

# The ART of Antiretroviral Therapy in Critically-ill Patients with HIV

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## Disclosure Statement

- I have no disclosures concerning financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation



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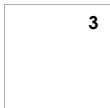
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## Pharmacist Objectives

- Describe available evidence regarding initiation of antiretroviral therapy (ART) in patients newly diagnosed with HIV with or without Opportunistic Infections
- Summarize literature on the continuation of ART in the inpatient setting for patients previously diagnosed with HIV and taking a complete antiretroviral regimen
- Recognize relevant drug-drug interactions between antiretroviral medications and other drugs commonly used in the inpatient setting



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### Technician Objectives

- Distinguish brand and generic names of HIV medications
- Recognize available dosage forms of HIV medications

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### 1981: The Beginning



<http://time.com/3503000/behind-the-picture-the-photo-that-changed-the-face-of-aids/>

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### HIV Therapy



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## HIV Medications

- **NRTIs**
  - Abacavir (Ziagen®)
  - Didanosine (Videx®)
  - Emtricitabine (Emtriva®)
  - Lamivudine (EpiVir®)
  - Stavudine (Zerit®)
  - Tenofovir alafenamide (Vemlidy®)
  - Tenofovir Disproxil Fumerate (Viread®)
  - Zidovudine (Retrovir®)
- **Entry Inhibitor**
  - Maraviroc (Selzentry®)
- **NNRTIs**
  - Delavirdine (Rescriptor®)
  - Efavirenz (Sustiva®)
  - Etravirine (Intence®)
  - Nevirapine (Viramune®)
  - Rilpivirine (Edurant®)
- **INSTIs**
  - Raltegravir (Isentress®)
  - Elvitegravir (Vitekta®)
  - Dolutegravir (Tivicay®)
- **Fusion Inhibitor**
  - Enfuvirtide (Fuzeon®)

<https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/58/da-approved-hiv-medications>

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## HIV Medications

- **Protease Inhibitors (PIs)**
  - Atazanavir (Reyataz®)
  - Darunavir (Prezista®)
  - Fosamprenavir (Lexiva®)
  - Indinavir (Crixivan®)
  - Nelfinavir (Viracept®)
  - Ritonavir (Norvir®)
- **Combination Products**
  - Abacavir/lamivudine (Epizicom®)
  - Abacavir/lamivudine/dolutegravir (Triumeq®)
  - Efavirenz/emtricitabine/tenofovir disoproxil fumerate (Atripla®)
- **Combination Products**
  - Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya®)
  - Elvitegravir/cobicistat/tenofovir disoproxil fumerate/emtricitabine (Stribild®)
  - Emtricitabine/rilpivirine/tenofovir alafenamide (Odefsey®)
  - Emtricitabine/rilpivirine/tenofovir disoproxil fumerate (Complera®)
  - Emtricitabine/tenofovir disoproxil fumerate (Truvada®)
  - Emtricitabine/tenofovir alafenamide (Descovy®)

<https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/58/da-approved-hiv-medications>

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## Opportunistic Infections

Morris A, Et al. Emerging Infectious Diseases 2004

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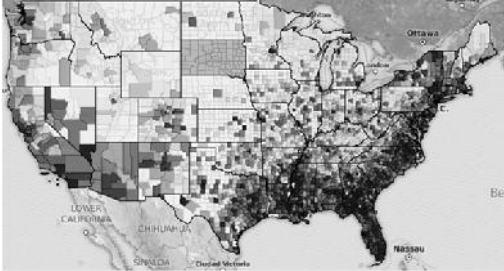
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### HIV Prevalence in the US



<http://aidsvu.org/map/>

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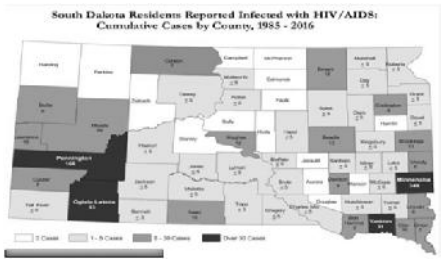
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### HIV in South Dakota



<https://doh.sd.gov/documents/statistics/ID/Nov2017.pdf>

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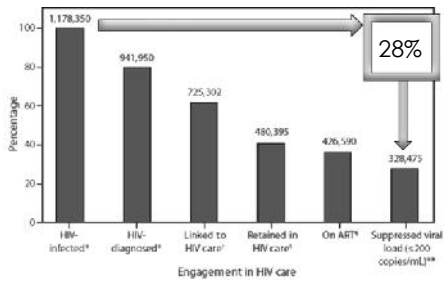
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### Recent Trends



<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6047a4.htm>

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### 2018: Why are patients with HIV in the ICU?

#### Unaware of HIV or Not in Effective Care

- Opportunistic infections
- HIV-associated neoplasms
- Non-HIV related conditions

#### Aware of HIV and Virally Suppressed

- Cardiovascular issues
- Respiratory Failure
- Sepsis
- Chronic Kidney Disease
- Gastrointestinal bleeding
- Liver disease
- Neurological conditions

Masur. HIV + Critical Illness: a Primer of ICU Management. 2015

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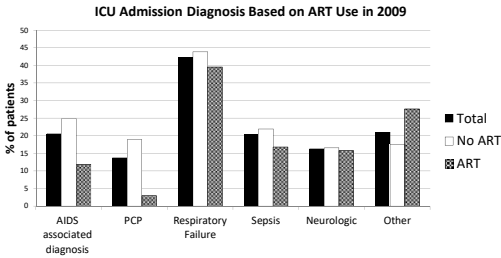
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### ICU Admission Diagnoses




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### Antiretroviral Therapy (ART) in Critically-ill Patients Newly diagnosed with HIV or Not in Effective Care

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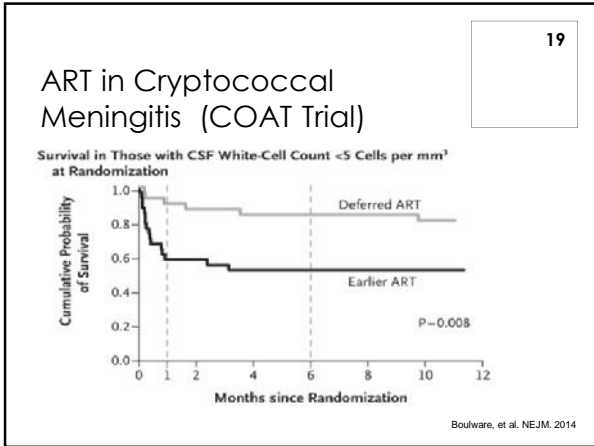
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### Continuation of ART in Patients Previously Diagnosed with HIV and Virally Suppressed

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- ### ART Continuation
- General consensus based on Expert Opinion
    - Continue ART if virally suppressed and minimal risk of drug-drug interactions or toxicity
    - Recommend drug resistance testing for any doubt of patient compliance before continuing
    - Consider drug delivery, dosing, and absorption factors
  - Holding ART can lead to viral resistance
    - Varying half lives of antiretrovirals
    - Short vs. long term interruptions
- Huang, et al. NEJM 2006  
Akgun, et al. Semin Resp Crit Care Med 2016

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### 2006: SMART Trial

■ CD4 Count Guided Interruptions in ART

	Continuation of ART (N=2752)	Interruption of ART (N=2720)	P- value
<b>All Cause Mortality</b>	30	55	0.007
<b>OIs</b>			
Serious	2	13	0.01
Non-serious	18	63	<0.001
<b>Major Cardiovascular, Renal, or Hepatic Disease</b>	39	65	0.009

OI: Opportunistic Infection

EI-Sadr, Et al. NEJM 2006

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### 2012: Continuing HAART in the ICU

	Continued ART in ICU (N=32)	Stopped ART in ICU (N=59)	P Value
Mortality at 6 months	11	27	0.04
AIDS related Events	5	20	0.07
Viral load at 6 months	2.42	3.37	0.03
Viral resistance	8	4	0.02

Maybeck, et al. AIDS Research and Therapy, 2012

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### Drug-Drug Interactions between ART and Other Medications Used in the Inpatient Setting

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### Clinical Conclusion

- ART should generally be started early in all newly diagnosed HIV+ patients presenting with OIs, or low CD4 Counts Except Cryptococcal Meningitis
- Continue ART in patients admitted to ICU who were on a complete regimen and virally suppressed
  - Improved outcomes, but possible increase in resistance due to absorption abnormalities
  - Interruption in ART can also lead to viral resistance
- Always Double check potential drug-drug interactions with ARVs and be aware of alternative methods of administering ARVs to patients in the ICU

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### Questions?




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### Assessment Question 1

**Initiation of antiretroviral therapy should be delayed in patients who present with which opportunistic infection?**

A. Pneumocystis Jiroveci Pneumonia  
 B. Toxoplasmosis  
**C. Cryptococcal Meningitis**  
 D. Mycobacterium Avium Complex

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### Assessment Question 2

**Which of the following outcomes has not been associated with the continuation of antiretrovirals in Critically-ill patients?**

A. Decreased mortality  
 B. Decreased AIDS-related events  
**C. Decreased antiretroviral resistance**  
 D. Potential drug toxicity due to drug-drug interactions

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Assessment Question 3

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A 25 yo woman with HIV as been tenofovir/emtricitabine and darunavir/ritonavir for 5 years. She was recently diagnosed with Hodgkin's Lymphoma for which she is currently being treated by an oncologist. Today, venous doppler reveals she has a lower extremity thrombus for which she will be treated with enoxaparin and transitioned to warfarin. Which of the following would be important regarding this patient's initial warfarin dosing?

- A. Initiate half the normal warfarin dose
- B. Use the standard initial warfarin dose**
- C. Double the initial warfarin dose
- D. Warfarin is contraindicated with this antiretroviral regimen

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Assessment Question 4

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Which medication is correctly matched to its commonly used brand name?

- A. Darunavir (Reyataz®)
- B. Tenofovir Disproxil Fumerate (Viread®)**
- C. Dolutegravir (Isentress®)
- D. Emtricitabine (Sustiva®)

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Assessment Question 5

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Which of the following antiretrovirals is available as an oral suspension?

- A. Dolutegravir
- B. Tenofovir alafenamide
- C. Efavirenz
- D. Raltegravir**

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