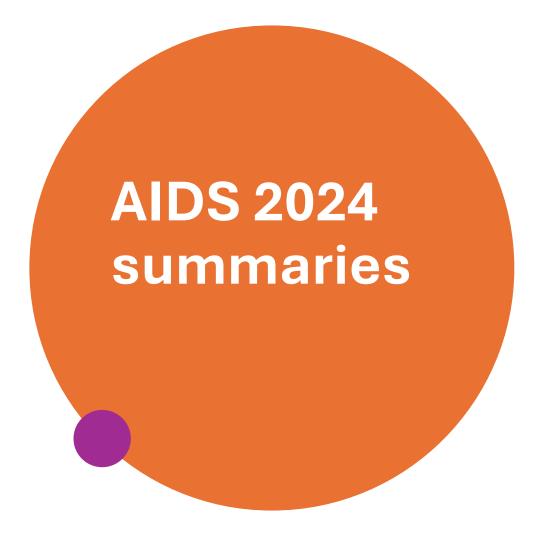
Update AIDS 2024 Conf Intl Munich 22-26 July

#### Albergue Las Memorias SD HIV Consortium





Dr. Marlet Nuno, Las Memorias, UABC Dr. Joe Caperna UCSD

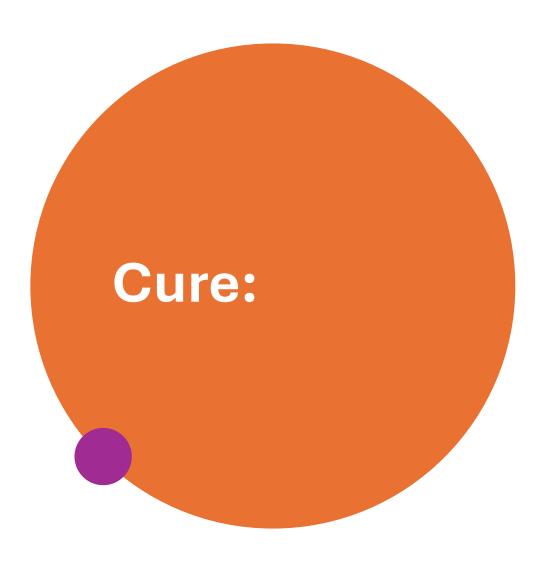


CURE patient

- By Days Pre-conference, 1-3, 4, 5
- CROWD Strike
- 2 drug regimens
- Every 6-month injection 100% effective in preventing HIV in heterosexual woman in Africa

More than 40 oral abstract sessions, 50 invited-speaker sessions, 20 workshops, 17 preconferences, 30 symposia sessions, 100 satellite sessions and 2,200 posters.

- Abstracts >2000 over 3 days
- Under the skin Cabenuva more reactions than in the muscle
- Several two drug regimens, not standard, but effective in highly resistant patients.
- Depression
- Spirituality, Faith UZWELO
- Doxy-PEP and PrEP
- Women's health, low frequency of meeting heart disease prevention goals



- The tone was set that this would be a groundbreaking conference for HIV cure when three people known to have been cured of HIV came together in a <u>pre-conference</u>.
- Adam Castillejo (formerly known as the London Patient),
- Marc Franke (formerly the Düsseldorf Patient) and
- Paul Edmonds (formerly the City of Hope Patient) shared their stories.
- Their hope was to inspire researchers and people living with HIV to keep on track to find a cure that would work for everyone.
- Then came details about the "next Berlin patient", who appears to be the seventh person cured of HIV.

# Another CURE By Jeff Taylor

• We are lucky to have Jeff Taylor from HARP-Palm Springs, who participated in the panel discussion with 3 cured patients, and shares the following comments on the 2<sup>nd</sup> Berlin patient.

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• The "Towards a Truly Global HIV Cure" preconference workshop on Sunday, 21st featured a panel discussion with all three "out" people who have been cured of HIV. "Düsseldorf Patient" Marc Franke, "London Patient" Adam Castillejo, and "City of Hope Patient"

• Paul Edmonds joined a panel discussion chaired by IAS co-chair Sharon Lewin and <u>Jeff Taylor.</u>



- All three shared their amazing stories of receiving stem cell transplants that cured both their blood cancers and their HIV— the tribulations of the procedure, the challenges they still face living as transplant recipients, and the rather surreal experience of being cured, and the media attention, and how the media often distorts their stories.
- All three agreed they had gone public hoping their stories would inspire researchers and people living with HIV to continue to fight for a cure for everyone.

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• The audience of researchers & community advocates from around the world *flocked to the stage* afterwards to shake their hands, and of course take lots of selfies. All three gentlemen will be featured in other IAS sessions—especially around interrupting HIV treatment during cure trials, and in multiple media stories coming out of the conference.

 Both Adam Castillejo and Paul Edmonds will be in San Diego for a town hall meeting on cure research produced by the RID HIV cure research Collaboratory on Sunday, Oct 6.

• Stay tuned for more details...

## ANOTHER CURE!!

- Also announced at the conference was the latest person cured of HIV—<u>"The New</u> Berlin Patient".
- This 60-year-old man also received a stem cell transplant to treat his blood cancer, but with one key difference—the donor stem cells only had one, not two genes of the rare mutation in T-cells that makes them immune to HIV infection. People with these cells can acquire HIV, but typically are so-called "slow progressors" who don't get as sick nearly as quickly as most people and can go a long time before they need to start on HIV treatment. Session Abstract
- This is the first case like this, so it's unknown whether they could possibly become reinfected with HIV or not.

## ANOTHER CURE!!

- The 2<sup>nd</sup> Berlin Patient, has been cured of **HIV.** "The procedure used with the next Berlin Patient is yet another stem cell transplant and, thus, not a viable option for the vast majority of the nearly 40 million people living with HIV. But his case is unique in that, unlike most other successful stem cell transplant HIV cures, his donor has only one copy of the CCR5-delta32 mutation that renders a person almost completely immune to HIV, rather than two. It will require further study to determine to full ramifications of this case, but it could open the door to a cure for many more people who already require a stem cell transplant for the treatment of cancer; while only about 1% of people with northern European ancestry have two copies of the CCR5 mutation, as many as 16% have one copy."
- https://www.poz.com/article/next-berlin-patient-another-man-cured-hiv-stem-cell transplant

## Patients cured of HIV

- 1) The second Berlin patient represents the seventh case of HIV to be cured worldwide, reported July **2024** at International AIDS Conference.
- 2) Timothy Ray Brown (the "Berlin Patient," publication date **2009**),
- 3) Adam Castillejo (the "London Patient," publication date **2019**),
- 4) Marc Franke (the "Düsseldorf Patient," publication date **2023**),
- 5) The "New York Patient" (publication date **2023**) and
- 6) Paul Edmonds (the "City of Hope Patient," publication date **2023**)
- 7) "Geneva Patient," who received a stem cell donation from a person with exclusively a functioning CCR5 receptor, was presented at the International AIDS Conference in **2023**; because the follow-up observation period has been rather short, there are different assessments as to whether he has been fully cured of HIV. Probably the 6th case cured.

## Can the cured be re-infected?

• The "Geneva Patient" announced at last year's IAS conference in Brisbane received normal stem cells without that mutation, yet the transplant process appears to have eliminated HIV in their bodies anyway. Since these are the first cases like this, it's unknown whether they could possibly become reinfected with HIV or not. We have a lot more to learn...

# Another *Hope* for cure First Human CRISPR gene therapy

- Researchers are slowly finding a safer way to cure, than the reported stem cell transplants.
- "This study is highly unique," added Chantelle Ahlenstiel, PhD, a senior research fellow in immunovirology and pathogenesis at the Kirby Institute at the University of New South Wales in Sydney, Australia. "It was a high-risk study that showed a very promising safety profile," she said.
- HIV RNA levels rebounded in all four participants who had antiretroviral interruption, but One patient had a delayed rebound of almost 16 weeks along with a significant drop in the HIV reservoir.
- "This is the most promising result but only seen in one person," Presti said during an interview.
- https://www.medscape.com/viewarticle/first-human-trial-crispr-gene-therapy-hiv-2024a1000dx5

#### Day 4

- "Highlights"
- Day 4
- 26 July 2024
- by Joe Caperna

Many important reports today. Most of today's summary will focus on Artistry-1.

ARTRISTRY-1

- Efficacy and Safety of Bictegravir Plus Lenacapavir: 48-Week Outcomes in Virologically Suppressed People With HIV-1 on Complex Antiretroviral Regimens at Baseline." This was a switch study, meaning on an effective regimen, fully suppressed, and 'switched' to another treatment. Patients were on up to five drugs at a time, then switched to just two drugs, a simplified regimen of once daily oral bictegravir plus lenacapavir. (Lenacapavir was just announced in every 6-month injectable form to prevent 100% of HIV infections in African women. This study used daily oral.
- This study was randomized for drug doses, making the results stronger. The regimen was effective and tolerated. It is important to know that this is not a recommended regimen, only being studied. The study compared different doses and found the most effective dose of each medicine. This combination cannot be used with active Hepatitis B.

#### **ARTISTRY-1**

- Sorana Segal-Maurer, MD, principal investigator on the ARTRISTRY-1 trial, commented that
  - In general, we don't really focus on people with HIV who are virologically suppressed, because they're suppressed. We don't always think that it's burdensome to take multiple pills a day. And these persons are getting older, they're having more metabolic comorbid conditions, more drug interactions," she stated.

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• "This is the population of persons with HIV that was singled out as sort of being left behind—just because they're suppressed. I think maybe we put them out of our mind. I like the focus of the study: Let's make their lives simpler. Let's make those drug interactions better, or less. It was a complex group—but they were all virally suppressed. So, it was a great opportunity to step in. I think it's a tremendous study to offer persons with HIV," Segal-Maurer said.

#### **ARTISTRY-1**

• This was an 'older' group of 137 PLH on ARV's, median age 60, most had a history of drug resistance (81%), a majority had been on ARV's for 27 years and about 75% were on PI's. With PI's, there are food requirements, dangerous drug interactions and significant metabolic side-effects. About half were on twice a day regimen and a third were on 5 drugs, so this study made the regimen easier and safer. Females at birth were 19%, and Black race was 31%. This regimen was effective in almost everyone, with more than 90% of patients remain suppressed.

#### Day 4

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• Bictegravir has a "high barrier to resistance." Lenacapavir is a first-in-class capsid inhibitor, "where there's no underlying resistance that persons with HIV would have if they've never taken it. So the 2 together can really offer a significant benefit or a potential for a good combination if somebody has prior history of resistance. They have very limited drug-drug interactions and no food requirement. This combination cannot be used with active Hepatitis B.

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• ARTISTRY-2 is planned in a larger group, with a new single tablet that has both drugs., bictegravir 75 mg plus lenacapavir 50 mg. It holds promise for an easier, safer and effective regimen in older PLH on arv's for decades and with history of resistance. ARTISTRY-1 Reference

## DO-DO Dolutegravir/Doraravirine (Tivicay/Pilfeltro)

- Patients took dolutegravir with a newer NNRTI, doravirine (Pilfeltro©), which does not have the acid blocker restriction, metabolic effects and lower chance for drug interactions.
- 102/104 patients remained suppressed after median of 3 years.
- However, 13/104 (12%) stopped the regimen because of side-effects, 36/104 had no significant side-effects. This is another 2-drug combination that is not recommended yet but holds promise. This combination cannot be used in active Hepatitis B.

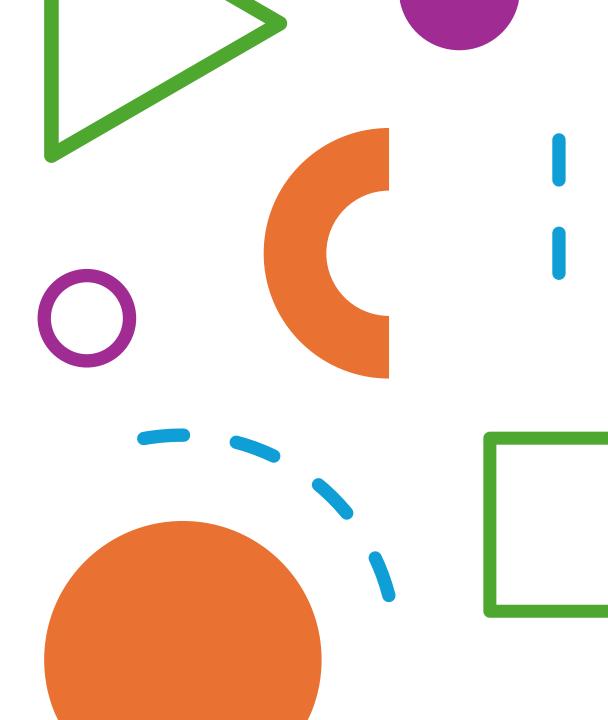
#### Do-Do Study (Dolutegravir and Doravirine

- This was another switch study, again in patients with resistance and this group was on arv's for median of 27 years.
- There was median 3-year f/u, with up to 5 years on some, so longer f/u compared to the 48 weeks in ARTISTRY-1.
- The researchers checked drug levels, important to understand why a regimen 'works' or not. We learned that checking drug levels is common in Europe, where insurance or the health system pays for these tests. We do not have these tests easily available in the US.
- Study sites were in Germany and Austria. Patients were recruited from a prior study, comparing dolutegravir-FTC (Dovato©) with dolutegravir plus rilpivirine (NNRTI class with druginteractions metabolic effects, and restriction to use acid blockers, PPI's like omeprazole (Prilosec©), esomeprazole (Nexium©), lansoprazole (Prevacid©), pantoprazole (Protonix©).

#### Depression in PLH

- By Michael Schulte, UCSD MS3
- Examining the relationship between psychological wellbeing, self-efficacy, resilience, and depression among people with HIV. M Schulte et al, UCSD.
- This study seeks to examine the relationship between psychological wellbeing, self-efficacy, resilience, and depression among people with HIV. Consistent with prior studies, we found that **people with HIV exhibited greater depressive symptom severity compared to people without HIV.**
- However, to our knowledge, this is the first study to report lower psychological wellbeing among PWH using the NIH Toolbox Emotions Battery.
- Surprisingly, HIV status was not a significant predictor of depressive symptom severity in our multivariable model. Instead, we found that lower psychological wellbeing and lower self-efficacy significantly predicted greater depressive symptom severity among people with and without HIV.
- This suggests that greater depressive symptom severity in PWH may be due partly to lower psychological wellbeing rather than disease-specific factors alone.

- By Michael Schulte, UCSD MS3
- Two other HIV-related mental health studies presented at AIDS 2024 stood out to me.
- One out of Florida International University found that inflammation at HIV onset predicts persistent depressive symptoms despite antiretroviral therapy (Chavez et al., 2024). This presents another step forward in characterizing a potential cause and overall profile of depression in people living with HIV. This study provides a biological counterpart to mine which seeks to characterize a potential psychosocial basis for depression in people living with HIV. Clearly, depression in people living with HIV is a complex phenomenon. It is exciting to see researchers of different backgrounds and fields of thought attempting to clarify this complexity with the common goal of improving the mental health of people living with HIV.
- Separately, AIDS 2024 was not saved from artificial intelligence. A randomized controlled trial of an AI-based HIV disclosure role-playing conversation simulator out of the University of North Carolina found that the app was an effective intervention to improve decision-making capacity in HIV disclosure among young men who have sex with men living with HIV (Stamp et al., 2024). This represents an important step forward in helping people living with HIV to reduce anxiety and make better decisions related to disclosure—a conversation that remains an act of courage.



#### Al and 'chatbot' psychotherapist?

- Dr Caperna:
- Day 5 of conference, the plenary session was on the rapid growth of AI in healthcare including with PLH. Surprisingly, or sadly, AI has been shown to be more compassionate than healthcare workers. It's faster, cheaper, and we all need chatbot psychotherapy?

The machine is less personal, less intimidating. Maybe more approachable. Selfservice gas. Self-checkout. These are inhuman. Antisocial.

- Real people need to understand and experience the benefits of compassion.
- The idea is to be other-centered. And remember the benefits of human community.
- A study from Georgia (the country) showed 50% of women with HIV have depression.

## Pablo Radusky from Fundación Huésped from the <u>TransCITAR study</u>, Argentina

- ......involved **480 trans participants** and found even higher rates of mental health impact among non-binary individuals.
- Radusky noted that police violence was found to be a recurring source of stigma and violence experienced by the community.
- For trans women living with HIV, this situation was found to be exacerbated by a higher probability of experiencing unstable housing, coming from a migrant background and holding less economic power.

• Another factor impacting the mental health of trans communities includes a crisis in Chemsex—using illicit substances to enhance sexual experiences—with severe consequences from dating app use including higher rates of depression, suicide, and cardiovascular diseases. Thiago Torres from Fundação Oswaldo Cruz, Brazil highlighted the widespread exclusion of trans and gender diverse individuals from studies on Chemsex but noted that the limited existing research that included disaggregated data from trans communities indicated a higher prevalence among trans women and non-binary people in Latin America. The research found a notable correlation between PrEP (pre-exposure prophylaxis) use and higher instances of chemsex, prompting discussions on harm reduction strategies tailored for trans and gender diverse individuals.

### UNAIDS report shows AIDS pandemic can be ended by 2030,

...but only if leaders boost resources and protect human rights now.

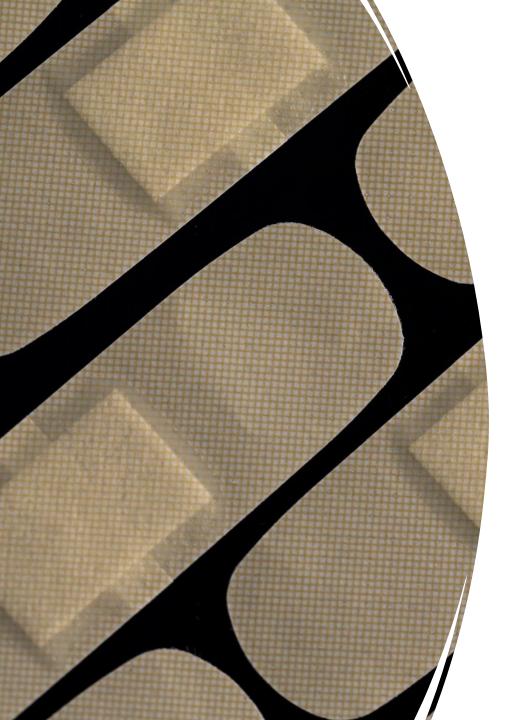
• The report demonstrates that HIV prevention and treatment services will only reach people if human rights are upheld, if unfair laws against women and against marginalized communities are scrapped, and if discrimination and violence are tackled head on. There is great concern that funding for research, prevention and treatment will be cut, globally, and never eliminate HIV.

#### Lenacapavir is safe in pregnancy

- . This is the medicine that is every 6 months, and shown to be 100% effective in preventing HIV in African cis-, heterosexual woman. A subgroup of this same PURPOSE-1 study were pregnant.
- Importantly, in this subset, this same injectable, lenacapavir, also known as Sunleca, HIV PrEP <u>can safely be used during pregnancy.</u>

"Increased incidence of emergent integrase drug resistance with cabotegravir versus dolutegravir in randomized switching trials." Abstract LB17

• The researchers looked at patients reported in prior studies (ATLAS, FLARIR, LATTITUDE, CARES), who were using regimens with dolutegravir, one of the most common HIV medicines used worldwide. Although researchers reported low virologic failure with the dolutegravir regimens, they found that 65% of patients had INSTI mutations. The significance is not certain now, but worrisome that they reported such high level of mutations (65%) that could later affect the efficacy of INSTI's.



## Sub-cutaneous rilpivirine/cabotegravir (Cabenuva©)

- Not sure if drug levels adequate
- Too many had very painful nodules form under the skin.
- Remember FUZEON©?
- In a sub-study of the FLAIR phase 3 trial found that 93 patients were virologically suppressed on intramuscular Cabenuva and changed to under the skin injections. Although most (91/93) remained virologically suppressed, participants favored intramuscular injection of Cabenuva© over the subcutaneous version due to pain and the development of nodules and reddening of the skin.2. See review.

#### Day 4--DoxyPrEP and DoxyPEP

AIDS 2024 saw the term, "DoxyPrEP" (doxycycline pre-exposure prophylaxis to describe taking the antibiotic before sex), make its debut to join the better-known "DoxyPEP" (doxycycline post-exposure prophylaxis).

So, daily doxycycline versus only as needed, which is the current recommendation.

Researchers from opposite sides of the world presented findings on daily doxycycline. A <u>trial</u> from Canada involving men who have sex with men, living with HIV and with a history of syphilis, showed reductions of 79% in syphilis, 92% in chlamydia and 68% in gonorrhoea in the doxycycline arm compared with the placebo arm.

#### Day 4--DoxyPrEP and DoxyPEP

A <u>study</u> from Japan among female sex workers showed a drop in STI incidence from 232.3 to 79.2 per 100 person-years. Syphilis incidence was reduced to zero; there was a marginally significant reduction in chlamydia and no significant change in gonorrhoea.

A big question mark hangs over the potential for antimicrobial resistance (AMR) with the prolonged use of doxycycline. Largescale and continued surveillance is crucial to gain further evidence around AMR.

#### **D-PrEP or D-PEP:**

• Dr Macias, UCLA ID

- "I believe both strategies are similarly effective in preventing STIs. The choice between them would depend on individual's sexual behaviors, specifically how frequent they engage in sex that might increase their risk of STIs.
- For instance, D-PrEP might be more suitable for someone using D-PEP more than four times per week, and vice versa."

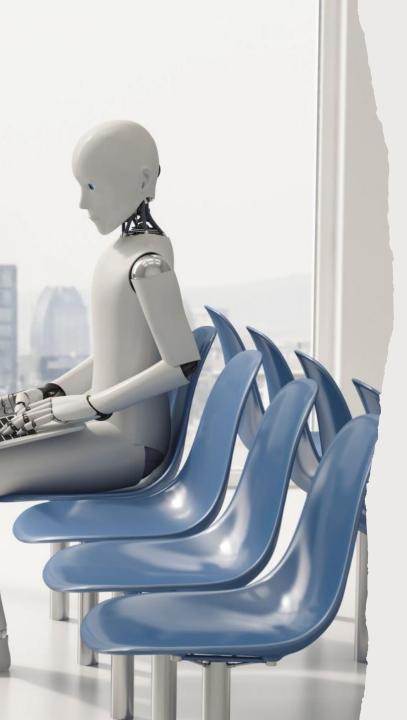
## Improving PrEP uptake by fewer appointments??:





Six-monthly PrEP monitoring as a standard of care, instead of every three months, could address an obstacle to PrEP uptake and reduce the total number of visits without resulting in increased STI positivity, leading to cost reductions of PrEP programs. These are preliminary results of the EZI-PrEP trial in the Netherlands. PrEP users monitored every six months made more additional STI visits than those who were monitored every three months but had fewer visits overall.

Dr Caperna: "I'm not so sure this is the way to go. Six months seems too long to wait to screen for STI's in PLH who have even one new partner a month. My take on this for now."



#### Day 5—last day

- AI
- Important session on the rapid growth of AI in healthcare including with PLH. Surprisingly, or sadly, AI has been shown to be more compassionate than healthcare workers. It's faster, cheaper, and we all need chatbot psychotherapy?

The machine is less personal, less intimidating. Maybe more approachable. Self-service gas. Self-checkout. These are inhuman. Antisocial.

- Real people need to understand and experience the benefits of compassion.
- The idea is to be other-centered. And remember the benefits of *human* community
- Robots as patients to train providers to be more compassionate?

#### Stigma and discrimination

A session peeled back the layers of <u>HIV stigma and discrimination</u>. A survey of 18,430 <u>healthcare workers across Europe</u> showed significant HIV stigma and discrimination: 69% did not agree with accurate statements related to HIV prevention and more than half are worried when providing care to people living with HIV.

Almost half of 8,128 respondents in a study on <u>HIV criminalization and enacted</u> stigma in eastern Europe and central Asia had experienced enacted stigma in healthcare settings. In Uganda, the <u>Tackle programme</u> uses football to reduce self-stigma (which affects almost 85% of people living with HIV), increase ART adherence and improve health outcomes for young people living with HIV.

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#### Day 5—We all need to get involved...

**Leadership, policy and funding:** One of the biggest obstacles to realizing the vision of ending the HIV pandemic as a threat to public health and individual well-being by 2030 is a **fall-off in funding**.

UNAIDS points to international resources for HIV in 2023 being almost 20% lower than at their peak in 2013. This will lead to more infections, and no hope for elimination.

## Last day—one of my patients shares this poem

Still Not Stopping,
by David B. Prather –
The Ekphrastic Review
Published 7/28/2024



 Just as my body was ready for desire, AIDS crept into daily life, even into the hidden hinterland

of West Virginia. I was terrified of sex before I knew what it was, what it could be. I was terrified

of the red serpent I knew must slither through the woods waiting for me to be baptized in those intimate waters.

All those years ago, such desires. And all these years later, still no stopping.

 Overwhelmed by attraction, my blood flowed inconveniently at the sight of women, the visions of men. • I didn't know I could separate pleasure and love and still be human. I grew up where religion was a disease, not a path

to enlightenment.
It got into an open wound and flourished in my body until I hated myself.

I cocooned my fear, let it butterfly into self-destruction, all those unprotected nights, those at-risk days.

Somehow, I'm still here. But so is that viper with its needle-sharp fangs, its venom in so many lovers' veins.

#### Long-acting technologies

A "miracle prevention tool" is how UNAIDS Executive Director Winnie Byanyima described Gilead's twice-yearly injectable lenacapavir for HIV prevention. Full results from the <u>PURPOSE 1 trial</u>, presented at AIDS 2024, confirmed that lenacapavir gave 100% protection against HIV acquisition in cisgender women; between 1% and 2% of women using daily F/TAF or F/TDF acquired HIV.

#### Leadership, policy and funding

• : One of the biggest obstacles to realizing the vision of ending the HIV pandemic as a threat to public health and individual well-being by 2030 is a **fall-off in funding**. UNAIDS points to international resources for HIV in 2023 being almost 20% lower than at their peak in 2013. This will lead to more infections, and no hope for elimination.

#### AIDS is still with us

: UNAIDS shared updated global HIV data. There is real concern that the world will not meet the UNAIDS 2030 95-95-95 targets. The report shows that 39.9 million people were living with HIV in 2023 (from 39 million in 2022). About 1.3 million people acquired HIV in 2023 – more than three times the 2025 target of 370,000. About 630,000 people died from AIDS-related illnesses worldwide in 2023 – a death every minute and way above the 2025 target of 250,000.

A study led by UNAIDS set out the cost of inaction

and failure to meet the targets. It found that if we fail to meet the 95-95-95 targets, the human cost will include 34.9 million new HIV acquisitions and 17.7 million AIDS-related deaths from 2021 to 2050. The economic cost of inaction will be huge, more than USD 8,200 per person.

One of my patients shared this poem with me:

Still Not Stopping, by David B. Prather
- The Ekphrastic Review

 Stop AIDS, by Keith Haring (USA) 1989



#### **Still No Stopping**

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David B. Prather

David B. Prather still lives a life of Sunday dinners and lawn mowing in Parkersburg, WV. He is the author of three poetry collections: We Were Birds (Main Street Rag, 2019), Shouting at an Empty House (Sheila-Na-Gig, 2023), and the forthcoming Bending Light with Bare Hands (Fernwood Press, 2024).

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#### Spirituality PLH

- Enhanced engagement for individuals with interrupted HIV treatment through person-centered empathetic communication ("Uzwelo/Empathy"): a quasi-experimental study
- Zimbabwe

#### My Experience at AIDS 2024, PLHA

- My Experience at AIDS 2024
- By Wanda London
- PLHA
- Peer Navigator / UCSD, Christie's Place/Board of Director's

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- Global Village:
- Tuesday, July 23<sup>rd</sup>

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• Global Village's official opening was on July 23rd. This year we marked the 20th anniversary of the Global Village. The Global Village was initially launched in Bangkok in 2004, to bring together ideals from different perspectives from sciences, community, and leadership in the global HIV response. The mission was, and remains, to increase public awareness and participation and to create a dynamic environment with learning opportunities for everyone involved.

#### My Experience at AIDS 2024

• Summary:

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- No one size fits all (ex. Mick Jagger vs King Charles) different approach, lifestyle.
- You have to go where the female population resides.
- Women's infection rates in the US are 25% vs the world's 55%
- Shared decision-making should be the norm. Communities of color do not feel heard.
- Achieve one voice "By the Community for the Community"
- Honor people's time/ value = reimbursement.
- Even tho HIV is treatable with medication. The stigma is still there. A strong reason why
  people are out of care.
- Going back to the basic
- Developing language to use in treatment
- Active listening and not assuming
- Ensuring that everyone is present at the table.