HIV and COVID-19: Impact on Susceptibility, Disease, and Long-Term Complications

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Financial Relationships With Commercial Entities

Dr Gandhi has no relevant financial affiliations to disclose. (Updated 05/20/21)

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe the potential impact of HIV on COVID-19 outcomes
- Discuss the impact of COVID-19 disruptions to the HIV care cascade
- Propose novel solutions to increasing HIV testing in the aftermath of COVID-19

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The two great viral pandemics of our day





Adults and children estimated to be living with HIV | 2019

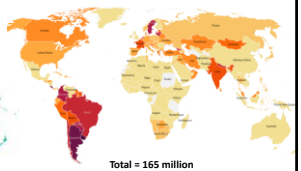


Total: 38.0 million [31.6 million–44.5 million]

Deaths = 37.2 million since beginning of pandemic

Although first reported June 5, 1981, declared an epidemic in 1985

COVID-19 cases around the world (May 20, 2021)

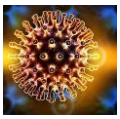


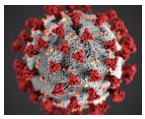
Total = 165 million

Deaths = 3.4 million since beginning of pandemic

Pandemic declared March 11, 2020

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Next….

What is the effect of HIV on COVID-19?

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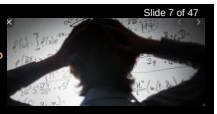
ARS 1: Which antiretroviral(s) have been studied in clinical trials against SARS-CoV-2?

1) Tenofovir disoproxil fumarate (TDF)
2) Tenofovir alafenamide (TAF)
3) Lopinavir/ritonavir
4) Atazanavir/ritonavir
5) TDF + lopinavir/ritonavir

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Are there reasons to think PWH could have worse outcomes with COVID-19?



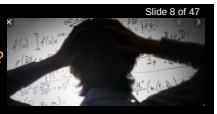
Theoretically yes

- PWH (especially those with low CD4 counts and high viral loads) are immunosuppressed, risk factor for ARDS in other viral infections
  - Severe immunosuppression, such in the case of solid organ transplants, appears to be a risk factor for severe COVID-19; while biologics appear less associated[1]
- PLHIV have an increased frequency of some of the known risk factors associated with severe COVID-19[1]
  - Nearly half of the PWH in the U.S. are >50 years[2]
  - PWH have a higher rate of cardiovascular disease and pulmonary disease, including chronic obstructive pulmonary disease, than general population[3,4]
  - Higher rates of poverty and marginal housing among our safety-net populations[5]

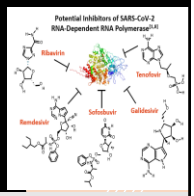
[1]Fung CID 2020 and CDC. https://www.cdc.gov/media/releases/2020/p0625-update-expands-covid-19.html; [2] CDC. HIV over 50. https://www.cdc.gov/hiv/group/age/olderamericans/index.html; [3]Triant. Curr HIV/AIDS Rep. 2013; [4]Fitzpatrick. AIDS 2020; Sachdev JAIDS 2020

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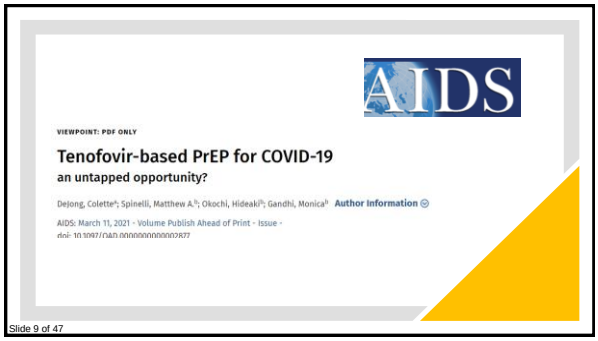
Are there reasons to think PWH could have better outcomes with COVID-19?



- ***Theoretically yes***
  - Tenofovir may inhibit replication of the SARS-CoV-2 virus[1] (looks like remdesivir which decreases hospitalization with SARS-CoV-2[2])
  - Lopinavir/ritonavir and atazanavir/ritonavir MAY have effects but not in studies
  - HIV or tenofovir could have immunomodulatory effects and could help w/ inflammation in severe disease with COVID-19
  - Study in Spain of HCW randomized to TDF/FTC versus placebo on susceptibility to SARS-CoV-2 (NCT04334928; results pending)
  - Cohort study of HIV/COVID-19 in Spain vs. no impact in PrEP[5]
  - Those with HIV may be social distancing more from concern



[1]Elfiky NEJM 2020; [2]Beigel NEJM 2020; [3]Goldman NEJM 2020; [4]Cao NEJM 2020; SOLIDARY trial WHO June 4, 2020 [5]Ayerdi OFID



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ARS 2: What is the current state of knowledge regarding HIV influencing COVID-19 in the U.S. and Europe?

1) HIV increases susceptibility to COVID
2) HIV increases severe outcomes with COVID
3) HIV does not seem to make COVID outcomes worse
4) HIV decreases susceptibility to COVID
5) HIV does not seem to (by itself) increase susceptibility to or severe outcomes with COVID

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Many smaller studies, but three larger studies on HIV influencing COVID-19

Spain, VA system in U.S., South Africa

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Annals of Internal Medicine ORIGINAL RESEARCH

Incidence and Severity of COVID-19 in HIV-Positive Persons Receiving Antiretroviral Therapy

A Cohort Study

Julia del Amo, MD, PhD; Rosa Polo, MD, PhD; Santiago Moreno, MD, PhD; Asunción Díaz, MD, PhD; Esteban Martínez, MD, PhD; José Ramón Arribas, MD, PhD; Inma Jarrín, PhD; and Miguel A. Hernán, MD, DrPH; for The Spanish HIV/COVID-19 Collaboration*

- One of largest studies to date of HIV and COVID-19
- Of 77,590 PWH receiving ART, 236 were diagnosed with COVID-19 in February – April 2020
  - 151 were hospitalized, 15 admitted to the ICU
  - 20 died
- HIV did not increase susceptibility to SARS-CoV-2 and did not increase outcome severity of COVID-19
- Effect of ART?

Ann Intern Med. 2020;[Epub]

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Risk and Outcomes of COVID-19 in Persons With HIV Receiving ART in Spain

- Patients receiving TDF (but not TAF) had *BETTER* outcomes: Is TDF protective or are those receiving TDF healthier (due to propensity to switch patients with comorbidities to TAF) – channeling bias?

Risk per 100,000 Persons Among PWH Receiving ART (95% CI)		PCR-Confirmed COVID-19 Diagnosis	COVID-19 Hospital Admission	COVID-19 ICU Admission	COVID-19 Death
Overall		30.4 (26.7-34.6)	19.5 (16.5-22.8)	1.9 (1.1-3.2)	2.6 (1.6-4.0)
Standardized*		30.0 (29.8-30.2)	17.8 (17.7-18.0)	2.5 (2.4-2.6)	3.7 (3.6-3.8)
Sex	• Men	35.1 (30.4-40.3)	23.4 (19.6-27.7)	2.1 (1.1-3.6)	2.8 (0.6-4.5)
	• Women	16.4 (11.2-23.2)	7.7 (4.3-12.7)	1.5 (3-4.5)	2.1 (0.6-5.3)
Age, yrs	• 20-39	28.3 (20.3-38.3)	10.3 (5.8-17.6)	0.7 (0-3.8)	0 (-2.9)†
	• 40-49	27.9 (20.9-36.4)	20.1 (14.3-27.5)	0.5 (0-2.9)	1.0 (0.1-3.7)
	• 50-59	26.3 (21.0-32.5)	16.7 (12.6-21.8)	2.2 (0.9-4.5)	2.2 (0.9-4.5)
	• 60-69	38.8 (26.9-54.2)	27.4 (17.6-40.8)	4.6 (1.2-11.7)	4.6 (1.2-11.7)
	• 70-79	83.7 (52.4-126.7)	72.3 (43.5-112.9)	7.6 (0.9-27.5)	26.6 (10.7-54.9)
NRTI	• FTC/TDF	16.9 (10.5-25.9)	10.5 (5.6-17.9)	0 (-2.9)†	0 (-2.9)†
	• FTC/TAF	39.1 (31.8-47.6)	20.3 (15.2-26.7)	2.7 (1.1-6.5)	3.9 (1.9-7.2)
	• ABC/3TC	28.3 (21.5-36.7)	23.4 (17.2-31.1)	3.0 (1.1-6.5)	4.0 (1.7-7.8)
	• Other regimens	29.7 (22.6-38.4)	20.0 (14.2-27.3)	1.0 (0.1-3.7)	1.0 (0.1-3.7)

COVID-19 outcomes among PWH in New York State

- The largest study to date of HIV and COVID-19 in U.S. 2988 PWH diagnosed with COVID-19
- Similar rate of COVID-19 diagnosis to those without HIV, (RR 0.94) but higher hospitalization (RR 1.38: 95%CI: 1.29-1.47), and elevated mortality (RR 1.23; 95% CI: 1.07-1.40)
- Higher mortality rate among those with CD4<200 and unsuppressed viral load


Original Investigation | Infectious Diseases

February 3, 2021

COVID-19 Outcomes Among Persons Living With or Without Diagnosed HIV Infection in New York State

James M. Tesoriero, PhD[1,2,3]; Carol-Ann E. Swain, PhD[1]; Jennifer L. Pierce, BS[1]; et al

Author Affiliations | Article Information

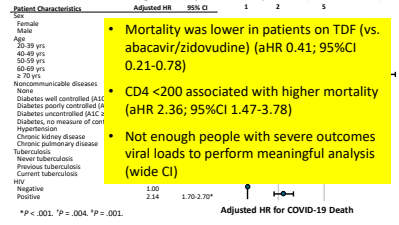
JAMA Netw Open. 2021;4(2):e2037069. doi:10.1001/jamanetworkopen.2020.37069

COVID-19 Resource Center

[1] Tesoriero et al. JAMA Network Open 2021

COVID-19 and HIV: Routine Public Sector Data in Western Cape, South Africa

- Evaluated factors among all adult public sector patients (N = 3,460,932)



*P < .001. †P = .004. ‡P = .001.

- Mortality was lower in patients on TDF (vs. abacavir/zidovudine) (aHR 0.41; 95%CI 0.21-0.78)
- CD4 <200 associated with higher mortality (aHR 2.36; 95%CI 1.47-3.78)
- Not enough people with severe outcomes viral loads to perform meaningful analysis (wide CI)

22,308 total persons diagnosed with COVID-19; 3978 PWH diagnosed with COVID-19

Standard mortality ratio for COVID-19 death with vs without HIV: 2.39 (95% CI: 1.96-2.86)

Boulle. CID. 2020

DHHS Interim Guidance Feb 26, 2021: Newer data suggests some additional cause for concern

"Many people with HIV have one or more comorbidities that may put them at increased risk for a more severe course of COVID-19. Both COVID-19 and HIV disproportionately affect communities of color. Based on the available literature, close monitoring is warranted for all people with HIV and SARS-CoV-2 infection, especially those with advanced HIV or with comorbidities."

REVIEW

The first 6 months of HIV-SARS-CoV-2 coinfection: outcomes for 6947 individuals

Rowena Johnston

DHHS. Interim Guidance on HIV and COVID-19. Updated Feb 26, 2021; Johnston R. Current Opinion HIV/AIDS. January 2021

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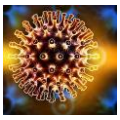
THE LANCET
HIV

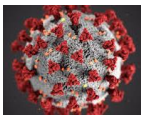
SARS-CoV-2 seroprevalence, and IgG concentration and pseudovirus neutralising antibody titres after infection, compared by HIV status: a matched case-control observational study

Matthew A Spinelli, Kara L Lynch, Cassandra Yun, David V Glidden, Michael J Peluso, Timothy J Henrich, Monica Gandhi, Lillian B Brown

Response to COVID-19 vaccines in those with HIV being studied

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Next….

What about the effect of COVID-19 on HIV?

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ARS 3: What are estimates of decreases in HIV testing from large urban centers in U.S. with COVID-19 pandemic?

1) HIV testing down 5%
2) HIV testing down 10%
3) HIV testing down 15-30%
4) HIV testing down 50-85%
5) HIV testing down 100%

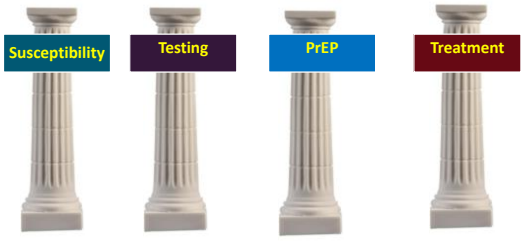
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The Pandemic's Hidden Victims: Sick or Dying, but Not From the Virus

Impact of COVID-19 on HIV – Expected to derail treatment, PrEP, increase loneliness, substance use, depression

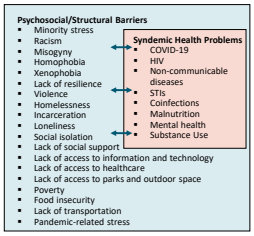
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What is impact of COVID-19 on pillars of HIV control?



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Physical, Emotional, and Social Well-being of PWH Threatened



- Mental health
- Substance use
- Poverty
- Loneliness
- Medical mistrust
- Food insecurity
- Housing insecurity
- Racism, homophobia

….from COVID-19 public health response all likely to affect PWH disproportionally

Shiau. AIDS Behav. 2020;24:2244.

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POLITICS

If COVID-19 isn't driving a dramatic increase in homeless deaths in SF, then what is?

San Francisco Chronicle

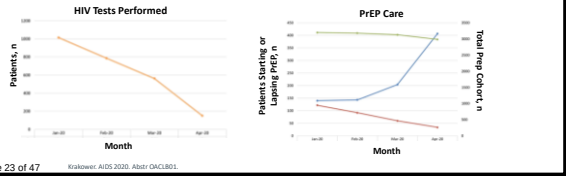
New numbers provided to The Chronicle show 1,070 bodies were examined by the San Francisco Medical Examiner's Office from Jan. 1 through Aug. 31. And 468 of them died of an overdose.

~123 deaths from COVID-19 during same period in San Francisco

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Access to HIV Testing and PrEP Care in Boston

- Analysis of electronic health records data from January 2020 through April Fenway Health, a community health center in Boston specializing in LGBTC healthcare
  - HIV tests decreased by 85.1%; lapses in refilling PrEP prescriptions rose by 191%
  - Patients starting PrEP fell by 72.1%, starting PrEP fell by 72.1%, total number of patients with an active PrEP prescription decreased by 18.3%



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Krakower. AIDS 2020. Abstr OACLB01.

Viral Suppression Rates and Retention in Care at Ward 86 in San Francisco, CA Following Shelter-in-Place

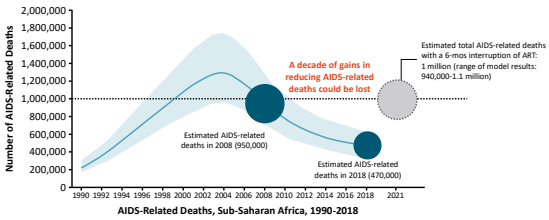
- Assessed viral suppression and retention in care after transition to telemedicine at Ward 86
  - January/February 2020 vs April 2020
  - Used propensity score analysis to assess the primary outcome of viral suppression
- **Odds of viral non-suppression 32% higher in April 2020 vs pre-COVID (aOR: 1.32; 95% CI: 1.08-1.53)**
  - Odds 3-fold higher for homeless individuals in April 2020 vs other groups
  - Black patients had lower odds of viral suppression both before and after start of COVID-19
- 54% of scheduled visits were telephone visits after shelter-in-place
- 31% did not attend visits pre-COVID vs 30% after shelter-in-place order
  - Younger individuals (< 35 yrs) had fewer no shows after transition to telemedicine
  - Fewer no shows for telephone visits
  - Homeless individuals had stable to improved retention in care



Spinelli. AIDS. 2020;

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Potential Cost of Interruption of HIV Services in Sub-Saharan Africa



UNAIDS. Modelling the extreme—COVID-19 and AIDS-related deaths. May 25, 2020. Jewell. Lancet HIV. 2020;[Epub].

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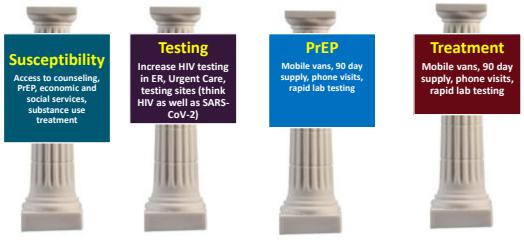
Impact of COVID-19 Response on ART Availability and Other Epidemic Diseases

- UNAIDS: generic ART availability in low- and middle-income countries[1]
  - *"Lockdowns have impacted both the transport of goods across the value chain of production and the distribution of HIV medicines"*
  - *"Barriers to the supply chain and a forecasted economic shock indicate possible fluctuation in the availability of antiretroviral medicines and an increase in cost"*
  - *"Coordinated action by governments is necessary to ease the supply chain and the distribution of medicines to facilities"*
- Healthcare workers in Africa are reporting disruptions in testing and treatment for HIV, TB, and malaria[2,3]

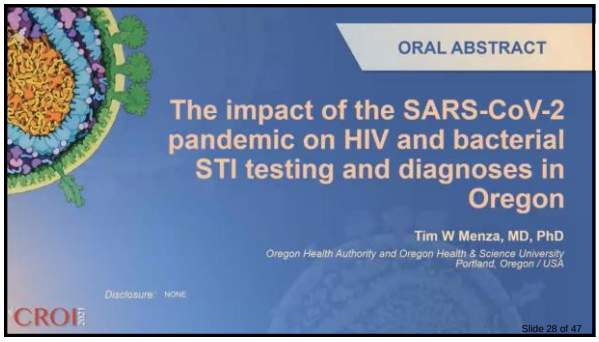
1. UNAIDS. The impact of the COVID-19 response on the supply chain, availability and cost of generic antiretroviral medicines for HIV in low- and middle-income countries. June 22, 2020. 2. Adepoju. Lancet HIV. 2020;7:E319. 3. Amimo. Tropical Medicine and Health. 2020;48:32.

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What can we do?



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Background

- Mitigation measures for SARS-CoV-2 have had unprecedented effects on public HIV and STI programs [ASM, 2020; Tao et al, 2021]
  - Elimination of services, including outreach and partner services
  - Reduction of in-person visits
  - Increase in telehealth
  - Testing supply shortages
- National declines in STI diagnoses despite previously increasing case counts [CDC, 2020]
- Reports of decreased access to sexual health services but an increase sexual partners among MSM [Sanchez et al, 2020; Fredrickson et al,

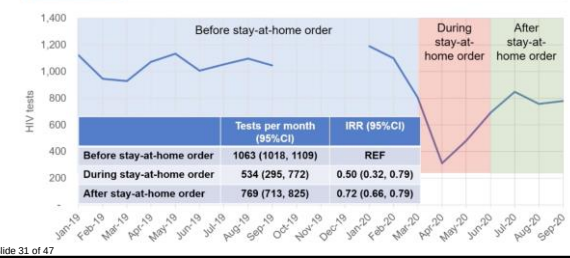
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Methods

- January through September of 2019 and 2020
- Outcomes
  - Monthly HIV, NG/CT, and syphilis tests
  - Monthly HIV, NG, CT, and primary and secondary syphilis diagnoses
- Predictors
  - **Before stay-at-home order (reference)**
    - January 2019 through September 2019 ***AND*** January through February 2020
  - **During stay-at-home order**
    - March 2020 through May 2020
  - **After stay-at-home order**
    - June 2020 through September 2020

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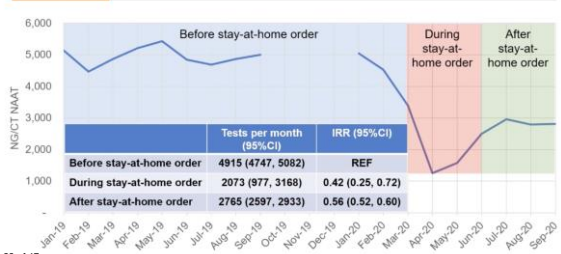
4th generation Ag/Ab HIV tests



	Tests per month (95%CI)	IRR (95%CI)
Before stay-at-home order	1063 (1018, 1109)	REF
During stay-at-home order	534 (295, 772)	0.50 (0.32, 0.79)
After stay-at-home order	769 (713, 825)	0.72 (0.66, 0.79)

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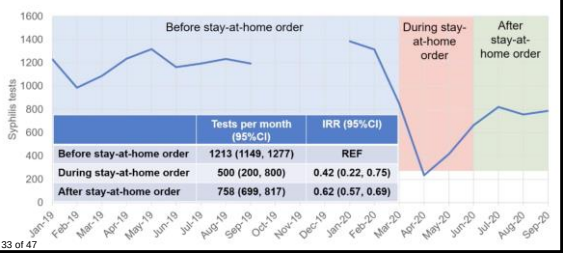
NG/CT nucleic acid amplification tests



	Tests per month (95%CI)	IRR (95%CI)
Before stay-at-home order	4915 (4747, 5082)	REF
During stay-at-home order	2073 (977, 3168)	0.42 (0.25, 0.72)
After stay-at-home order	2765 (2597, 2933)	0.56 (0.52, 0.60)

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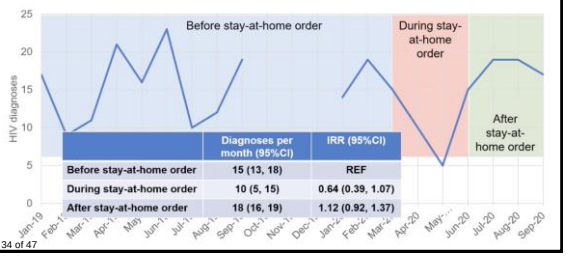
Syphilis tests



	Tests per month (95%CI)	IRR (95%CI)
Before stay-at-home order	1213 (1149, 1277)	REF
During stay-at-home order	500 (200, 800)	0.42 (0.22, 0.75)
After stay-at-home order	758 (699, 817)	0.62 (0.57, 0.69)

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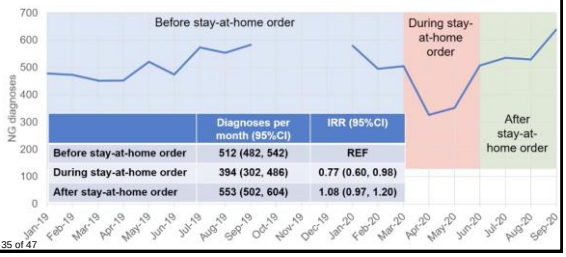
HIV diagnoses



	Diagnoses per month (95%CI)	IRR (95%CI)
Before stay-at-home order	15 (13, 18)	REF
During stay-at-home order	10 (5, 15)	0.64 (0.39, 1.07)
After stay-at-home order	18 (16, 19)	1.12 (0.92, 1.37)

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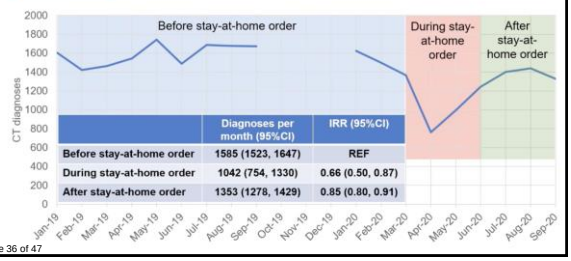
Gonorrhea diagnoses



	Diagnoses per month (95%CI)	IRR (95%CI)
Before stay-at-home order	512 (482, 542)	REF
During stay-at-home order	394 (302, 486)	0.77 (0.60, 0.98)
After stay-at-home order	553 (502, 604)	1.08 (0.97, 1.20)

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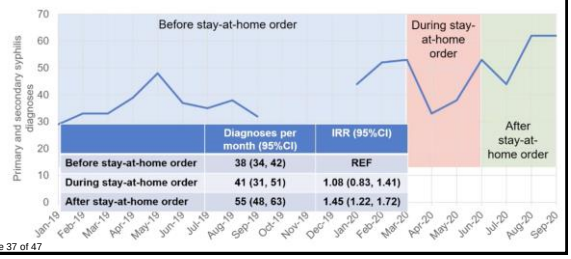
Chlamydia diagnoses



	Diagnoses per month (95%CI)	IRR (95%CI)
Before stay-at-home order	1585 (1523, 1647)	REF
During stay-at-home order	1042 (754, 1330)	0.66 (0.50, 0.87)
After stay-at-home order	1353 (1278, 1429)	0.85 (0.80, 0.91)

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Primary and secondary syphilis diagnoses



	Diagnoses per month (95%CI)	IRR (95%CI)
Before stay-at-home order	38 (34, 42)	REF
During stay-at-home order	41 (31, 51)	1.08 (0.83, 1.41)
After stay-at-home order	55 (48, 63)	1.45 (1.22, 1.72)

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Summary

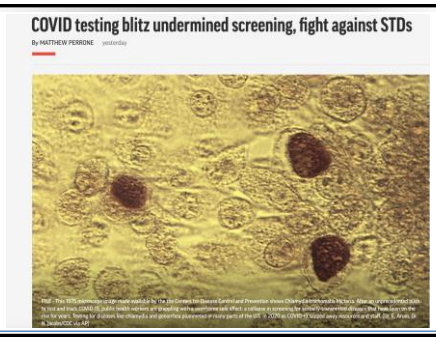
- Public sector testing
  - Testing for HIV and bacterial STI declined dramatically during the stay-at-home order in Oregon
  - Testing did not recover to 2019 levels by September 2020
- Diagnoses
  - Diagnoses of CT (more likely to present asymptomatically) were lower during ***and*** after the stay-at-home order
  - Primary and secondary syphilis diagnoses increased 45% after the stay-at-home order
  - While not statistically significant, HIV and NG diagnoses rose 12% and 8%, respectively, after the stay-at-home order

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Public health implications

- The mismatch in the availability of sexual health services and ongoing sexual behavior during the pandemic may result in increased HIV and STI transmission
- Ongoing monitoring of HIV testing and diagnoses in the context of SARS-CoV-2 is critical
- Public health agencies must find ways to provide sexual health services during the SARS-CoV-2 pandemic and beyond

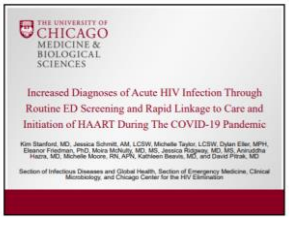
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COVID testing blitz undermined screening, fight against STDs

By MATTHEW PERRONE yesterday

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New study from University of Chicago (e.g. what can we do?)


THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

Increased Diagnoses of Acute HIV Infection Through Routine ED Screening and Rapid Linkage to Care and Initiation of HAART During The COVID-19 Pandemic

Kim Stanford, MD, Jessica Schmitt, AM, LCSW, Michelle Taylor, LCSW, Dylan Eller, MPH, Eleanor Friedman, PhD, Moira McNulty, MD, MS, Jessica Roggeay, MD, MS, Aniruddha Hazra, MD, Michelle Moore, RN, APN, Kathleen Beavis, MD, and David Pitrak, MD

Section of Infectious Diseases and Global Health, Section of Emergency Medicine, Clinical Microbiology, and Chicago Center for the HIV Elimination

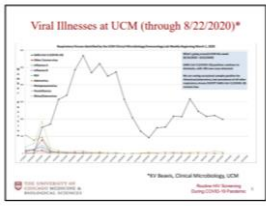

IDWeek

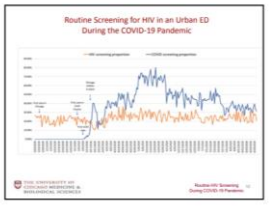
Advancing Science. Improving Care

Chasing the Sun

24 hours of COVID-19 followed by IDWeek

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Testing volumes for HIV decreased from 22,502 to 11,766 tests from Jan-Feb to April-May in this U. of Chicago system (15 health care sites South/West Chicago with expanded testing)

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Expanded HIV testing during COVID-19 testing

- Drew tube of blood if indicated in U. of Chicago system
- Sent for HIV Ag/Ab screening
- Identified 13 acute HIV infections in 40 days since starting program
- Can also think of rapid HIV testing (saliva)
- Think creatively on how to keep our testing, prevention, treatment goals up during this time

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UNAIDS

PREVAILING AGAINST PANDEMICS
BY PUTTING PEOPLE AT THE CENTRE

2020 World AIDS Day report



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ARS 4: How many deaths from AIDS occurred in 2019?

1) 200,000
2) 300,000
3) 500,000
4) 700,000
5) 1 million

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Collective global efforts that prioritize people can transform the COVID-19 crisis into an opportunity to accelerate the HIV response.

Five years after a global commitment to Fast-Track the HIV response and end AIDS by 2030, the world is off track. A promise to build on the momentum created in the first decade of the twenty-first century by front-loading investment and accelerating HIV service provision has been fulfilled by too few countries. Important gains in the most affected regions of sub-Saharan Africa and the Caribbean have been counterbalanced by rising epidemics in Latin America, eastern Europe and central Asia, and the Middle East and North Africa. Combined, these successes and failures result in global progress that is far too slow. Agreed milestones for 2020 have been missed. Nearly 700 000 deaths from AIDS-related causes and an 1.7 million new HIV infections in 2019 are unacceptable when effective therapeutics and prevention options are affordable and readily available.

Insufficient investment and action on HIV and other long-running pandemics have also left the world exposed to a new global health threat: COVID-19. Had health systems and social safety nets been even stronger, the world would have been better positioned to slow the spread of the novel coronavirus and withstand its impact.

The need for decisive action against deadly pandemics has never been clearer. Humanity must heed this latest warning to pay much greater attention to building global pandemic response capacity and fulfilling the right to health. There is a solid foundation to build on. The architecture,

Emergency use authorizations, fast reviews, nimble pivoting, vaccines, etc. in COVID-19 all informed by HIV

2025 targets



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Harm reduction can inform both HIV and COVID-19 prevention





Message kindly and effectively





Harm reduction—when applied to disease prevention for infectious diseases—is the principle of advising individuals how to mitigate risk, while acknowledging the real world conditions that may lead individuals to take some risks

IDEAS *The Atlantic*

The Danger of Assuming That Family Time Is Dispensable

Americans who are desperate to see their loved ones need advice that goes beyond "Just say no."

DECEMBER 8, 2020

Julia Marcus

Epidemiologist and professor at Harvard Medical School

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Question-and-Answer Session