HIV Primary Care Update

Cara McAnaney, MD, AAHIVS
Assistant Professor, Director of the HIV Primary Care Track
Department of Family Medicine, UPSOM
March 8, 2025

Disclosures

No financial disclosures

Bias Disclosure

- Our biases relate to our identities
- I do not intend to perpetuate bias or stigma in this presentation
- If I do, I am likely not aware that I have done so
- If you feel comfortable, please raise your hand or enter a message into the chat that I have done so during the presentation so that I may correct my messaging and we as a group can learn from my mistakes
- Gendered language is present in parts of the presentation- this reflects the limitations in the data

Outline

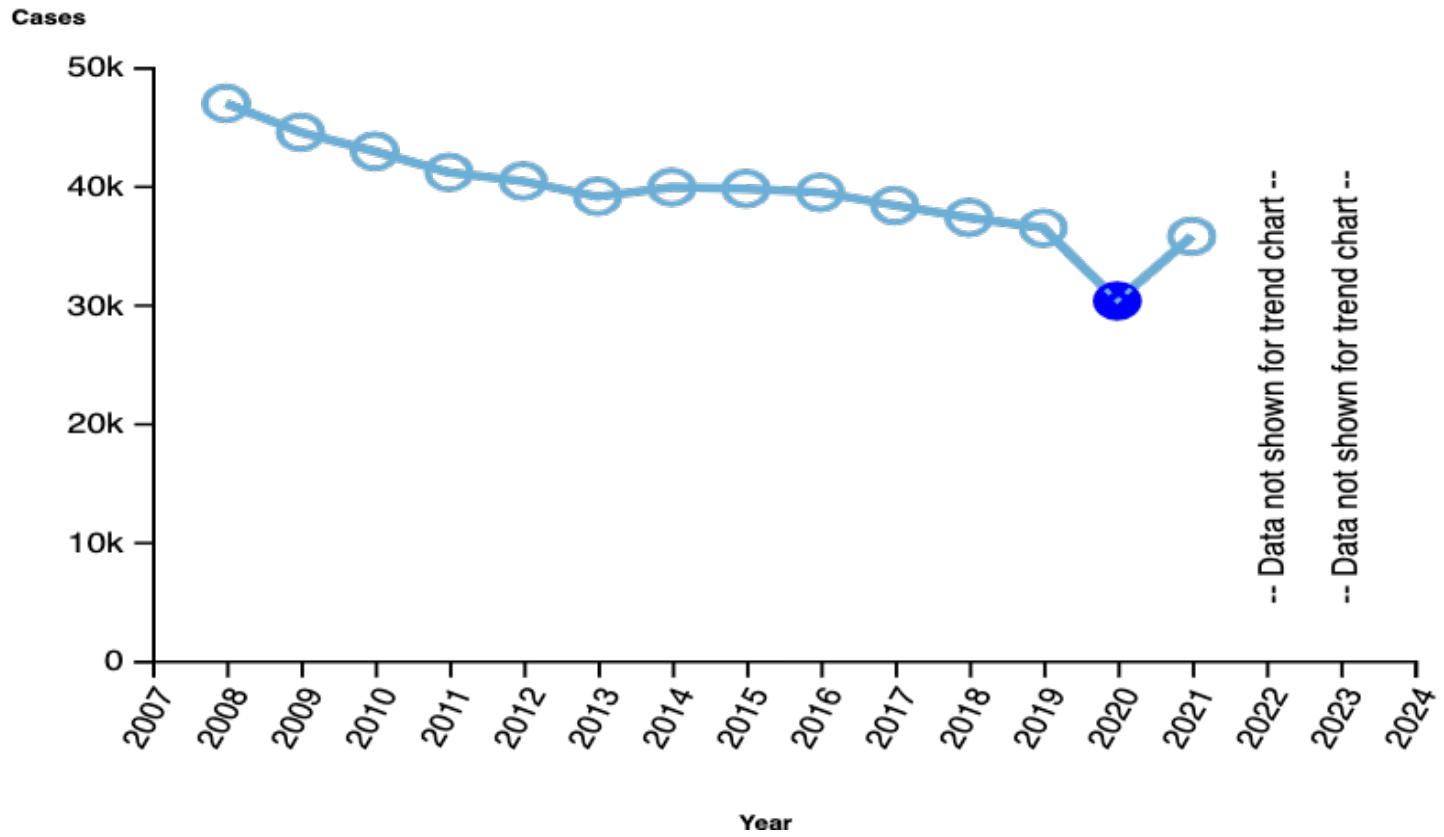
- Epidemiology
- Diagnosis
- Initial Evaluation
- Rapid Start
- Advances in Antiretroviral Therapy
- Statins
- Infant feeding
- Health maintenance

Objectives

- Describe current epidemiology of HIV in the US
- Outline initial steps following diagnosis of HIV including laboratory tests and first line medications
- Identify new treatment strategies for HIV, including injectable regimens
- Review recommendations for primary care of people living with HIV, including CVD prevention, infant feeding, and cancer screenings

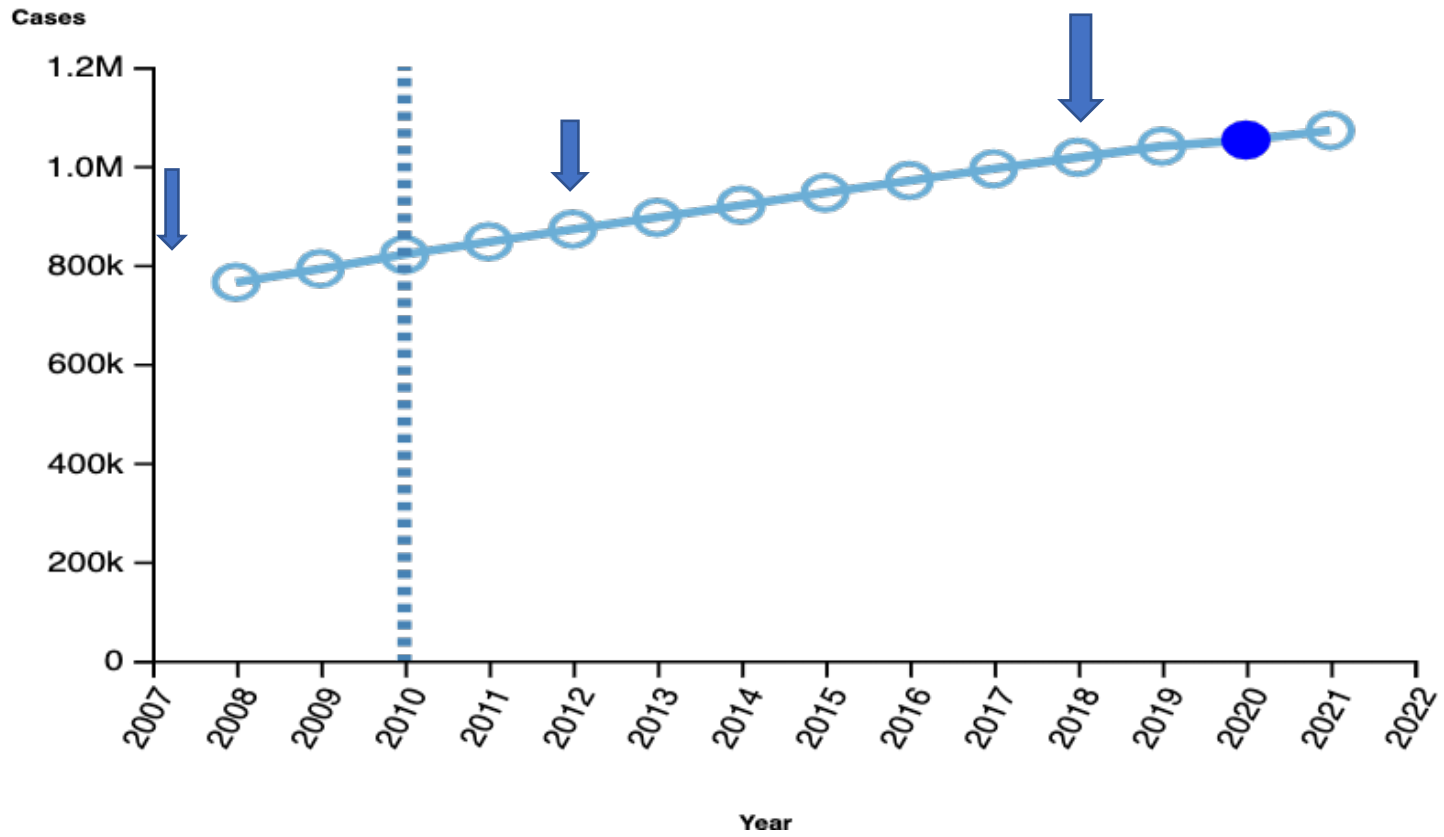
Epidemiology

HIV diagnoses | 2021 | Ages 13 years and older | All races/ethnicities | Both sexes | All transmission categories | United States



Footnotes: Data for 2022 and 2023 are preliminary and based on data received by CDC as of September 2023. Inclusion of preliminary data in trend assessments is discouraged. See Notes on second slide for details. NA - Not Applicable.

HIV prevalence | 2021 | Ages 13 years and older | All races/ethnicities | Both sexes | All transmission categories | United States



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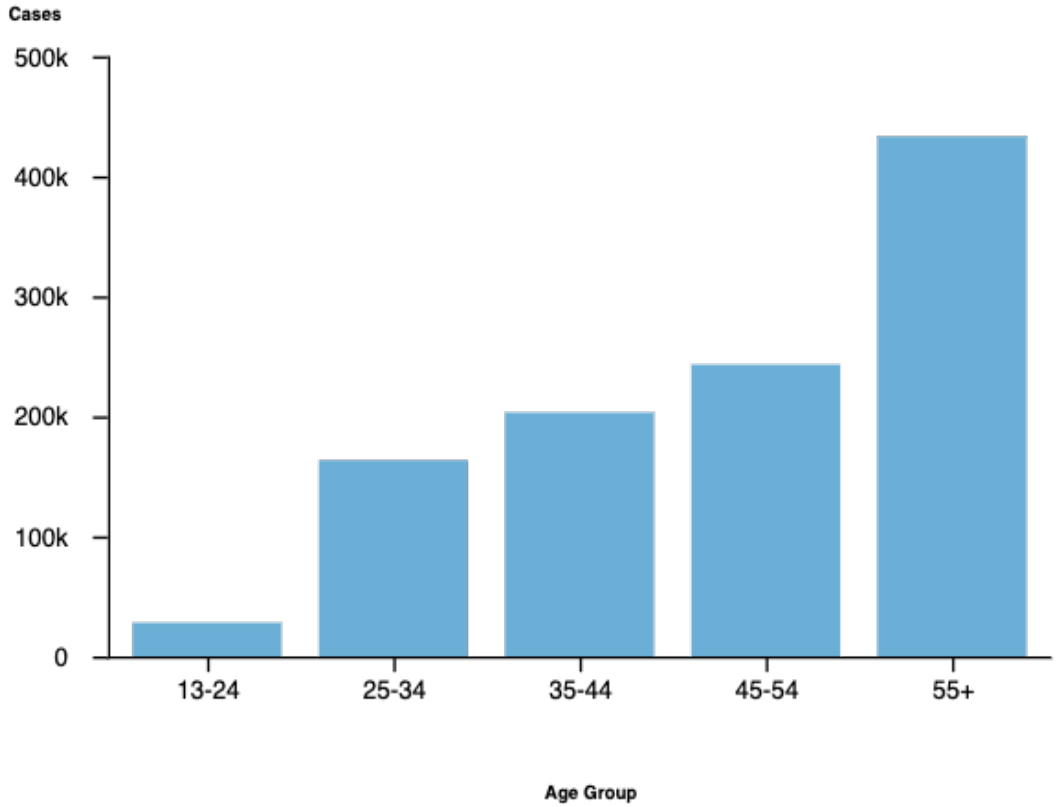

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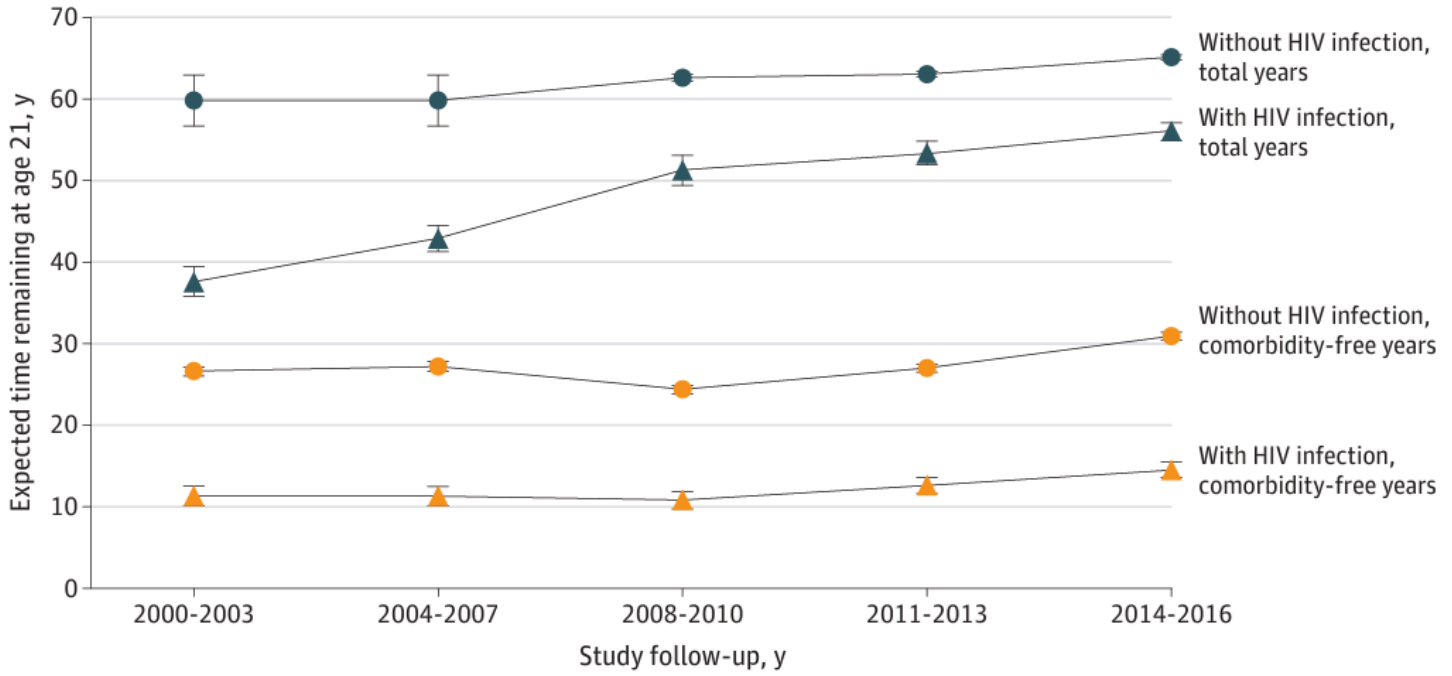
Figure 1. Overall and Comorbidity-Free Life Expectancy at Age 21 Years for Individuals With and Without HIV Infection, Kaiser Permanente, 2000-2016



JAMA Network Open. 2020;3(6):e207954. doi:10.1001/jamanetworkopen.2020.7954

Marcus JL, Leyden WA, Alexeeff SE, et al. Comparison of Overall and Comorbidity-Free Life Expectancy Between Insured Adults With and Without HIV Infection, 2000-2016. *JAMA Netw Open*. 2020;3(6):e207954. Published 2020 Jun 1. doi:10.1001/jamanetworkopen.2020.7954

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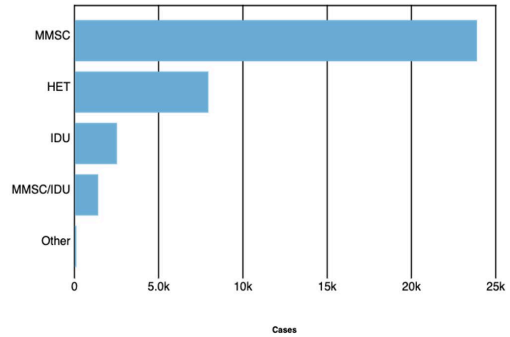

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Atlas Plus

Centers for Disease Control and Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

CDC

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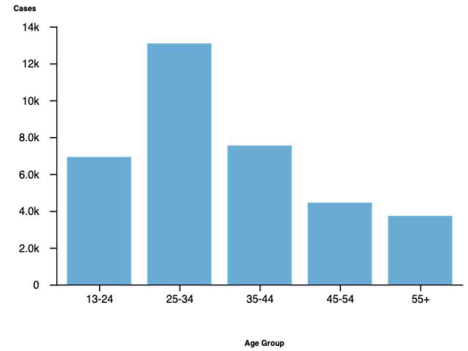

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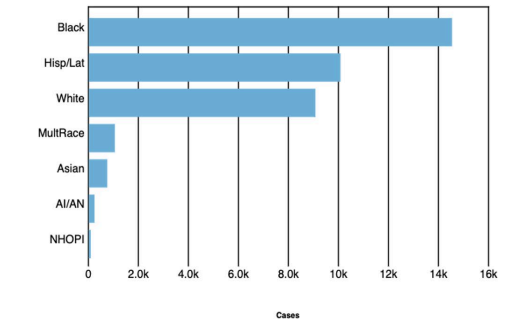

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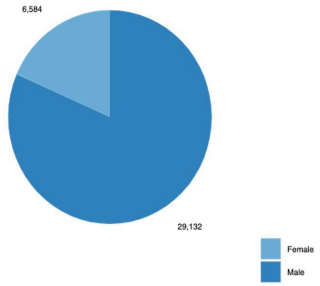

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CDC

HIV and Transgender People

Nearly

1 million

adults in the United States **identify as transgender**[1]

HIV diagnoses among transgender adults and adolescents

increased 7%

between 2015 and 2019[2]

Approximately

1 in 7

transgender people with HIV already had AIDS when they were diagnosed[3]

Disproportionately high numbers of transgender people of color were diagnosed with HIV in 2019:

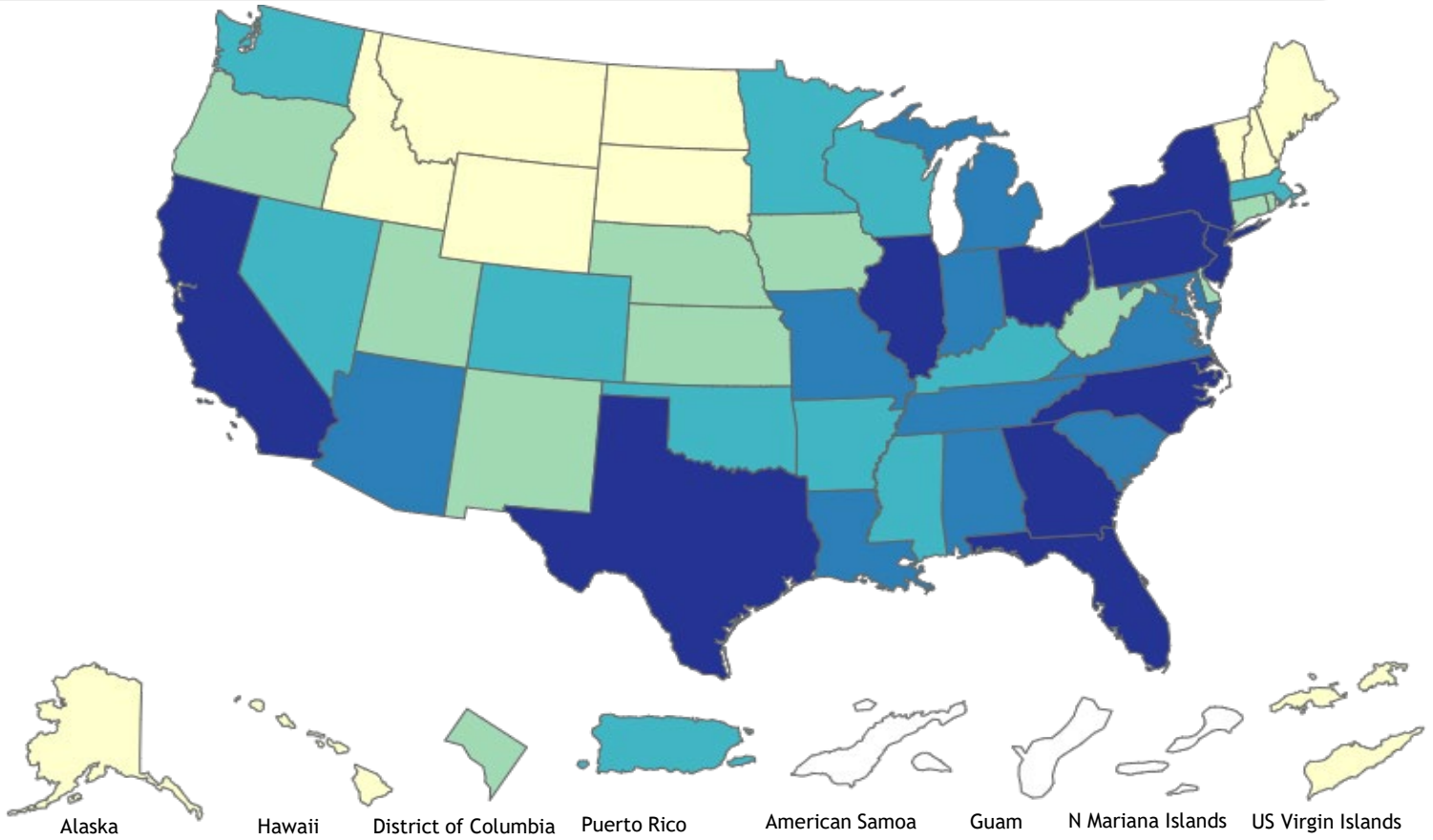
48% were **Black or African American,**

and **37%** were **Hispanic or Latino**[2]

[1] Becasen JS, Denard CL, Mullins MM, Higa DH, Sipe TA. Estimating the prevalence of HIV and sexual behaviors among the US transgender population: a systematic review and meta-analysis, 2006-2017. *Am J Public Health*. 2018;109(1);e1-e8.
[2] Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance* Report. 2021;32:57. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2018-updated-vol-32.pdf
[3] Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using surveillance data: United States and 6 dependent areas, 2019. *HIV Surveillance Report: Supplemental Report.* 2021;26(2):69. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-vol-26-no-2.pdf

Centers for Disease Control and Prevention. Ending the HIV Epidemic: Screening, Treatment, and Prevention- A Guide for Health Care Providers 2022 [Slide set}. (2022). https://www.cdc.gov/hiv/clinicians/materials/slidedecks.html. Accessed April 13, 2024.

HIV diagnoses | 2021 | Ages 13 years and older | All races/ethnicities | Both sexes | All transmission categories | US Map-State Level



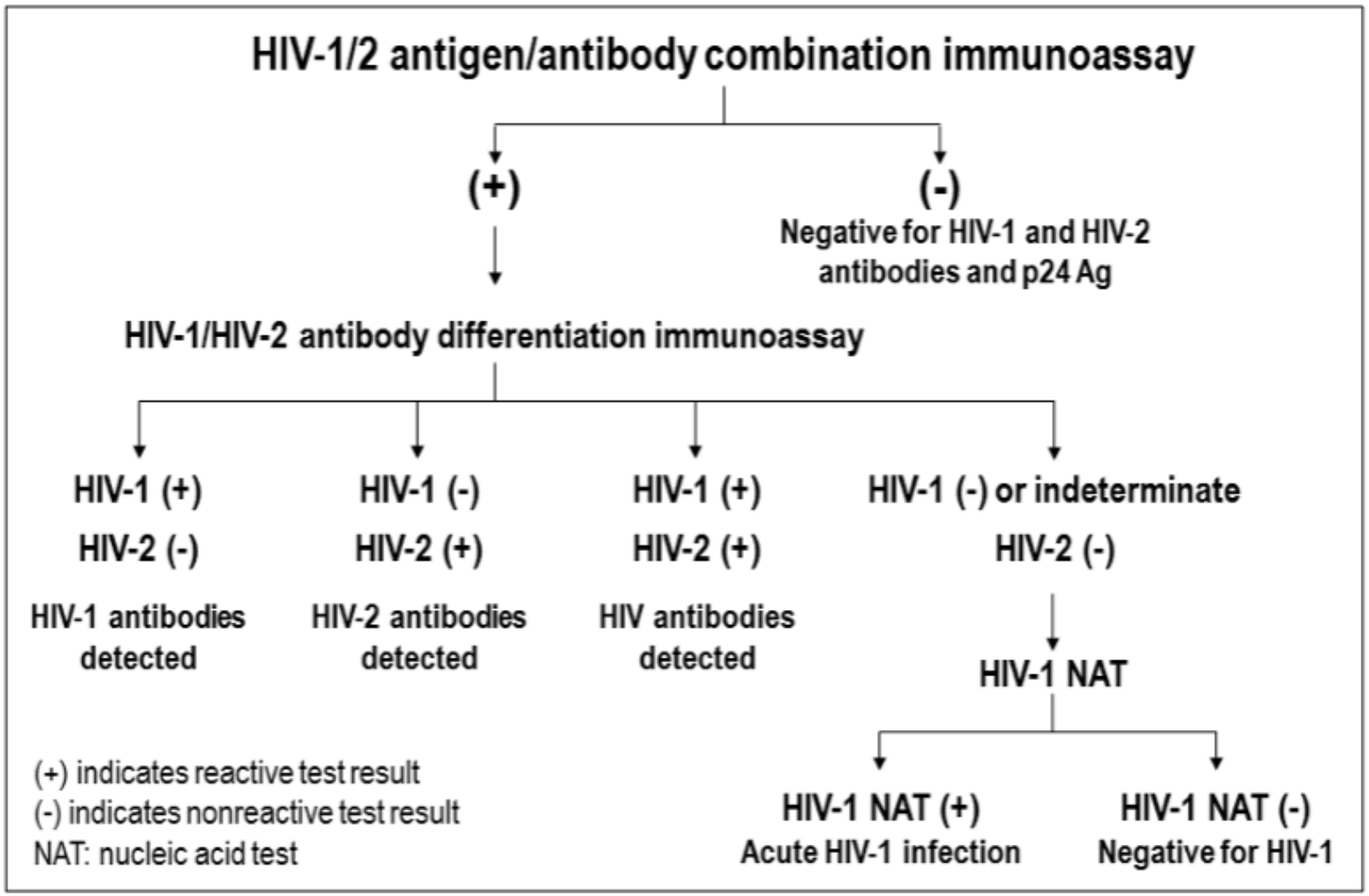
Rate per 100,000 among selected population

0	7 - 65	68 - 233	253 - 501	528 - 899	909 - 4,399

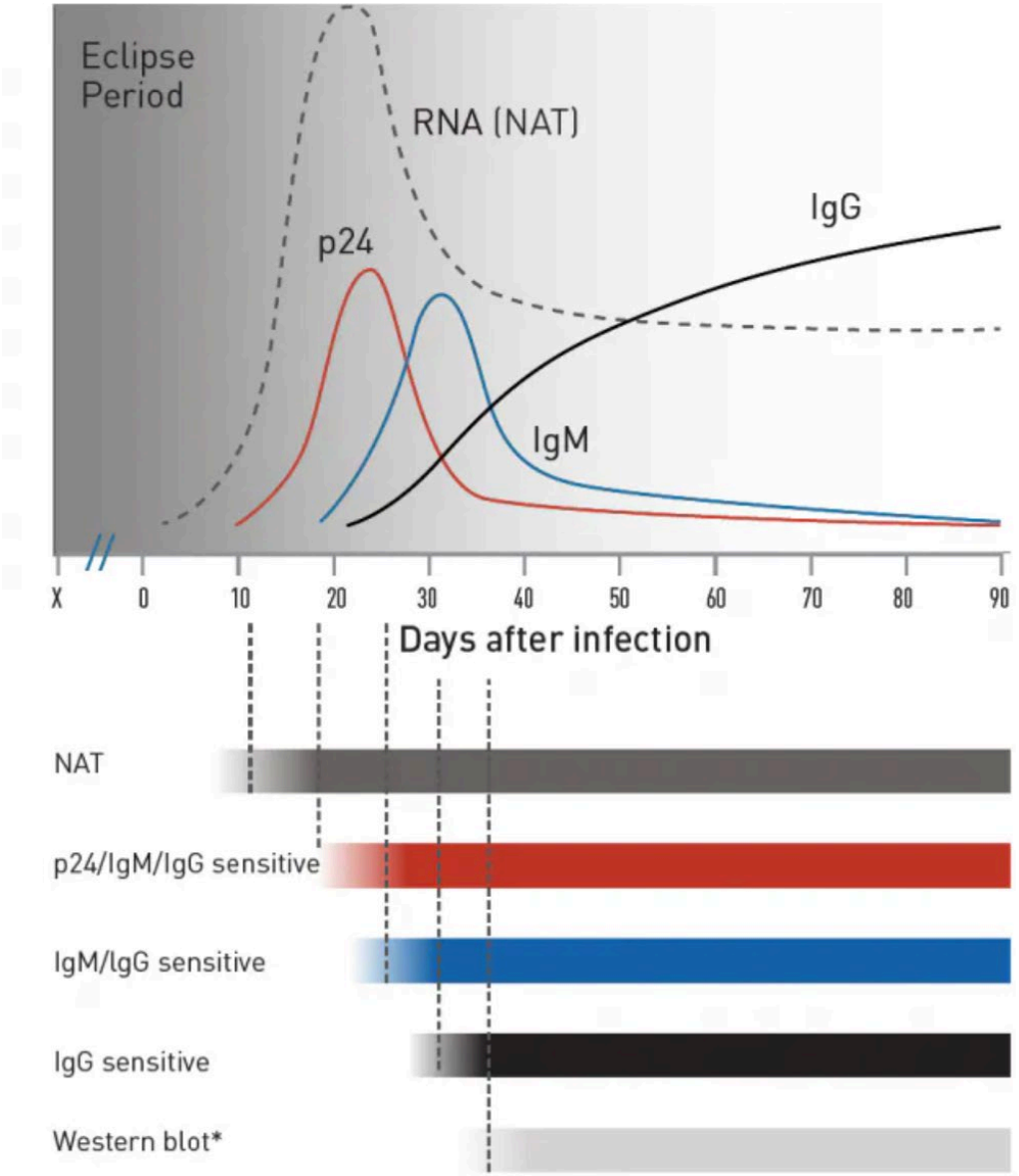
Footnotes: Data for 2022 and 2023 are preliminary and based on data received by CDC as of September 2023. Inclusion of preliminary data in trend assessments is discouraged. See Notes on second slide for details. NA - Not Applicable.

Diagnosis

Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens



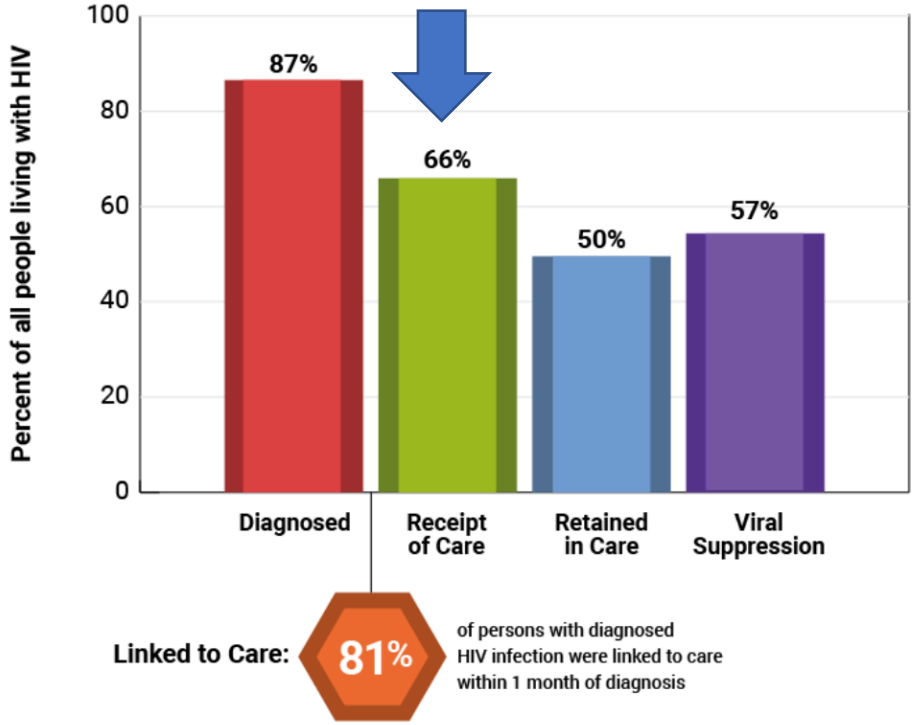
Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. 2014. http://stacks.cdc.gov/view/cdc/23447. Accessed April 12, 2024.



* Western blot is no longer used for HIV.

CDC- HIV Nexus Clinician Resources: HIV Screening. Which HIV Tests Should I Use?. https://www.cdc.gov/hiv/clinicians/screening/tests.html. Updated June 1, 2023. Accessed April 12, 2024.

Prevalence-based HIV Care Continuum, U.S. and 6 Dependent Areas, 2019



Note: Receipt of medical care was defined as ≥1 test (CD4 or VL) in 2019. Retained in medical care was defined as ≥ 2 tests (CD4 or VL) ≥ 3 months apart in 2019. Viral suppression was defined as < 200 copies/mL on the most recent test in 2019. Linkage to care is defined as having ≥ one CD4 or VL test within 30 days (1 month) of diagnosis. (Linkage is calculated differently from the other steps in the continuum, and cannot be directly compared to other steps.)

CDC, Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2019. HIV Surveillance Supplemental Report 2021; 26(No. 2). Published May 2021.

Initial evaluation

HIV Specific Labs for All Patients
HIV-1 RNA quantitative
CD4 count
Genotype for Reverse Transcriptase and Protease Inhibitor Resistance
Genotype for Integrase resistance IF previously on injectable PrEP

Labs to assess for comorbid conditions
CBC (also helps with interpretation of CD4)
CMP
UA
Lipids
Fasting or random glucose*
Pregnancy test if indicated

Screen for substance use behaviors, do not need to collect a UDS

Assess for co-infections	
Hepatitis B	HBsAg HBsAb HBcAb total (not IgM)
Hepatitis C	HCV Ab HCV RNA if history of prior HCV
Hepatitis A (susceptibility)	Anti-HAV total (IgG)
Sexually transmitted infections	Syphilis (RPR if prior history) GC/CT (site based) Trichomonas (AFAB patients)
Tuberculosis	Quantiferon Gold

Rapid Start

Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of ART during pregnancy should be guided by recommendations from the Perinatal Guidelines.

For people who do not have a history of CAB-LA use as PrEP, the following regimens are recommended:

INSTI plus Two NRTIs

- BIC/TAF/FTC **(AI)**[a]
- DTG/ABC/3TC **(AI)**—**if HLA-B*5701 negative**
- DTG plus (TAF or TDF)[c] plus (FTC or 3TC) **(AI)**

INSTI plus One NRTI

- DTG/3TC **(AI),** except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

For people with HIV and a history of CAB-LA use as PrEP, INSTI genotypic resistance testing should be performed before the start of ART. If treatment is begun prior to results of genotypic testing, the following regimen is recommended:

- DRV/c[b] or DRV/r with (TAF or TDF)[c] plus (FTC or 3TC)—pending the results of the genotype test **(AIII)**

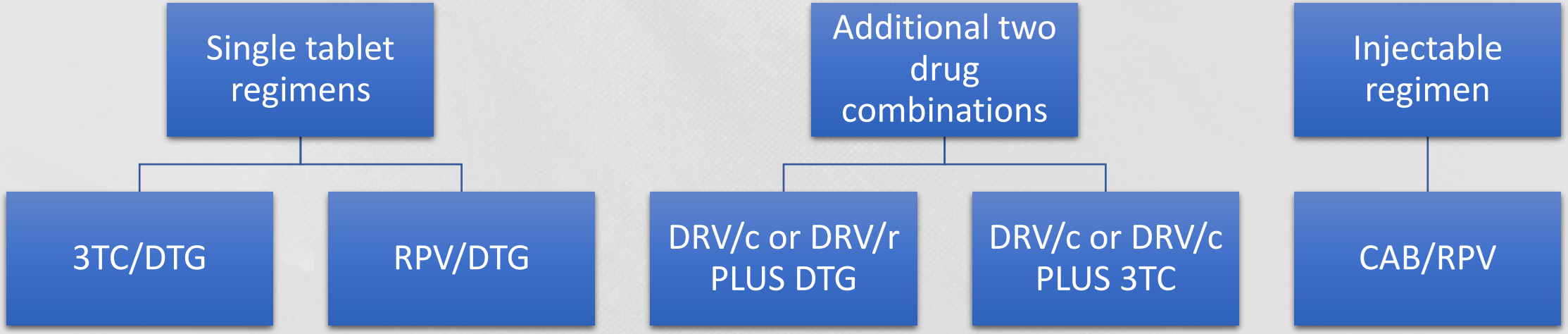
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. 2024. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed April 12, 2024. Table 6.

Suspected low CD4 count
Assess for any neurological symptoms
If concern for opportunistic infection (OI), consult with an HIV specialist
Counsel on the possibility of immune reconstitution inflammatory syndrome (IRIS)- if feeling worse after starting medications, should continue taking but contact office immediately

Drug Prescribing and Counseling
Check drug drug interactions (https://www.hiv-druginteractions.org/)
Advise patient to take the pill at the same time every day
If taking BIC or DTG, avoid taking ART with supplements or dairy products
Side effects are usually mild (GI upset, fatigue, or headache) and improve after the first few days

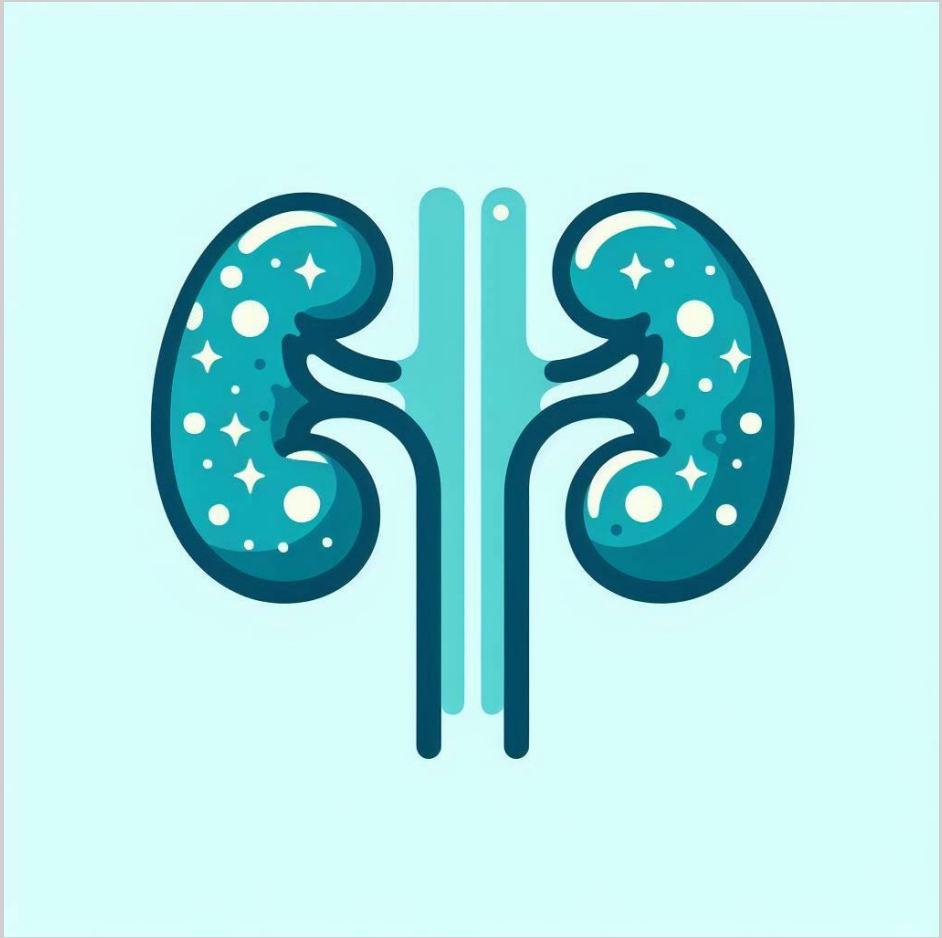
Advances in ART

Two drug regimens



Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. 2024. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed April 12, 2024.

What’s the deal with tenofovir?



Produced by Microsoft Copilot

Clinical Trial > N Engl J Med. 2020 Mar 19;382(12):1112-1123. doi: 10.1056/NEJMoa1904398.
Epub 2020 Mar 4.

Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression

Susan Swindells [1], Jaime-Federico Andrade-Villanueva [1], Gary J Richmond [1], Giuliano Rizzardini [1], Axel Baumgarten [1], Mar Masiá [1], Gulam Latiff [1], Vadim Pokrovsky [1], Fritz Bredeek [1], Graham Smith [1], Pedro Cahn [1], Yeon-Sook Kim [1], Susan L Ford [1], Christine L Talarico [1], Parul Patel [1], Vasiliki Chounta [1], Herta Crauwels [1], Wim Parys [1], Simon Vanveggel [1], Joseph Mrus [1], Jenny Huang [1], Conn M Harrington [1], Krischan J Hudson [1], David A Margolis [1], Kimberly Y Smith [1], Peter E Williams [1], William R Spreen [1]

Affiliations + expand

PMID: 32130809 DOI: 10.1056/NEJMoa1904398

Cabotegravir/Rilpivirine Highlights
Approved by the FDA January 2021
First injectable regimen available for the treatment of HIV
Not a first line agent
Can be given monthly or every two months
Intramuscular gluteal injections (one for each medication)
Increasing support for use in patients with viremia
Requires careful coordination of team to ensure appropriate administration and monitoring

Clinical Trial > Lancet HIV. 2023 Aug;10(8):e497-e505. doi: 10.1016/S2352-3018(23)00113-3.
Epub 2023 Jul 11.

Efficacy and safety of the novel capsid inhibitor lenacapavir to treat multidrug-resistant HIV: week 52 results of a phase 2/3 trial

Onyema Ogbuagu [1], Sorana Segal-Maurer [2], Winai Ratanasuwan [3], Anchalee Avihingsanon [4], Cynthia Brinson [5], Kimberly Workowski [6], Andrea Antinori [7], Yazdan Yazdanpanah [8], Benoit Trottier [9], Hui Wang [10], Nicolas Margot [10], Hadas Dvory-Sobol [10], Martin S Rhee [10], Jared M Baeten [10], Jean-Michel Molina [11]; GS-US-200-4625 investigators

Collaborators, Affiliations + expand

PMID: 37451297 DOI: 10.1016/S2352-3018(23)00113-3

Statins

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

Authors: Steven K. Grinspoon, M.D., Kathleen V. Fitch, M.S.N., Markella V. Zanni, M.D., Carl J. Fichtenbaum, M.D., Triin Umbleja, M.S., Judith A. Aberg, M.D., Edgar T. Overton, M.D., +19, for the REPRIEVE Investigators* Author Info & Affiliations

Published July 23, 2023 | N Engl J Med 2023;389:687-699 | DOI: 10.1056/NEJMoa2304146 | VOL. 389 NO. 8

Table 1: Number Needed to Treat over 5 Years Based on REPRIEVE

	Population	N	NNT_5
10-Year Atherosclerotic Cardiovascular Disease Risk Score	>10%	563	35
	5-10%	2,995	53
	2.5% to <5.0%	2,065	149
	0% to <2.5%	2,156	199
Overall		7,769	106

Key: NNT_5= number needed to treat over 5 years

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Recommendations for the Use of Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease in People with HIV. Department of Health and Human Services. 2024. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed April 12, 2024. Table 1.

DHHS Guidelines Update (2/27/2024)

Panel's Recommendations

For people with HIV who have low-to-intermediate (<20%) 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimates

- Age 40–75 years
  - When 10-year ASCVD risk estimates are 5% to <20%, the Panel for the Use of Antiretroviral Agents in Adults and Adolescents with HIV (the Panel) recommends initiating at least moderate-intensity statin therapy **(AI).**
    - Recommended options for moderate-intensity statin therapy include the following:
      - Pitavastatin 4 mg once daily **(AI)**
      - Atorvastatin 20 mg once daily **(AII)**
      - Rosuvastatin 10 mg once daily **(AII)**
  - When 10-year ASCVD risk estimates are <5%, the Panel favors initiating at least moderate-intensity statin therapy **(CI).** The absolute benefit from statin therapy is modest in this population; therefore, the decision to initiate a statin should take into account the presence or absence of HIV-related factors that can increase ASCVD risk.[a]
    - Same options for moderate-intensity statin therapy as recommended for 10-year ASCVD risk estimates of 5% to <20% (see above)
- Age <40 years
  - Data are insufficient to recommend for or against statin therapy as primary prevention of ASCVD in people with HIV. In the general population, lifestyle modifications are recommended for people age <40 years, with statin therapy considered only in select populations (see American Heart Association (AHA)/American College of Cardiology (ACC)/Multisociety Guidelines).

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Recommendations for the Use of Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease in People with HIV. Department of Health and Human Services. 2024. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed April 12, 2024.

Key Recommendations for the General Population (Including People with HIV) Based on AHA/ACC/Multisociety Guidelines

For people age 40–75 years who have high (≥20%) 10-year ASCVD risk estimates

- Initiate high-intensity statin therapy.

For people age 20–75 years who have low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL

- Initiate high-intensity statin therapy at maximum tolerated dose.

For people age 40–75 years with diabetes mellitus

- Initiate at least moderate-intensity statin therapy. Perform further risk assessment to consider using a high-intensity statin.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Recommendations for the Use of Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease in People with HIV. Department of Health and Human Services. 2024. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed April 12, 2024.

Infant feeding

Panel's Recommendations

- People with HIV should receive evidence-based, patient-centered counseling to support shared decision-making about infant feeding. Counseling about infant feeding should begin prior to conception or as early as possible in pregnancy; information about and plans for infant feeding should be reviewed throughout pregnancy and again after delivery **(AIII).** During counseling, people should be informed that—
  - Replacement feeding with properly prepared formula or pasteurized donor human milk from a milk bank eliminates the risk of postnatal HIV transmission to the infant **(AI).**
  - Achieving and maintaining viral suppression through antiretroviral therapy (ART) during pregnancy and postpartum decreases breastfeeding transmission risk to less than 1%, but not zero **(AI).**
- Replacement feeding with formula or banked pasteurized donor human milk is recommended to eliminate the risk of HIV transmission through breastfeeding when people with HIV are not on ART and/or do not have a suppressed viral load during pregnancy (at a minimum throughout the third trimester), as well as at delivery **(AI).**
- Individuals with HIV who are on ART with a sustained undetectable viral load and who choose to breastfeed should be supported in this decision **(AIII).**
- Individuals with HIV who choose to formula feed should be supported in this decision. Providers should ask about potential barriers to formula feeding and explore ways to address them **(AIII).**
- Engaging Child Protective Services or similar agencies is not an appropriate response to the infant feeding choices of an individual with HIV **(AIII).**

Clinicians are encouraged to consult the national Perinatal HIV/AIDS hotline (1-888-448-8765) with questions about infant feeding by individuals with HIV **(AIII).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States. Infant Feeding for Individuals with HIV in the United States. Department of Health and Human Services. 2024. Available at https://clinicalinfo.hiv.gov/en/guidelines/perinatal. Accessed April 12, 2024.

Health care maintenance

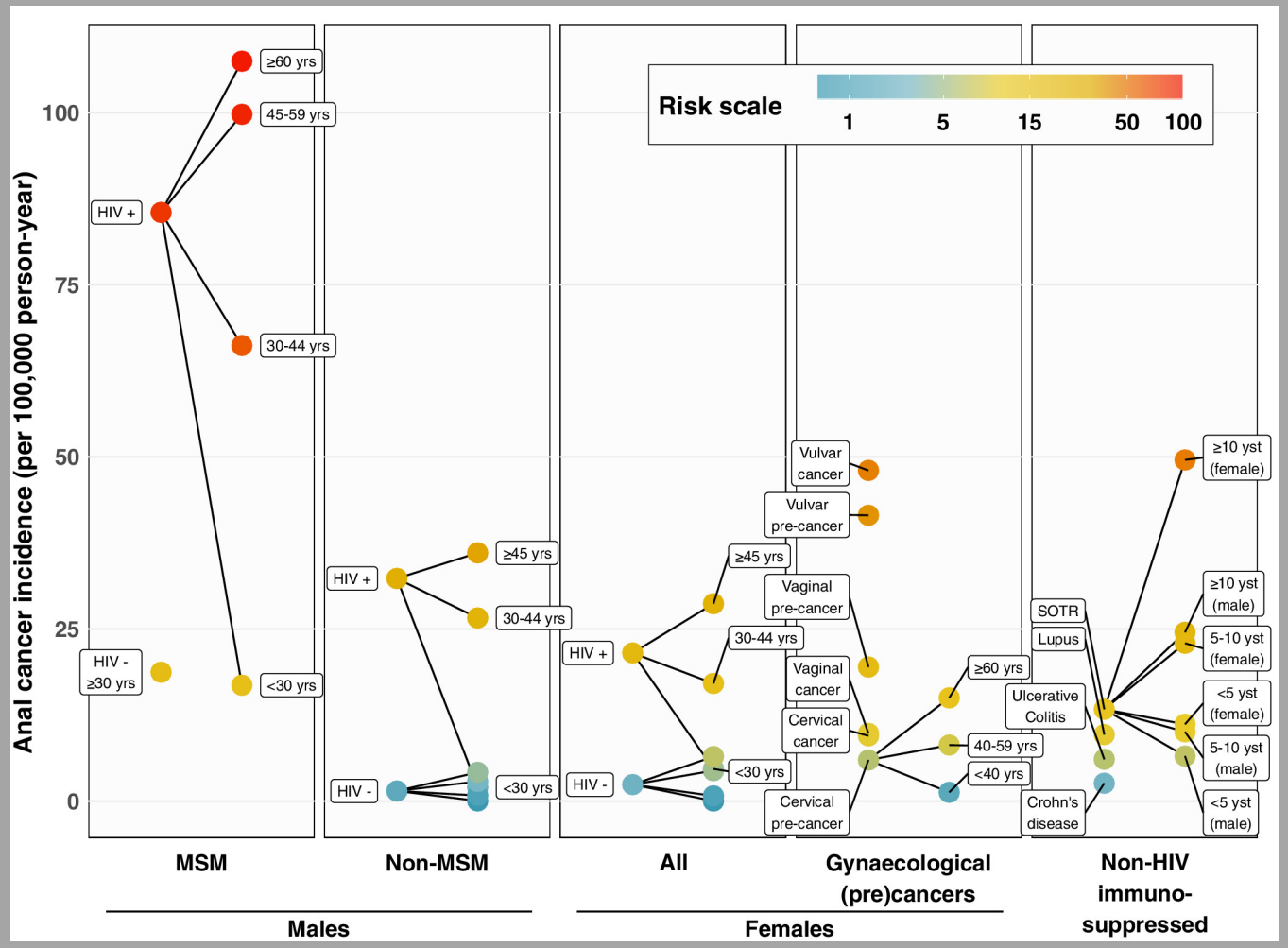
Cancer screening recommendations	
Lung cancer	General guidelines (higher rates of smoking in PWH)
Colon cancer	General guidelines
Breast cancer	General guidelines
Prostate cancer	General guidelines
Hepatocellular carcinoma	General guidelines (higher risk of cirrhosis with HBV or HCV coinfection)

*Hirsch B, Fine SM, Vail R, et al. Screening for Anal Dysplasia and Cancer in Adults With HIV [Internet]. Baltimore (MD): Johns Hopkins University; 2022 Aug. Available from: https://www.ncbi.nlm.nih.gov/books/NBK556472/

Cervical cancer screening	
Assigned female at birth <21 years old	No Pap indicated
Assigned female at birth 21-29 years old	Perform Pap with reflex testing at baseline (time of diagnosis or age of 21) and then annually Once 3 consecutive tests are normal, can space to every three years
Assigned female at birth ≥ 30 years old	Perform Pap and HPV cotesting at baseline If results are negative, can space to every 3 years Do not space to every 5 years
Assigned female at birth s/p hysterectomy	Done for benign conditions: no vaginal Pap indicated Hx of high grade CIN or invasive cervical cancer: annual vaginal cuff Pap tests

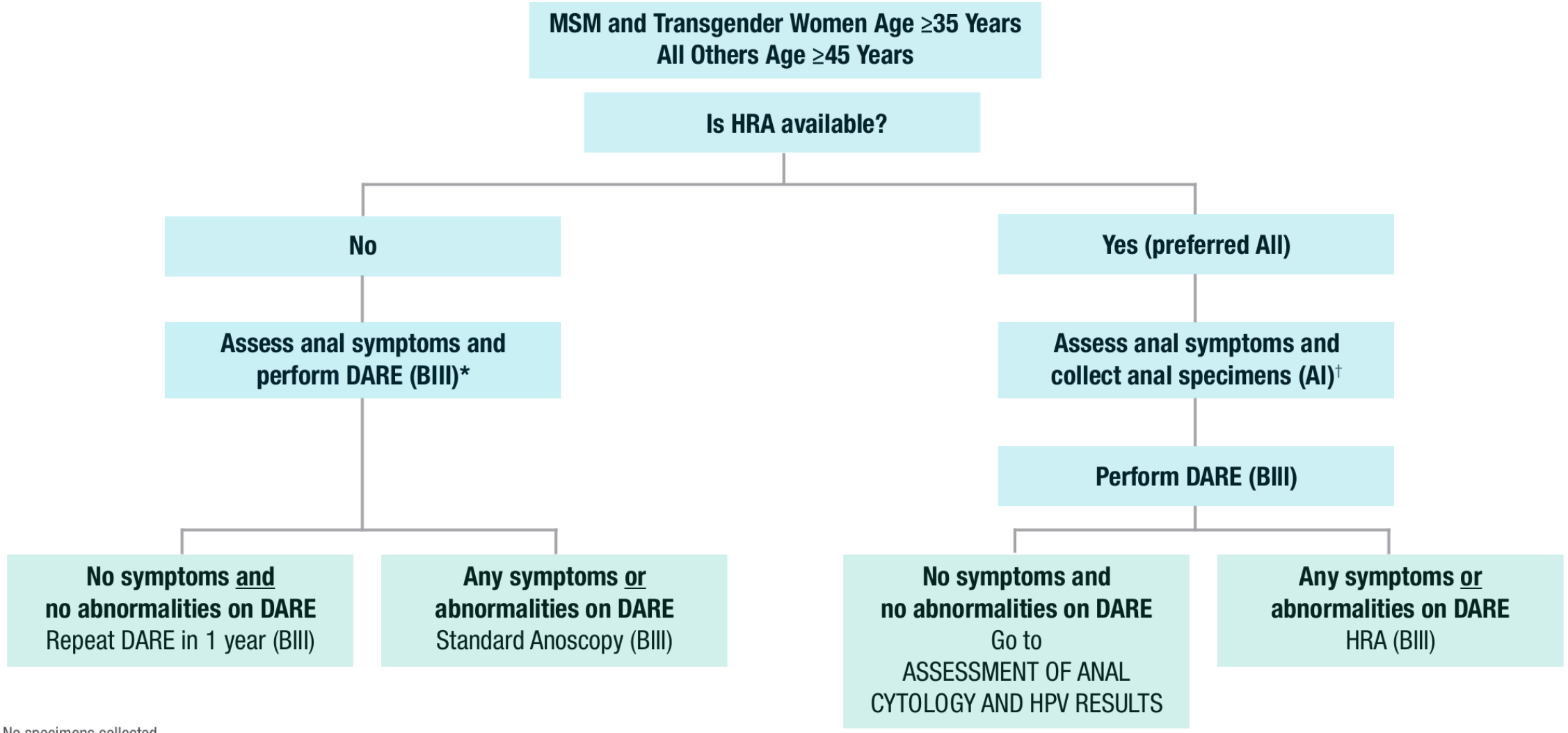
Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Human Papillomavirus Disease. National Institutes of Health, Centers for Disease Control and Prevention, HIV Medicine Association, and Infectious Diseases Society of America. 2024. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection. Accessed April 12, 2024.

A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale



Intl Journal of Cancer, Volume: 148, Issue: 1, Pages: 38-47, First published: 04 July 2020, DOI: (10.1002/ijc.33185)

SCREENING ALGORITHM FOR ANAL CANCER IN ASYMPTOMATIC PEOPLE WITH HIV



* No specimens collected

† Collect any specimens either for cytology or for cytology with HPV co-testing prior to DARE. HPV testing without cytology is not recommended (BIII)

Key: DARE = digital anorectal exam; HPV = human papillomavirus; hr-HPV = high-risk HPV; HRA = high-resolution anoscopy; MSM = men who have sex with men

ASSESSMENT OF ANAL CYTOLOGY AND HPV RESULTS IN PEOPLE WITH HIV

Was hr-HPV co-testing performed?

No

Cytology Normal
Repeat cytology in 1 year (BIII)

Normal x 3 consecutive years
Repeat cytology in 3 years (BIII)

Cytology ≥ ASC-US
HRA (BIII)

Yes

Cytology Normal
Assess hr-HPV results

hr-HPV Negative	Repeat cytology and hr-HPV in 3 years (BIII)
hr-HPV Positive, No HPV typing	Repeat cytology and hr-HPV in 6 months† (BIII)
hr-HPV Positive, HPV 16 and 18 negative	Repeat cytology and hr-HPV in 1 year† (BIII)
hr-HPV Positive, HPV 16 or 18 positive	HRA (BIII)

Cytology ASC-US
Assess hr-HPV results

hr-HPV Negative	Repeat cytology and hr-HPV in 1 year† (BIII)
hr-HPV Positive	HRA (BIII)

Cytology ≥ LSIL
HRA (BIII)

† If at repeat testing either cytology is ≥ ASC-US or any hr-HPV is detected, refer for HRA (BIII)

Key: ASC-US = atypical squamous cells of undetermined significance; HPV = human papillomavirus; hr-HPV = high-risk HPV; HRA = high-resolution anoscopy; LSIL = low-grade squamous intraepithelial lesion

Vaccinations
PCV20 or PCV21
Hepatitis B if not immune (preferably use two dose recombinant with adjuvant)
Hepatitis A if not immune
MenACWY
Shingles
MMR booster if not immune (contraindicated if CD4 <200)
HPV series if not previously completed (≤45 years)
Flu (live vaccine contraindicated)
COVID19 (if not previously vaccinated and CD<200 or not on ART, will need 3 total doses of Pfizer or Moderna)
Mpox (if at increased risk)

Questions?

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UPMC LIFE CHANGING MEDICINE

Pulmonary embolism: a practical overview

47th Annual Family Medicine Refresher Course

Richard H. Zou, MD, MS

March 8, 2025

Disclosures

Verona Pharma PLC

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Learning Objectives

- To recognize **clinical and radiographic features** of PE
- To **risk stratify** PE
- To understand PE **treatments** and controversies

Overview

Pre-Diagnosis
- ❑ Definition
- ❑ Epidemiology
- ❑ Pathophysiology
- ❑ Risk Factors

Diagnosis
- ❑ Clinical Presentation
- ❑ Diagnostic Testing
- ❑ Risk Stratification
- ❑ Thrombophilia Testing

Treatment
- ❑ Anticoagulation
- ❑ Post-PE Care

Overview

Pre-Diagnosis
- ❑ **Definition**
- ❑ Epidemiology
- ❑ Pathophysiology
- ❑ Risk Factors

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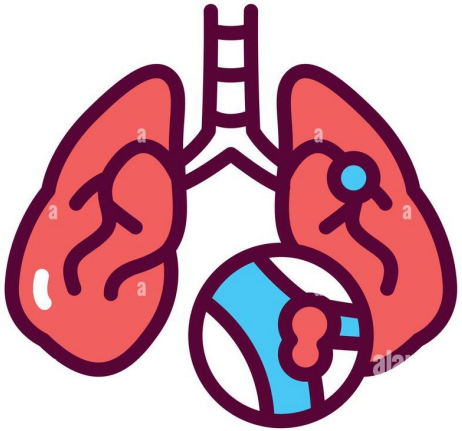
- ❑ Anticoagulation
- ❑ Post-PE Care

Definition

- **Occlusion of blood flow** in the pulmonary arterial circulation due to embolus from systemic vasculature
- **Restricts normal pulmonary ventilation and perfusion** [1,2]



1 Giri et al, *Circulation*, 2019.
2 Freund et al, *JAMA*, 2022.

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Overview

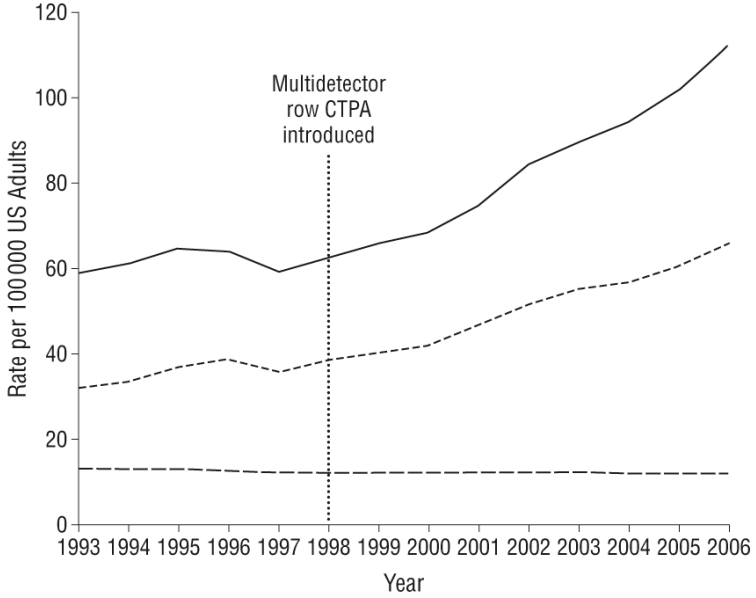
Pre-Diagnosis
- ❑ Definition
- ❑ **Epidemiology**
- ❑ Pathophysiology
- ❑ Risk Factors

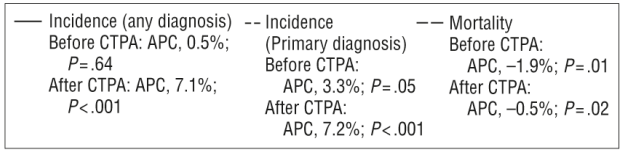
Diagnosis
- ❑ Clinical Presentation
- ❑ Diagnostic Testing
- ❑ Risk Stratification
- ❑ Thrombophilia Testing

Treatment
- ❑ Anticoagulation
- ❑ Post-PE Care

Morbidity and Mortality in PE

- **Third leading cause** of cardiovascular mortality [3]
- General population incidence of **60-120 cases per 100,000** [4]





Weiner et al, *JAMA*, 2011.

3 Goldhaber et al, *Lancet*, 2012.
4 Wendelboe et al, *Circ Res*, 2016.

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Morbidity and Mortality in PE

- ~900,000 VTE events/year → **1.8 VTE events every minute** [5]
- ~100,000 PE deaths/year → **1 PE death every 5 minutes** [5]
- **14% in-hospital mortality** [2]
- **20% all-cause 90-day mortality** [2]

2 Freund et al, *JAMA*, 2022.
5 Centers for Disease Control and Prevention, Apr 2022.

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Clinical Question #1

How does PE compare to other major causes of cardiovascular mortality in the US?

PE is the third leading cause of cardiovascular mortality (*behind only myocardial infarction and stroke*).

Overview

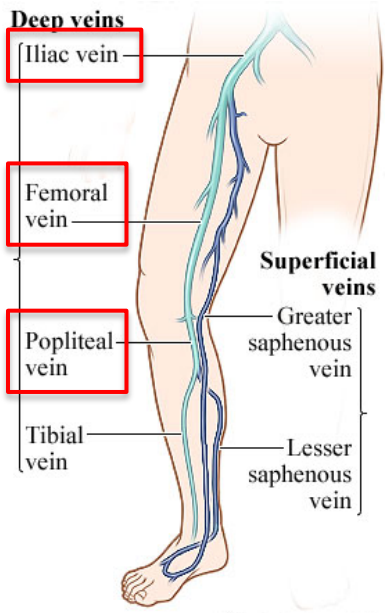
Pre-Diagnosis
- ❑ Definition
- ❑ Epidemiology
- ❑ **Pathophysiology**
- ❑ Risk Factors

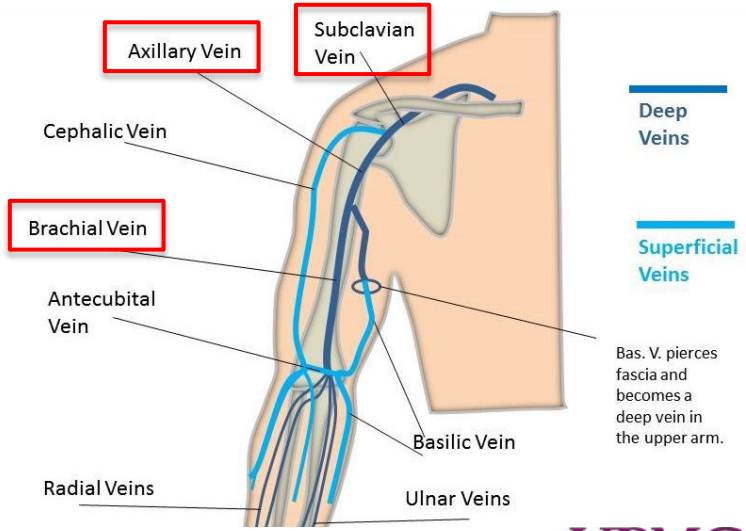
Diagnosis
- ❑ Clinical Presentation
- ❑ Diagnostic Testing
- ❑ Risk Stratification
- ❑ Thrombophilia Testing

Treatment
- ❑ Anticoagulation
- ❑ Post-PE Care

Where Does It Start?

- ~90% originate from **deep veins of lower extremity or pelvis** [8]
- ~10% originate from deep veins of upper extremity [9]





8 Hyeres, *Am J Respir Crit Care Med*, 1999.
9 Previtali et al, *Blood Transfus*, 2011.

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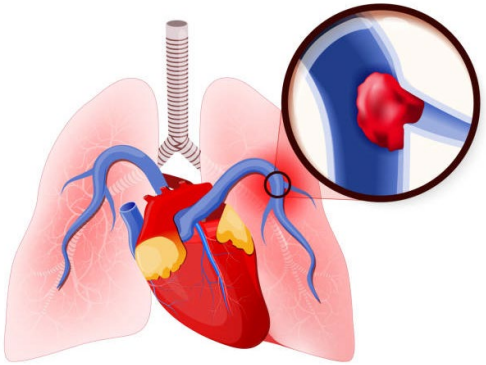
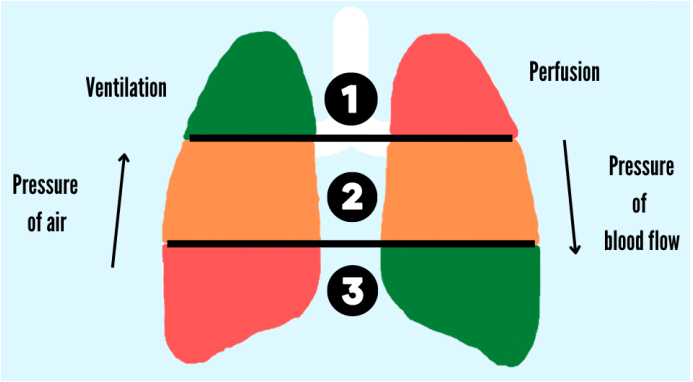
Where Does It End?

- Migration to pulmonary arterial vasculature
- Typically multiple, **lower lobe > upper lobe** predominance [10]





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10 Moser, *Am Rev Respir Dis*, 1990.

Pathophysiology

V/Q mismatch

Obstruction of pulmonary vascular bed

↓

Impaired gas exchange

↓

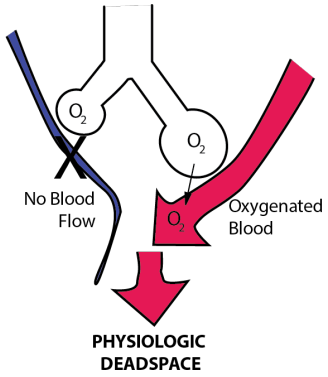
Ventilation/perfusion mismatch

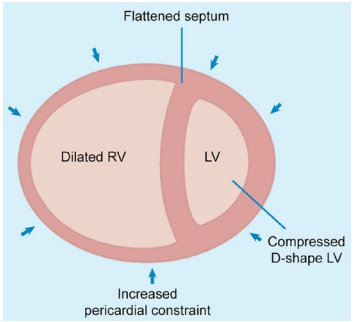
↓

Dead space ventilation

↓

Hypoxemia





RV spiral of death

Increased pulmonary vascular resistance

↓

Increased RV afterload

↓

RV dilation

↓

Interventricular septal flattening

↓

Reduced LV preload

↓

Decreased cardiac output

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Clinical Question #2

In patients with PE, where do the majority of clot burden originate?

90% of PEs originate from proximal deep veins of the lower extremity (*femoral, popliteal*) and pelvis (*iliac*).

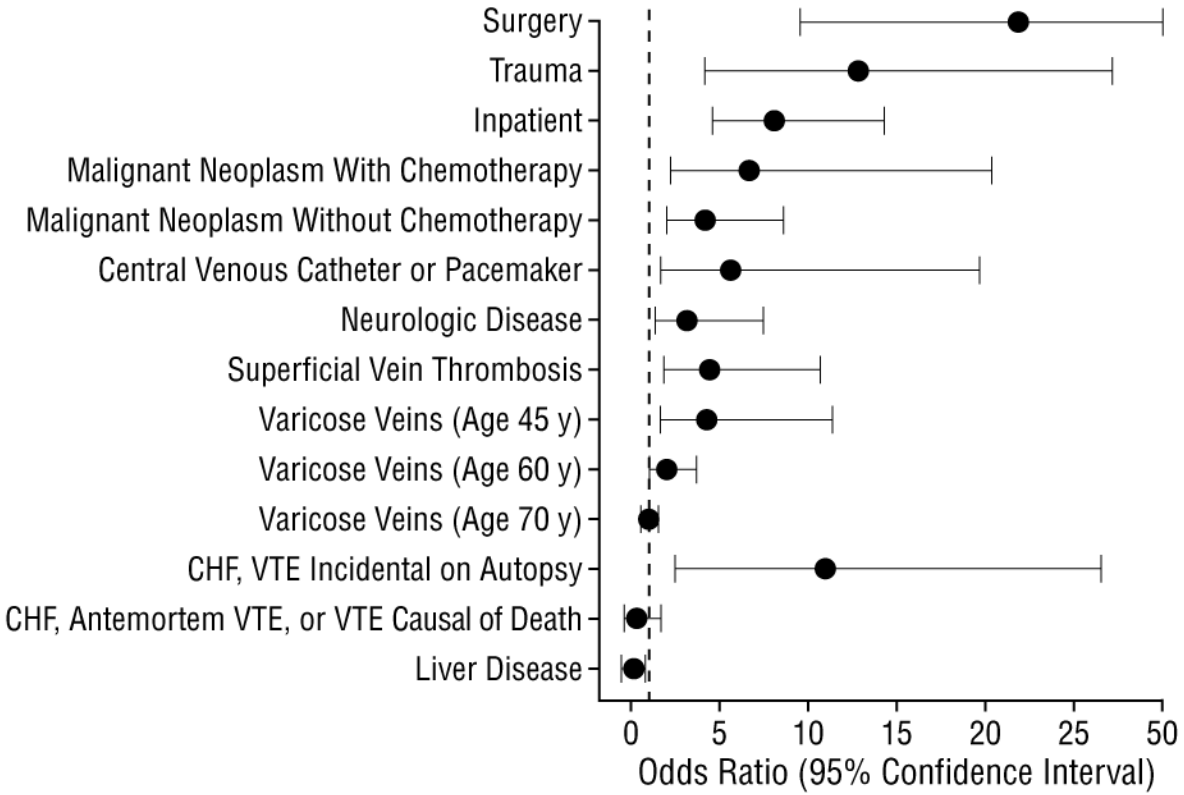
Overview

Pre-Diagnosis
- ❑ Definition
- ❑ Epidemiology
- ❑ Pathophysiology
- ❑ **Risk Factors**

Diagnosis
- ❑ Clinical Presentation
- ❑ Diagnostic Testing
- ❑ Risk Stratification
- ❑ Thrombophilia Testing

Treatment
- ❑ Anticoagulation
- ❑ Post-PE Care

Provoking Risk Factors



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11 Heit et al, *JAMA*, 2000.

Provoking Risk Factors

- **Hospitalization is important (and often underestimated)** [11]
  - Relative immobilization, severe illness, acute inflammation, etc.
  - DVT prophylaxis alone does not absolve inpatient VTE risk
- COVID-19 infection [12]
  - ~4% of hospitalized patients in US
  - Higher risk of **mechanical ventilation** (HR 1.38) and **mortality** (HR 1.36)

11 Heit et al, *JAMA*, 2000.
12 Gul et al, *Respir Res*, 2023.

Clinical Question #3

What is the single most provoking risk factor for PE?

Recent lower extremity musculoskeletal (*orthopedic*) surgery.

Overview

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- ❑ Definition
- ❑ Epidemiology
- ❑ Pathophysiology
- ❑ Risk Factors

Diagnosis
- ❑ **Clinical Presentation**
- ❑ Diagnostic Testing
- ❑ Risk Stratification
- ❑ Thrombophilia Testing

Treatment
- ❑ Anticoagulation
- ❑ Post-PE Care

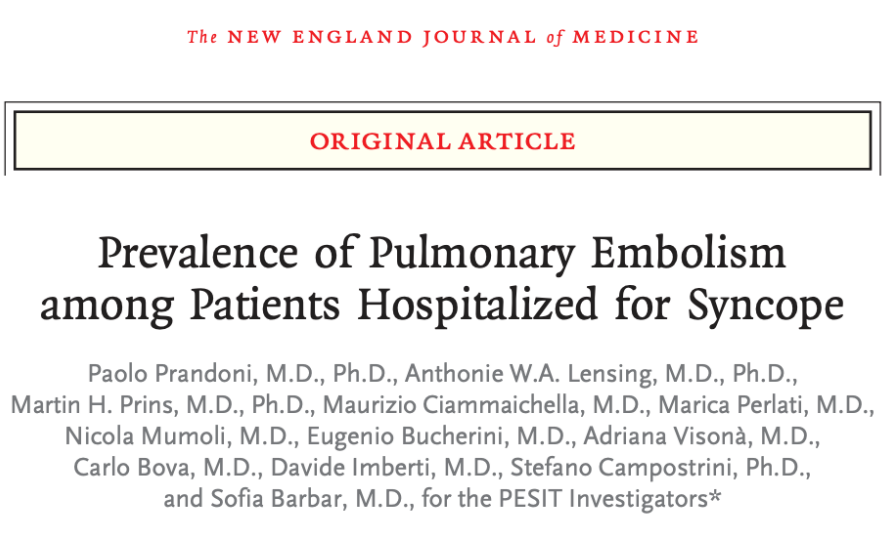
Clinical Presentation

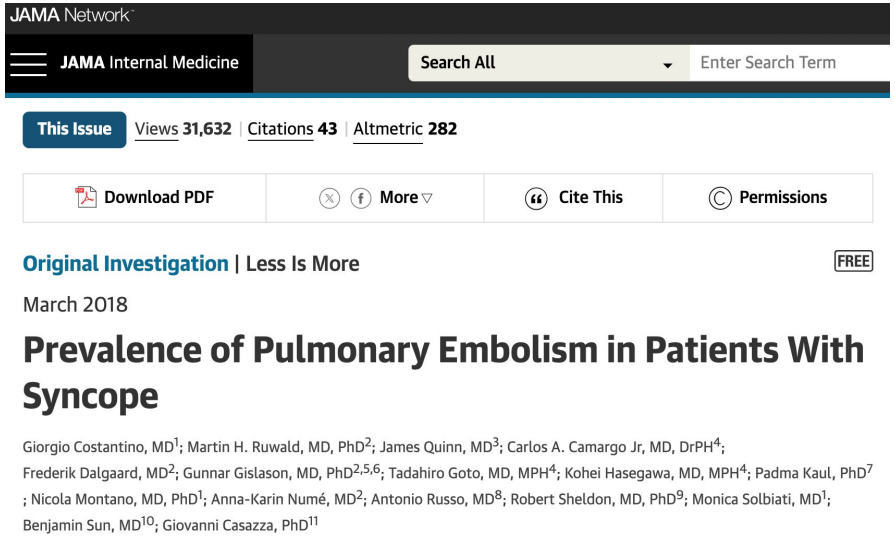
- **Dyspnea**
- **Pleurisy**
- **Unilateral calf pain/swelling**
- Non-productive cough
- Hemoptysis
- Hypoxemia *
- Syncope *
- Arrythmia (atrial fibrillation)
- Hemodynamic collapse
- Sudden cardiac arrest

Not All Hypoxemia Needs PE Evaluation

- Significant hypoxemia due to PE is associated with **considerable clot burden, likely with hemodynamic compromise**
- What is your pretest probability?

Syncope in PE





17% prevalence!
n = 560

→

0.15-2% prevalence
n = 1.67 million

13 Prandoni et al, *N Engl J Med*, 2016.
14 Costantino et al, *JAMA Intern Med*, 2018.

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Overview

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- ❑ Post-PE Care

My Diagnostic Workflow

Pretest Probability	Clot Assessment	Biomarkers	RV Dysfunction	Vital Signs	Perfusion	Risk Scores	Classification
Well's	CTA	HS troponin	TTE	HR	Lactate	PESI	European (ESC)
D-dimer	Duplex	BNP	CTA	BP	Cr		American (AHA)
				SpO_2	Na		

What Is Your Pretest Probability?

Wells' Criteria for Pulmonary Embolism

Objectifies risk of pulmonary embolism.

When to Use | Pearls/Pitfalls | Why Use

Clinical signs and symptoms of DVT	No 0	Yes +3
PE is #1 diagnosis OR equally likely	No 0	Yes +3
Heart rate > 100	No 0	Yes +1.5
Immobilization at least 3 days OR surgery in the previous 4 weeks	No 0	Yes +1.5
Previous, objectively diagnosed PE or DVT	No 0	Yes +1.5
Hemoptysis	No 0	Yes +1
Malignancy w/ treatment within 6 months or palliative	No 0	Yes +1

Well's Score	Well's Tier	Prevalence
0-1	Low	1.3%
2-6	Moderate	16.2%
7-12.5	High	37.5%

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15 Wells et al, *Ann Intern Med*, 2001.

D-Dimer

- **High negative predictive value** (97-99%) [16]
- Poor positive predictive value (44-67%) [16]
  - **Alternative causes**: malignancy, AKI, infection, etc.
- *Remember: use age-adjusted cutoff values*

16 Kearon et al, *N Engl J Med*, 2019.

My Diagnostic Workflow

Pretest Probability	Clot Assessment	Biomarkers	RV Dysfunction	Vital Signs	Perfusion	Risk Scores	Classification
Well's	CTA	HS troponin	TTE	HR	Lactate	PESI	European (ESC)
D-dimer	Duplex	BNP	CTA	BP	Cr		American (AHA)
				SpO_2	Na		

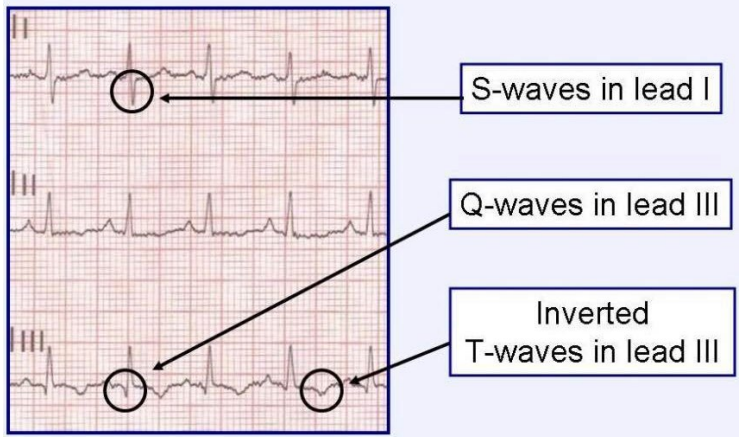
Biomarkers of RV Strain

- Elevations in **HS troponin** and **BNP** reflect subendothelial RV ischemia and strain/stretch [17, 19]
- Associated with **clinical deterioration and mortality** in PE [18, 20]

17 Meyer et al, *J Am Coll Cardiol*, 2000.
18 Becattini et al, *Circulation*, 2007.
19 Binder et al, *Circulation*, 2005.
20 Coutance et al, *Crit Care*, 2008.

EKG

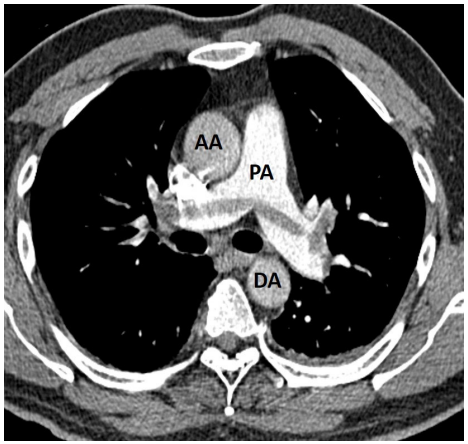
- Most common finding is **sinus tachycardia** (>50%)
- **S1Q3T3** (~20%) *
- New **right bundle branch block** (~20%) *



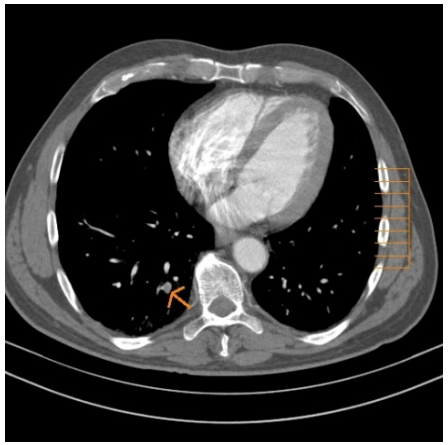
CT Pulmonary Angiogram

- Evaluation of **clot burden** in the pulmonary arterial circulation
- Evaluation of **right heart strain**
  - May not always be accurate (in comparison with TTE)
  - Based on relationship between heart and cross-sectional cuts
- Assess for **reflux of contrast into IVC**
  - Correlates with degree of tricuspid regurgitation (TR) and pulmonary artery systolic pressure (PASP)
- *Remember: order CT angiogram (PE protocol), not CT chest w/ contrast*

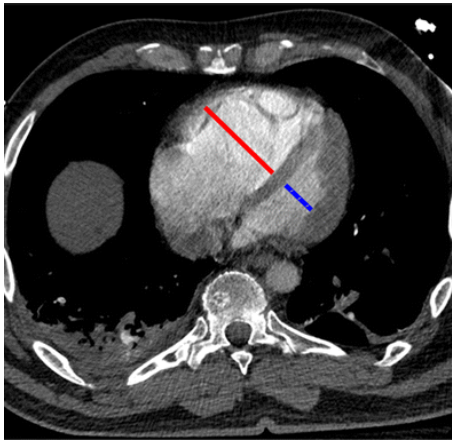
CT Pulmonary Angiogram



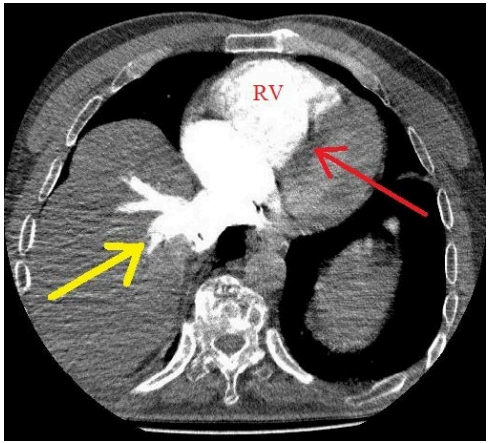
Proximal (saddle)



Distal (subsegmental)



RV/LV >1



Reflux of contrast

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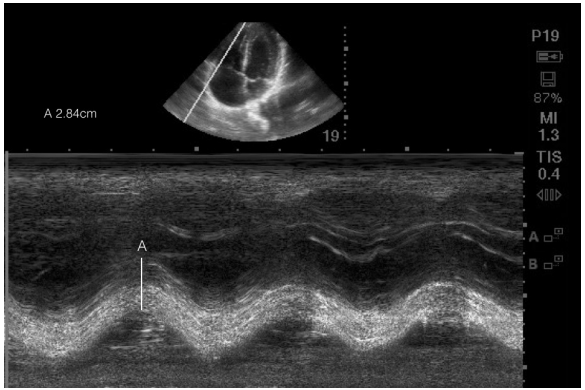
TTE



- Measurement of left ventricular function
- Ideal evaluation of true **right heart strain**
  - **McConnell's sign** (*specific, but not sensitive*)
- Tricuspid annular plane systolic excursion (TAPSE)
  - Poor man's measure of "RV function"
  - Predicts short- and long-term adverse events [23]

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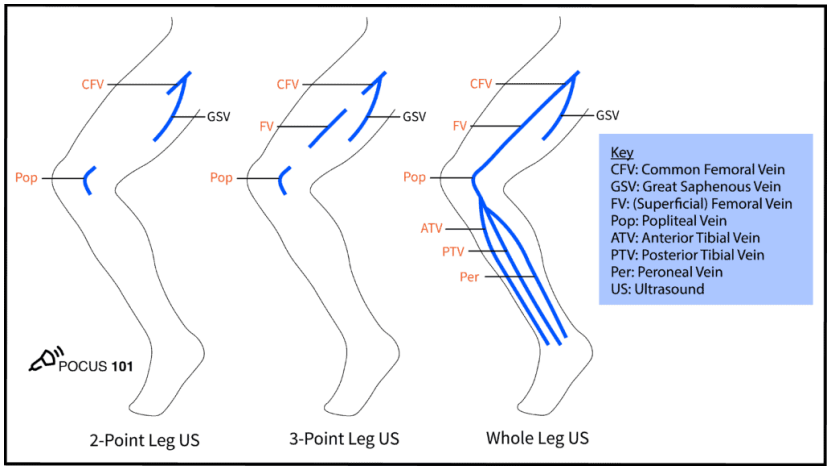
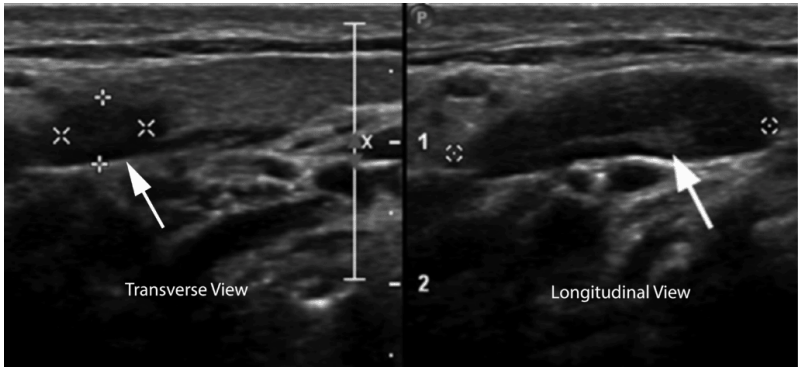
23 Lyhne et al, *Eur Heart J Cardiovasc Imaging*, 2021.

Venous Duplex

- DVT is identified in only **~50%** of PE cases [24]





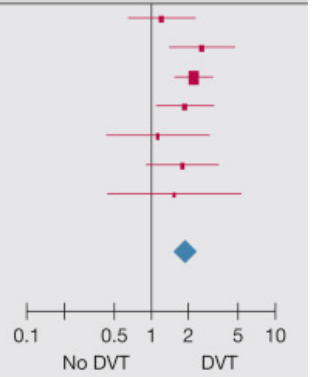
24 van Langevelde et al, *Haemotologica*, 2013.

DVT + PE Matters

- Should we care about DVT if we already know there is a PE?
- Increased odds of **PE-related 30-day mortality** (OR 1.9) [25]
- Increased risk **recurrent VTE** (~4x) [25]

Study or Subgroup	DVT Events	DVT Total	No DVT Events	No DVT Total	Weight	Odds Ratio M-H, Random, 95% CI
Jiménez, Chest 2007	21	266	22	333	12.8%	1.21 [0.65, 2.25]
Jiménez, AJRCCM 2010	40	362	16	345	13.7%	2.55 [1.40, 4.65]
RIETE, AJRCCM 2010	137	2,803	38	1,673	37.1%	2.21 [1.54, 3.18]
Jiménez, Thorax 2011	31	228	28	361	16.9%	1.87 [1.09, 3.21]
Vedovati, Chest 2012	17	271	6	108	5.4%	1.14 [0.44, 2.97]
Jiménez, AJRCCM 2014	22	375	15	445	10.9%	1.79 [0.91, 3.50]
Kabhrel, Thorax 2014	4	74	8	224	3.3%	1.54 [0.45, 5.28]
Total (95% CI)		**4,379**		**3,489**	**100.0%**	**1.89 [1.52, 2.36]**
Total events	272		133			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 4.87$, df = 6 ($P = .56$); $I^2 = 0\%$
Test for overall effect: $z = 5.63$ ($P < .00001$)



25 Becattini et al, *Chest*, 2016.

My Diagnostic Workflow

Pretest Probability	Clot Assessment	Biomarkers	RV Dysfunction	Vital Signs	Perfusion	Risk Scores	Classification
Well's	CTA	HS troponin	TTE	HR	Lactate	PESI	European (ESC)
D-dimer	Duplex	BNP	CTA	BP	Cr		American (AHA)
				SpO_2	Na		

UPMC LIFE CHANGING MEDICINE

Overview

Pre-Diagnosis
- ❑ Definition
- ❑ Epidemiology
- ❑ Pathophysiology
- ❑ Risk Factors

Diagnosis
- ❑ Clinical Presentation
- ❑ Diagnostic Testing
- ❑ **Risk Stratification**
- ❑ Thrombophilia Testing

Treatment
- ❑ Anticoagulation
- ❑ Post-PE Care

Nomenclature Is Confusing!

Crashing massive PE

Intermediate high risk PE

Intermediate low risk PE

Submassive PE

Subacute PE

Saddle PE ?

Massive PE

Non-crashing massive PE

Chronic thromboembolic disease (CTED)

Chronic thromboembolic pulmonary hypertension (CTEPH)

Acute PE

UPMC LIFE CHANGING MEDICINE

Classification Dictates Treatment

	Category	Shock or hypotension	PESI III-IV or sPESI ≥1	RV dysfunction	Biomarkers
American Heart Association (AHA)	Massive	+	+	+	+
	Submassive	–	+	Either or both +	
	Low	–	–	–	–

	Category	Shock or hypotension	PESI class III-IV or sPESI ≥1	RV dysfunction	Biomarkers
European Society of Cardiology (ESC)	High	+	+	+	+
	Intermediate high	–	+	Both +	
	Intermediate low	–	+	Either +	
	Low	–	–	–	–

UPMC LIFE CHANGING MEDICINE

PE Severity Index (PESI)

Age		years
Sex	Female 0	Male +10
History of cancer	No 0	Yes +30
History of heart failure	No 0	Yes +10
History of chronic lung disease	No 0	Yes +10
Heart rate ≥110	No 0	Yes +20
Systolic BP <100 mmHg	No 0	Yes +30
Respiratory rate ≥30	No 0	Yes +20
Temperature <36°C/96.8°F	No 0	Yes +20
Altered mental status (disorientation, lethargy, stupor, or coma)	No 0	Yes +60
O2 saturation <90%	No 0	Yes +20

PESI Score	PESI Class	30-day Mortality
0-65	I	0-1.6%
66-85	II	1.7-3.5%
86-105	III	3.2-7.1%
106-125	IV	4.0-11.4%
126-220	V	10.0-24.5%

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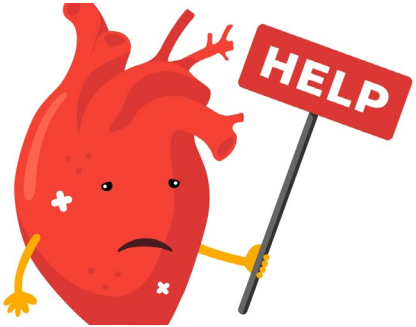
26 Aujesky et al, *Am J Respir Crit Care Med*, 2005.

Biomarkers Associated with Mortality

- Hemodynamic instability
  - **Tachycardia (HR >110)** [27]
  - **Shock index (HR/SBP) >1** [28]
- Poor end organ perfusion
  - **Lactate >2** [29]
  - **AKI (eGFR <60)** [30]
- Hyponatremia (**Na <135**) [31]
  - RV dysfunction → activation of RAAS



27 Jaureguizar et al, *Chest*, 2022.
28 Otero et al, *Eur Respir J*, 2007.
29 Vanni et al, *Ann Emerg Med*, 2013.
30 Kostrubiec et al, *Thomb Haemostat*, 2019.
31 Zhou et al, *Int J Cardiol*, 2017.

UPMC LIFE CHANGING MEDICINE

My Diagnostic Workflow

Pretest Probability	Clot Visualization	Biomarkers	RV Dysfunction	Vital Signs	Perfusion	Risk Scores	Classification
Well's	CTA	HS troponin	TTE	HR	Lactate	PESI	European (ESC)
D-dimer	Duplex	BNP	CTA	BP	Cr		American (AHA)
				SpO_2	Na		

UPMC LIFE CHANGING MEDICINE

Clinical Question #4

Why is saddle PE not a very helpful descriptor for PE treatment?

Saddle PE only describes the geographic location but does not provide meaningful information about risk stratification and classification, which dictates treatment options.

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Diagnosis
- ❑ Clinical Presentation
- ❑ Diagnostic Testing
- ❑ Risk Stratification
- ❑ **Thrombophilia Testing**

Treatment
- ❑ Anticoagulation
- ❑ Advanced Therapies
- ❑ Post-PE Care

Thrombophilia Testing Not Required

- Patients with **clearly provoked VTE event**
  - Treat for 3-6 months
- Patients with **first unprovoked VTE event**
  - Indefinite treatment (benefit > risk)
  - Testing would not change management

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32 Middeldorp et al, *Blood Adv*, 2023.

Thrombophilia Testing Beneficial

- Patients with **strong family history** of thromboembolic events
- Patients with **first VTE event w/o clear "major" provoking event**
  - ASH 2023: "non-surgical transient risk factors"
  - If negative, reasonable to spare indefinite full dose A/C
- Patients with **multisite clotting events** (venous and arterial)
  - Higher suspicion for antiphospholipid syndrome
  - Management differs (warfarin > DOAC)

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32 Middeldorp et al, *Blood Adv*, 2023.

Which Thrombophilia Tests to Order?

- **Not affected** by presence of VTE or systemic anticoagulation:
  - **Prothrombin gene mutation**
  - **Factor V Leiden**
  - **Anti-beta-2-glycoprotein antibody**
  - **Anti-cardiolipin antibody**

- **Affected** by presence of VTE or systemic anticoagulation:
  - Protein C and S
  - Activated protein C
  - Antithrombin III
  - Lupus anticoagulant panel

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32 Middeldorp et al, *Blood Adv*, 2023.

Clinical Question #5

In patients with PE who meet criteria for thrombophilia testing, when should testing be ordered?

Prothrombin gene mutation, Factor V Leiden, anti-beta-2-glycoprotein antibody, and anti-cardiolipin antibody at time of diagnosis. Remainder of tests should be completed as an outpatient, after 3-6 months of treatment, off anticoagulation.

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- ❑ Thrombophilia Testing

Treatment
- ❑ **Anticoagulation**
- ❑ Post-PE Care

Unfractionated Heparin (UFH)

- One of most common systemic anticoagulants in the hospital
- Benefits:
  - Quick on, quick off
  - Reversible with protamine sulfate
  - Different therapeutic ranges for different diseases

UFH or LMWH?

- Compared to LMWH, UFH is associated with:
  - **Longer time to first therapeutic anti-Xa level**

UFH only (n=12)	Enoxaparin only (n=2)
13 hours (6-46 hours)	4 hours (3-5 hours) *

* After single subQ dose, per available UPMC SMH pharmacokinetic data

  - **Longer duration (days) of use in the hospital**

UFH only (n=12)	Enoxaparin only (n=2)
5.3 days	2.5 days

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Courtesy of Brianna Ordons, PharmD, BCPS, BCCCP; data from May 2022.

UFH or LMWH?

- Compared to UFH, LMHW is associated with:
  - **Decreased anti-Xa monitoring**
    - Decreased lab draws (and increased patient satisfaction)
    - Decreased cost

Month/Year	# of anti-Xa levels drawn at SMH
January 2021	730
February 2021	552
January 2022	324
February 2022	392

Courtesy of Brianna Ordons, PharmD, BCPS, BCCCP; data from May 2022.

Prioritize LMWH over UFH

- Why: time to **early therapeutic level** matters
- Who: **low risk PE** or **intermediate risk PE**
- How: **1mg/kg Q12H**
- Duration: assess clinical stability over **36-48 hours** [33]
- *Remember: data is sparse for severe obesity (BMI ≥40 or >150kg)* [34, 35]

33 Klok et al, *Lancet Haematol*, 2021.
34 Nutescu et al, *Ann Pharmacother*, 2009.
35 Freeman et al, *Am J Hematol*, 2012.

Oral Anticoagulants

- **Similar efficacy** between apixaban and rivaroxaban [36]
- **Decreased bleeding events** with apixaban c/w rivaroxaban [36]
- **Higher bleeding risk** with warfarin compared to DOACs [37, 38]
- Warfarin remains the treatment of choice for:
  - Failure of other anticoagulants
  - Valvular heart disease
  - Antiphospholipid syndrome

36 Aryal et al, *Blood Adv*, 2019.
37 Buller et al, *N Engl J Med*, 2012.
38 Agnelli et al, *N Engl J Med*, 2013.

Fibrinolysis

- Standard of care for **massive/high risk PE**
  - Decreased risks of **mortality and recurrent PE** (OR 4.5) [39]
- Not routinely used for submassive/intermediate risk PE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

Guy Meyer, M.D., Eric Vicaut, M.D., Thierry Danays, M.D., Giancarlo Agnelli, M.D., Cecilia Becattini, M.D., Jan Beyer-Westendorf, M.D., Erich Bluhmki, M.D., Ph.D., Helene Bouvaist, M.D., Benjamin Brenner, M.D., Francis Couturaud, M.D., Ph.D., Claudia Dellas, M.D., Klaus Empen, M.D., Ana Franca, M.D., Nazzareno Galiè, M.D., Annette Geibel, M.D., Samuel Z. Goldhaber, M.D., David Jimenez, M.D., Ph.D., Matija Kozak, M.D., Christian Kupatt, M.D., Nils Kucher, M.D., Irene M. Lang, M.D., Mareike Lankeit, M.D., Nicolas Meneveau, M.D., Ph.D., Gerard Pacouret, M.D., Massimiliano Palazzini, M.D., Antoniu Petris, M.D., Ph.D., Piotr Pruszczyk, M.D., Matteo Rugolotto, M.D., Aldo Salvi, M.D., Sebastian Schellong, M.D., Mustapha Sebbane, M.D., Bozena Sobkowicz, M.D., Branislav S. Stefanovic, M.D., Ph.D., Holger Thiele, M.D., Adam Torbicki, M.D., Franck Verschuren, M.D., Ph.D., and Stavros V. Konstantinides, M.D., for the PEITHO Investigators*

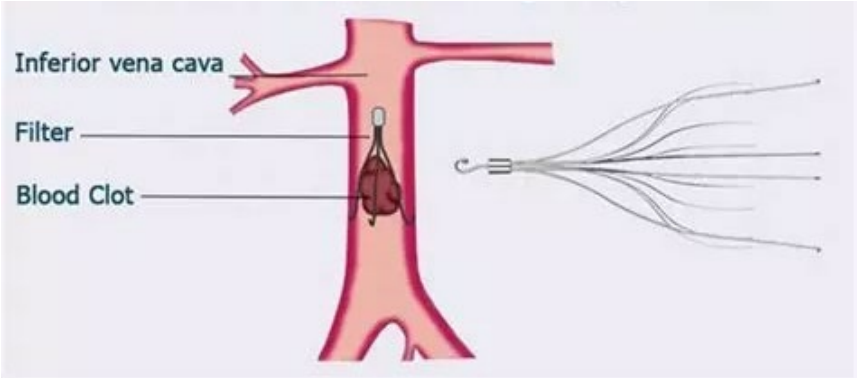
Mortality/decompensation: OR 0.44, NNT 33
Recurrent PE: OR 0.20, NNT 125

Major extracranial bleed: OR 5.55, NNH 20
Stroke: OR 12.1, NNH 45

39 Wan et al, *Circulation*, 2004.
40 Meyer et al, *N Engl J Med*, 2014.

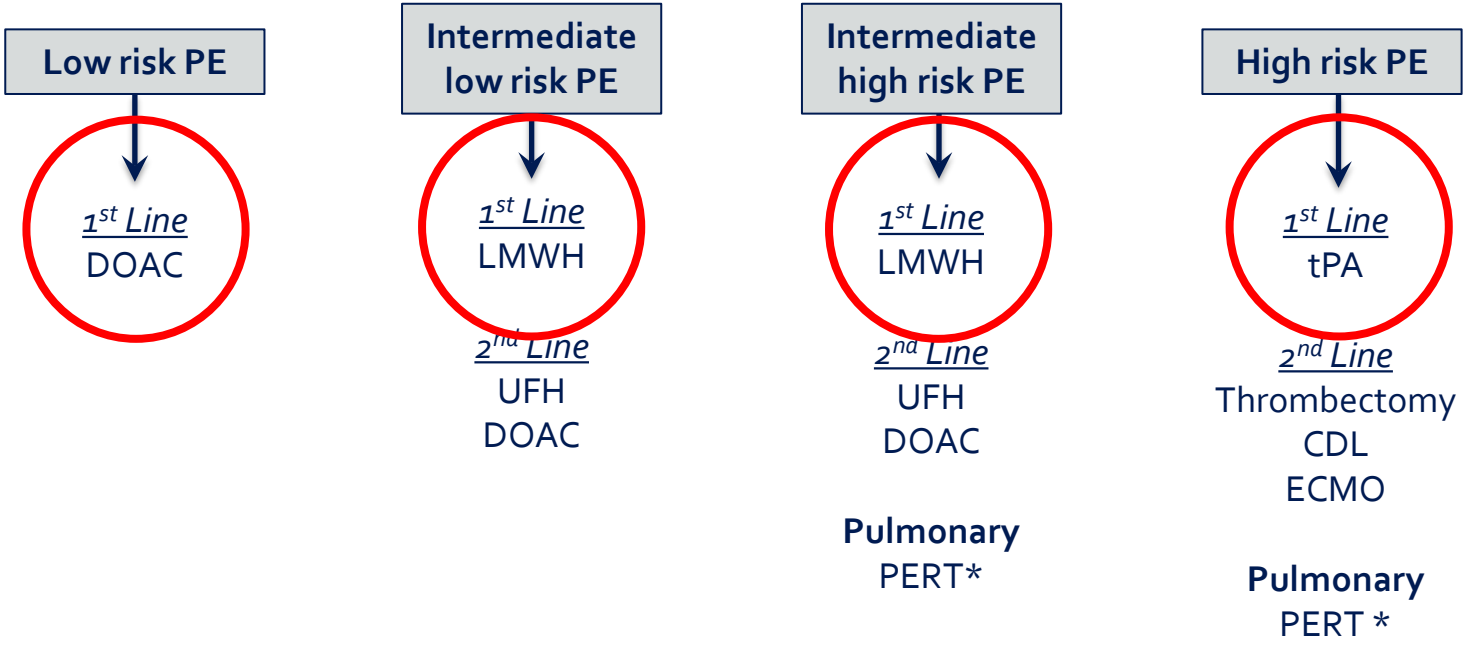
IVC Filter

- Absolute contraindication (or failure of) systemic anticoagulation
- Ideally **removed after acute insult resolves**
- Substantially **increases risk of recurrent DVT** [41]
- Retrievable filters preferred over historic Greenfield filters



41 PREPIC Study Group, *Circulation*, 2005.

My Therapeutic Workflow



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Is Bedrest a Thing of the Past?

- Prior recommendations to avoid ambulation due to concerns about disease progression and/or hemodynamic collapse
- **Early ambulation reduces VTE progression** (RR 0.79)

ELSEVIER

International Journal of Cardiology

Volume 137, Issue 1, September 2009, Pages 37-41

A meta-analysis of bed rest versus early ambulation in the management of pulmonary embolism, deep vein thrombosis, or both ☆

Nadia Aissaoui [a], Edith Martins [b], Stéphane Mouly [c], Simon Weber [a], Christophe Meune [a]

42 Aissaoui et al, *Int J Cardiol*, 2009.

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Treatment
- ❑ Anticoagulation
- ❑ **Post-PE Care**

Timing of Procedures Post-PE

- Ideally postpone ≥**3 months**
- At a minimum, postpone ≥**4-6 weeks**
  - Highest VTE recurrence in the first 4 weeks [42]
  - Consider peri-operative IVC filter placement
- **Risk/benefit discussion** with **multidisciplinary involvement**

UPMC LIFE CHANGING MEDICINE

43 Caron et al, *JAMA*, 2019.

In Summary…

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Well's	CTA	HS troponin	TTE	HR	Lactate	PESI	European (ESC)
D-dimer	Duplex	BNP	CTA	BP	Cr		American (AHA)
				SpO_2	Na		

Low risk PE

↓

1st Line
DOAC

Intermediate low risk PE

↓

1st Line
LMWH

Intermediate high risk PE

↓

1st Line
LMWH

High risk PE

↓

1st Line
tPA

UPMC LIFE CHANGING MEDICINE

Thank You! Questions?

Email: zour@upmc.edu

Cell: 510-672-1617

UPMC LIFE CHANGING MEDICINE

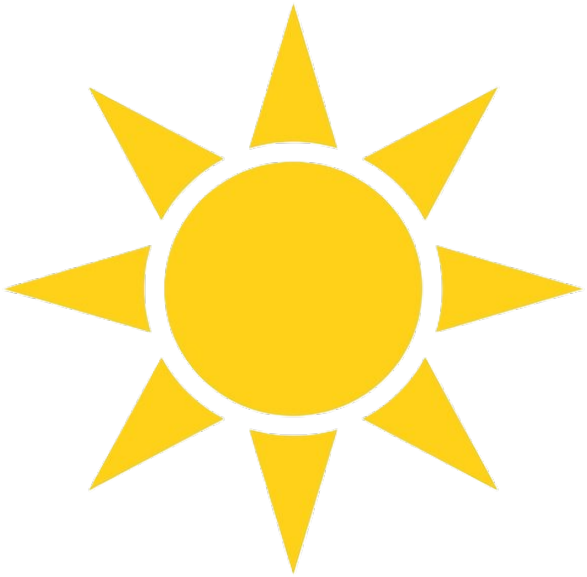
YOU CAN (and should!) DO IT! Opioid Use Disorder Management in Primary Care

ALYSSA BRUEHLMAN, MD
UPMC ST MARGARET FAMILY MEDICINE RESIDENCY PROGRAM

3/6/2025

DISCLOSURES

No financial disclosures



OBJECTIVES

Describe	opioid-related harms at the patient and population level
Recognize	diagnostic criteria for opioid use disorder (OUD)
Compare	medications for the treatment of opioid use disorder (MOUD)
Examine	strategies for buprenorphine initiation and maintenance
Empower	to incorporate OUD care into primary care practice

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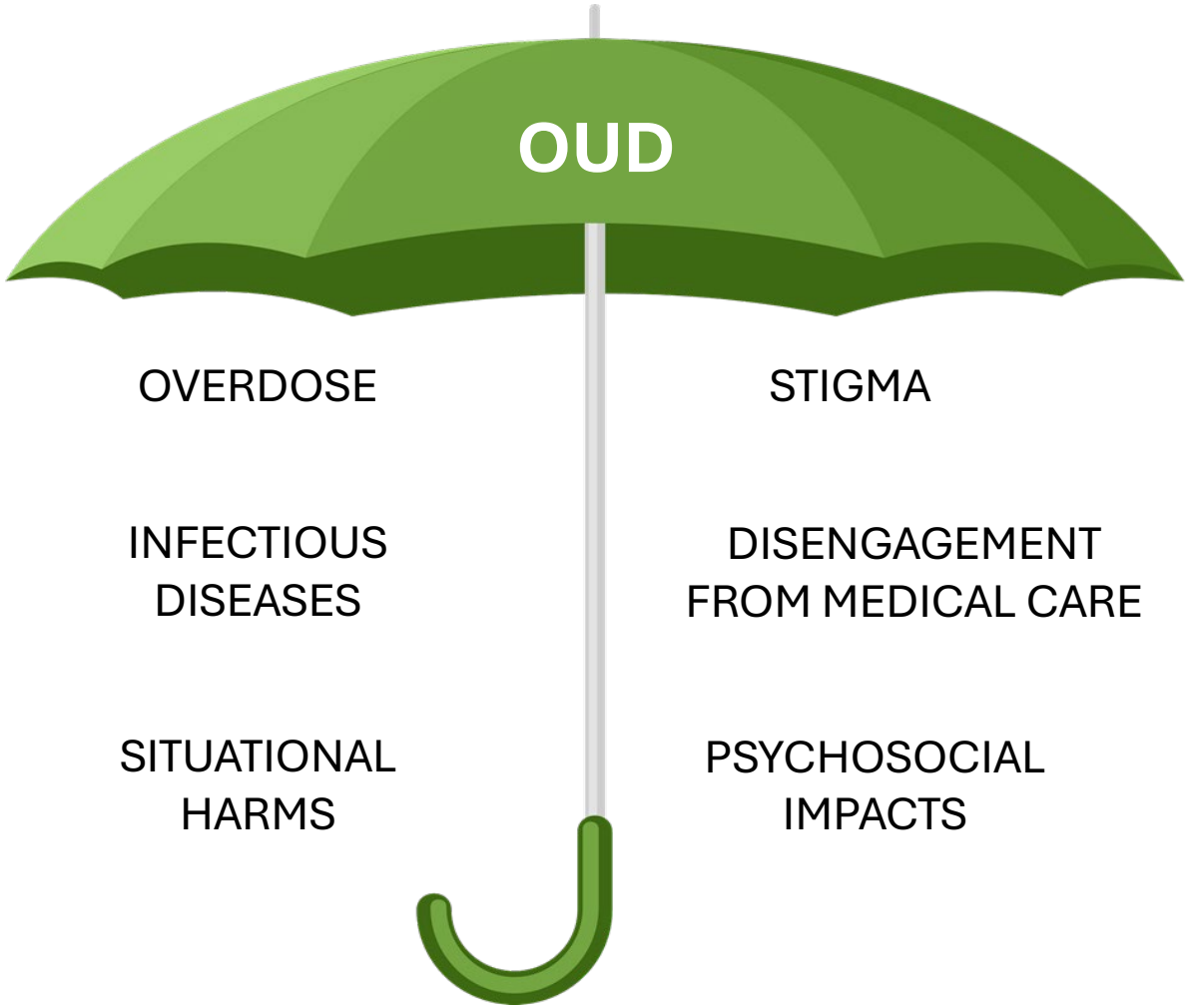
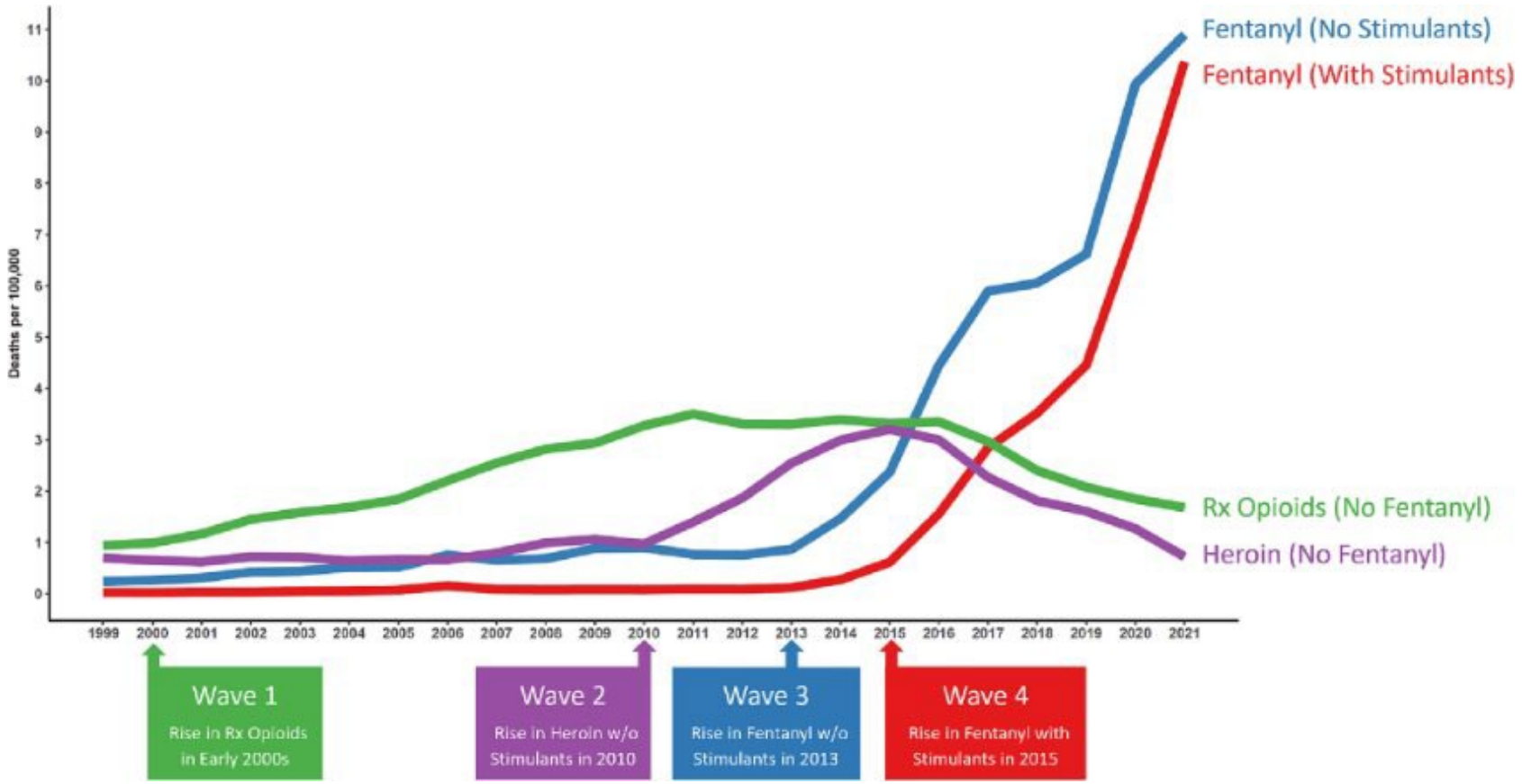
Why We Care: Individual Harms



Why We Care: Population-Wide Harms



Friedman et al. *Addiction* 2023.

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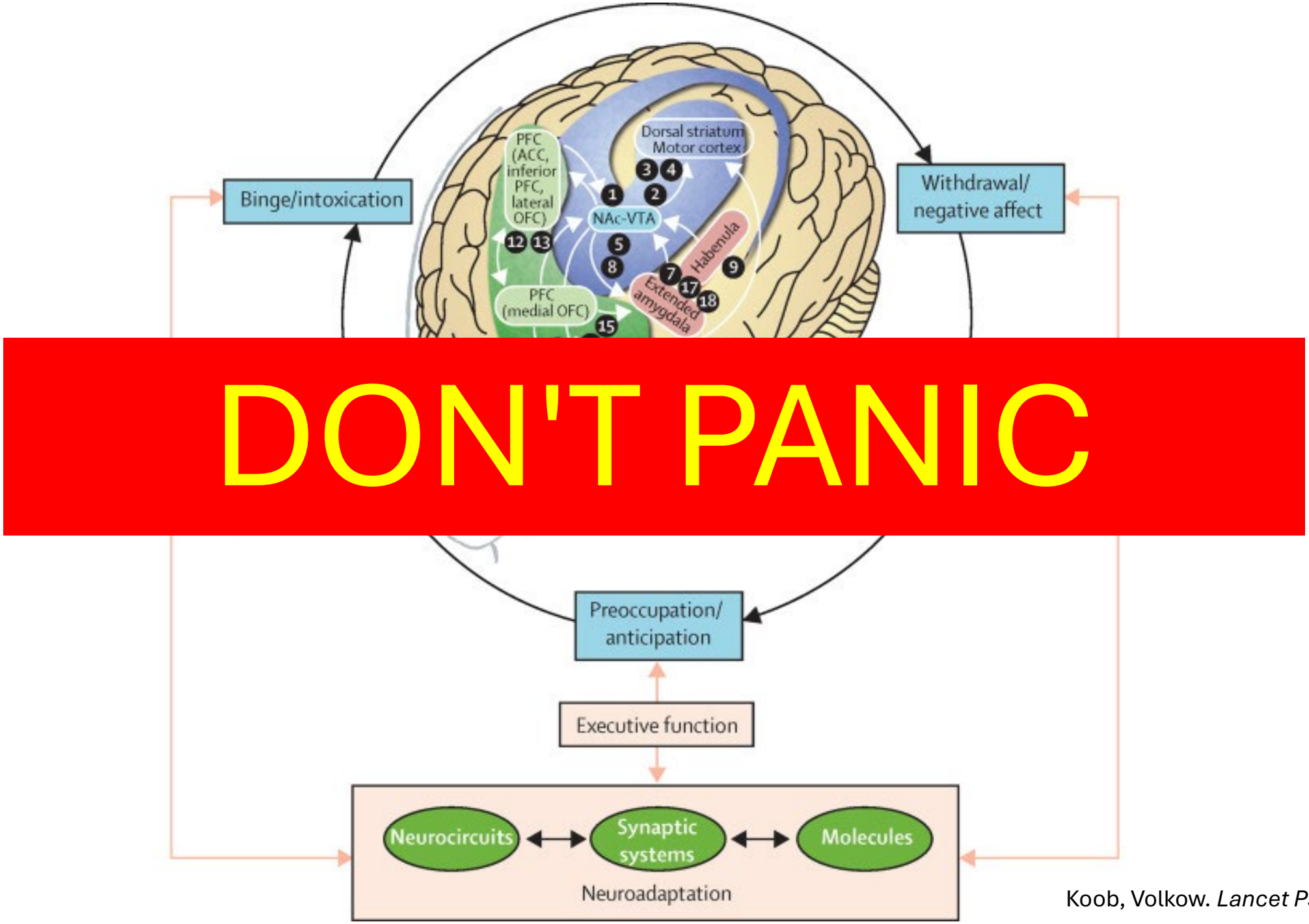


Koob, Volkow. *Lancet Psychiatry* 2016.

Screening

Population	Recommendation	Grade
Adults age 18 years or older	The USPSTF recommends screening by asking questions about unhealthy drug use in adults age 18 years or older. Screening should be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred. (Screening refers to asking questions about unhealthy drug use, not testing biological specimens.)	B
Adolescents	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for unhealthy drug use in adolescents. See the "Practice Considerations" section for suggestions for practice regarding the I statement.	I

USPSTF 2020.

Screening Tools

Tool	Substance type		Patient age		How tool is administered	
	Alcohol	Drugs	Adults	Adolescents	Self-administered	Clinician-administered
Screening to Brief Intervention (S2BI)	X	X		X	X	X
Brief Screener for Alcohol, Tobacco, and other Drugs (BSTAD)	X	X		X	X	X
Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)	X	X	X			
Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide (NIAAA)	X			X		
Opioid Risk Tool – OUD (ORT-OUD) Chart		X	X			

Tool	Substance type		Patient age		How tool is administered	
	Alcohol	Drugs	Adults	Adolescents	Self-administered	Clinician-administered
Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)	X	X	X		X	X
CRAFFT	X	X		X	X	X
Drug Abuse Screen Test (DAST-10)* *For use of this tool - please contact Dr. Harvey Skinner*		X	X		X	X
Drug Abuse Screen Test (DAST-20: Adolescent version)* *For use of this tool - please contact Dr. Harvey Skinner*		X		X	X	X
NIDA Drug Use Screening Tool (NMASSIST) *(discontinued in favor of TAPS screening above)*	X	X	X			X
Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide (NIAAA)	X			X		X

NIDA 2023.

Diagnosing OUD

In the last 12 months…	
Craving	Withdrawal from activities
Larger amounts or longer than intended	Use in physically hazardous situations
Persistent desire or attempts to cut down or stop	Use despite knowing its harm
Excessive time using, getting, recovering	To[illegible]n
Failure to fulfill a major role	Wi[illegible]al
Use despite social/interpersonal conflicts	

Compulsion

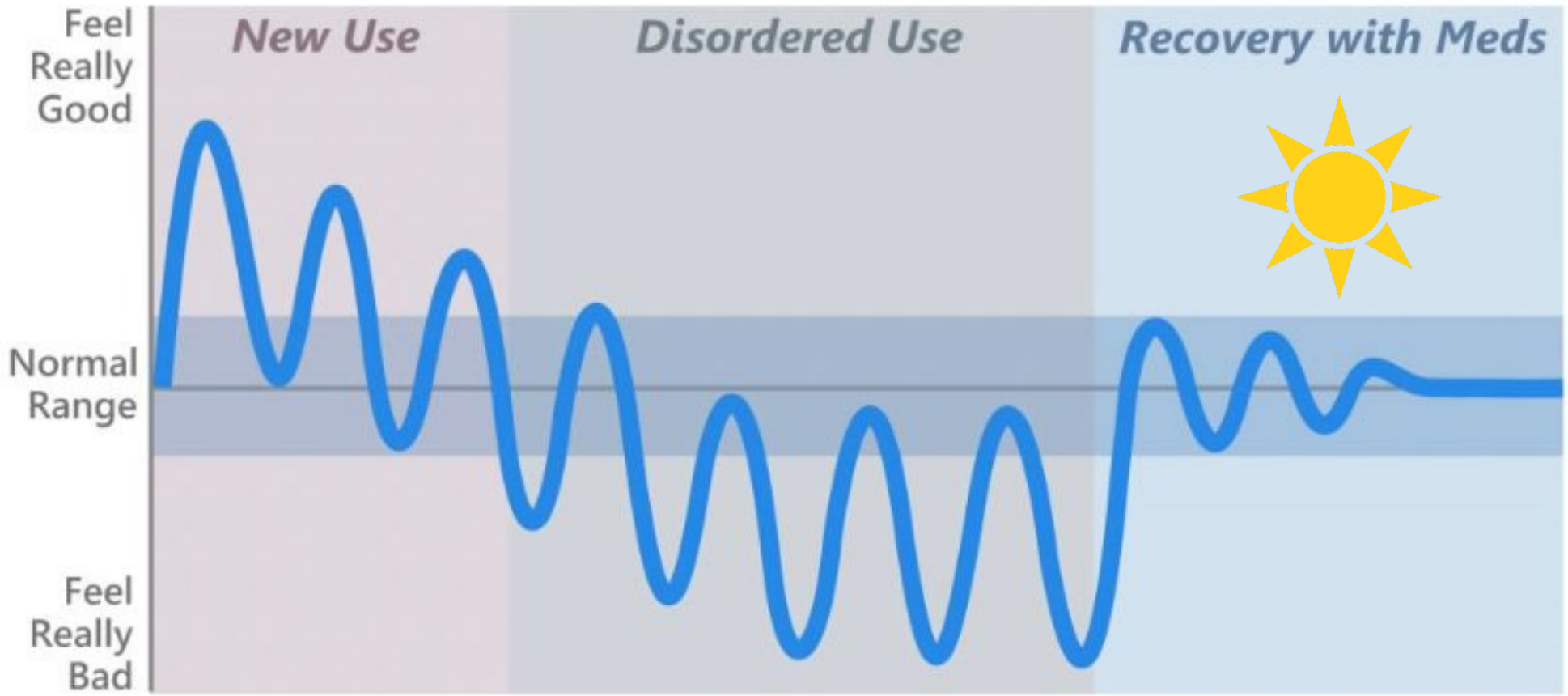
Craving

Consequences

Control

Am Psychiatric Assoc. *DSM-5* 2013.

Opioid Use Disorder



Univ of Washington Addictions, Drug, & Alcohol Institute 2023.

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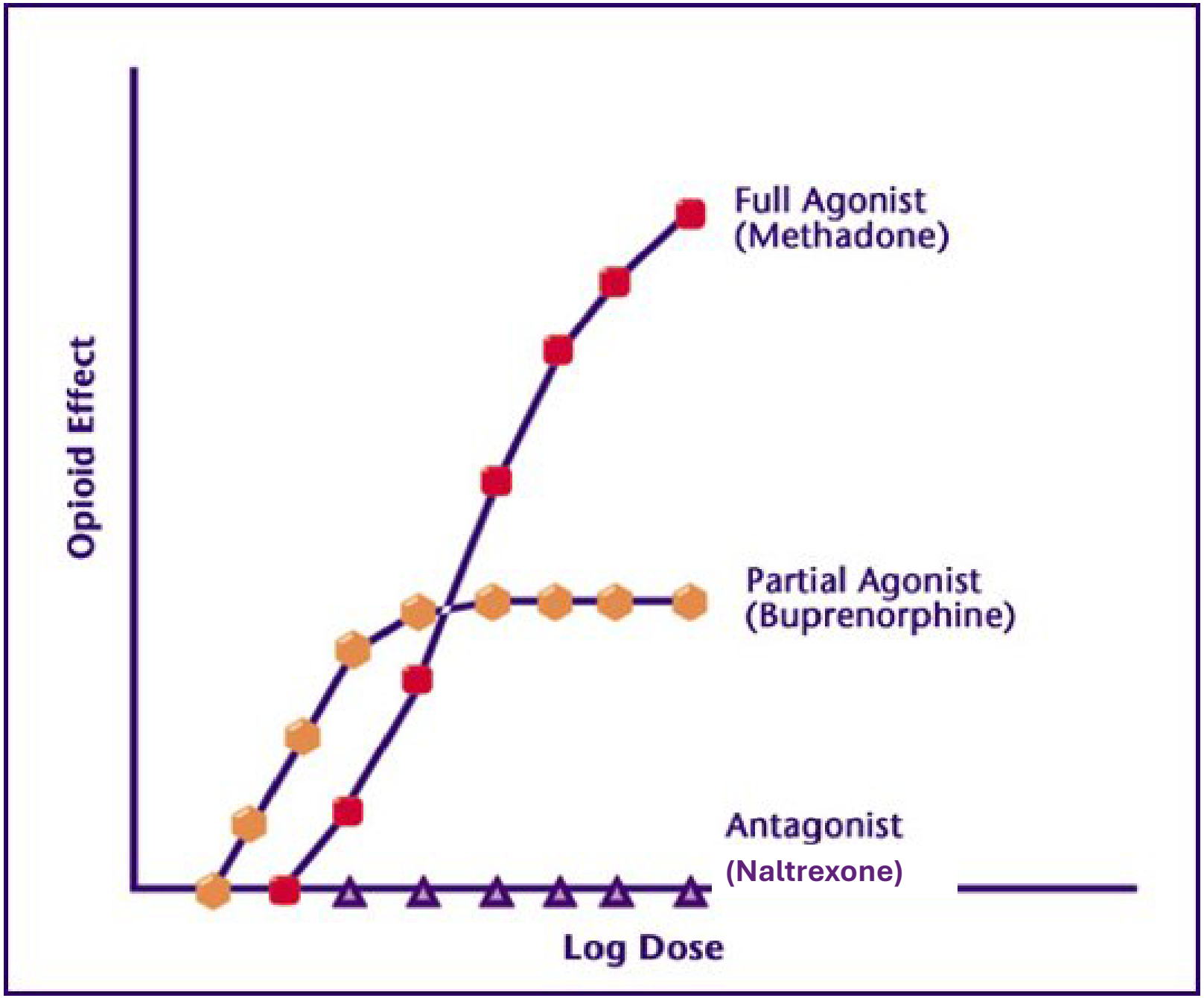
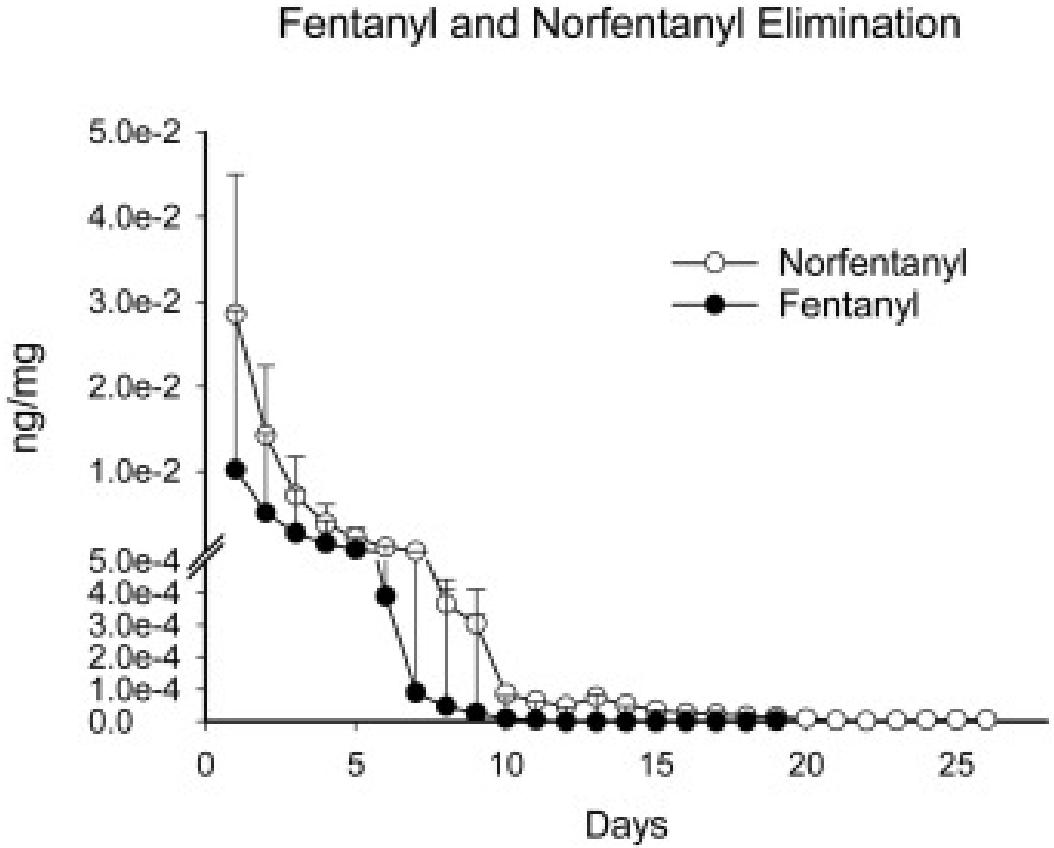


Adapted from naabt.org

The fentanyl problem

- Potency
  - 50-100x more than morphine
- Lipophilicity
  - Rapidly crosses BBB
  - **Chronic heavy use: accumulation in adipose tissue, delayed clearance**



Huhn et al. *Drug Alcohol Dependence* 2020.

	METHADONE	BUPRENORPHINE	NALTREXONE
Mechanism	**Agonist**	**Partial** agonist	**Antagonist**
Regulation	Schedule **II**	Schedule **III**	N/A
Dosing	QD or BID 	QD-QID  WEEKLY OR MONTHLY 	MONTHLY 
Primary Care Rx	**NO**	YES	YES
Initiation	Start at low doses	**Variable strategies**	**7-14 days withdrawal**
Diversion/misuse	Observed dosing	Co-formulation with naloxone Self-treatment of OUD	N/A
Overdose risk	If rapid titration With polysubstance use	**Less risk** **Ceiling effects**	After discontinuation
Mortality reduction	**50%**	**50%**	**?**

Adapted from NEJM 2023

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Mortality reduction	**50%**	**50%**	**?**

Adapted from NEJM 2023

Methadone

- Proactive ROI
- Learn about their dose!
- Monitor QTc: EKG at least yearly

*Eventual changes? S.644 Modernizing Opioid Treatment Access (MOTA) Act

	METHADONE	BUPRENORPHINE	NALTREXONE
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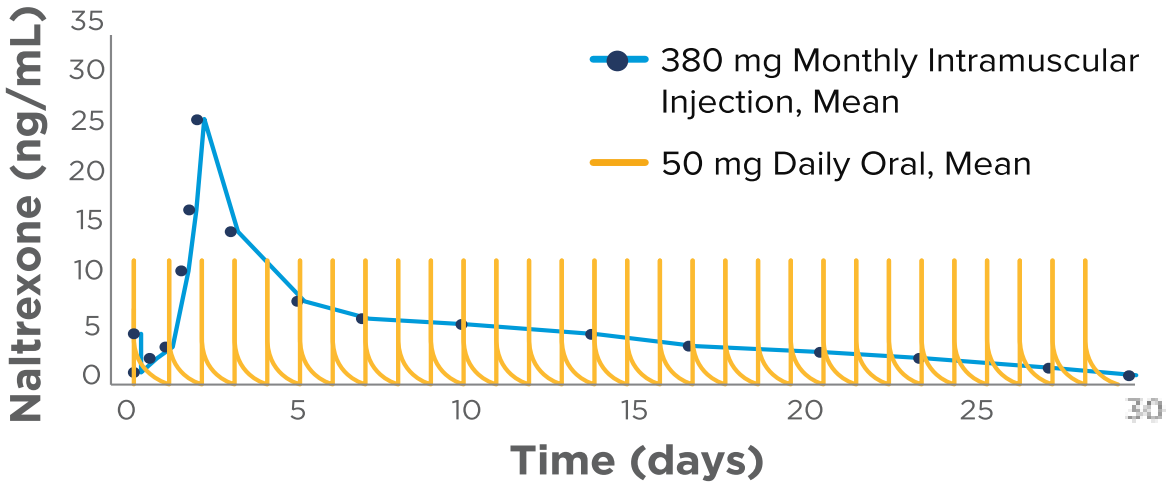
Mortality reduction	**50%**	**50%**	**?**

Adapted from NEJM 2023

XR-Naltrexone

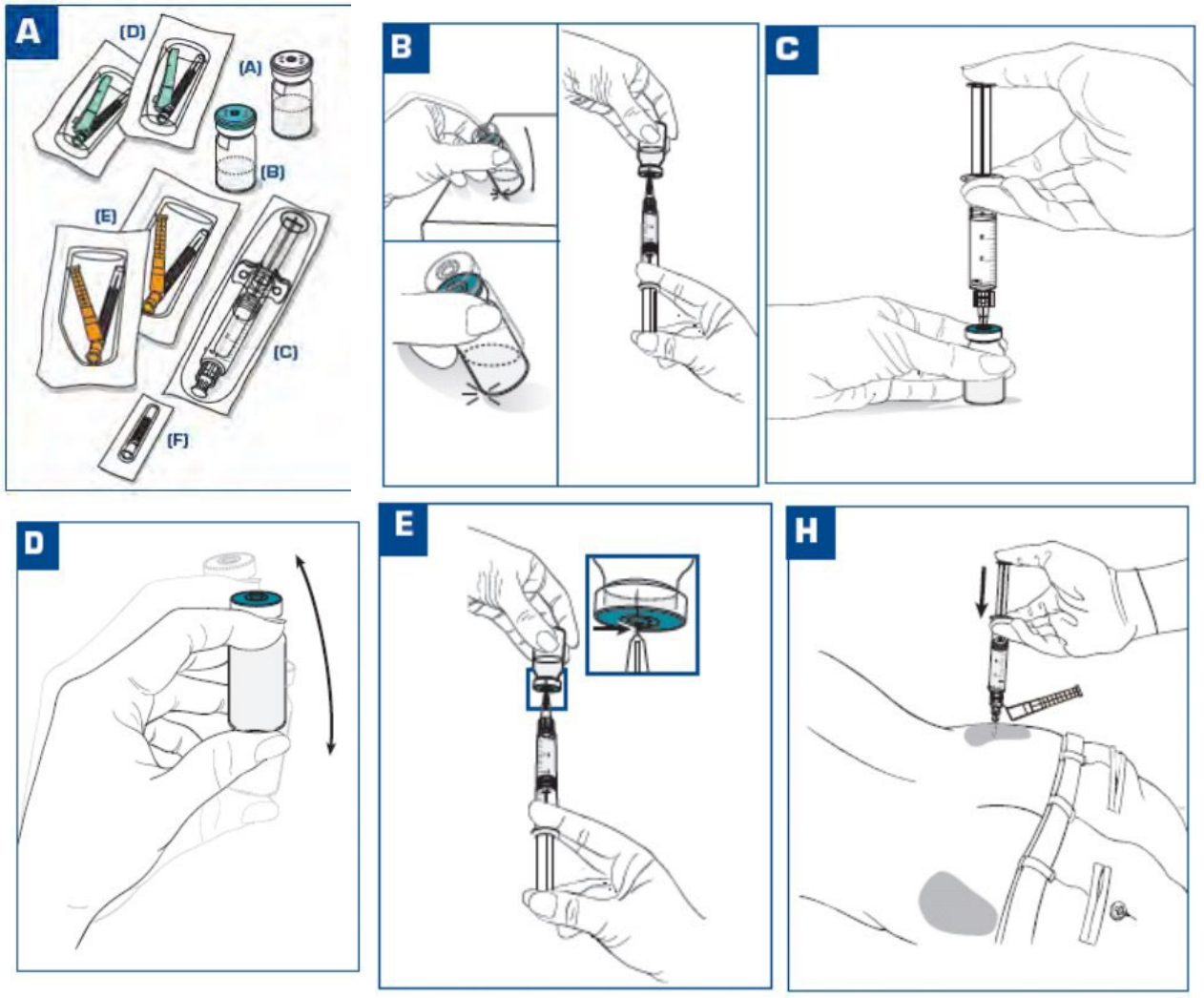
- Requires withdrawal
  - 7-14 days
  - PO naltrexone, IN/IM naloxone challenge
- Hepatoxicity warning
  - Avoid in acute hepatitis, decompensated cirrhosis
- **Overdose risk with treatment discontinuation**
  - Treatment retention lower than MET or BUP



Vivitrol: US Prescribing Information. Alkermes, Inc. 2024.

XR-Naltrexone: Administration

- Storage
  - Refrigerate
  - Remove 45min prior to administration
- Preparation
  - 1 syringe
  - 2 vials
  - 3 needles
- Administration
  - IM gluteal
  - 1.5" or 2" 20-guage



Alkermes, Inc. 2024.

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Primary Care Rx	NO	YES	YES
Initiation	Start at low doses	**Variable strategies**	**7-14 days withdrawal**
Diversion/misuse	Observed dosing	Co-formulation with naloxone Self-treatment of OUD	N/A
Overdose risk	Rapid titration Polysubstance use	**Less risk** **Ceiling effects**	After discontinuation
Mortality reduction	**50%**	**50%**	**?**

Adapted from NEJM 2023

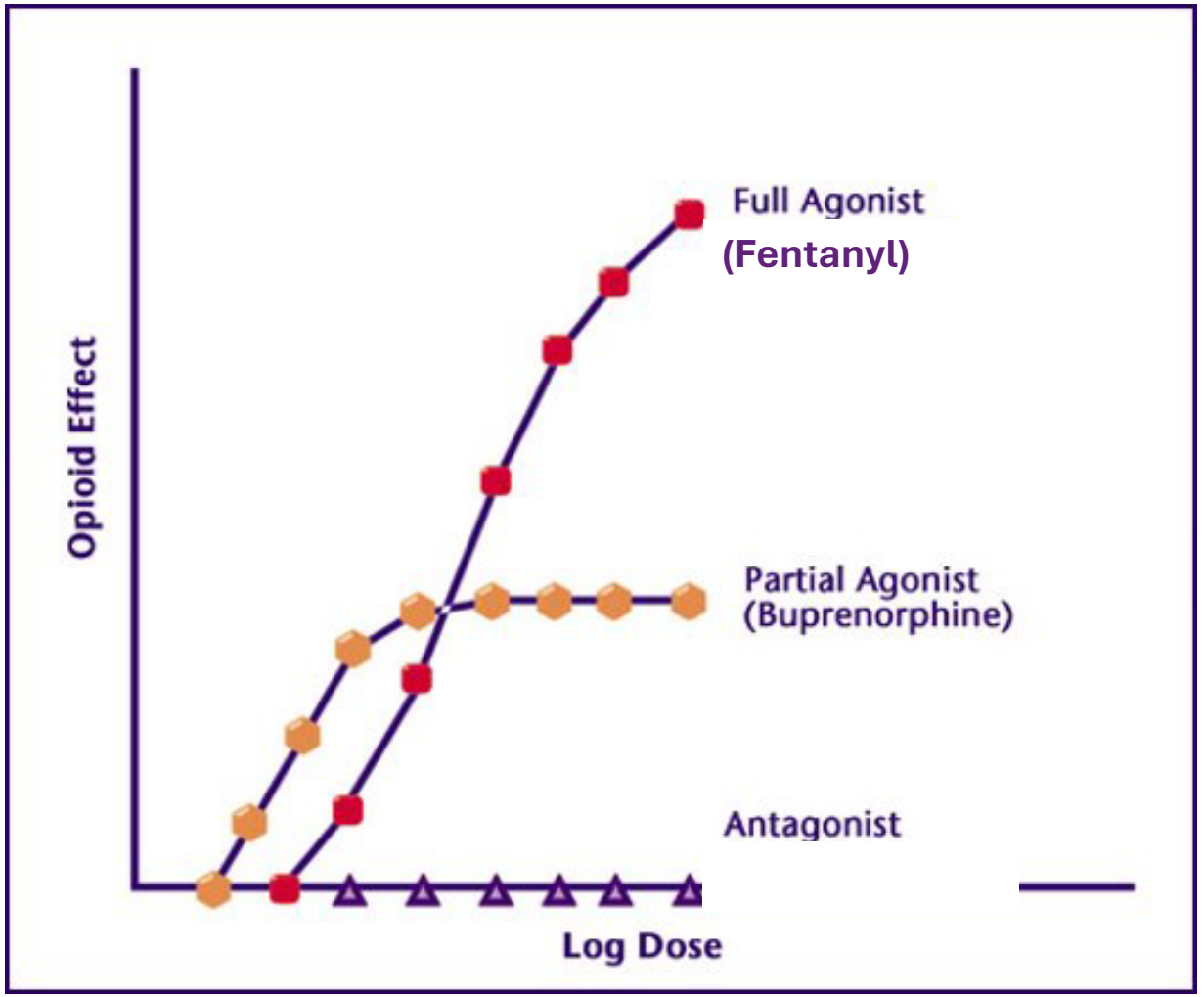
OBJECTIVES

Describe	opioid-related harms at the patient and population level
Recognize	diagnostic criteria for opioid use disorder (OUD)
Compare	medications for the treatment of opioid use disorder (MOUD)
Examine	**strategies for buprenorphine initiation and maintenance**
Empower	to incorporate OUD care into primary care practice

BUP-Precipitated Withdrawal

* Naloxone is not the culprit

MGH 2021.

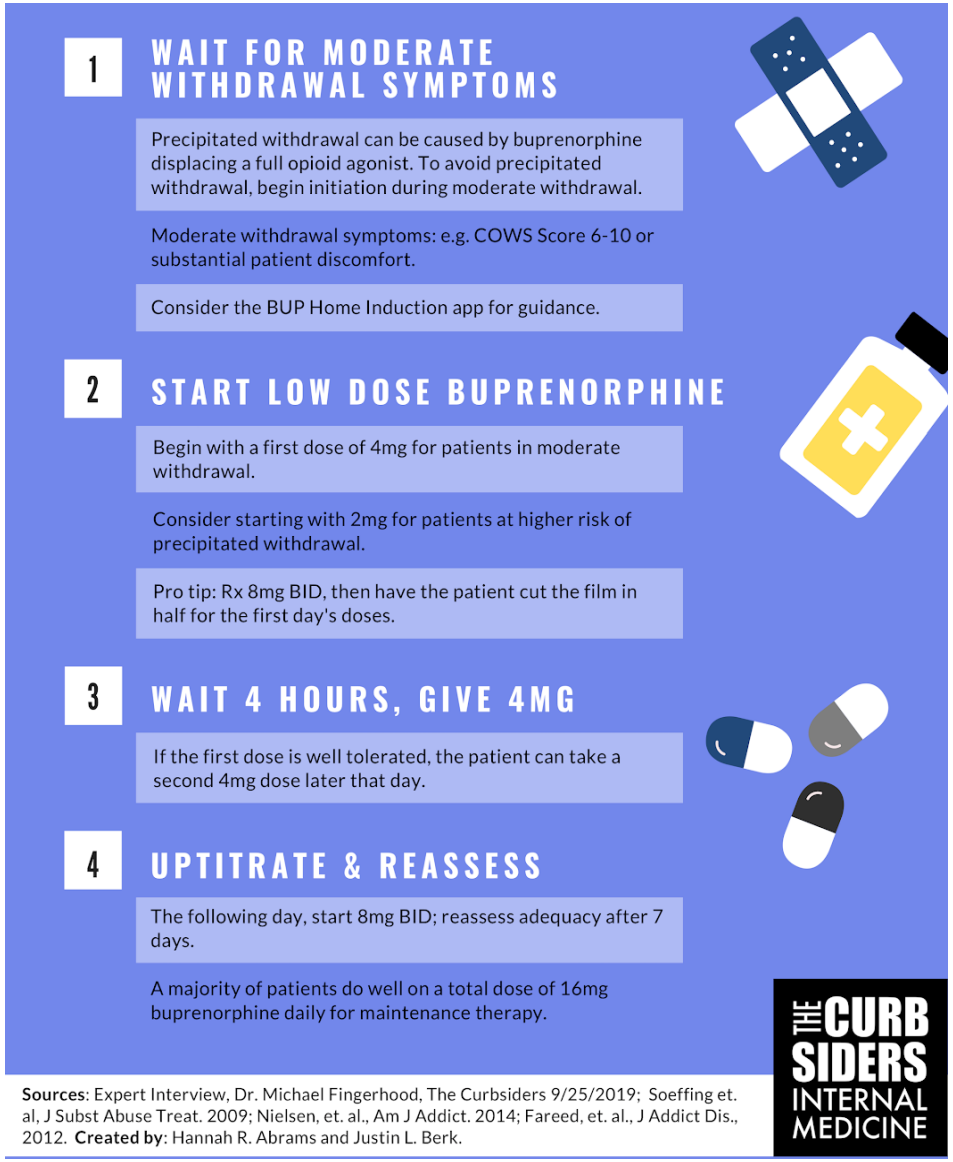


Adapted from naabt.org

SL BUP Initiation: Approaches

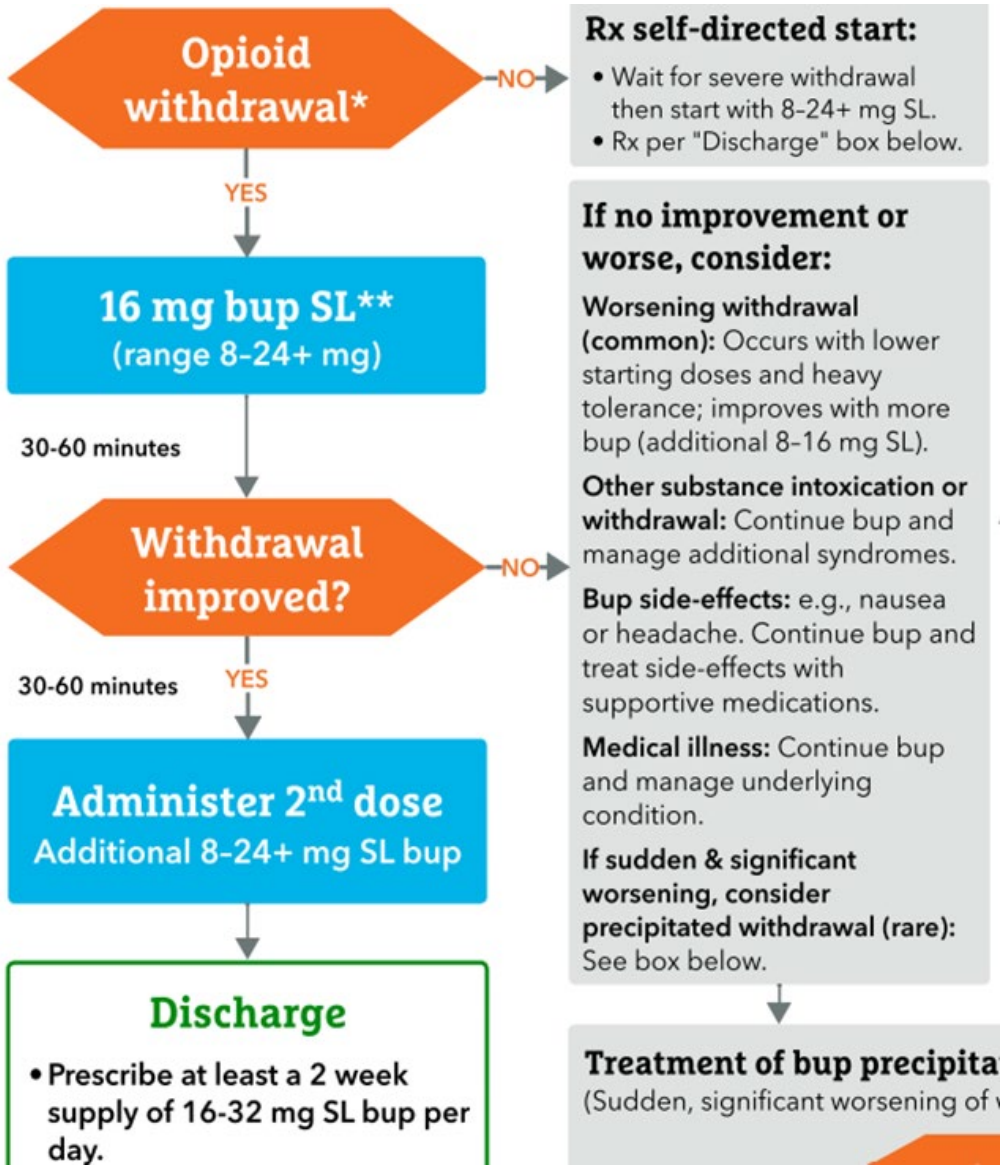
	Instructions for other opioid use	Requires withdrawal to start?	Initial dose
Standard	**STOP**	YES	2mg, 4mg
High-dose ("macro")	**STOP**	YES	8-16mg
Low-dose ("macro")	Continue until goal dose BUP	**NO**	< 2mg

Standard initiation



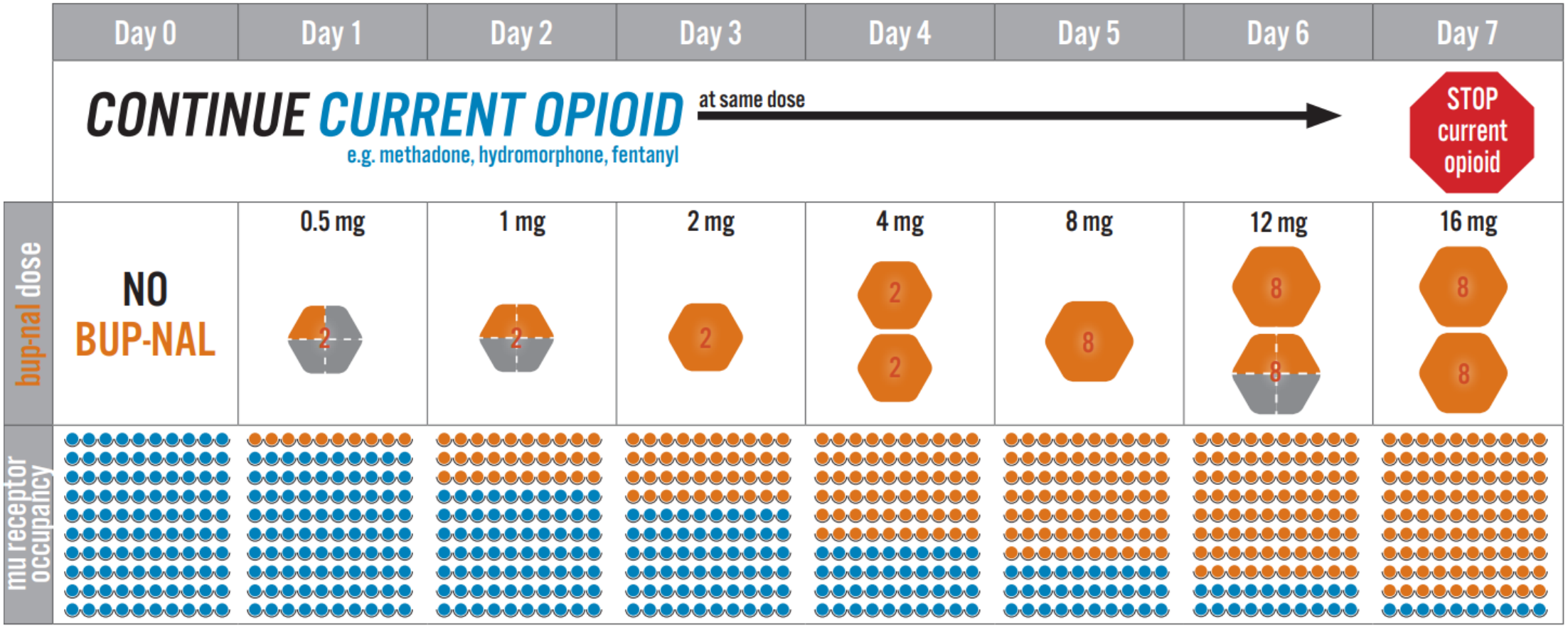
Curbsiders Addiction Medicine 2022.

High-dose initiation



CA Bridge Project 2024.

Low-dose initiation

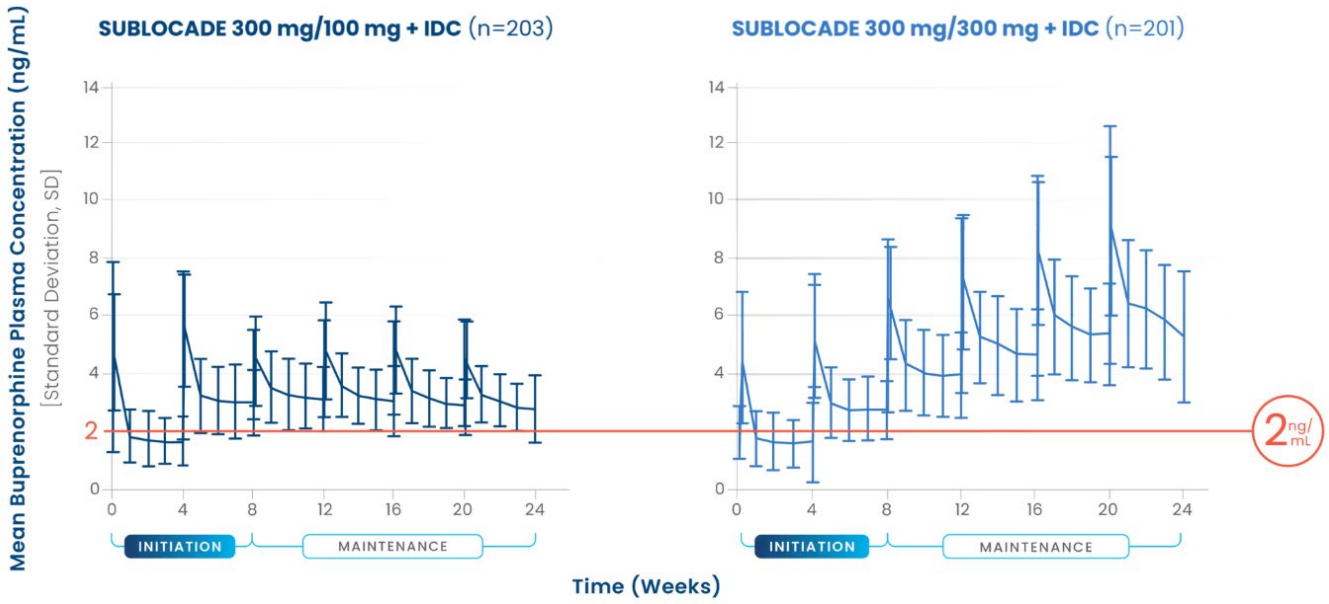


SL BUP: Finding a therapeutic Dose

- Short answer: The dose at which the patient feels comfortable
  - Withdrawal controlled
  - Return to use minimized
  - Overdose protection maximized

- Higher doses (> 16mg) associated with improved treatment retention
- Split dosing is common
- Variations in symptoms during daytime, diversion concern, sick of taking SL BUP --> consider LAI

BUP-XR: Sublocade®



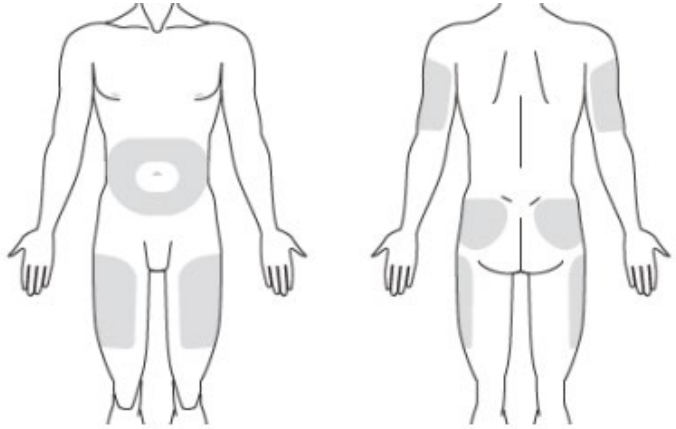
Previous Dose of TM BUP	TM BUP	SUBLOCADE		
	Initial Dose	Injection #1	Injection #2[a]	Maintenance Dose[b]
Initiation in patients not already receiving buprenorphine				
NA	4 mg[c]	300 mg	300 mg	100 mg
Transition of patients already receiving transmucosal buprenorphine				
8 – 24 mg/day	NA	300 mg	300 mg[d]	100 mg

Storage: room temp

Preparation: 1 syringe, 1 needle

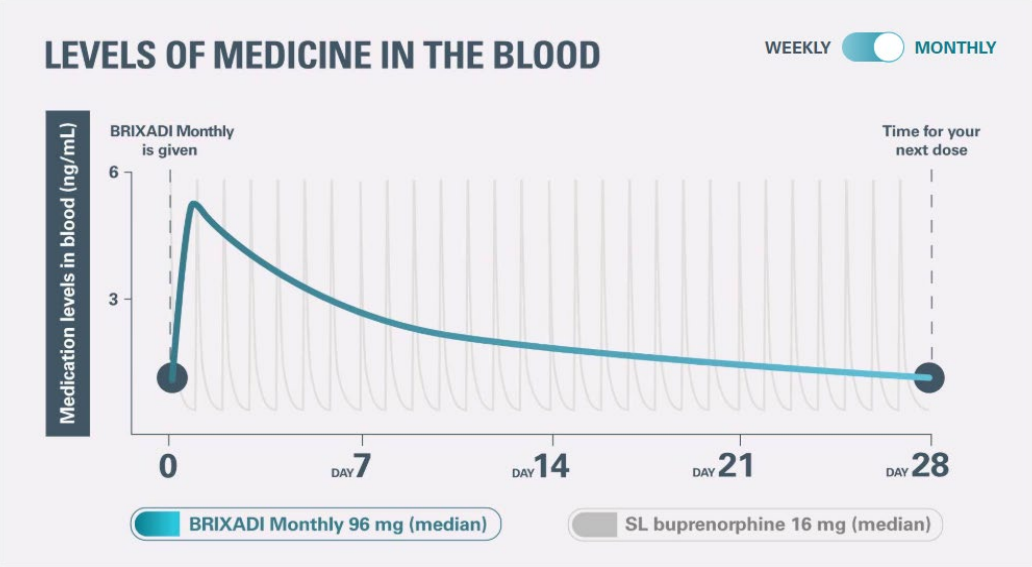
Administration: Monthly SubQ

*Consider lidocaine



**Potential teratogenicity

BUP-XR: Brixadi®

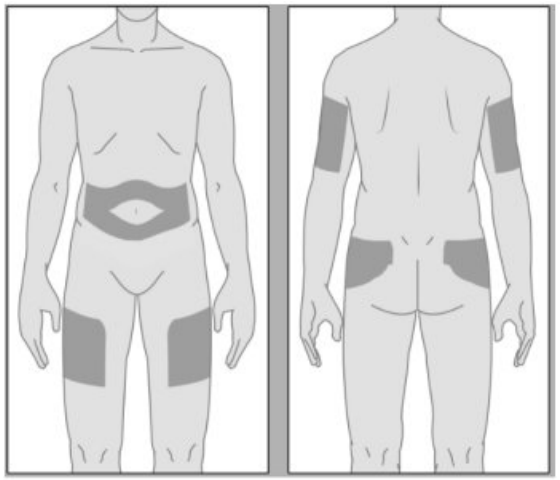


Daily dose of sublingual buprenorphine*	BRIXADI Weekly	BRIXADI Monthly
Less than or equal to 6 mg	8 mg	—
8-10 mg	16 mg	64 mg
12-16 mg	24 mg	96 mg
18-24 mg	32 mg	128 mg

Storage: room temp

Preparation: preloaded syringe and plunger

Administration: Monthly or weekly SQ injection



Braeburn Inc. 2023.

Common Questions

- Telehealth rules
- Buprenorphine vs Bup/Naloxone
- Precipitated withdrawal management
- Diversion
- Acute pain management
- Urine drug testing
- Comorbid substance use
- Requirement of counseling

Beyond MOUD

- Naloxone for ALL
- Safe medication storage
- Harm reduction and safe use strategies
- Risk-adjusted primary care: ID, contraception, pain
- Recovery supports (more than NA)
- Advocacy

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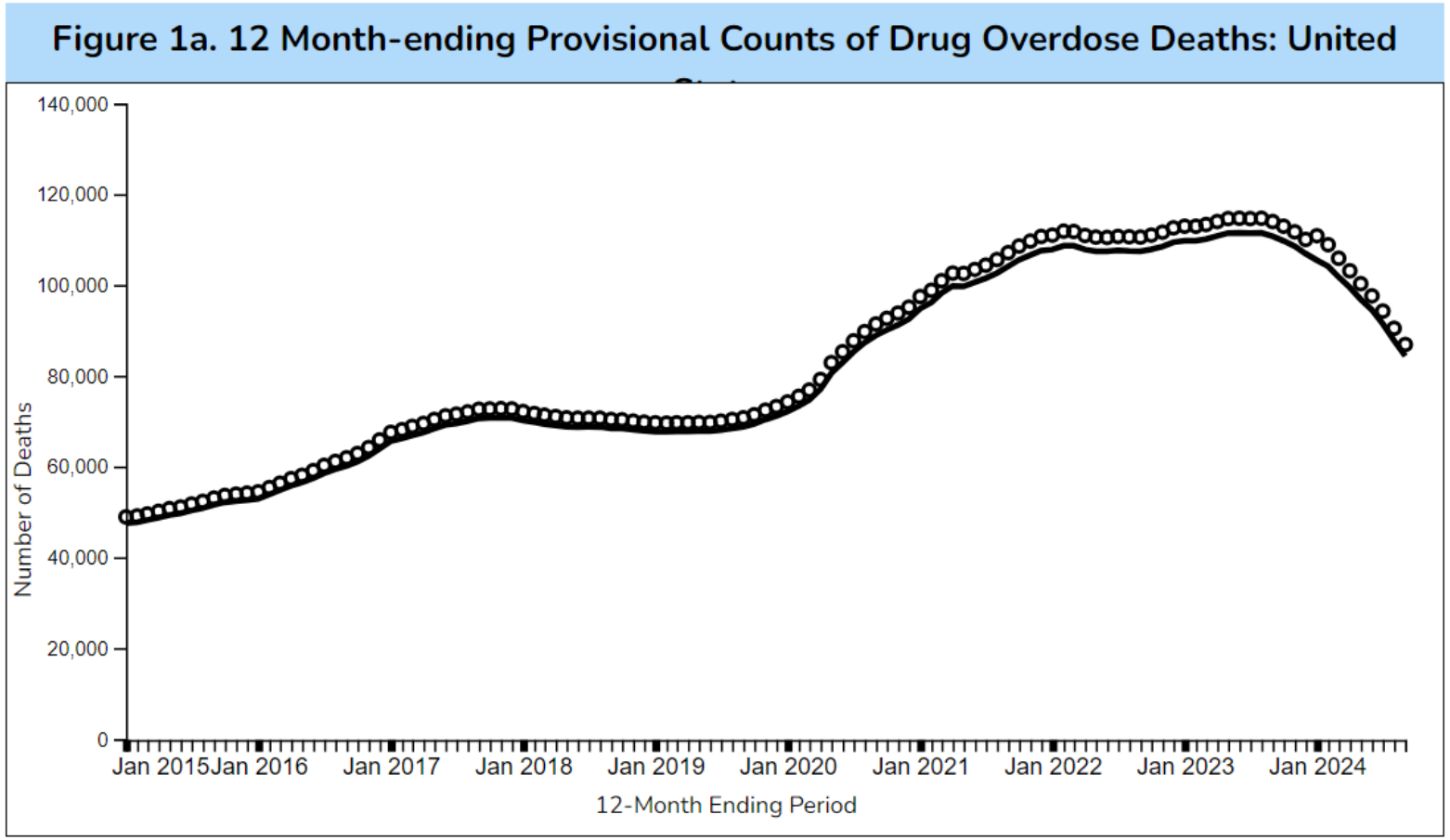
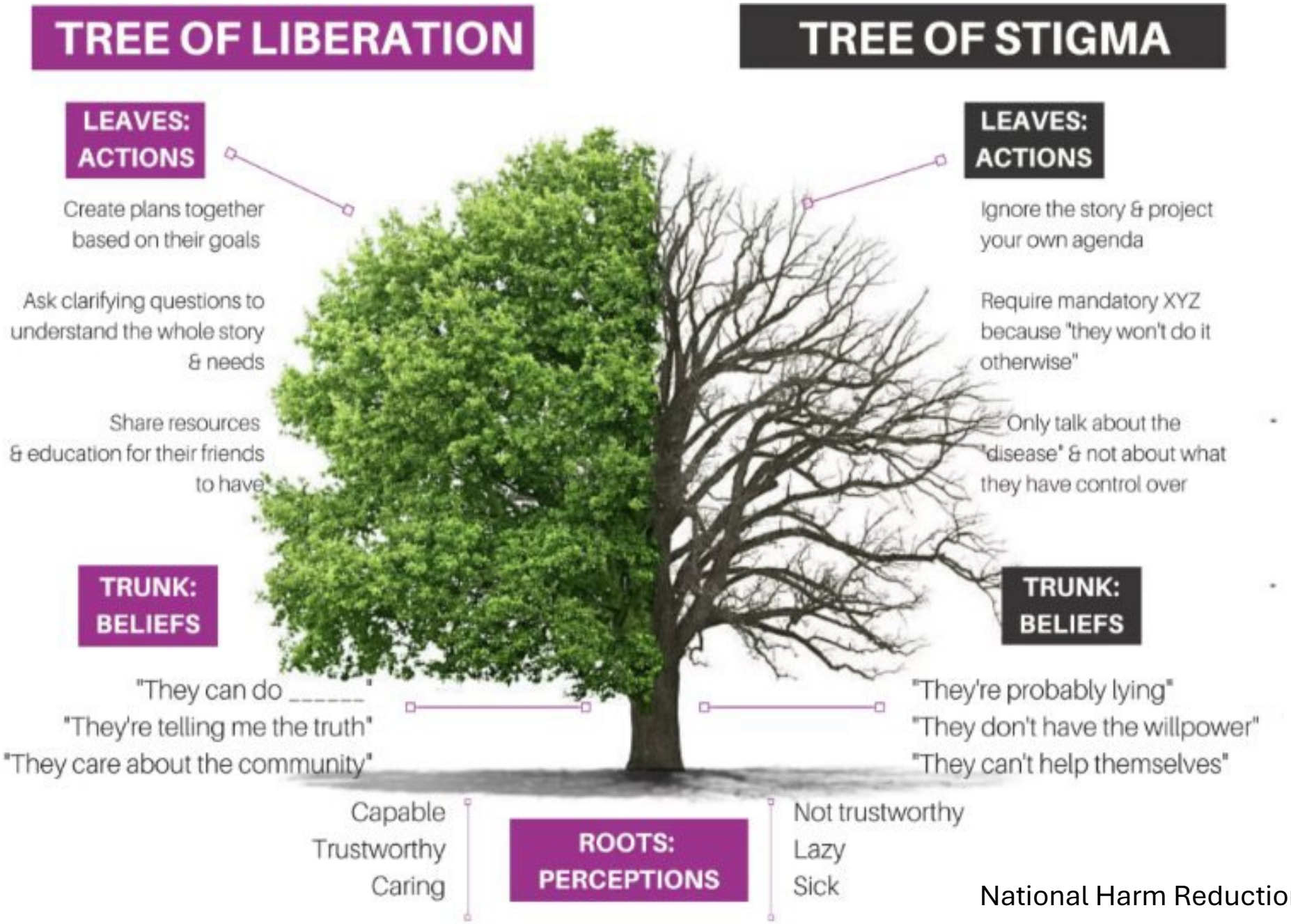
Why We Care



National Center for Health Statistics 2025.



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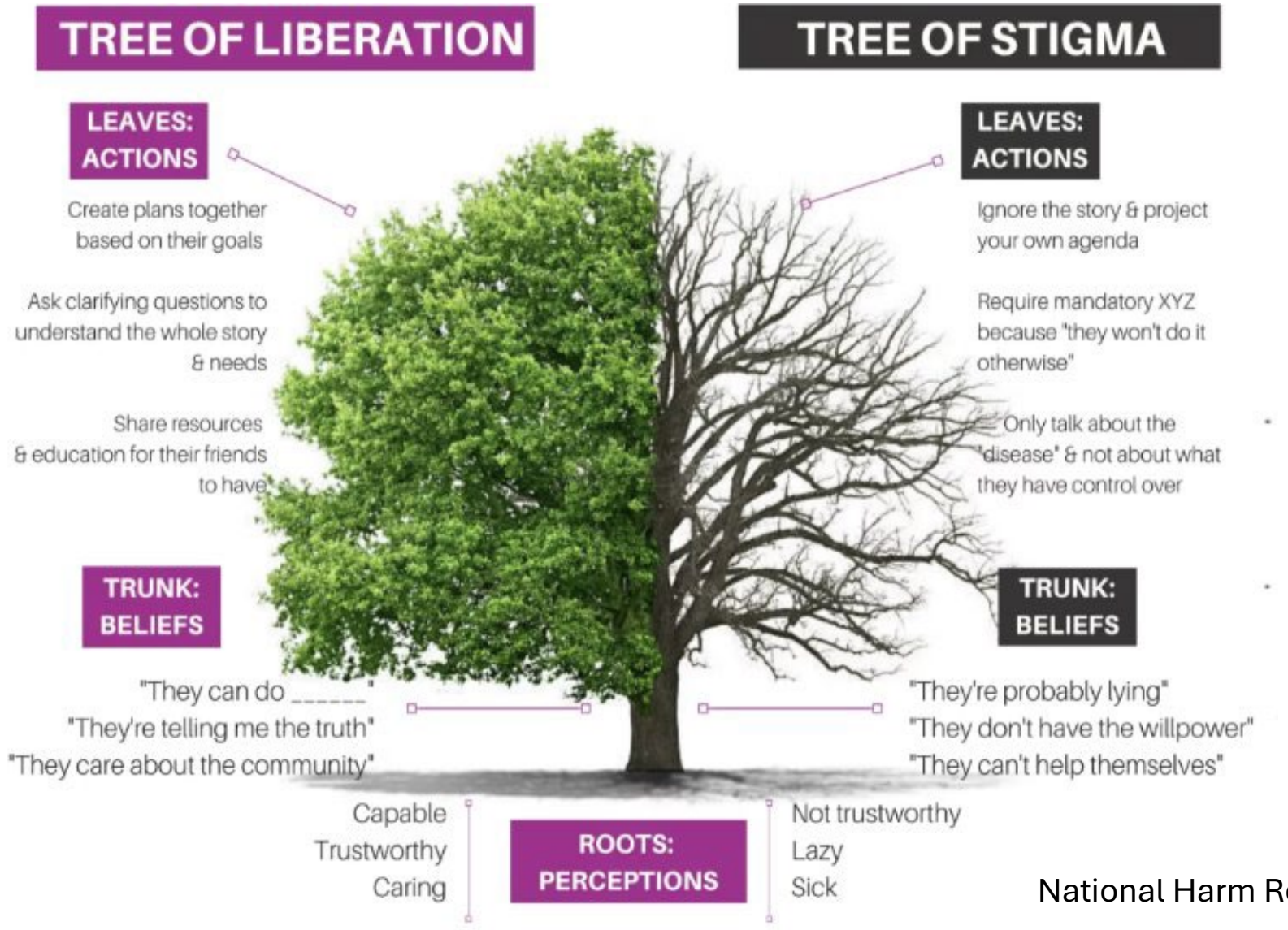
Thank you!

Alyssa Bruehlman
412-977-2996
Bruehlmanak@upmc.edu



National Harm Reduction Coalition 2024.