What's New in Opportunistic Infections and…Washington, DC

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe trends in HIV and opioid use disorder in Washington, DC
- Identify preferred regimens for tuberculosis chemoprophylaxis
- Prescribe newer immunizations appropriately in their medical practices

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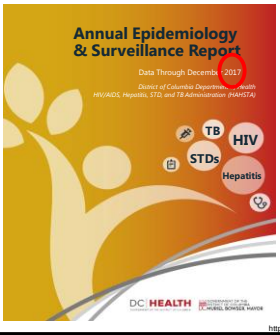

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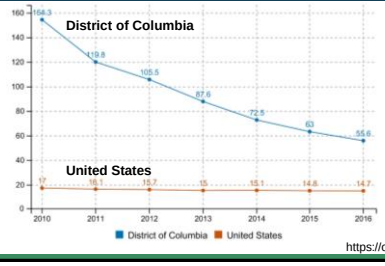
https://dchealth.dc.gov/HAHSTA2018AnnualReport

New HIV Diagnoses per 100,000 In Washington DC and the United States



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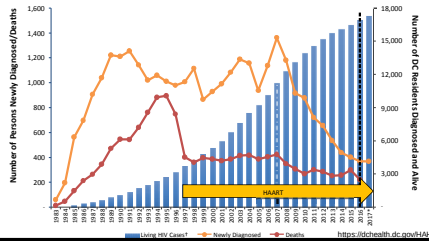
https://opioid.amfar.org/DC

Newly Diagnosed HIV Disease Cases, Deaths, and Living HIV Cases, by Year, District of Columbia, 1983-2017



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https://dchealth.dc.gov/HAHSTA2018AnnualReport

Of Those Newly Diagnosed with HIV in the District, 2013-2017

1 in 5
Black Women

1 in 3
Men Who Have Sex with Men of Color

1 in 3
20-29 YO

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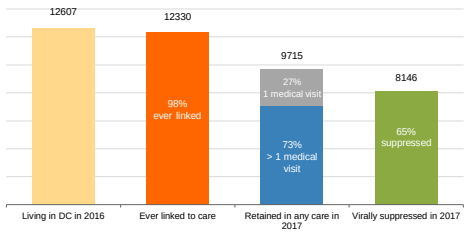
2017 Care Dynamics HIV Cases Living in DC, District of Columbia



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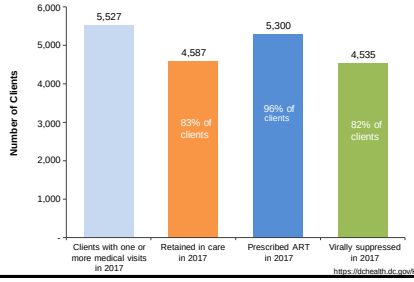
2017 Care Dynamics among Ryan White Clients, District of Columbia



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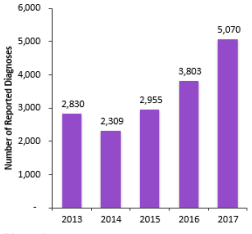
STDs Are An Ominous Indicator: Gonorrhea

Newly Reported Diagnoses of Gonorrhea, by Year, District of Columbia, 2013-2017



Of those newly reported with Gonorrhea in DC in 2017...

1 in 7 were aged 15-19	**7 in 10** were Men
1 in 5 were aged 20-24	**1 in 5** Men had an extra-genital diagnosis

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HIV Co-Morbidities and Co-Factors

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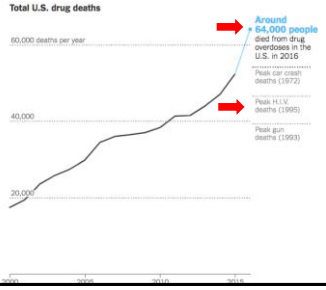
Rise in Overdose Deaths, 2000-2016



NYTimes

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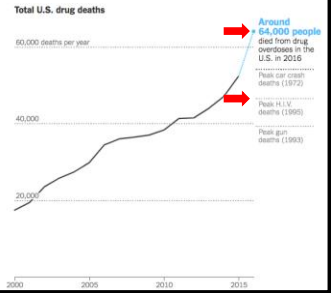
Rise in Overdose Deaths, 2000-2016

- **Washington, DC**
  - 30 overdose deaths per 100,000 residents
- **Baltimore City**
  - 35 overdose deaths per 100,000 residents



NYTimes

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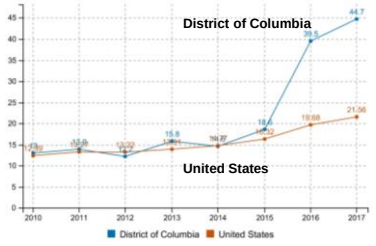
Drug-related Deaths per 100,000



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https://opioid.amfar.org/DC

DC Opioid Overdose Deaths Driven by Heroin and Synthetic Opiates

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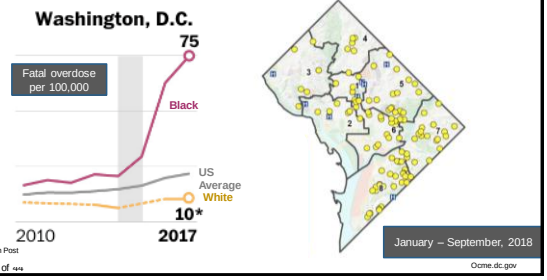
https://sanjaybasu.shinyapps.io/opioid_geographic/

Overdose Rates Highest in Black Residents



Washington Post

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Opportunistic Infections

What's New from CROI and Elsewhere

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What's New In Opportunistic Infections: 2019

- MAC
  - Primary prophylaxis no longer recommended for patients starting ART
  - (If not starting ART, MAC prophylaxis is likely "an academic issue"
- HPV
  - Recommended for males and females 9-26 yo, but discussions about use to age 45yo, and revaccinating persons who received earlier vaccines (quadrivalent)
- Zoster
- HBV
- PCP
- TB
- Talaromyces

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ARS Question 1

One of your HIV infected patients who is now 51 years of age (CD4>350/mm^3, VL<20 copies/uL on a standard ART regimen) inquires about zoster vaccine. The patient had an episode of dermatomal zoster 5 years ago that was extremely painful and prolonged, and he does not want to have another episode. He had never been received immunization for zoster.

What should you recommend

1. No vaccine is needed; the patient now has adequate immunity
2. Give attenuated vaccine
3. Give recombinant attenuated
4. Wait until the patient is 60 years old and then give a vaccine when the guidelines have better data

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Zoster Vaccine: Zostavax (LZV)
Live Attenuated Virus Vaccine-No Longer Preferred

- HIV Negative Adults
  - 1 Dose Regimen Recommended for Adults> 60 years old
  - Robust data on safety, immunogenicity, efficacy
- PLWH
  - Safe, immunogenic, reduces Zoster
  - Expert Opinion for PLWH
    - CD4>200: Effective and safe
    - CD4<200: Contraindicated

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Zoster Vaccine: Shingrix (RZV)
Recombinant VZV Glycoprotein E and Adjuvant AS01B

- HIV Negative Adults
  - 2 Dose Regimen Recommended for Adults> 50 years old
  - Robust data on safety, immunogenicity, efficacy (n=30,000)
  - Possible concerns for patients with transplants or autoimmune diseases
- PLWH
  - ACIP has not commented yet
  - Published: 94 heterogeneous HIV patients
    - Safe, immunogenic with longer lasting immunity than Zostavax

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Zoster Vaccine: Shingrix (RZV)
Recombinant VZV Glycoprotein E and Adjuvant AS01B

Expert Opinion for PLWH

- Because the vaccine is safe and immunogenic, and the risk of zoster is high, many experts are using 2 dose regimen of this vaccine
  (if available and covered by insurance)

Questions for PLWH:

- **Age less than 50 years**
- **Give pre ART or pre VL <50**
- **Duration of immunogenicity**

Safe, immunogenic with longer lasting immunity than Zostavax

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ARS Question 2

A 22 year old MSM with multiple partners was recently found to be HIV positive (CD4 =150 cells/uL, VL= 2 million copies/uL), started on an approved HIV regimen, and is now part of your patient panel for long term management.

He is Hepatitis B negative (HBsAg, HbsAb, HbcAb) and was never immunized

What do you advise him regarding HBV

1. Practice safe sex-no vaccine is indicated
2. No vaccine: wait until CD4 is >350 cells/mm^3
3. Recombinant HBsAg (3 doses)
4. Hep B recombinant, adjuvanted vaccine

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HBV Vaccine

- Who should be immunized
  - All HIV infected persons who are susceptible (HBsAb negative)
  - All family members and sexual contacts of HBV positive patients
  - HBcAb positive, HBsAb negative-controversial-probably immunize
- What Vaccine to Use
  - Recombinant HBsAg
    - Less immunogenic in PLWH but recommended by ACIP
  - Recombinant CpG1018 with TLR-9 agonist
    - One dose HIV Negative
    - More immunogenic than Engerix B 3 doses
    - Trend: more cardiovascular events---a concern!
  - PLWH: Limited data
- What Do Experts Do
  - Not certain: some use Hep B recombinant, adjuvanted vaccine ….some don't!

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ARS Question 3

A 28 year old male was found to be HIV positive at the STD clinic and is referred to you for initial management. CD4 = 100 cells/mm^3, VL = 1 million copies/uL. He has lived in Washington DC all his life and has no unusual exposures.

The patient will start on dolutegravir-emtricitabine-tenofovir-alafenamide and seems like he will be compliant.

What do you recommend for opportunistic infection chemoprophylaxis?

1. PCP prophylaxis only
2. MAC prophylaxis only
3. PCP and MAC prophylaxis only
4. PCP, MAC, and fungal (crypto/candida) prophylaxis

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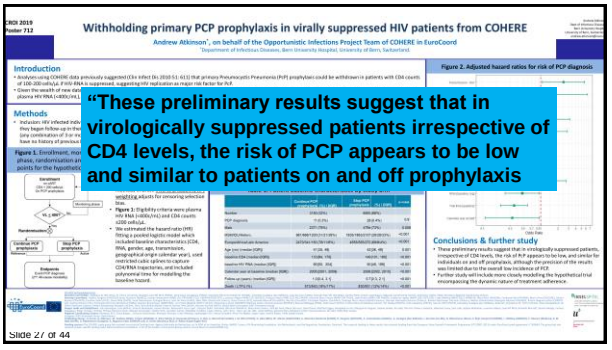

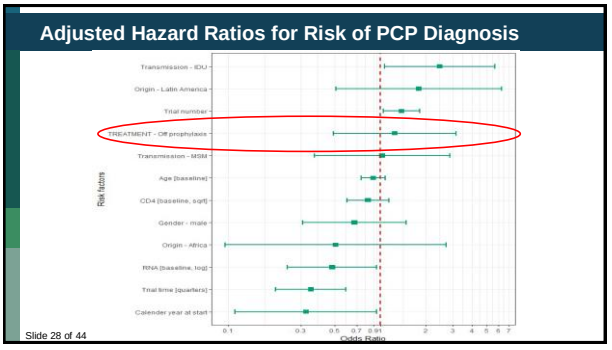

Conclusions

- But
  - Patients grouped <200 cells/mm^3
  - Prior manuscript separated 0-100 and 100-200 cells/mm^3

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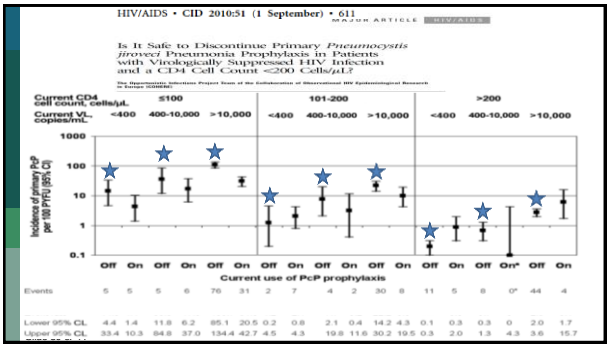

Conclusions

- What should you do?

Continue PCP prophylaxis until CD4 count >200 cells for everyone, regardless of VL or adherence to ART

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ARS Question 4

What is Talaromyces?

1. An emerging world wide pathogen that is increasingly being acquired in certain parts of the US
2. An important pathogen in immigrants and travelers from Central and South America
3. An important pathogen in immigrants and travelers from Asia
4. An important pathogen only in Asia, almost never seen in the US

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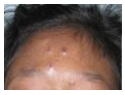
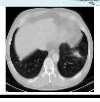
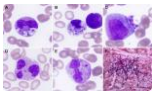
Talaromyces (Penicilliosis)







Abstracts 706 and 710

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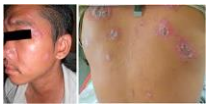
Lessons Learned



- New Development of Serum Antigen
  - Screening asymptomatic persons
  - Pre-emptive therapy

Abstracts 706 and 710

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Results of Screening

- Results for Positive Antigen
  - Mp1p 20%
  - Galactomannan 16%
  - Crypt antigen 3%
- Follow Up: Symptomatic Disease in Antigen Positive Patients
  - Mp1p 97% developed talaromyces
  - Galact 79% developed talaromyces
  - Crypt ag 62% developed cryptococcosis
- Follow Up: Symptomatic Disease in Antigen Negative Patients
  - Mp1p 4% developed talaromyces
  - Galact 14% developed talaromyces
  - Crypt ag 0% developed cryptococcosis

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Conclusions
New Technology

- Talaromyces is significantly more common in Southern China than cryptococcosis
- Screening is highly predictive of the development of active disease
- Screening and preemptive therapy would plausibly reduce morbidity and mortality
- There might be cases in US due to recent travelers and immigrants
- Does reactivation occur months or years later?

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What Regimen Should You Be Using for TB Prophylaxis in Your Practice?

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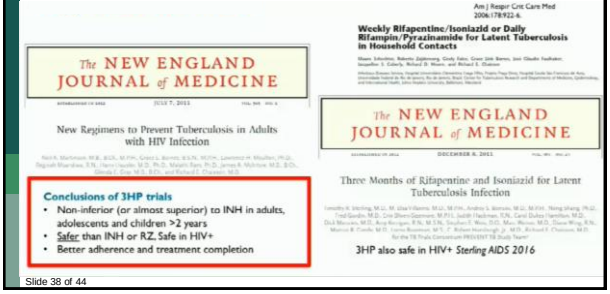
TB Preventive Therapy: Shorter & Safer Regimens are Here



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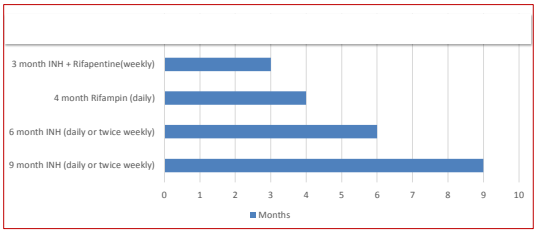
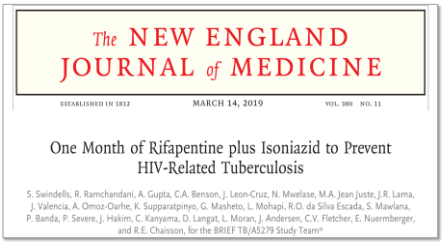
LTBI Treatment Options




The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 14, 2019 VOL. 380 NO. 11

One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis

S. Swindells, R. Ramchandani, A. Gupta, C.A. Benson, J. Leon-Cruz, N. Mwelase, M.A. Jean Juste, J.R. Lama, J. Valencia, A. Omoz-Oarhe, K. Supparatpinyo, G. Masheto, L. Mohapi, R.O. da Silva Escada, S. Mawlana, P. Banda, P. Severe, J. Hakim, C. Kanyama, D. Langat, L. Moran, J. Andersen, C.V. Fletcher, E. Nuermberger, and R.E. Chaisson, for the BRIEF TB/A5279 Study Team*

BRIEF TB

Inclusion Criteria

- HIV +
- > 13 yr old
- Positive test for LTBI or Live in an area with TB prevalence of ≥ 60 cases of TB per 100,000 population
- If on ART, receiving either EFV or NVP – at least for the 1st month

Primary Endpoint – Time to event –
- 1st diagnosis of active TB, death from TB, or death from unknown cause

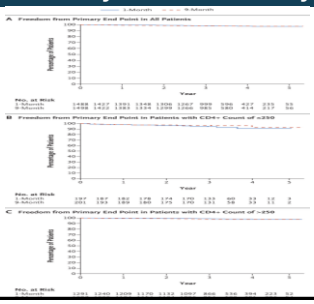
Secondary Endpoints –
- Safety, side-effect profile, deaths from other causes unrelated to TB

Kaplan–Meier Analysis of the Primary End Point

All Patients

CD4 <250

CD4 > 250



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Grade 3 or Greater Adverse Events

Table 3. Adverse Events of Grade 3 or Greater.*

Adverse Event	1-Month Group (N = 1488)				9-Month Group (N = 1498)			
	Grade 3	Grade 4	Grade 5	Grades 3–5	Grade 3	Grade 4	Grade 5	Grades 3–5
	number of patients (percent)							
Targeted adverse event†	34	9	1	44 (3)	32	20	0	52 (3)
Serious adverse event	41	22	12	75 (5)	49	25	19	93 (6)
Any systemic event	101	9	1	111 (7)	123	12	0	135 (9)
Any adverse event	198	47	5	250 (17)	213	59	2	274 (18)
Hematologic event	41	22	0	63 (4)	36	21	0	57 (4)
Thrombocytopenia	0	3	0	3 (<1)	4	1	0	5 (<1)
Anemia	6	14	0	20 (1)	8	18	0	26 (2)
Neutropenia	28	8	0	36 (2)	16	2	0	18 (1)
Hepatic event	19	9	0	28 (2)	24	18	0	42 (3)
Gastrointestinal event	29	1	1	31 (2)	22	2	0	24 (2)
Dermatologic event	8	0	0	8 (1)	11	0	0	11 (1)
Neurologic event	12	2	0	14 (1)	25	4	1	30 (2)

* There was a significant between-group difference in neutropenia and in neurologic events ($P = 0.02$ for both comparisons) at an alpha level of 0.05 with no adjustment for multiple comparisons.
† Targeted adverse events included nausea and vomiting, rash, drug-associated fever, elevated liver-enzyme levels, and peripheral neuropathy.

OR for stopping or withholding drugs during study 2.09 (95% CI 1.32, 3.33) – favoring 1 HP

	1 HP	9 H
d/c due to toxicities	16	25
Stopped for >7 days	11	31
SAE	83 (6%)	108 (7%)

Conclusions

- A 1-month regimen of rifapentine plus isoniazid was noninferior to 9 months of isoniazid alone for preventing tuberculosis in HIV-infected patients
- The percentage of patients who completed treatment was significantly higher in the 1-month group (97%) than the 9 month regimen (90%).
- Only EFV or RAL based regimens and only TDF/FTC or ABC/3TC can be used with once weekly rifapentine

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Concerns About Study

- Non Inferiority Trial
- Not Validated for Low Endemic Area
  - High Endemic Areas (90%) and Low Endemic (10%)
- Latent TB Rarely Assessed
  - Only 110/3815 (23%) were skin test or IGRA positive
- Many not on ART (50%)
- End Points
  - Included deaths of unknown cause

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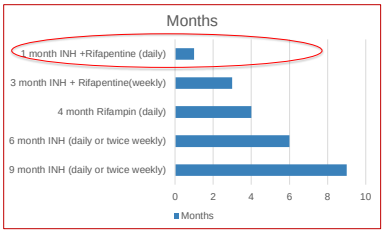
LTBI Treatment Options - 2019



1 HP is non-inferior to 9 H with better tolerability

Relevant in US?

Only use wittch raltegravir and either abv/tc or teno/emtric

Measles?

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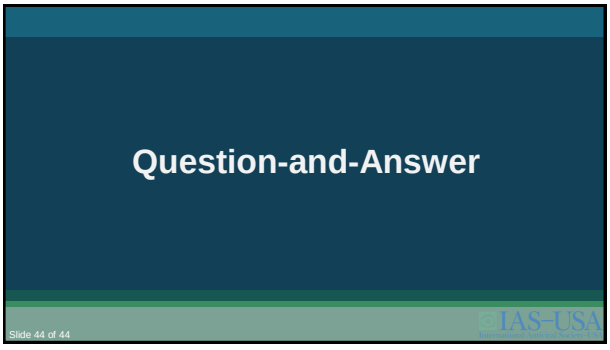
Question-and-Answer
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