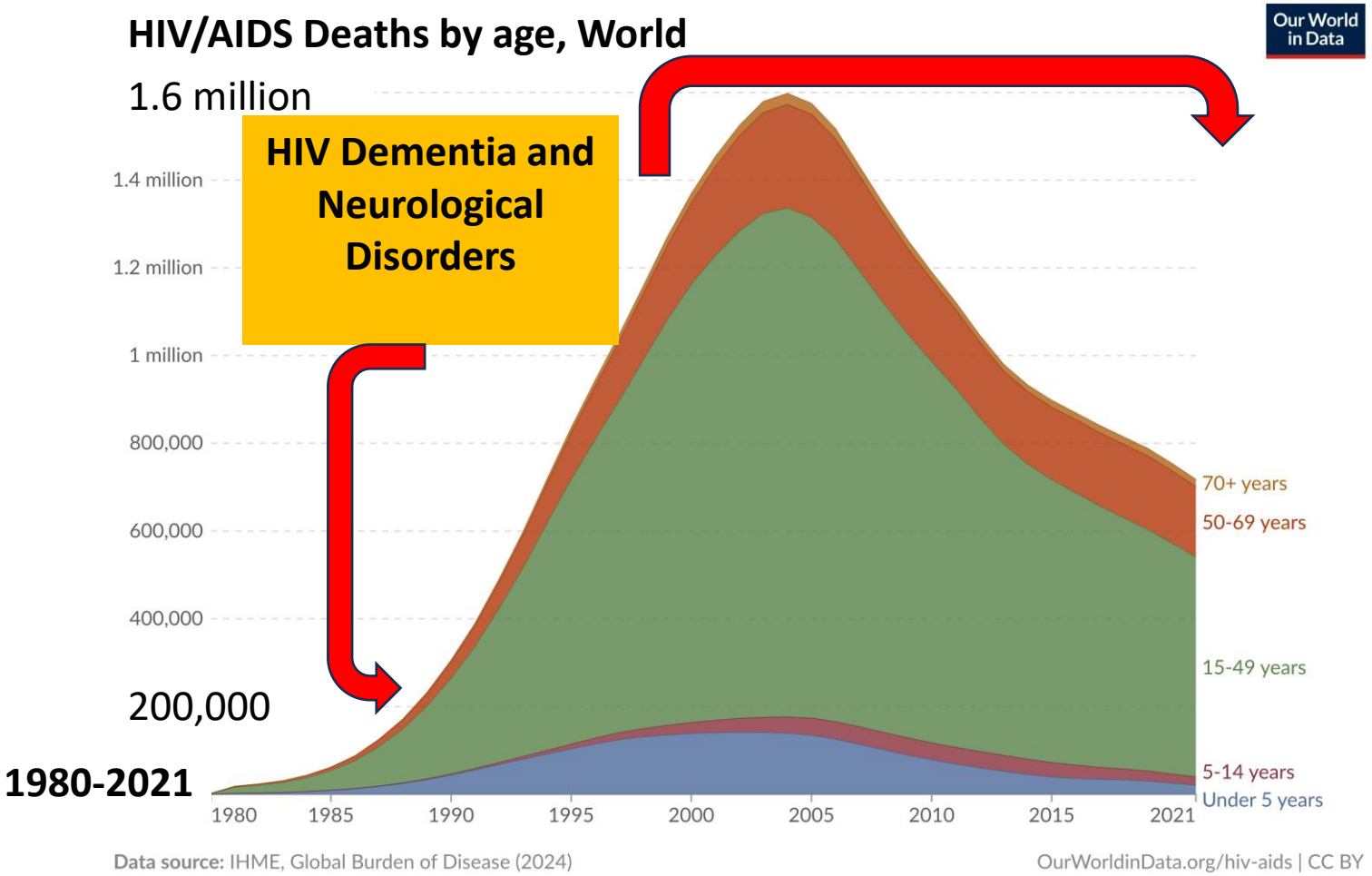
Fairfield Hospital, Victoria

http://en.wikipedia.org/wiki/Fairfield_Infectious_Diseases_Hospital



1980-2021

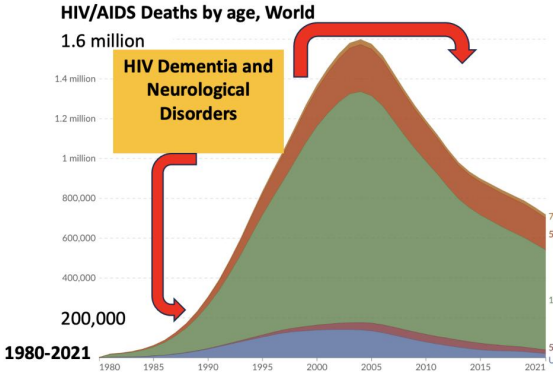
https://ourworldindata.org/hiv-aids from https://www.healthdata.org/; https://imagebank.asrs.org/



https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

HIV Dementia & Neurological Disorders

- Asia Pacific NeuroAIDS Consortium
- SMART Neurology Sub- Study
- START Neurology Sub- study
- Australian National NeuroAIDS Brain Tissue Bank
- Neurocognitive Health clinic at Alfred



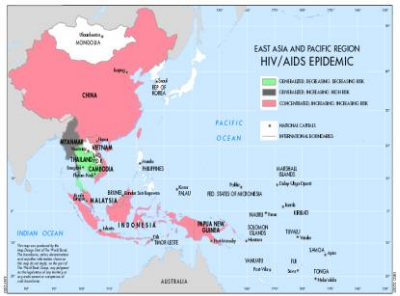
BrainBank
AUSTRALIAN NATIONAL NEUROAIDS BRAIN & TISSUE BANK

insight

HIV Dementia & Neurological Disorders- Epidemiology

The Asia-Pacific NeuroAIDS Consortium Formed 2002

- PNG
- Cambodia
- India
- Fiji
- Indonesia
- Thailand
- Hong Kong
- Singapore
- Malaysia
- China
- Australia



Neurologic disorders are prevalent in HIV-positive outpatients in the Asia-Pacific region

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ABSTRACT

Background: A total of 8.3 million HIV-positive people live in the Asia-Pacific region. The burden of HIV-associated neurocognitive impairment and symptomatic sensory neuropathy in this region is unknown.

Methods: Between July 2005 and March 2006, we undertook a cross-sectional study at 10 sites

Neurological disorders were prevalent in the Asia-Pacific region

certain nucleoside analogues, or both.[4]

In patients with advanced HIV disease in Western countries prior to highly active antiretroviral therapy (HAART) the prevalence of HAD was approximately 16% and the prevalence of symptomatic SN was 30%.[4,5] The data for the Asia-Pacific (AP) region have not been rigorously evaluated. Reported rates of HAD from individual countries in the region range from

From The Alfred Hospital (E.W., M.H., C.C., S.W.), Melbourne Burnet Institute (E.W., M.L., J.L., G.M., M.H., C.C., S.W.), Melbourne, Australia; Monash University (E.W., L.L., B.D., S.W.), Victoria, Australia; St Vincent's Hospital (B.B., M.P.B.), Sydney, University of New South Wales (B.B.), Sydney, Australia; Taipei Veterans General Hospital (A.A.), Ubon Rachathani, Thailand; University of North Carolina at Chapel Hill (K.R.); Lampang Hospital (K.S.), Thailand; Rajavithi Hospital (S.K.), Bangkok, Thailand; National Centre for HIV/AIDS (S.V., C.S., S.H.), Dermatology and STDs, Phnom Penh, Cambodia; Queen Elizabeth Hospital (P.L.), Kowloon, Hong Kong; Cipto Mangunkusumo Hospital (D.I.), Jakarta, Indonesia; Dian Hospital (W.H.L.), Beijing, China; University of Malaya Medical Centre (A.K.), Kuala Lumpur, Malaysia; Port Moresby General Hospital (G.T.), Port Moresby, Papua New Guinea; Fiji School of Medicine (S.T.A., K.K.), Suva, and Johns Hopkins Hospital (J.M.), Baltimore, MD.

Supplemental data at www.neurology.org

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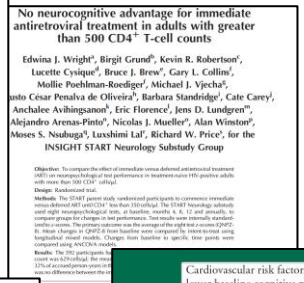
Disclosure: The authors report no disclosures.

Wright et al, Neurology 2008

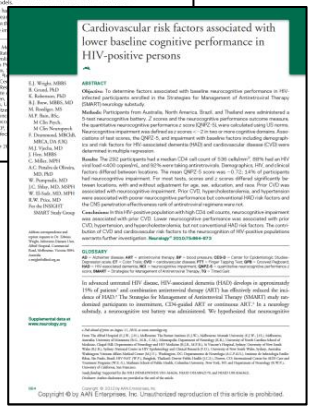
HIV Dementia & Neurological Disorders- Intermittent and Early Treatment


Improved neurocognitive test performance in both arms of the SMART study: impact of practice effect


No neurocognitive advantage for immediate antiretroviral treatment in adults with greater than 500 CD4+ T-cell counts


ORIGINAL RESEARCH

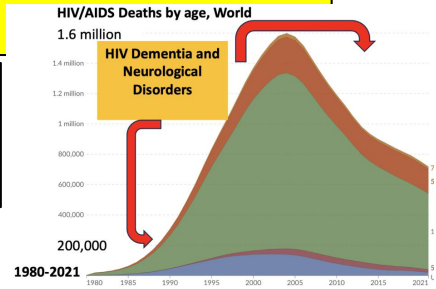
Factors associated with neurocognitive test performance at baseline: a substudy of the INSIGHT Strategic Timing of AntiRetroviral Treatment (START) trial


Cardiovascular risk factors associated with lower baseline cognitive performance in HIV-positive persons

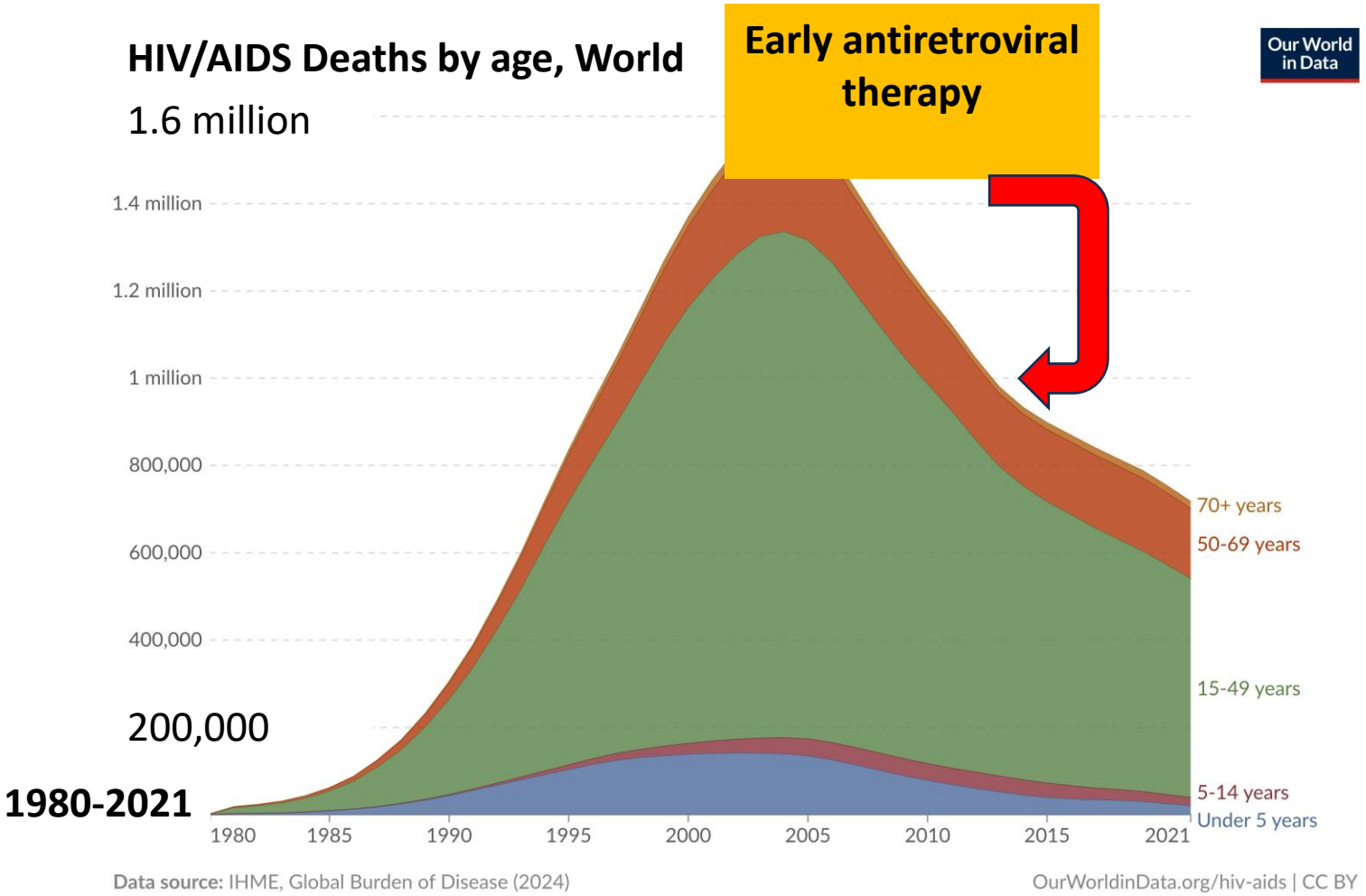
SMART and START Neurology Sub studies

International RCTs to determine benefits of intermittent ART (SMART n=292) and immediate vs deferred ART (START n=592)

- ❖CV risk factors play a key role in cognitive impairment in PLWH
- ❖Immediate vs deferred ART was not associated with improved neurocognitive function

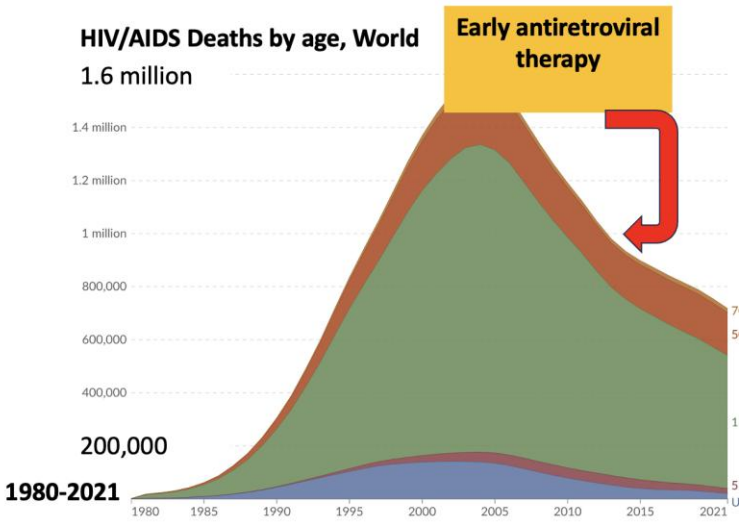


Wright et al, Neurology 2010; Grund et al, J Neurovirol 2013; Wright et al, HIV Med 2015; Wright et al, AIDS 2017



https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

Early Antiretroviral Therapy



2013

- Clear evidence for benefits of early ART on HIV transmission and mixed evidence clinical benefit
- START study results were a long way off!
  - BUT Community wanted access to early ART

ASHM CEO Levinia Crooks supported the community

- As ASHM President => tasked with leading a major community submission to PBAC to remove CD4+ cell restrictions limiting ART initiation

SUCCESS in 2014!!!!

- **All people able to access antiretroviral therapy**

PBAC Community Submission Team & Acknowledgments

ASHM

Assoc Prof Levinia Crooks (CEO)

ASHM

Anna Roberts

NAPWHA

Bill Whittaker

AFAO

Rob Lake

Prof David Wilson

- ViiV Healthcare
- Jannsen
- PBS- fee waiver
- Vic, NSW, Qld, WA, Tas, ACT Governments
- Prof Sunil Ahuja
- Covance

Early Antiretroviral Therapy

Research

Original Investigation

Influence of the Timing of Antiretroviral Therapy on the Potential for Normalization of Immune Status in Human Immunodeficiency Virus 1–Infected Individual

Jason F. Okulicz, MD; Tuan D. Le, MD, DrPH; Brian K. Agan, MD; Jose F. Camargo, MD; Michael L. Landrum, MD; Edwina Wright, MD; Matthew J. Dolan, MD; Anuradha Ganesan, MD; Tomas M. Ferguson, MD; Davey M. Smith, MD; Douglas D. Richman, MD; Susan J. Little, MD; Robert A. Clark, MD; Weijing He, MD; Sunil K. Ahuja, MD

IMPORTANCE In individuals with human immunodeficiency virus 1 (HIV-1) infection who are receiving antiretroviral therapy (ART), factors that promote full immune recovery are not well characterized.

OBJECTIVE To investigate the influence of the timing of ART relative to HIV-1 infection on normalization of CD4+ T-cell counts, AIDS risk, and immune function.

DESIGN, SETTING, AND PARTICIPANTS Participants in the observational US Military HIV Natural History Study with documented estimated dates of seroconversion (EDS) who achieved virologic suppression with ART were evaluated. Markers indicative of immune activation, dysfunction, and responsiveness were determined. Responses to hepatitis B virus (HBV) vaccine, an indicator of in vivo immune function, were also assessed. The timing of ART was indexed to the EDS and/or entry into the cohort. The CD4+ counts in HIV-1–uninfected populations were surveyed.

MAIN OUTCOMES AND MEASURES Normalization of CD4+ counts to 900 cells/μL or higher, AIDS development, HBV vaccine response, as well as T-cell activation, dysfunction, and responsiveness.

RESULTS The median CD4+ count in HIV-1–uninfected populations was approximately 900 cells/μL. Among 1119 HIV-1–infected participants, CD4+ normalization was achieved in 38.4% vs 28.3% of those initiating ART within 12 months vs after 12 months from the EDS (P = .001). Incrementally higher CD4+ recovery (<500, 500-899, and ≥900 cells/μL) was associated with stepwise decreases in AIDS risk and reversion of markers of immune activation, dysfunction, and responsiveness to levels approximating those found in HIV-1–uninfected persons. Participants with CD4+ counts of 500 cells/μL or higher at study entry (adjusted odds ratio [aOR], 2.00; 95% CI, 1.51-2.64; P < .001) or ART initiation (aOR, 4.08; 95% CI, 3.14-5.30; P < .001) had significantly increased CD4+ normalization rates compared with other participants. However, even among individuals with a CD4+ count of 500 cells/μL or higher at both study entry and before ART, the odds of CD4+ normalization were 80% lower in those initiating ART after 12 months from the EDS and study entry (aOR, 0.20; 95% CI, 0.07-0.53; P = .001). Initiation of ART within 12 months of EDS vs later was associated with a significantly lower risk of AIDS (7.8% vs 15.3%; P = .002), reduced T-cell activation (percent CD4+HLA-DR+ effector memory T cells, 12.0% vs 15.6%; P = .03), and increased responsiveness to HBV vaccine (67.9% vs 50.9%; P = .07).

CONCLUSIONS AND RELEVANCE Deferral of ART beyond 12 months of the EDS diminishes the likelihood of restoring immunologic health in HIV-1–infected individuals.

JAMA Intern Med. 2015;175(1):88-99. doi:10.1001/jamainternmed.2014.4010
Published online November 24, 2014.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Enhanced CD4+ T-Cell Recovery with Earlier HIV-1 Antiretroviral Therapy

Tuan Le, M.D., Dr.P.H., Edwina J. Wright, M.D., Davey M. Smith, M.D., Weijing He, M.D., Gabriel Catano, M.D., Jason F. Okulicz, M.D., Jason A. Young, Ph.D., Robert A. Clark, M.D., Douglas D. Richman, M.D., Susan J. Little, M.D., and Sunil K. Ahuja, M.D.

ABSTRACT

BACKGROUND
The relationship between the timing of the initiation of antiretroviral therapy (ART) after infection with human immunodeficiency virus type 1 (HIV-1) and the recovery of CD4+ T-cell counts is unknown.

METHODS
In a prospective, observational cohort of persons with acute or early HIV-1 infection, we determined the trajectory of CD4+ counts over a 48-month period in partially overlapping study sets: study set 1 included 384 participants during the time window in which they were not receiving ART and study set 2 included 213 participants who received ART soon after study entry or sometime thereafter and had a suppressed plasma HIV viral load. We investigated the likelihood and rate of CD4+ T-cell recovery to 900 or more cells per cubic millimeter within 48 months while the participants were receiving viral-load–suppressive ART.

RESULTS
Among the participants who were not receiving ART, CD4+ counts increased spontaneously, soon after HIV-1 infection, from the level at study entry (median, 495 cells per cubic millimeter; interquartile range, 383 to 622), reached a peak value (median, 765 cells per cubic millimeter; interquartile range, 573 to 987) within approximately 4 months after the estimated date of infection, and declined progressively thereafter. Recovery of CD4+ counts to 900 or more cells per cubic millimeter was seen in approximately 64% of the participants who initiated ART earlier (≤4 months after the estimated date of HIV infection) as compared with approximately 34% of participants who initiated ART later (>4 months) (P<0.001). After adjustment for whether ART was initiated when the CD4+ count was 500 or more cells per cubic millimeter or less than 500 cells per cubic millimeter, the likelihood that the count would increase to 900 or more cells per cubic millimeter was lower by 65% (odds ratio, 0.35), and the rate of recovery was slower by 56% (rate ratio, 0.44), if ART was initiated later rather than earlier. There was no association between the plasma HIV RNA level at the time of initiation of ART and CD4+ T-cell recovery.

CONCLUSIONS
A transient, spontaneous restoration of CD4+ T-cell counts occurs in the 4-month time window after HIV-1 infection. Initiation of ART during this period is associated with an enhanced likelihood of recovery of CD4+ counts. (Funded by the National Institute of Allergy and Infectious Diseases and others.)

N ENGL J MED 368;3 NEJM.ORG JANUARY 17, 2013

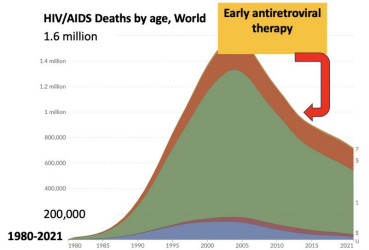
HIV Seroconversion Cohort (n=468)

- ART within vs > 4 months of seroconversion led to CD4+ normalization* in 64% vs 34% of people, respectively

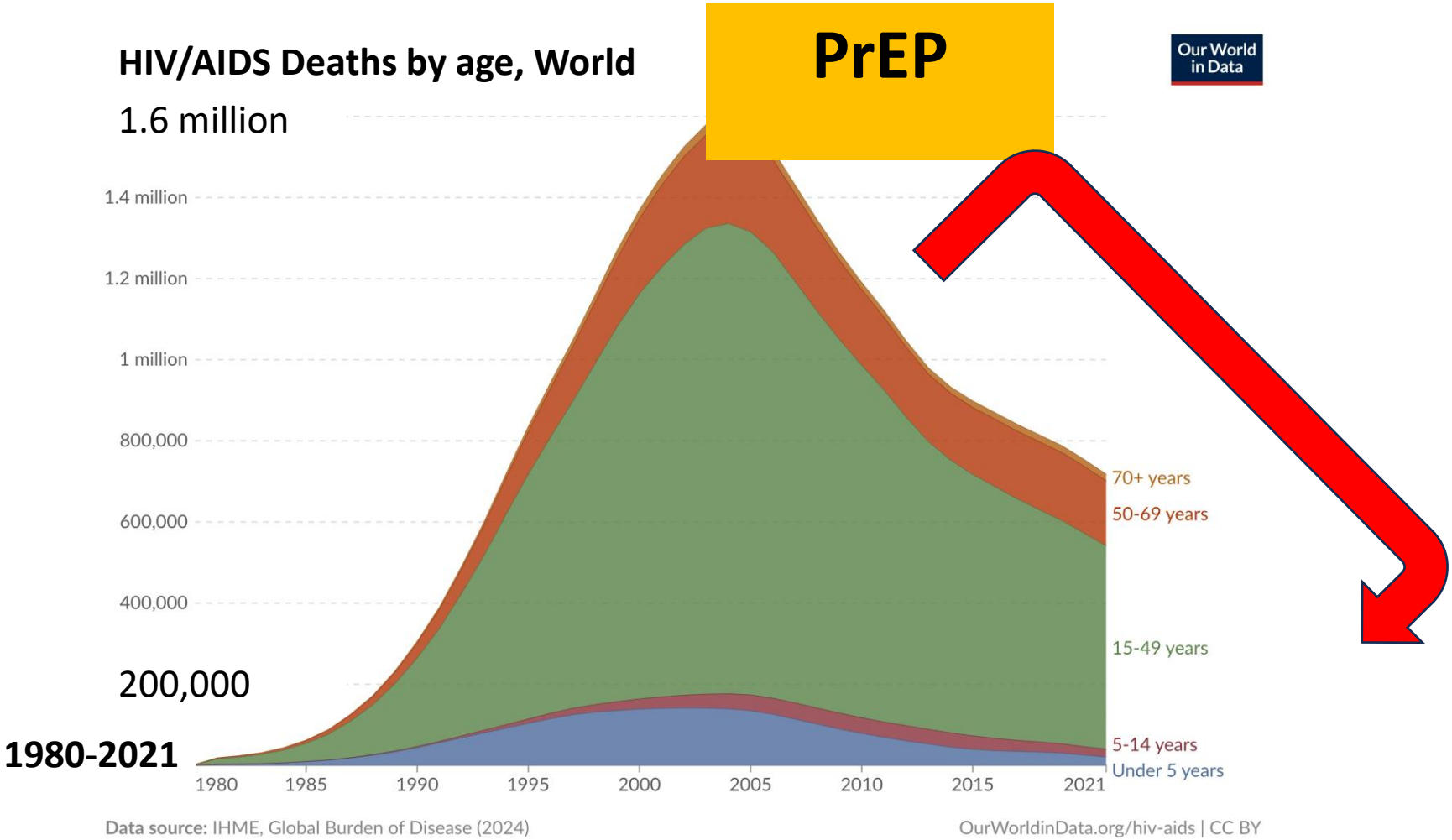
HIV Seroconversion Cohort (n=1119)

- ART within vs > 12months of seroconversion was associated lower risk of AIDS, T-cell activation and HBV responsiveness

** Defined as CD4+ cells > 900/uL*

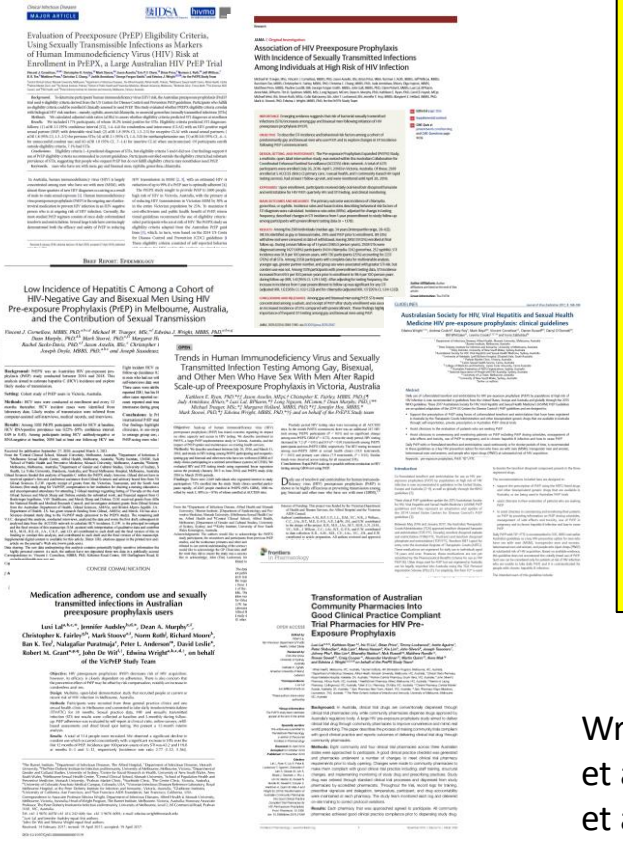


Le et al, NEJM 2013; Okulicz et al, JAMA Int Med 2015



https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

PrEP



VicPREP- 2014

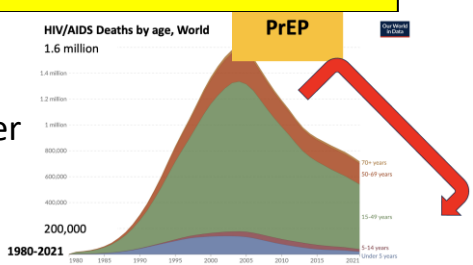
- ❖ First PrEP trial in Australia, n=100

PrEPX study- 2016, n > 5,000 Vic, SA and Tasmania

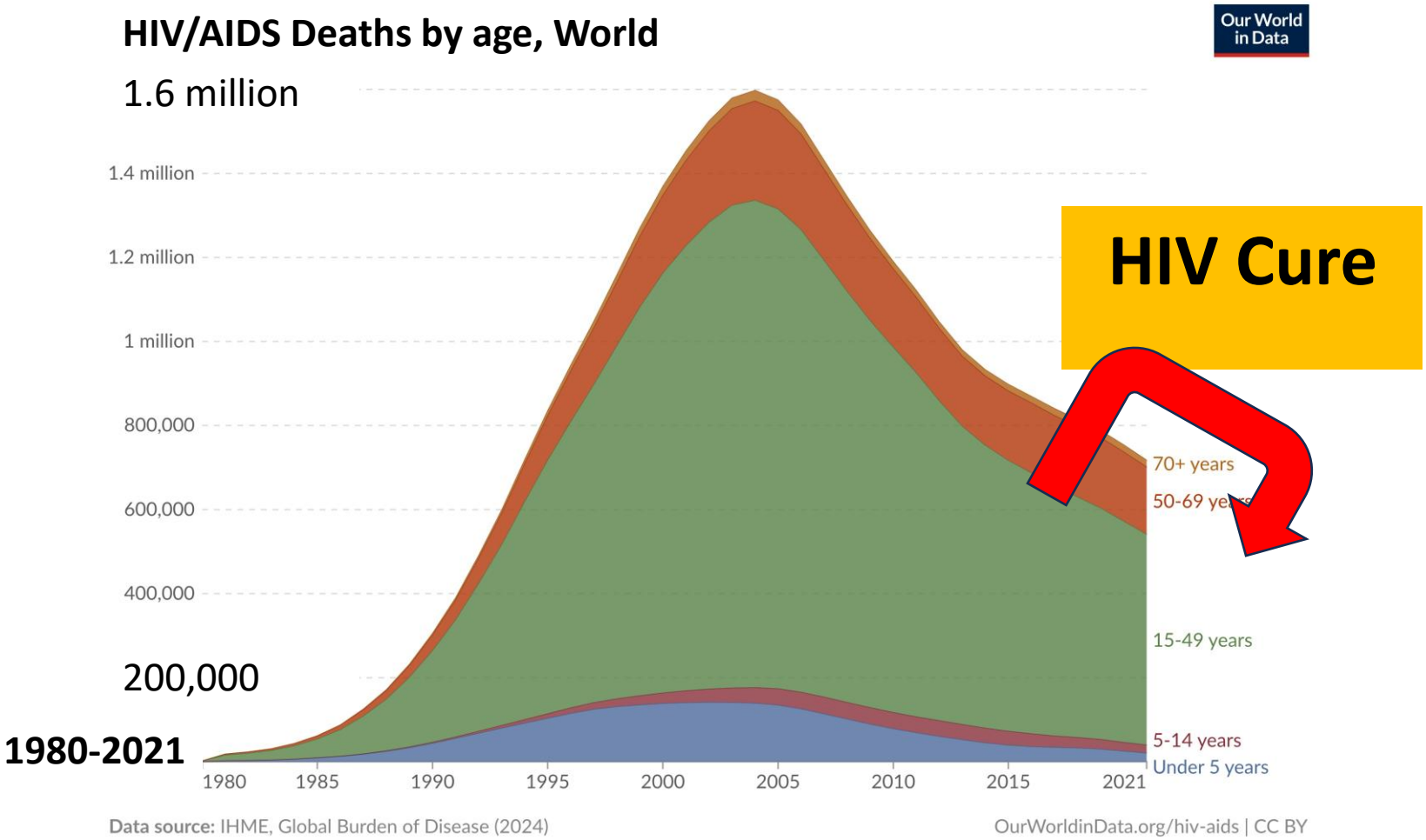
- ❖ 30% reduction HIV incidence in MSM in Victoria, 2017-2019
- ❖ STI and HCV incidence
- ❖ Impact of PrEP on service delivery in clinics
- ❖ Pharmacy as clinical trial sites

Chair ASHM PrEP guidelines

Worked pro bono with colleagues to advocate for TGA and PBS listing of PrEP products

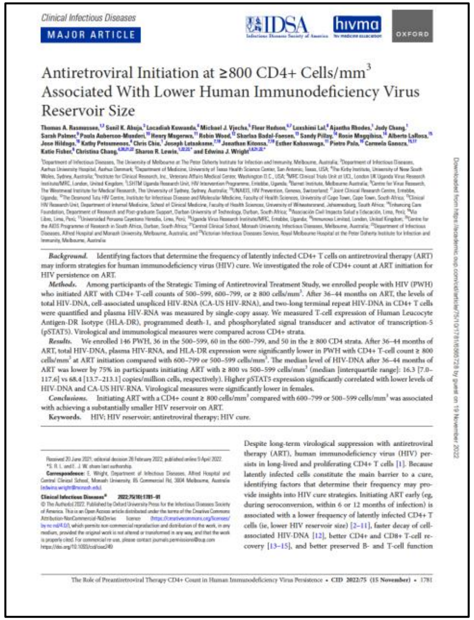


Wright et al, JVE, 2017; Cornelisse et al, CID 2018; Traeger et al, JAMA, 2019; Lal et al, Front Pharmacol 2019; Ryan et al, STD 2020; Cornelisse et al, JAIDS 2021



https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

HIV Cure


Clinical Infectious Diseases
MAJOR ARTICLE

Antiretroviral Initiation at ≥800 CD4+ Cells/mm^3 Associated With Lower Human Immunodeficiency Virus Reservoir Size

Background. Identifying factors that determine the frequency of latently infected CD4+ T cells on antiretroviral therapy (ART) may inform strategies for human immunodeficiency virus (HIV) cure. We investigated the role of CD4+ count at ART initiation for HIV persistence on ART.

Methods. Among participants of the Strategic Timing of Antiretroviral Treatment Study, we enrolled people with HIV (PWH) who initiated ART with CD4+ T-cell counts of 500–599, 600–799, or ≥ 800 cells/mm^3. After 36–44 months on ART, the levels of total HIV-DNA, cell-associated unspliced HIV-RNA (CA-US HIV-RNA), and two-long terminal repeat HIV-DNA in CD4+ T cells were quantified and plasma HIV-RNA was measured by single-copy assay. We measured T-cell expression of Human Leucocyte Antigen-DR Isotype (HLA-DR), programmed death-1, and phosphorylated signal transducer and activator of transcription-5 (pSTAT5). Virological and immunological measures were compared across CD4+ strata.

Results. We enrolled 146 PWH, 36 in the 500–599, 60 in the 600–799, and 50 in the ≥ 800 CD4 strata. After 36–44 months of ART, total HIV-DNA, plasma HIV-RNA, and HLA-DR expression were significantly lower in PWH with CD4+ T-cell count ≥ 800 cells/mm^3 at ART initiation compared with 600–799 or 500–599 cells/mm^3. The median level of HIV-DNA after 36–44 months of ART was lower by 75% in participants initiating ART with ≥ 800 vs 500–599 cells/mm^3 (median [interquartile range]: 16.3 [7.0–117.6] vs 68.4 [13.7–213.1] copies/million cells, respectively). Higher pSTAT5 expression significantly correlated with lower levels of HIV-DNA and CA-US HIV-RNA. Virological measures were significantly lower in females.

Conclusions. Initiating ART with a CD4+ count ≥ 800 cells/mm^3 compared with 600–799 or 500–599 cells/mm^3 was associated with achieving a substantially smaller HIV reservoir on ART.

Keywords. HIV; HIV reservoir; antiretroviral therapy; HIV cure.

Despite long-term virological suppression with antiretroviral therapy (ART), human immunodeficiency virus (HIV) persists in long-lived and proliferating CD4+ T cells [1]. Because latently infected cells constitute the main barrier to a cure, identifying factors that determine their frequency may provide insights into HIV cure strategies. Initiating ART early (eg, during seroconversion, within 6 or 12 months of infection) is associated with a lower frequency of latently infected CD4+ T cells (ie, lower HIV reservoir size) [2–11], faster decay of cell-associated HIV-DNA [12], better CD4+ and CD8+ T-cell recovery [13–15], and better preserved B- and T-cell function

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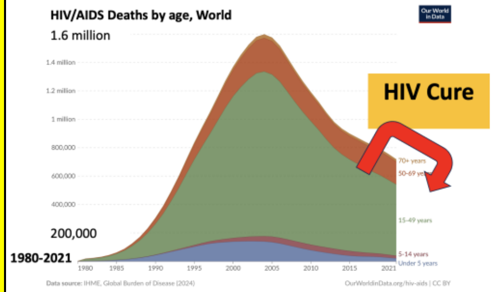
https://doi.org/10.1093/cid/ciac249

The Role of Preantiretroviral Therapy CD4+ Count in Human Immunodeficiency Virus Persistence • CID 2022:75 (15 November) • 1781

START HIV Reservoir Study

- After 36-44 months of ART, people who initiated ART with ≥800 cells/uL vs 600-799 cells/uL vs 500-599 cells/uL had significantly smaller HIV reservoir*



Rasmussen et al, CID 2022

**Measured as total HIV- DNA in CD4+ T cells*

The Arc of Science:
What It Asks of Us

HIV/AIDS Deaths by age, World

1.6 million

HIV Dementia and Neurological Disorders

Know yourself

Why have you come?

1.4 million

1.2 million

1 million

800,000

600,000

400,000

200,000

1980-2021

1980 1985 1990 1995 2000 2005 2010 2015

Data source: IHME, Global Burden of Disease (2024)

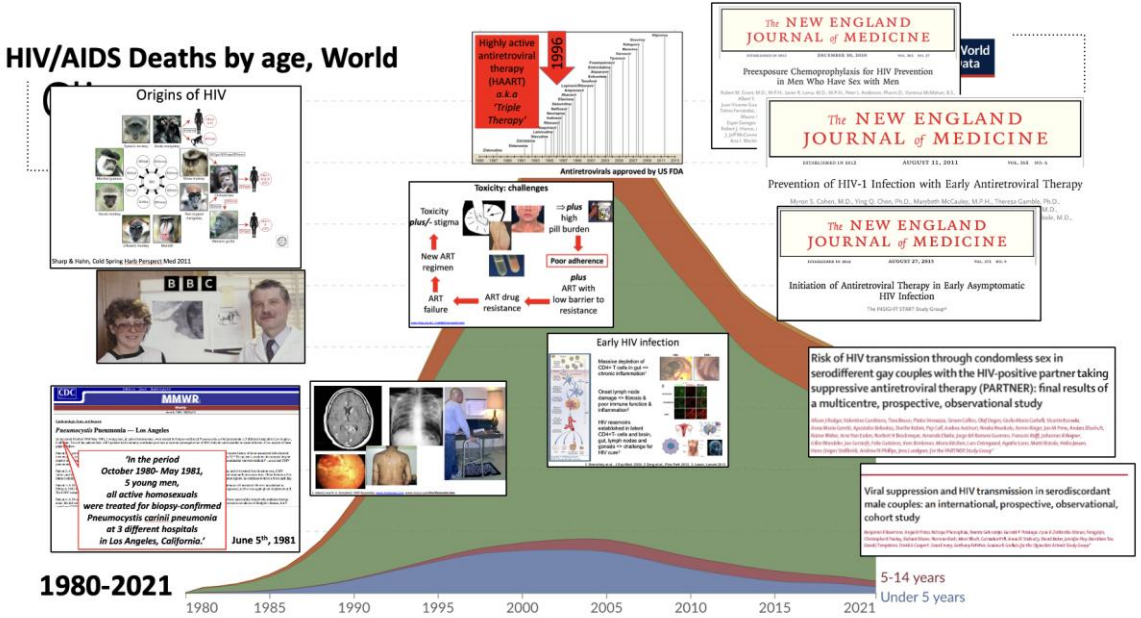
https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

Know yourself- *Why have you come?*

This may largely remain a mystery to you

https://en.wikipedia.org/wiki/Kilbreda_College, https://www.loretotoorak.vic.edu.au/; https://onlinepublichealth.gwu.edu/; https://www.sydney.edu.au/

Know yourself- *What is your capacity for change?*



https://ourworldindata.org/hiv-aids from https://www.healthdata.org/ https://wspartners.bbc.com/. Grant et al, NEJM 2010; INSIGHT Group NEJM 2015; Roger et al, Lancet 2019; Bavinton et al, Lancet HIV 2018

Change will be on offer but it may be challenging and take time to adapt!

Know the science and the politics of science- *What can you really offer people?*

Pregnancy and syphilis[1] are ancient health conditions

- *No vaccines for pregnancy, syphilis or HIV infection*
- *No cure for HIV*
- *Prevention is available for pregnancy, syphilis and HIV but it can be withheld*
- *Treatment is available for HIV but it too can be withheld, as can abortion*
- *Pregnancy can be enforced*

Wise to be humble if what we have to offer is modest and may change with the political times

1. Barquera et al, Nature 2023

Science asks
but it also gives

The propensity for suffering in humans and all creatures is enormous

The key driver of our behaviour throughout life is to move away from suffering and towards peace

Science rewards the clinician's endeavours and relieves people's suffering, hence it fosters peace

Acknowledgements

Ron Lucas
Anne Mijch
Suzanne Crowe
Jenny Hoy
Allen Yung
Jo Lucas
& many others

Bruce Brew
Steve Wesselingh
Lucette Cysique
Luxshimi Lal & all others

Richard Price
Mike Vjecha
Birgit Grund
Jim Neaton

Olga Vujovic
Brian Price
Vincent Cornelisse
Andrew Way
Mary Bowes
Sandy Beach
Christine Bowtell-Harris &
many others

insight

Sharon Lewin

Doherty Institute

Mark Stoové
Michael Traeger
Kat Ryan & others

Levinia Crooks
Bill Whittaker
Dash Heath-Paynter
Jo Watson
PAN, PrEP'd4 change
& many others

Sunil Ahuja

ashm

Alexis Apostolellis
Jessica Michaels
Benjamin Riley
Bek Lamb

LA TROBE UNIVERSITY

Dean Murphy
Jeanne Ellard

thorne harbour health

Colin Batrouney
Simon Ruth
& many others

NHMRC, NIH, ACH2, Vic, SA, Tas Governments, Alfred Health, Gilead, MSD, Jannsen, ViiV Healthcare

All the patients who have taught me and all the researchers and study participants (humans and animal) who have shaped the arc of HIV science

Thank you

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HIV/AIDS Deaths by age, World

Our World in Data

1.6 million

HIV Dementia and Neurological Disorders

1.4 million
1.2 million
1 million
800,000
600,000
400,000
200,000

1980-2021

1980 1985 1990 1995 2000 2005 2010

Data source: IHME, Global Burden of Disease (2024)

Know yourself

Why have you come?

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& many others

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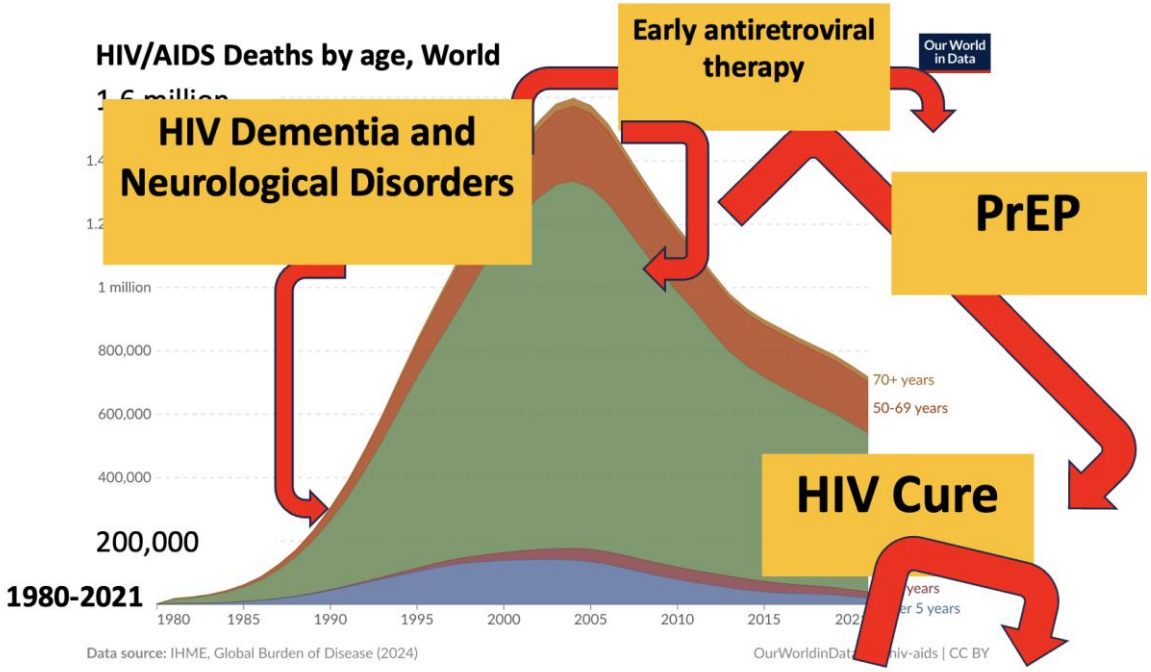
& many others

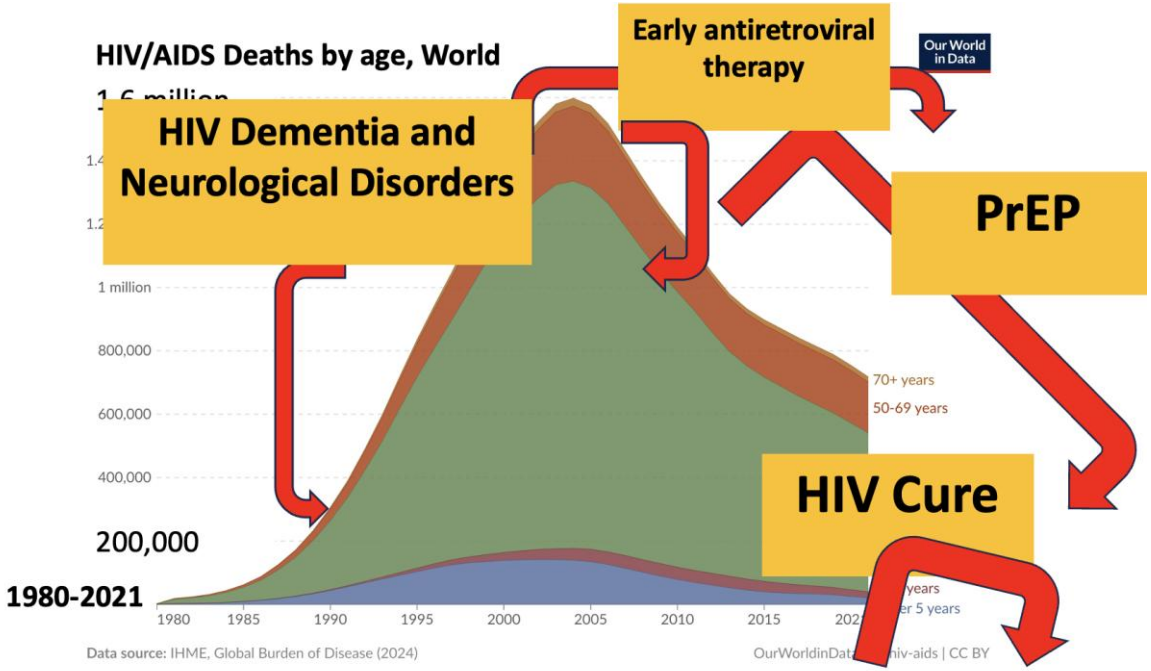
Sunil Ahuja

Know yourself- *what is your capacity for change and adaptation?*

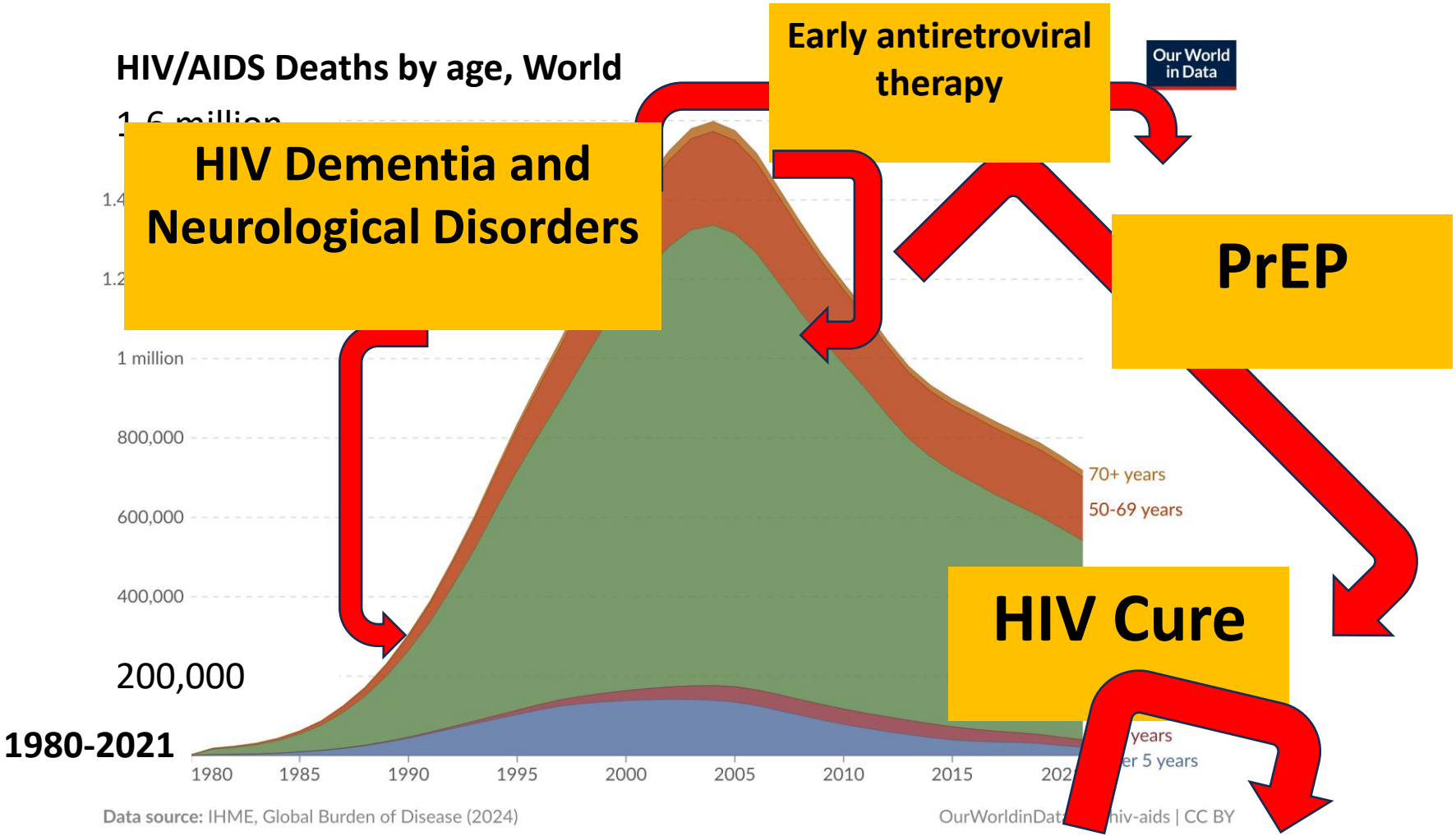


Change will be on offer but it can be challenging to adapt!

Know yourself- *what is your aptitude for adaptation?*



Adaptation is likely to be on offer but can be challenging!



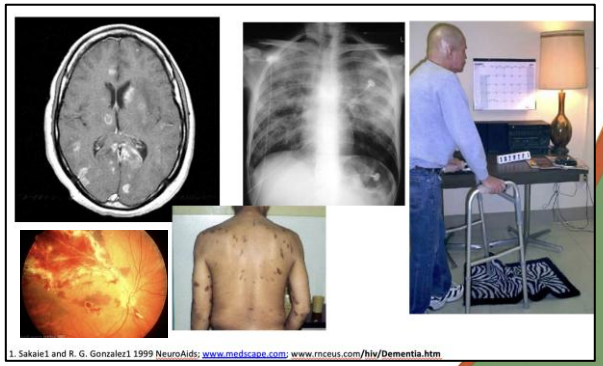
https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

Challenges- know yourself

-Why have you come?

Fairfield Hospital, Victoria

http://en.wikipedia.org/wiki/Fairfield_Infectious_Diseases_Hospital



1. Sakaie1 and R. G. Gonzalez1 1999 NeuroAids; www.medscape.com; www.rnceus.com/hiv/Dementia.htm

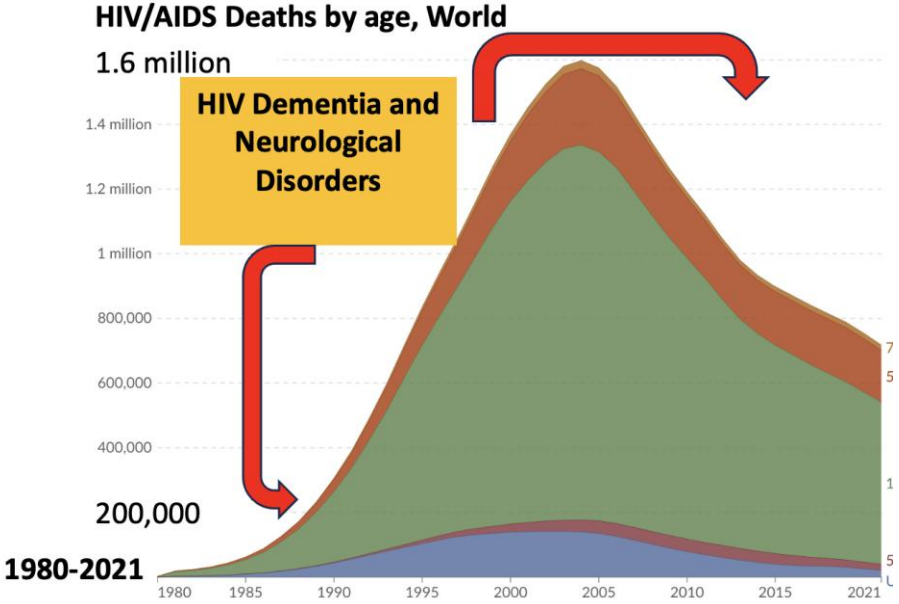
1980-2021

Data source: IHME, Global Burden of Disease (2024)

OurWorldinData.org/hiv-aids | CC BY

https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

HIV Dementia & Neurological Disorders

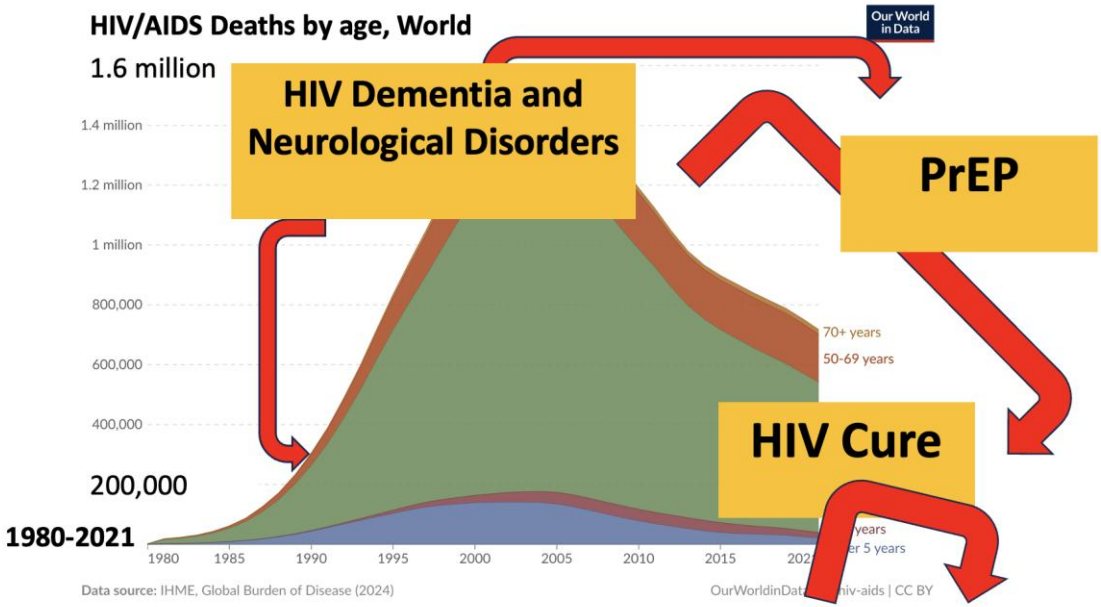


- Asia Pacific NeuroAIDS Consortium
- SMART Neurology Sub- Study
- START Neurology Sub- study
- Australian National NeuroAIDS Brain Tissue Bank
- Neurocognitive Health clinic at Alfred

insight

Brain Bank
AUSTRALIAN NATIONAL NEUROAIDS BRAIN & TISSUE BANK

Adaptation- *can you adapt as the science progresses?*



Adaptation may be necessary and may be uncomfortable as you move out of your areas of expertise

Social Landscape- Homophobia

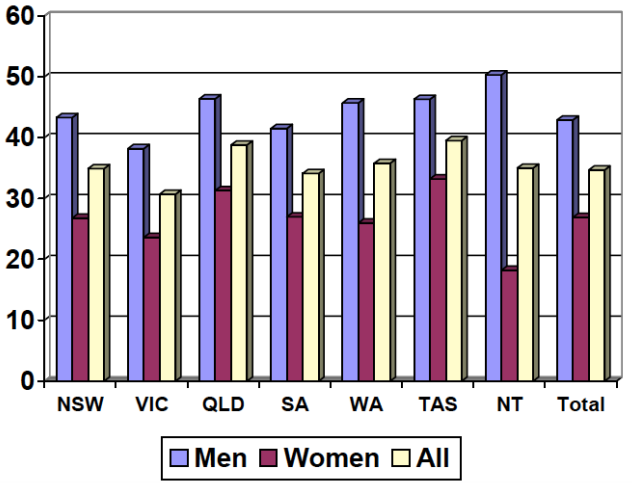
2005: 35% people considered homosexuality to be immoral

Mapping Homophobia in Australia

Australia Institute Webpaper July 2005

Michael Flood and Clive Hamilton[1]

Figure 1 Percent who consider homosexuality to be immoral, by state



Abc.net.au/news; Flood & Hamilton. The Australia Institute, 2005 https://www.tai.org.au/sites/default/files/WP79_8.pdf ; The Australia Institute, 2005 https://www.tai.org.au/sites/default/files/WP79_8.pdf

1981- Political Landscape in Australia

ACT
- Paul Everingham

WA
- Sir Charles Court

Victoria
- Rupert Hamer

SA
- David Tonkin

NSW
- Neville Wran

Tasmania
- Doug Lowe

Queensland
- Joh Bjelke-Petersen

Sir Garfield Barwick

Sir Zelman Cowen

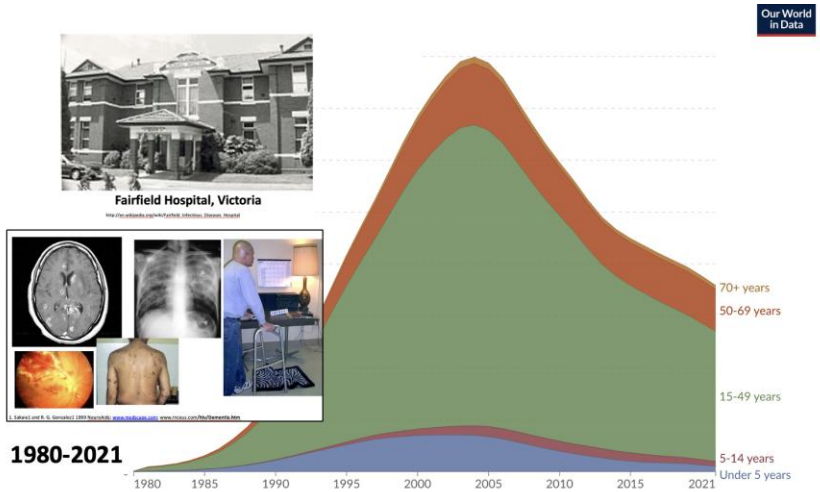
Prior pandemics in 20th century

- **Cholera pandemics**
  - 1899-1923
  - 1961-1975
- **Third Plague pandemic**
  - 1855 China and seen in San Francisco, 1900-1904
- **Influenza plagues**
  - 1918-19, H1N1, Spanish flu
  - 1957-58, H2N2, Asian flu
  - 1968-69, H3N2, Hong Kong flu
- **Tuberculosis pandemic**
  - Treated with triple therapy since 1955

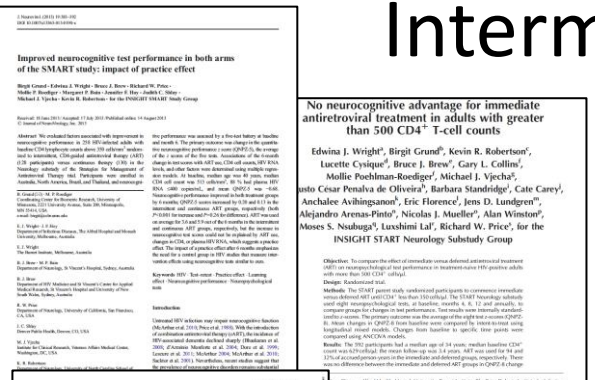
Sexual transmission not the key driver of any of these pandemics


CLAWDIA
OR JUST PLAIN CLAUDIA?

You will be asked to adapt as the science progresses



HIV Dementia & Neurological Disorders- Intermittent and Early Treatment



Improved neurocognitive test performance in both arms of the SMART study: impact of practice effect

No neurocognitive advantage for immediate antiretroviral treatment in adults with greater than 500 CD4+ T-cell counts

ORIGINAL RESEARCH

Factors associated with neurocognitive test performance at baseline: a substudy of the INSIGHT Strategic Timing of AntiRetroviral Treatment (START) trial

Cardiovascular risk factors associated with lower baseline cognitive performance in HIV-positive persons

SMART and START Neurology Sub studies

International RCTs to determine benefits of intermittent ART (SMART n=292) and immediate vs deferred ART (START n=592)

- CV risk factors play a key role in cognitive impairment in PLWH
- Immediate vs deferred ART was not associated with improved neurocognitive function

insight

The ask of the ASHRA Oration

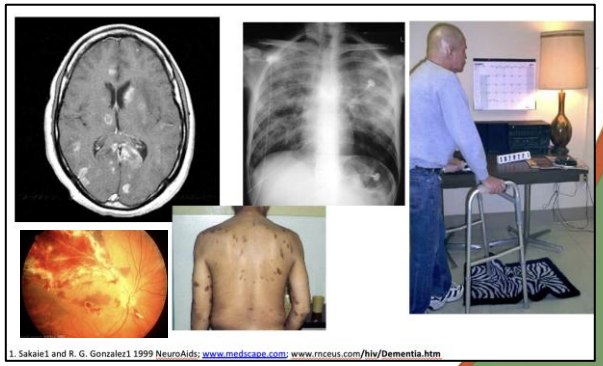
'The Oration aims to capture past, current and future challenges and opportunities in sexual or reproductive health from the orator's personal perspective'

Know yourself

-Why have you come?

Fairfield Hospital, Victoria

http://en.wikipedia.org/wiki/Fairfield_Infectious_Diseases_Hospital

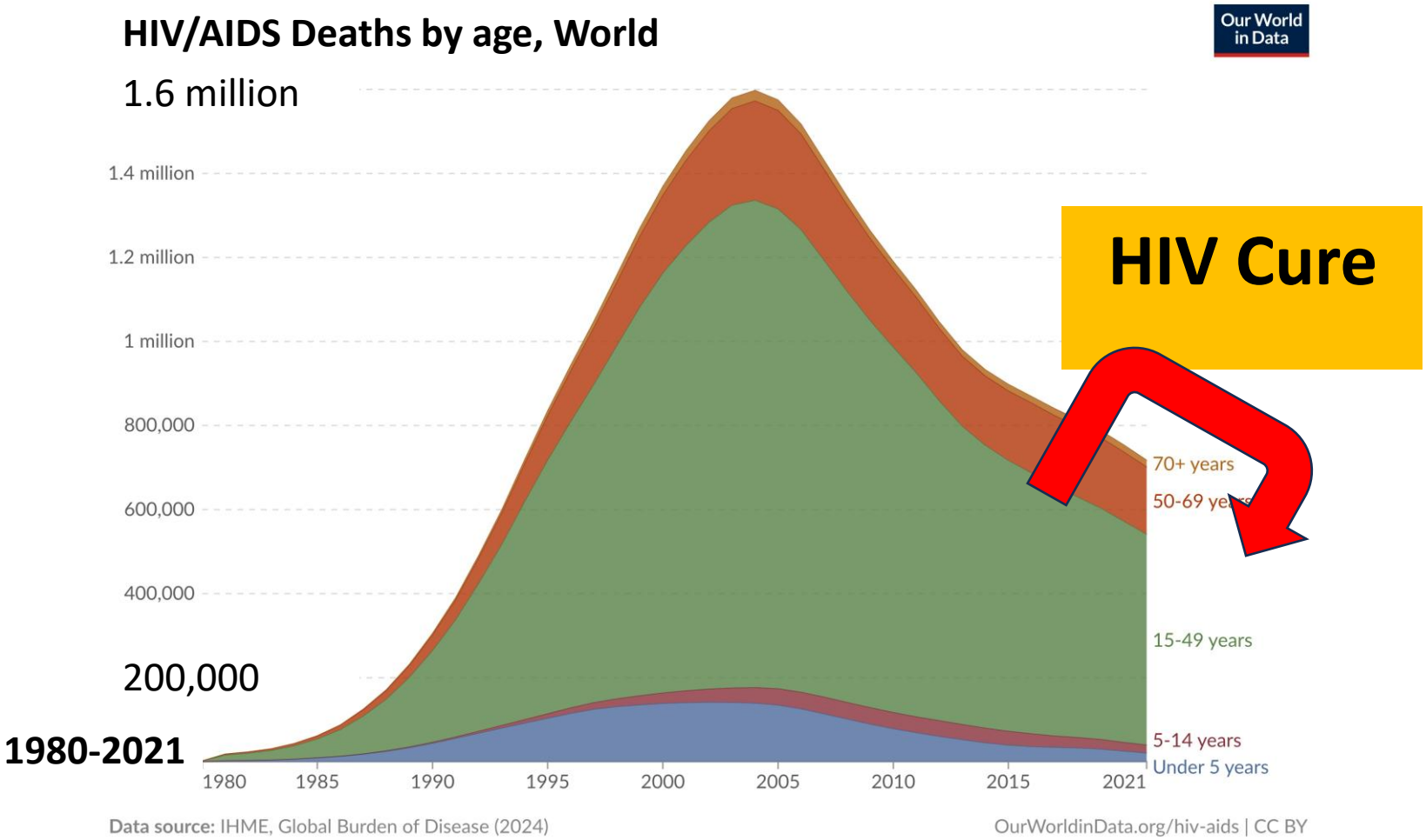


1980-2021

Data source: IHME, Global Burden of Disease (2024)

OurWorldinData.org/hiv-aids | CC BY

https://ourworldindata.org/hiv-aids from https://www.healthdata.org/



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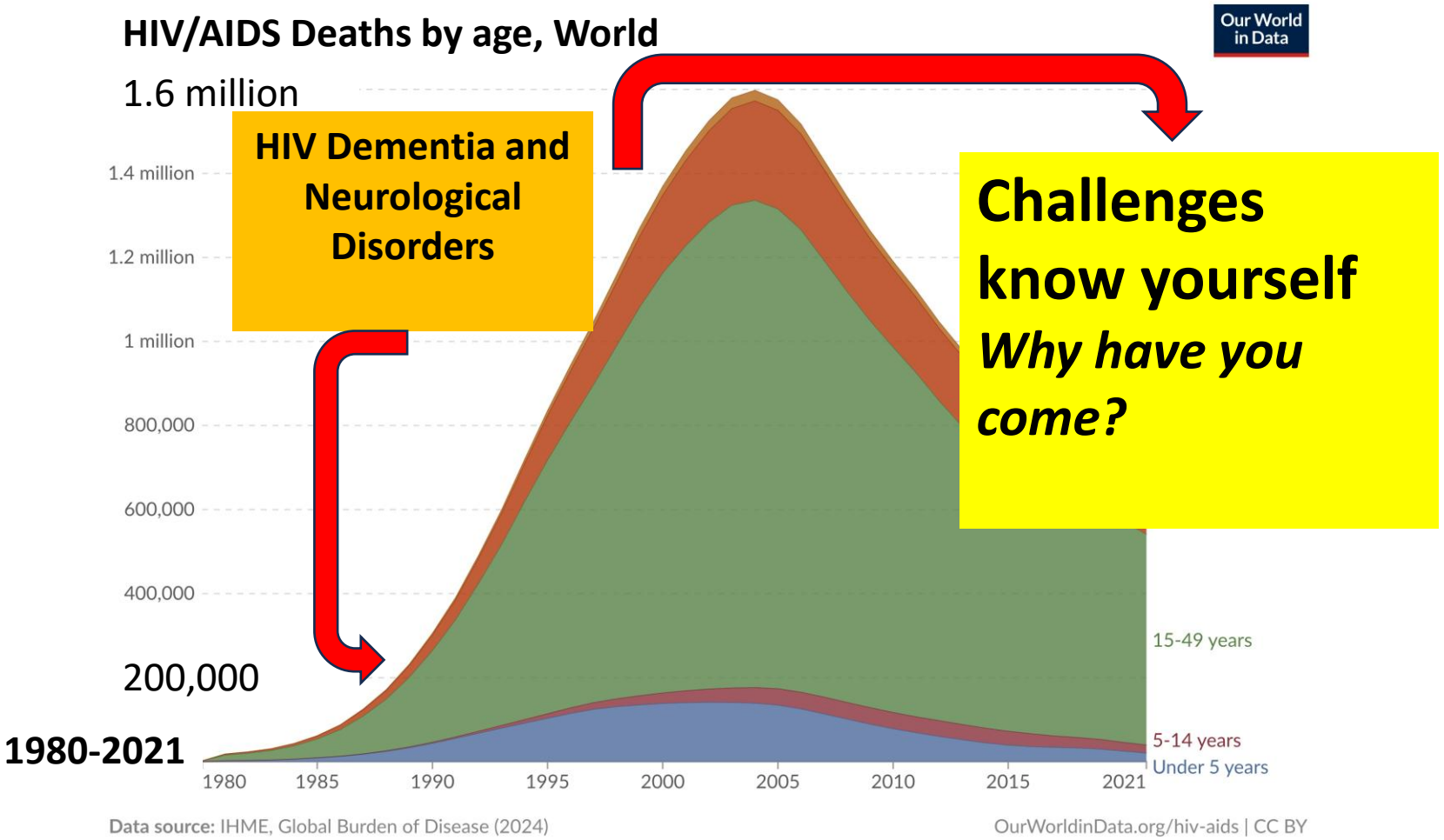


https://ourworldindata.org/hiv-aids from https://www.healthdata.org/

DOI: 10.1111/hiv.12238
HIV Medicine (2015), 16 (Suppl. 1), 97–108

ORIGINAL RESEARCH

Factors associated with neurocognitive test performance at baseline: a substudy of the INSIGHT Strategic Timing of AntiRetroviral Treatment (START) trial

EJ Wright,[1,2] B Grund,[3] LA Cysique,[4,5] KR Robertson,[6] BJ Brew,[4,5] G Collins,[7] JC Shlay,[8,9] A Winston,[10] TRH Read[11,12] and RW Price[13] for the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT) START Study Group

[1]*Department of Infectious Diseases, Alfred Hospital and Monash University, Melbourne, Victoria, Australia,* [2]*Burnet Institute, Melbourne, Victoria, Australia,* [3]*School of Statistics, University of Minnesota, Minneapolis, MN, USA,* [4]*University of New South Wales, Sydney, New South Wales, Australia,* [5]*Peter Duncan Neurosciences Unit St Vincent's Centre for Applied Medical Research, St Vincent's Hospital, Sydney, New South Wales, Australia,* [6]*AIDS Neurological Center, Neurology, University of North Carolina, Chapel Hill, NC, USA,* [7]*Division of Biostatistics, University of Minnesota, Minneapolis, MN, USA,* [8]*Denver Public Health, Denver Health and Hospital Authority, Denver, CO, USA,* [9]*Department of Family Medicine, University of Colorado School of Medicine, Denver, CO, USA,* [10]*Division of Medicine, Imperial College London, London, UK,* [11]*Melbourne Sexual Health Centre, Alfred Health, Melbourne, Victoria, Australia,* [12]*Victorian Infectious Diseases Service, Royal Melbourne Hospital, Melbourne, Victoria, Australia and* [13]*Department of Neurology, University of San Francisco California, San Francisco, CA, USA*

insight

BrainBank

AUSTRALIAN NATIONAL TISSUE BANK

Neurologic diso
positive outpatie
region

E. Wright, MBBS, FRACP
B. Brew, MBBS, MD, FRACP

ABSTRACT

Background: A total of 8.3 million HI
HIV-associated neurocognitive impa

Neurologic disorders are prevalent in HIV-positive outpatients in the Asia-Pacific region

E. Wright, MBBS, FRACP
B. Brew, MBBS, MD, FRACP
A. Arayawichanont, MD
K. Robertson, PhD
K. Samintharapanya, MD
S. Kongsaengdao, MD
M. Lim, BBioMedSci
S. Venthanak, MD
L. Lal, BPharm, BAppSci
C. Sarim, MD
S. Huffam, MBBS, MPH
P. Li, MD
D. Imran, MD
J. Lewis, BSc, MBiomed
W.H. Lan, MD
A. Kamarulzaman, MBBS, FRACP
G. Tau, MBBS
S.T. Ali, MD
K. Kishore, MBBS
M. Peggy Bain, BSc(Psych)A, MClinPsych
R. Dwyer, MBBS, BMedSci
G. McCormack, MBBS
M. Hellard, MBBS, PhD, FRACP, MPH
C. Cherry, MBBS

ABSTRACT

Background: A total of 8.3 million HIV-positive people live in the Asia-Pacific region. The burden of HIV-associated neurocognitive impairment and symptomatic sensory neuropathy in this region is unknown.

Methods: Between July 2005 and March 2006, we undertook a cross-sectional study at 10 sentinal sites within eight Asia-Pacific countries to determine the prevalence of moderate to severe HIV-related neurocognitive impairment and symptomatic sensory neuropathy. We clinically assessed and administered sensitive neuropsychological and peripheral neuropathy screening tools to 658 patients infected with HIV. Univariate and logistic regression analyses were applied to the data.

Results: The results showed that 76 patients (11.7%) (95% CI 9.3–14.2) were significantly neurocognitively impaired, 235 patients (36.4%) (95% CI 32.7–40.2) were depressed, and 126 patients (19.7%) (95% CI 16.6–22.8) had either definite or probable symptomatic sensory neuropathy; 69% of this last group had exposure to stavudine, didanosine, or zalcitabine. Several potential confounders including depression (OR 1.49, 95% CI 0.88–2.51, $p = 0.11$) and prior CNS AIDS illness (OR 1.28, 95% CI 0.50–2.89, $p = 0.54$) were not significantly associated with neurocognitive impairment.

Conclusions: A total of 12% of patients had moderate to severe HIV-related neurocognitive impairment, 20% of patients had symptomatic sensory neuropathy, and 36% of patients had evidence of depression. This study provides a broad regional estimate of the burden of HIV-related neurologic disease and depression in the Asia-Pacific region. *Neurology*® 2008;71:53–59

GLOSSARY

AP = Asia-Pacific; **APNAC** = Asia Pacific NeuroAIDS Consortium; **ARV** = antiretroviral; **CES-D** = Center for Epidemiologic Studies-Depression Scale; **HAART** = highly active antiretroviral therapy; **HAD** = HIV-associated dementia; **NCI** = neurocognitive impairment; **SN** = sensory peripheral neuropathy.

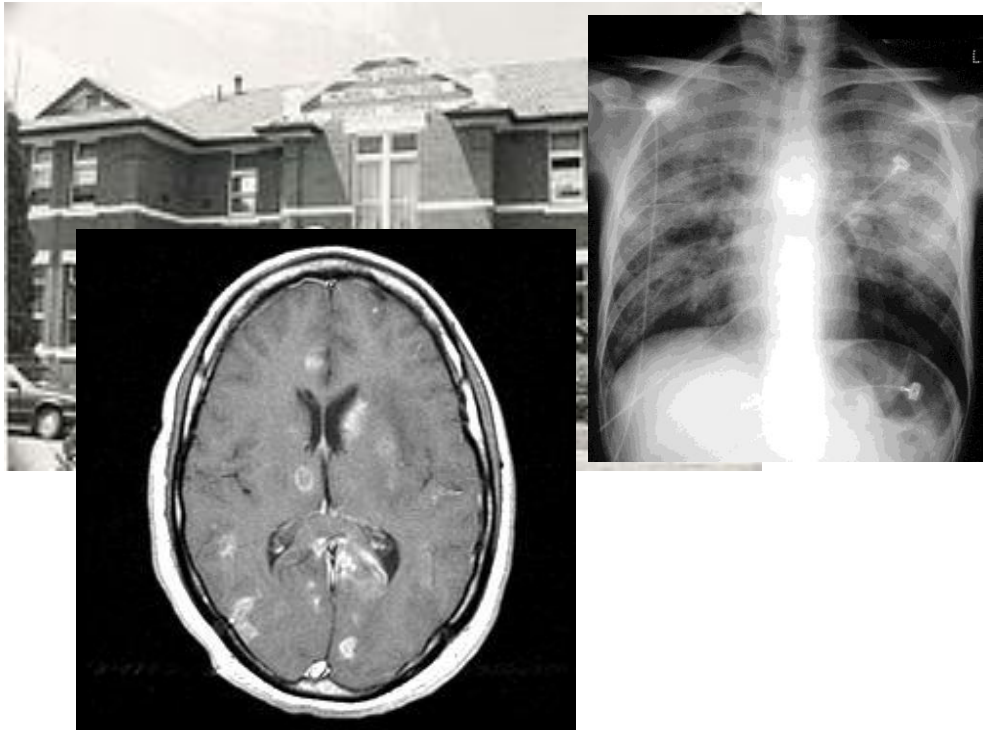
Why do you stay?

Remarkable medicine, science, people

Care is always needed

Solved an unsolvable problem

Medical Landscape- Treatment for OIs



1. Sakaie1 and R. G. Gonzalez1 1999 NeuroAids

www.rnceus.com**/hiv/Dementia.htm**

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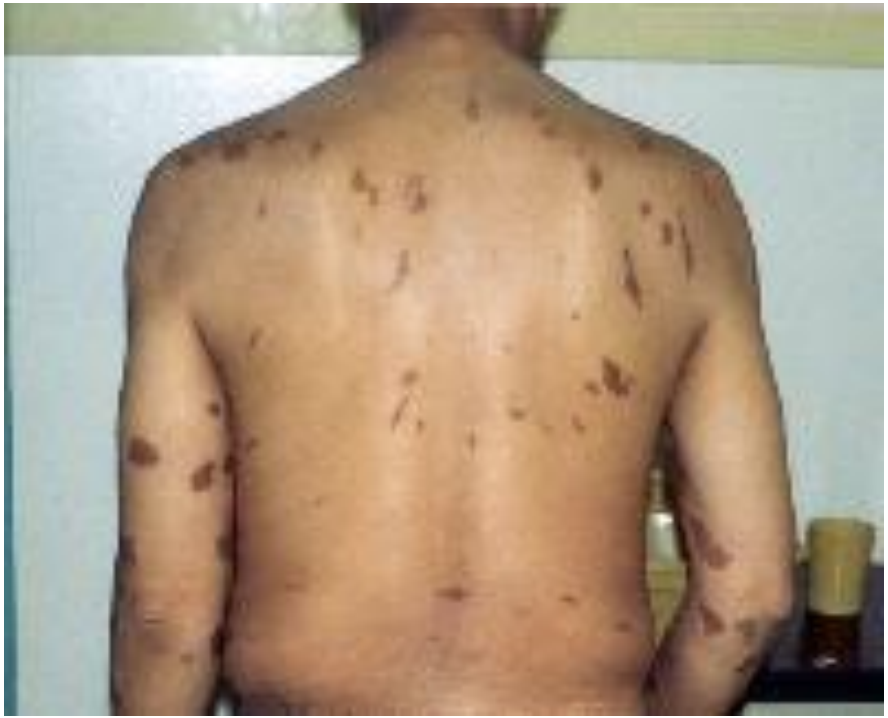


Source: www.medscape.com

Medical Landscape- Treatment for Opportunistic Diseases

Available in 1981 for use

- Pentamidine- since 1937
- Sulphadiazine- since 1940s
- Pyrimethamine- since 1960s
- Co-trimoxazole- since 1974
- Amphotericin-B- since 1958
- Radiotherapy

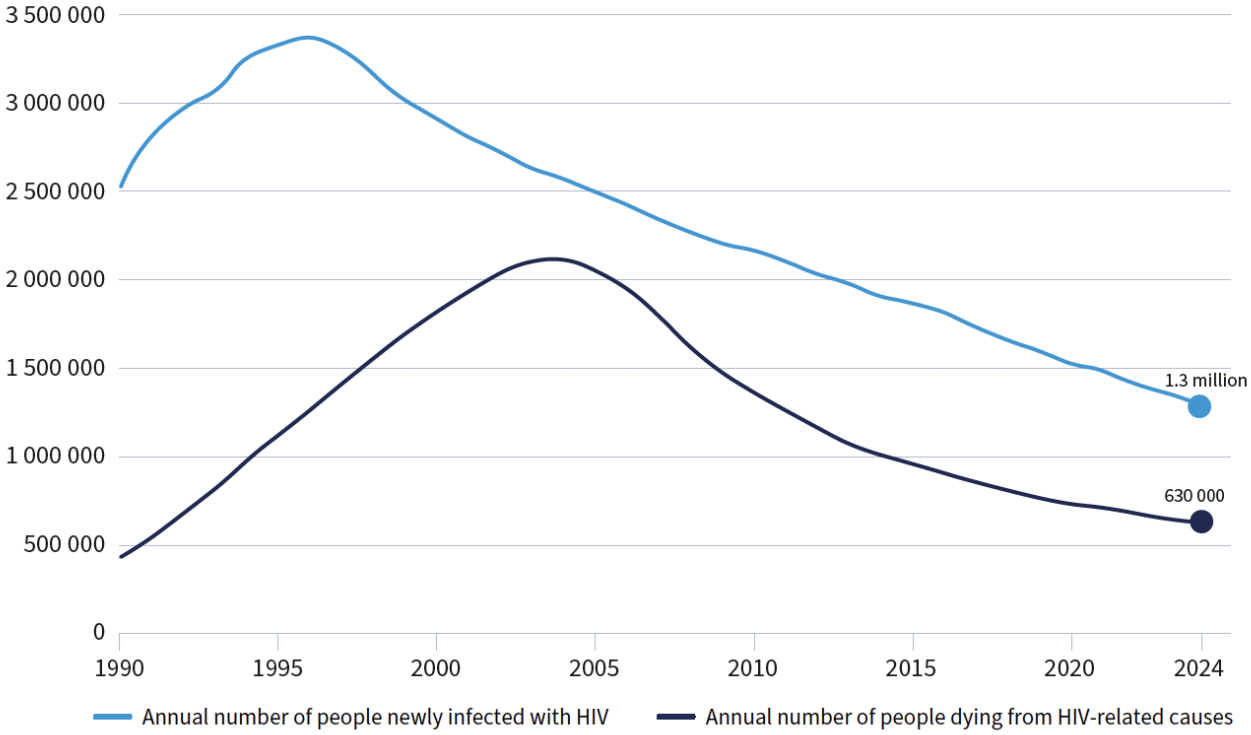
Subsequently available

- Topical Acyclovir- 1982
- Clofazimine-1986
- Ganciclovir-1988
- Clarithromycin-1990s
- Fluconazole-1990
- Vinca alkaloid- 2000s

Know yourself

- Why have you come to work on the line of this particular scientific arc?
- What are your expectations of what you can achieve?
- What conditioning have you brought with you?
- What can you actually offer?

Fig 2. Global trends in people acquiring HIV and people dying from HIV-related causes, 1990–2024

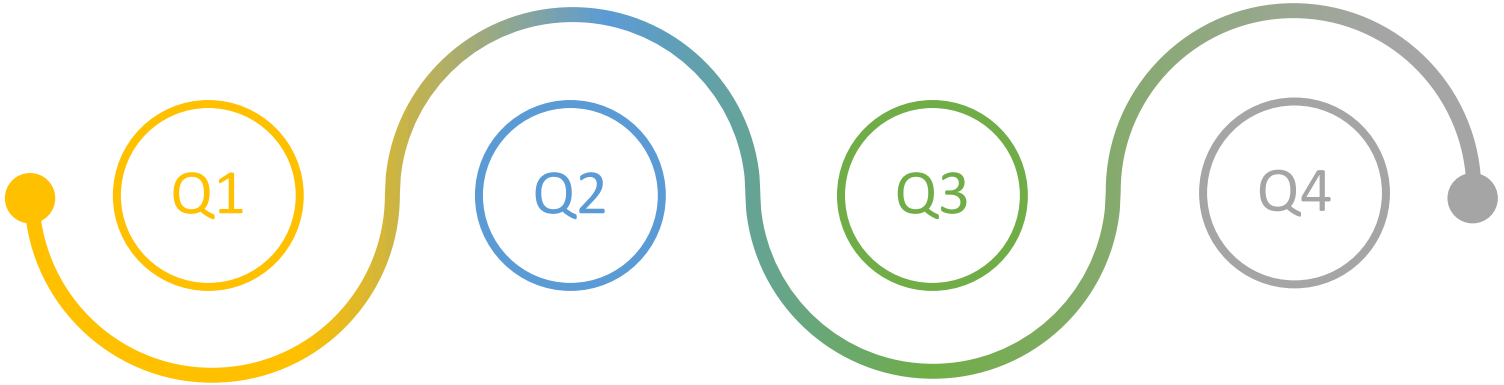


Note: These estimates were made before the implementation of cuts to foreign aid.

Source: UNAIDS/WHO estimates, 2025.

https://cdn.who.int/media/docs

Product Roadmap



MILESTONE

Successful completion and finalization of our innovative product

MILESTONE

Successful introduction of our innovative product to the market

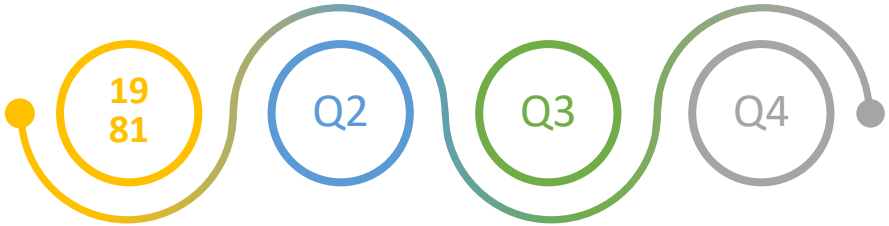
MILESTONE

Celebration of reaching a substantial user base, indicating growing demand

MILESTONE

Formation of a strategic alliance, expanding market presence and capabilities

PRODUCT ROADMAP



AIDS DESCRIBED

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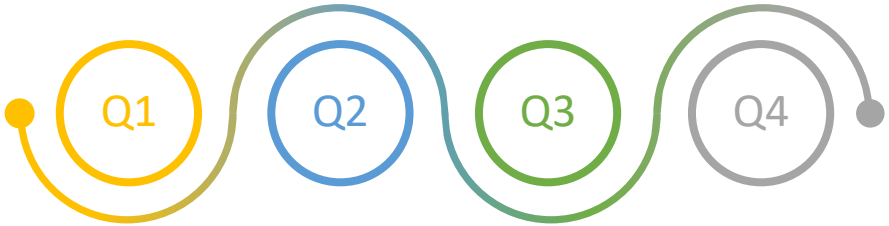

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