HCV & Addiction Medicine

Laura Maroldo, PA-C, AAHIVS

WMMG WEST MIDTOWN MEDICAL GROUP

Disclosures

- Advisory Boards
  - AbbVie
  - Gilead
- Speaker
  - AbbVie
  - Gilead

WMG WEST MIDTOWN MEDICAL GROUP

West Midtown Medical Group

- Our mission is to improve the quality of life of our patients by providing high quality and comprehensive medical and substance use disorder treatment services.
- Established in 1974
- Located in midtown Manhattan
- Patient population

WMMG WEST MIDTOWN MEDICAL GROUP

Services

- MOUD
  - Methadone
  - Buprenorphine/Naloxone
  - Naltrexone
- Counseling
  - Individual
  - Group
- Medical
  - MOUD
  - Primary Care
  - HIV specialty care
  - HCV specialty care
  - Psychiatry
  - Podiatry

WMMG WEST MIDTOWN MEDICAL GROUP

Opiate Use Disorder

- Opioid use disorder is a chronic and treatable mental health condition that involves a problematic pattern of opioid misuse.
- Measured as Mild, Moderate or Severe based on a series of questions.

Opioid use disorder diagnostic criteria

Difficulty cutting down or quitting?
Spending a lot of time obtaining opioids?
Cravings or strong desire to use opioids?
Taking opioids in larger amounts and for longer than intended? Repeated difficulty carrying out major obligations at work, school or home due to opioid use?
Continued use despite persistent or recurring social or interpersonal problems caused or made worse by opioid use?
Stopping or reducing important social, work or recreational activities due to opioid use?
Recurrent use of opioids in physically hazardous situations?
Persistent use of opioids despite awareness of persistent or recurrent physical or psychological consequences?
Tolerance?
Withdrawal symptoms?

(Minimum of 2 criteria required for mild opioid use disorder, 4 for moderate, 6 for severe)

WMMG WEST MIDTOWN MEDICAL GROUP

Transition from Heroin to Fentanyl

Heroin 10 times more potent than Morphine

Fentanyl 100 times more potent than Morphine

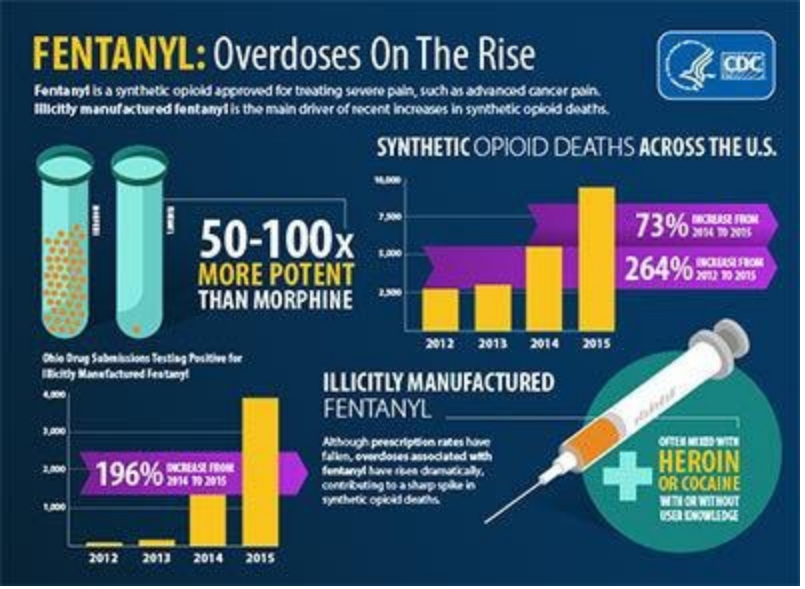
Inexpensive

Synthetic

Created in counterfeit labs and smuggled into US

Found in heroin, cocaine, pills, methamphetamine

WMG WEST MIDTOWN MEDICAL GROUP


FENTANYL: Overdoses On The Rise
Fentanyl is a synthetic opioid approved for treating severe pain, such as advanced cancer pain.
Illicitly manufactured fentanyl is the main driver of recent increases in synthetic opioid deaths.
CDC
SYNTHETIC OPIOID DEATHS ACROSS THE U.S.
50-100x MORE POTENT THAN MORPHINE
73% INCREASE FROM 2014 TO 2015
264% INCREASE FROM 2012 TO 2015
2012 2013 2014 2015
Ohio Drug Submissions Testing Positive for Illicitly Manufactured Fentanyl
196% INCREASE FROM 2014 TO 2015
2012 2013 2014 2015
ILLICITLY MANUFACTURED FENTANYL
Although prescription rates have fallen, overdoses associated with fentanyl have risen dramatically, contributing to a sharp spike in synthetic opioid deaths.
OFTEN MIXED WITH HEROIN OR COCAINE WITH OR WITHOUT USER KNOWLEDGE


2 mL NDC 0074-9093-32
FENTANYL Citrate
Injection, USP
100 mcg Fentanyl/2 mL
(50 mcg/mL) (0.05 mg/mL)
WARNING: May be habit forming.


HEROIN
FENTANYL


NDC 0378-9121-98
MYLAN
FENTANYL
TRANSDERMAL SYSTEM
25 mcg/hr
NOT FOR ACUTE OR POSTOPERATIVE USE
Five (25 mcg/hr) Systems
DO NOT USE IF SEAL ON POUCH IS BROKEN
KEEP OUT OF REACH OF CHILDREN AND PETS
© 2005


DanceSafe
HOW TO TEST YOUR DRUGS FOR FENTANYL

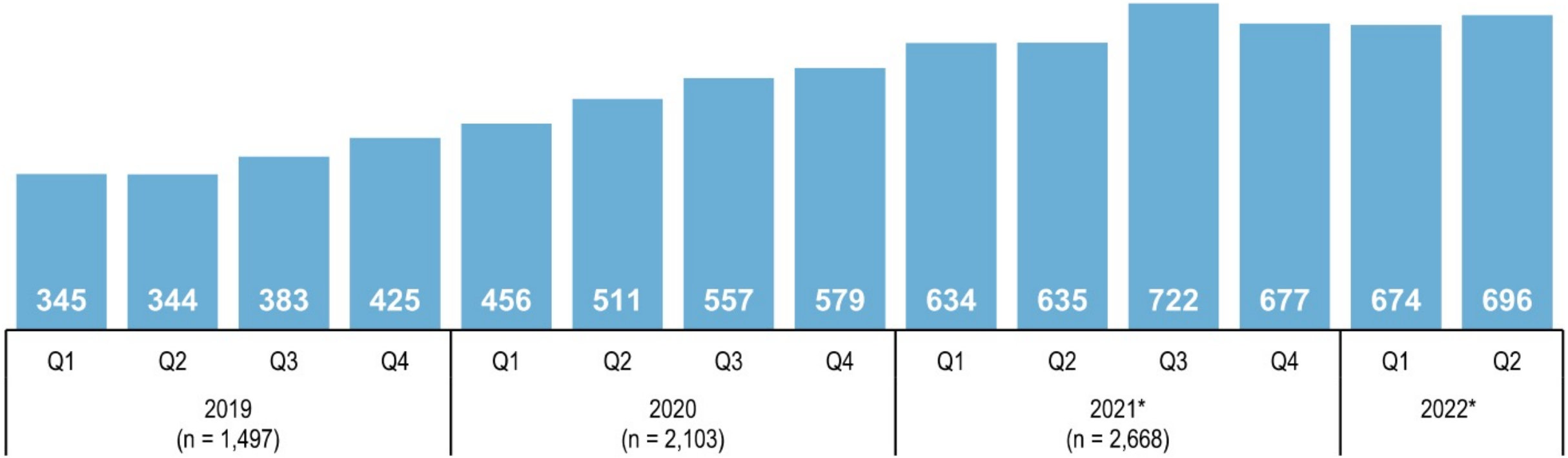

Rapid Response
100 Tests-100 Pruebas


HEROIN
FENTANYL
CARFENTANIL

There were 696 overdose deaths confirmed during the second quarter of 2022

Number of confirmed overdose deaths by quarter, New York City, 2019-2022

Deaths in 2021 and 2022 still pending final determinations; more recent quarters subject to larger increases



*Data for 2021 and 2022 are provisional and subject to change

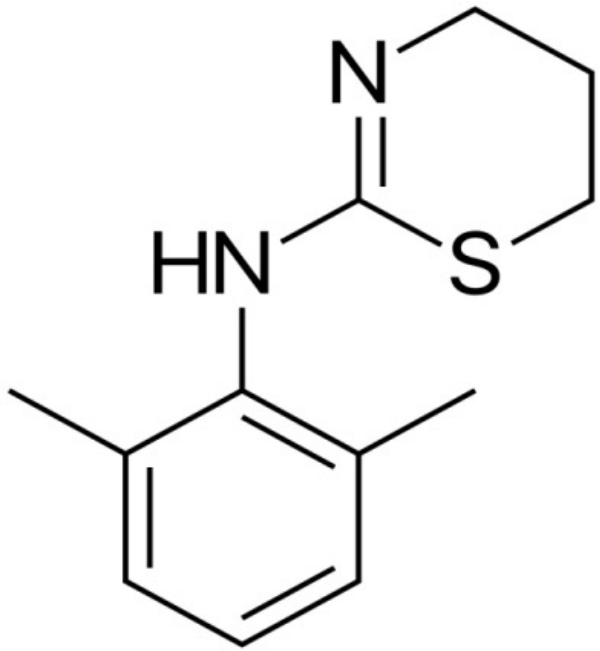
WMG WEST MIDTOWN MEDICAL GROUP

Xylazine pharmacology & Clinical Effects

Xylazine Pharmacology and Clinical Effects

- Alpha-2 adrenergic agonist that *stimulates central alpha-2 receptors:*
  - Decreases sympathetic nervous system outflow
    -> sedation (decreases the release of NE and dopamine)
  - **CNS DEPRESSION:** ***No effect on respiratory rate, blunted response to airway occlusion (hypoxia) similar to other sedatives (benzodiazepines, barbiturates), synergistic effect with opioids***
- Similar effects to *imidazoline* compounds, such as clonidine, dexmedetomidine, oxymetazoline, tetrahydrazoline, tizanidine, and lofexidine
  - **Major clinical effect is profound sedation**
  - **But *NO* imidazoline receptor activity, so *NO* hypotension/bradycardia**
  - Increase in vagal tone is reported in the veterinary literature
  - Acts on alpha-2 receptors in pancreatic beta cells, inhibiting insulin release->hyperglycemia
  - One of xylazine's metabolites, 2,6-xylidine, has been classified as potentially genotoxic and carcinogenic in humans based on animal studies
- Pharmacokinetics:
  - Typical anesthesia dose ranges (0.2-1 mg/kg IM or IV)
  - Time to effect is 1-2 minutes (depending on administration route); lipophilic, diffuses widely, good bioavailability
  - Average duration of substance effect up to 4 hours, but can last longer
  - Routes of Administration: IV, IM, SC, PO, inhalation, insufflation, ocular

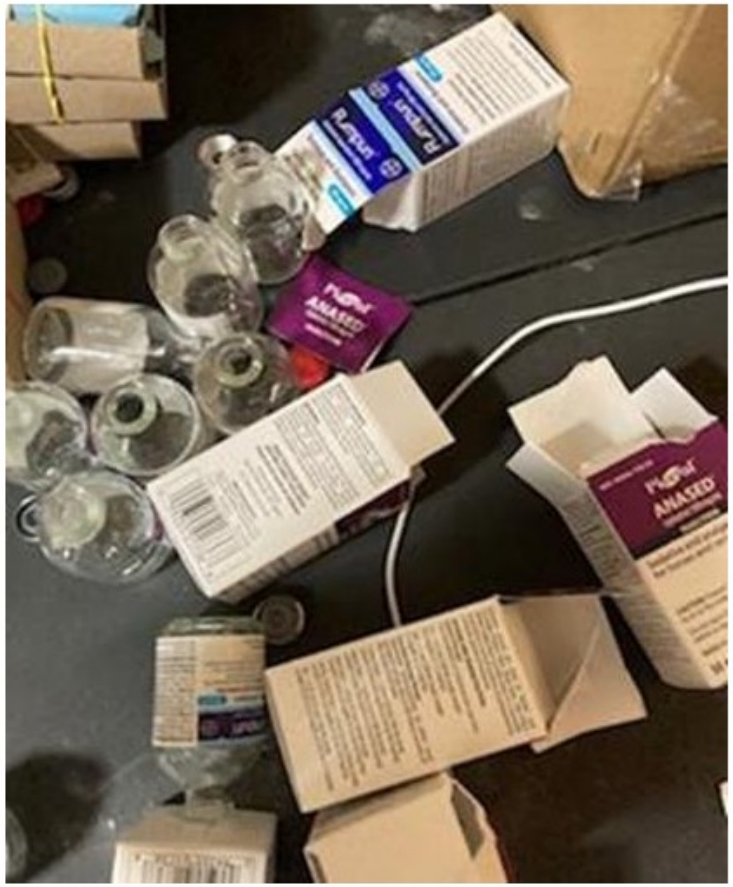
Xylazine Structure



Similar chemical structure to phenothiazines, TCAs, and clonidine

Thank you Dr. Kelly Ramsey!

Xylazine Use



- Xylazine (a colorless liquid in veterinary formulations) is converted to a bitter tasting, solid (“salted”), crystalline substance that then easily dissolves in water and can be mixed with other substances
- Xylazine is added to opioids to potentiate the opioid’s effects and to act as a filler (to add bulk to the substance being sold)

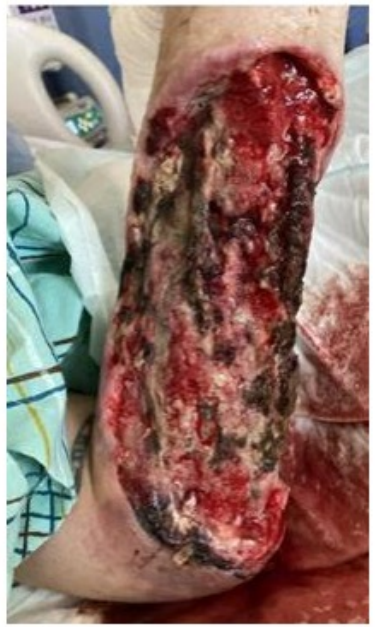
Source: DEA, Philadelphia Division

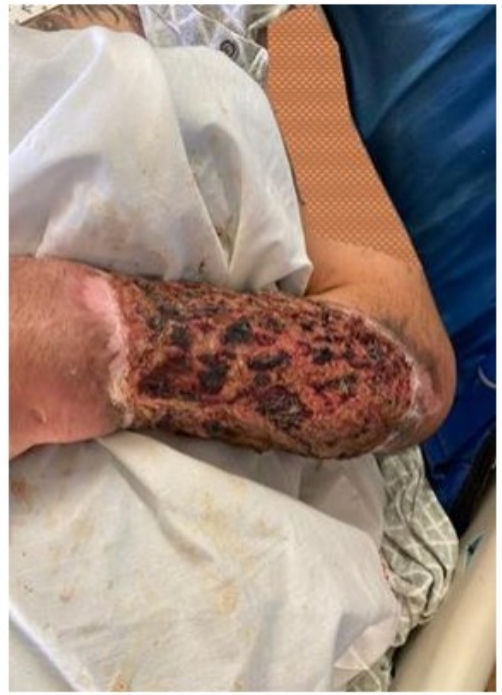
Xylazine and Skin Ulcers/Wounds

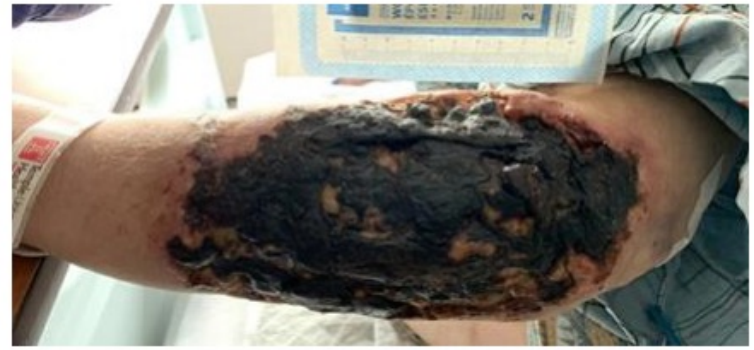
- Severe necrotic skin ulcerations, often necessitating complicated wound care
- Occur at skin sites associated with injection, *but also at skin sites not associated with injection and in individuals who don't inject*
- The pathophysiological mechanism which causes the ulcerations is unclear; they are not infectious, but can become superinfected with bacteria, particularly with skin picking

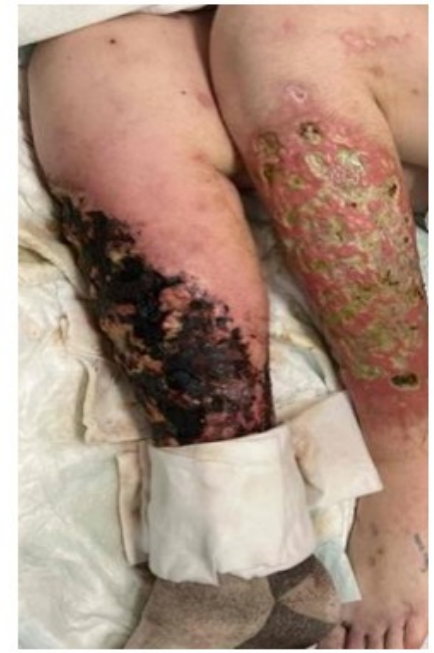
FDA Dear Colleague Letter: FDA Warns About the Risk of Xylazine Exposure in Humans, 11/8/22

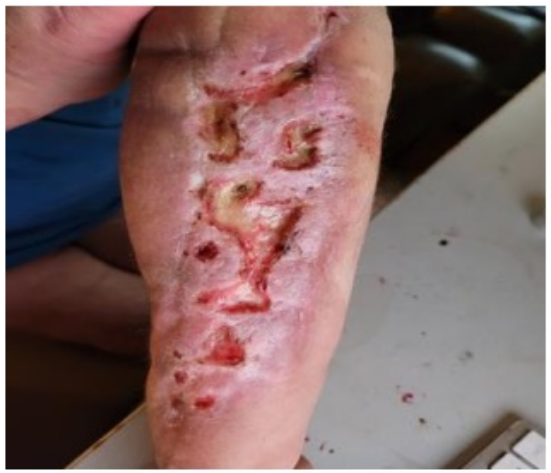
Xylazine and Skin Ulcers/Wounds

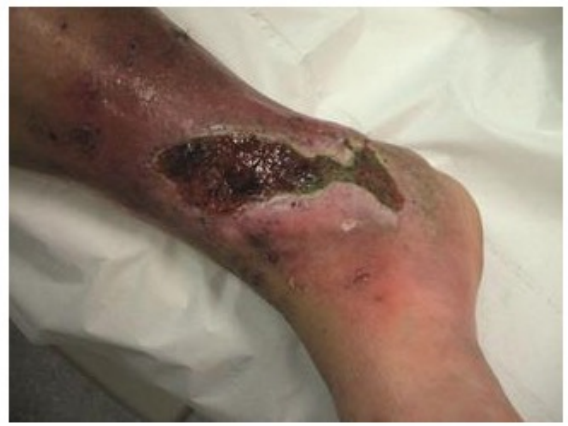


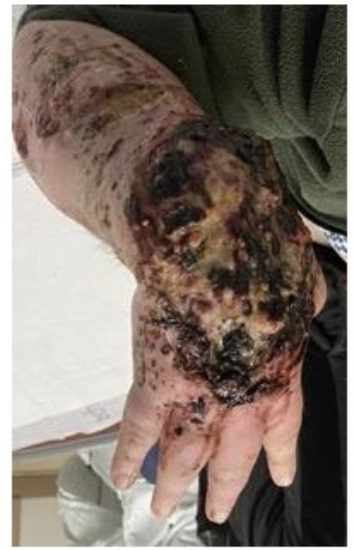


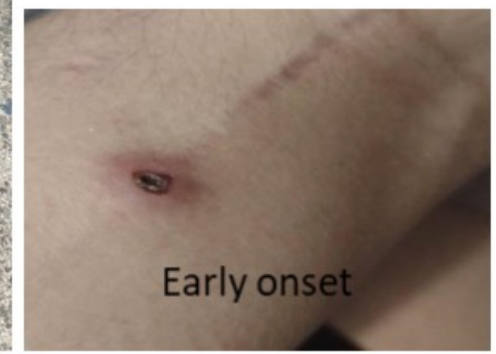












NHRC Xylazine Office Hours, 4/2022

NEW YORK STATE | Office of Addiction Services and Supports

OASAS. Every Step of the Way.

Medication for Opiate Use Disorder (MOUD)

- **Methadone**
  - Agonist
  - Binds to the opioid receptor (Mu)
  - OTP/MAT
  - Liquid, Tab, Disc
- **Buprenorphine (Naloxone)**
  - Partial agonist
  - Binds to the opioid receptor
  - OTP/MAT or medical office
  - Tab, film, injection or implant
- **Naltrexone (Vivitrol)**
  - Antagonist
  - Medical office
  - IM Injection – long acting
  - Oral tab – daily use

WMMG WEST MIDTOWN MEDICAL GROUP

Initial screening

- History of Substance Use Disorder(SUD)/Opiate Use Disorder(OUD)
- COWS – clinical opiate withdrawal scale
- Opiate Use Disorder Criteria
- Laboratory Screening (including Hepatitis C with reflex to RNA)

WMMG WEST MIDTOWN MEDICAL GROUP

Admission

- Deciding on MOUD
  - Methadone, Buprenorphine, Naltrexone
- Goals of treatment
  - Sobriety, Harm Reduction, Financial
- Length of treatment
  - 12 months to long term maintenance
- Stabilization – “blocking dose”
  - Higher due to fentanyl
- Comorbid conditions
  - HCV, HIV, HBV, STDs
  - Common primary care concerns
- Secondary substances
  - Cocaine, benzodiazepine, ETOH, xylazine, methamphetamine, hallucinogenic, MDMA

On MOUD, now What?

- Stabilize the MOUD dose
- Address secondary Substance Use
- Address Co-morbid conditions

WMG WEST MIDTOWN MEDICAL GROUP

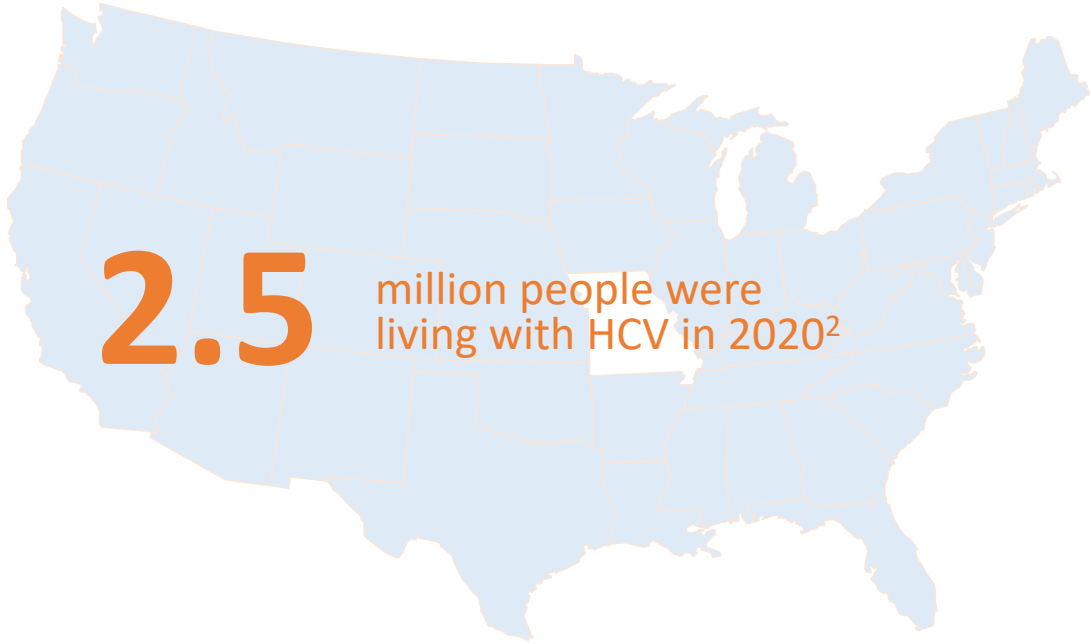
Estimated prevalence of hepatitis C virus

2013–2016 National Health and Nutrition Examination Survey (NHANES) data

- estimated 1.0% of all adults in the United States, or 2,386,100 persons, were living with HCV infection (HCV RNA positive) (*2*).
- Nine states comprise 51.9% of all persons living with HCV infection: California, Florida, New York, North Carolina, Michigan, Ohio, Pennsylvania, Tennessee, and Texas

During 2006–2012, the combined incidence of acute HCV infection in four states (Kentucky, Tennessee, Virginia, and West Virginia) increased 364% among persons aged ≤30 years.

- IDU was most commonly reported (73%).
- Primarily non-Hispanic white persons from nonurban areas (*8*).



* State estimates of HCV RNA positivity among all adults are based on a statistical model that allocated nationally representative hepatitis C prevalence from the 2013–2016 NHANES and additional previously published data for populations not sampled in NHANES to states according to the spatial demographics and distributions of 1999–2016 hepatitis C mortality and narcotic overdose deaths in the National Vital Statistics System.

† Data are from an analysis of 2015, National Center for Health Statistics birth certificate data (live births) (Schillie SF, Canary L, Koneru A, et al. Hepatitis C virus in women of childbearing age, pregnant women, and children. Am J Prev Med 2018;55:633–41).

§ Connecticut did not report maternal HCV infection on 2015 birth certificates and New Jersey reported infections from only a limited number of facilities; therefore, women residing in these two states were not included in the analysis.

1. MMWR Recommendations and Reports / April 10, 2020 / 69(2);1–17 2. Blach, S, et al. AASLD 2021: The Liver Meeting

Abbreviations: HCV = hepatitis C virus; RNA = ribonucleic acid; NHANES = National Health and Nutrition Examination Survey.

Injection Drug Use Is the Most Important Risk Factor for HCV Infection[1-7]

Young PWUD with propensity to share needles and preparation equipment

HCV often acquired shortly after individuals begin injecting

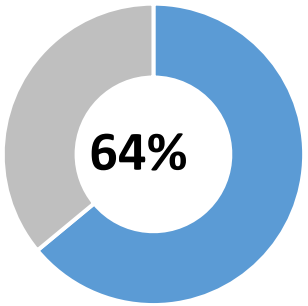
HCV can survive on cookers and cotton filters for days, and longer in needle barrel

10

HCV transmitted at a tenfold rate relative to HIV

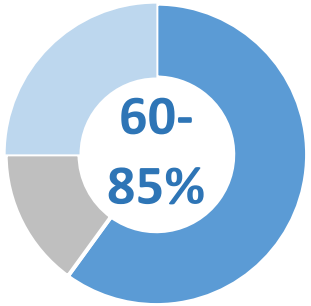
80

HCV is prevalent in 60-80% or more in people with IDU



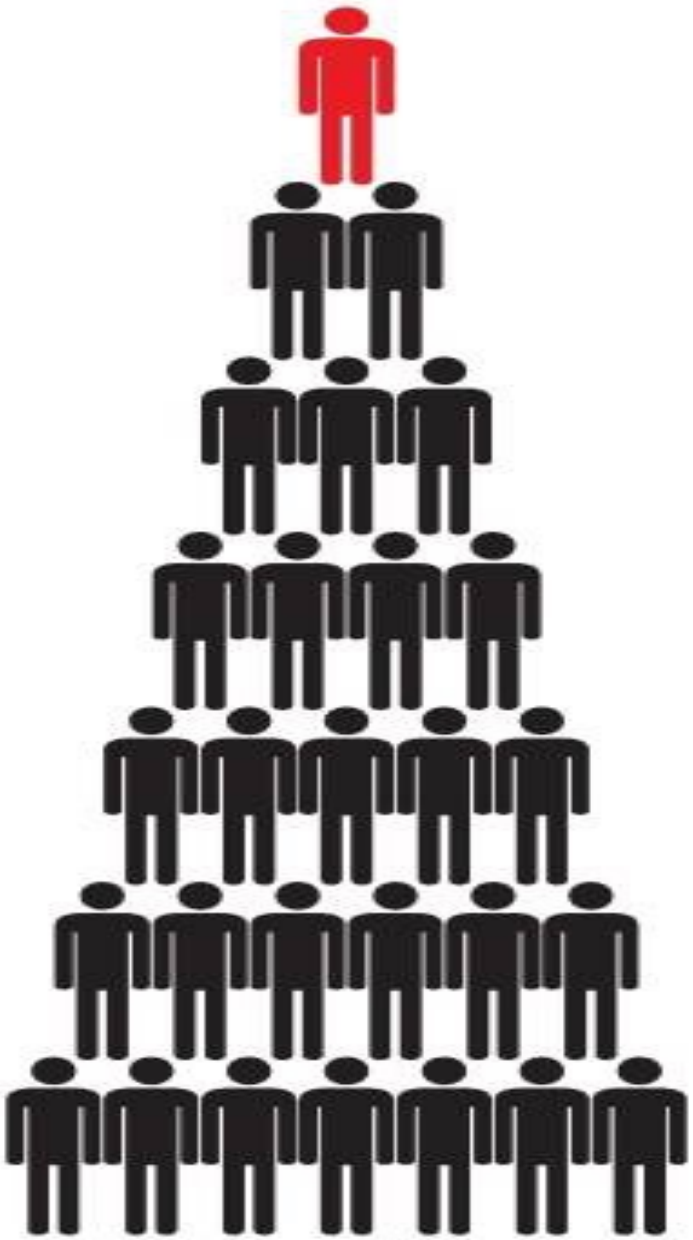
of PWUDs in the **United States** are chronically infected

PWUD make up between 60% and 85% of all new HCV infections in **USA**



1. https://www.hhs.gov/sites/default/files/viral-hepatitis-action-plan.pdf; 2. https://hepfree.nyc/wp-content/uploads/2017/08/hcv-and-young-pwid-consultation-report.pdf;
3. Paintsil E, et al. *J Infect Dis.* 2010;202:984-90; 4. Doerrbecker J, et al. *J Infect Dis*. 2013;207:281-7; 5. Clausen LN, et al. *World J Gastroenterol*.2014;20:12132-43.
6. Nelson PK, et al. *Lancet*. 2011;378:571-83. 7. Lourenço L, et al. *Can Commun Dis Rep*. 2021;47(12):561-70.

People who inject drugs (PWIDs) are the highest-risk group for acquiring hepatitis C (HCV) infection.



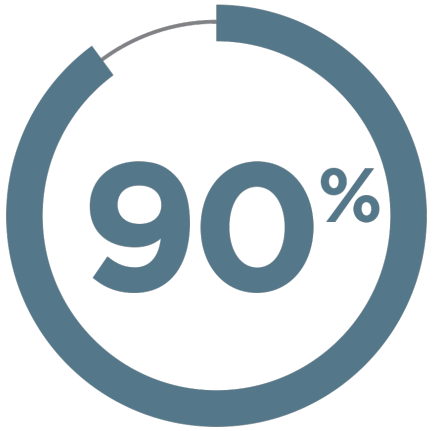
Each PWID infected with HCV is likely to infect 20 other people within the first 3 years of infection

WMG WEST MIDTOWN MEDICAL GROUP

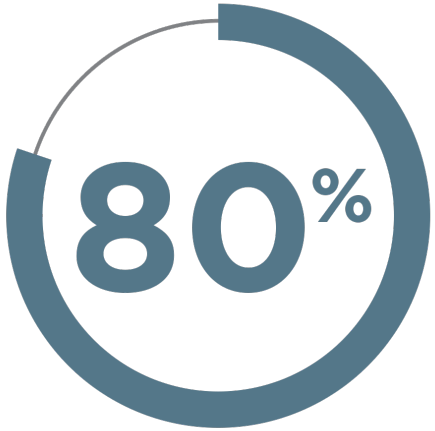
Why does heroin use create special risk for contracting HIV/AIDS and hepatitis B and C? | National Institute on Drug Abuse (NIDA) (nih.gov) updated June 2021

THE WHO HAS OUTLINED STEPS NEEDED TO ELIMINATE HCV AS A PUBLIC HEALTH THREAT BY 2030

According to the WHO, the elimination of HCV as a public health threat by 2030 will require:



of HCV cases diagnosed



of people diagnosed with HCV treated

HCV=hepatitis C virus; WHO=World Health Organization.

WHO. Accessed June 14, 2020. https://apps.who.int/iris/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1

WEST MIDTOWN MEDICAL GROUP

The Effect of COVID-19 on HCV[1-3]

30% Increase in drug overdose deaths between December 2019 and December 2020; United States eclipsed 100,000 in November 2021

73% Reduction in HCV screening/testing reported by local health departments[a]

22% Decrease in HCV treatment occurred from 2019 to 2020[b]

[a] Represents percentage of local health departments offering the service. [b] Data do not include Department of Corrections and Veterans Affairs

1. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm. 2. https://hepvu.org/state-of-viral-hepatitis-during-covid-19/.
3. IMS Monthly Data (Week of January 4, 2019 through January 1, 2021).

Guideline Recommendations: Screening

The following recommend screening for all people >18 years of age

USPSTF	AASLD-IDSA	CDC
• US Preventive Service Task Force • Grade B Recommendation[1]	• American Association for the Study of Liver Diseases and the Infectious Diseases Society of America[2]	• Centers for Disease Control and Prevention[3]

1. USPSTF Assessed April 14, 2023
2. AASLD-IDSA Updated January 21, 2021
3. Schille S. et al, MMWR Recomm Rep. 2020; 69(2):1-17

Guideline Recommendations: Treatment

Patient with HCV are recommended to receive treatment regardless of drug use[1,2]

ASAM Recommendation

- Active alcohol and/or drug use should not in itself exclude any persons from receiving treatment for their HCV infection[2]

AASLD-IDSA Guidelines

- Recommend treatment for all people with chronic HCV, except those with a short life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy [1]

1. AASLD-IDSA Updated January 21, 2021
2. ASAM Update April 5, 2017

Barriers to HCV Treatment Uptake

Systemic

- Lack of insurance
- Lack of provision of services
- PA process complicated
- Transportation

Patient

- Fear of side effects, stigmatization
- Mistrust of health care system
- IFN “PTSD”
- Lack of HCV-related knowledge / perceived need for treatment / lack of symptoms

Provider

- Concerns regarding adherence, reinfection
- Discomfort with coexisting mental health diagnoses or active drug use
- Lack of HCV Tx knowledge

Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis: Regimens & Monitoring[1]

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg)
taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

1. https://www.hcvguidelines.org/

Clinical Snapshot of Recommended Regimens or Most People with HCV[1,2]

Agent	Composition	Duration	Dosing	Contraindications
Sofosbuvir/ velpatasvir (± ribavirin) **Genotype 1-6**	Sofosbuvir, a HCV nucleotide analog NS5B polymerase inhibitor; velpatasvir, an HCV NS5A inhibitor	12 weeks	1 tablet daily	• Ribavirin combination regimen contraindicated in patients for whom ribavirin is contraindicated.
Glecaprevir/ pibrentasvir **Genotype 1-6**	Glecaprevir, a HCV NS3/4A protease inhibitor; pibrentasvir, an HCV NS5A inhibitor	8 weeks	3 tablets dosed once daily with food	• Patients with moderate or severe hepatic impairment (Child-Pugh B or C) or those with any history of prior hepatic decompensation • Coadministration with atazanavir or rifampin

1. https://hcp.epclusa.com/efficacy 2. https://www.mavyret.com/hcp/mavyret-efficacy

Drug-Interaction Potential Between Selected HIV Antiretroviral and Preferred HCV Direct-Acting Antiviral Agents

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Sofosbuvir/Velpatasvir/ Voxilaprevir
Atazanavir + RTV or COBI	x	√	√	x	x
Darunavir + RTV or COBI	x	√	√	x	≈
Lopinavir/ritonavir	x	≈	√	x	x
Doravirine	√	√	√	√	√
Efavirenz	x	x	≈	x	x
Rilpivirine	√	√	√	√	√
Raltegravir	√	√	√	√	√
Elvitegravir/COBI/FTC/TAF	√	√	√	x	√
Dolutegravir	√	√	√	√	√
Bictegravir/FTC/TAF		√	√	√	√
Tenofovir DF	√	≈	≈	√	≈
Tenofovir AF	√	√	√	√	√
Abacavir	√	√	√	√	√
Lamivudine	√	√	√	√	√

No clinically significant interaction expected Potential weak interaction Potential interaction Do not coadminister

HEP Drug Interactions. https://www.hep-druginteractions.org/.

Common Drug-Drug Interactions

SOFOSBUVIR/VELPATISVIR

Avoid

- Amiodarone
- Topotecan
- Carbamazepine, phenytoin, phenobarbital, oxcarbazepine
- Rifampin
- Atorvastatin
- St John's Wort

GLECAPREVIR/PIBRENTASVIR

Avoid

- Carbamazepine, phenytoin, phenobarbital, oxcarbazepine
- Rifampin
- Atorvastatin, lovastatin, simvastatin
- St John's Wort
- Oral estrogen

Efficacy Overview of Recommended Regimens for Most People With HCV[1-6]

Sofosbuvir/Velpatasvir

In pivotal clinical trials

98% overall cure rate

in GT 1-6 TN/TE NC/CC adult patients
(n = 1,015/1,035; ASTRAL-1, -2, -3 studies)

Real-world integrated analysis

99% overall cure rate

in effectiveness population in GT 1-6 TN/TE NC/CC patients
(n = 5,141/5,196; pooled analysis of 12 clinical cohorts and studies in Canada, Europe, and the USA, PP)

Glecaprevir/Pibrentasvir

Overall treatment-naïve efficacy
Proven 8-week efficacy in treatment-naïve patients without cirrhosis or with compensated cirrhosis

98% cure rate

(SVR12) based on integrated pooled analysis of GT 1-6 TN, NC, and CC patients across 8 clinical trials that included US study locations (n = 1,218/1,248, ITT)

8-week real-world evidence
Results from two TRIO Health Network studies

99% cure rate

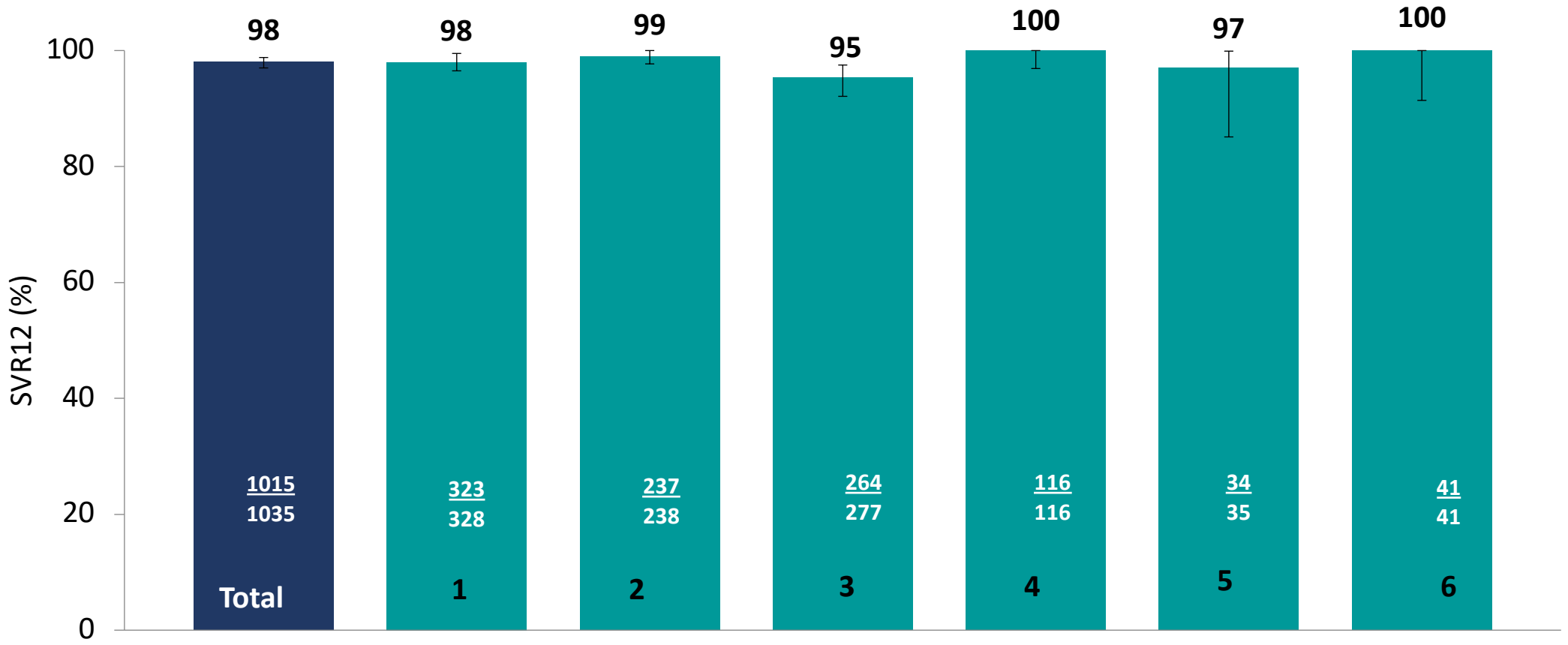
in per protocol population

In GT 1-4 and 6, TN, NC (n = 537/540) and TN, CC (n = 70/71) patients treated for 8 weeks

1. Gilead Sciences Canada, Inc. EPCLUSA product monograph. Date of revision: Aug. 8, 2022; 2. Mangia A, et al. *Liver Int*. 2020;40:1841-52;
3. AbbVie Corporation. MAVIRET product monograph. Date of revision: Apr. 7, 2022; 4. Zuckerman E, et al. *Clin Gastroenterol Hepatol*. 2020;18:2544-53;
5. Curry MP, et al. *GastroHep*. 2020;2:64-71; 6. Flamm SL, et al. *Adv Ther*. 2020;37:2267-74.

Persons with HCV genotype 1, 2, 3, 4, 5, or 6 infection can be effectively treated with 1 tablet daily for 12 weeks

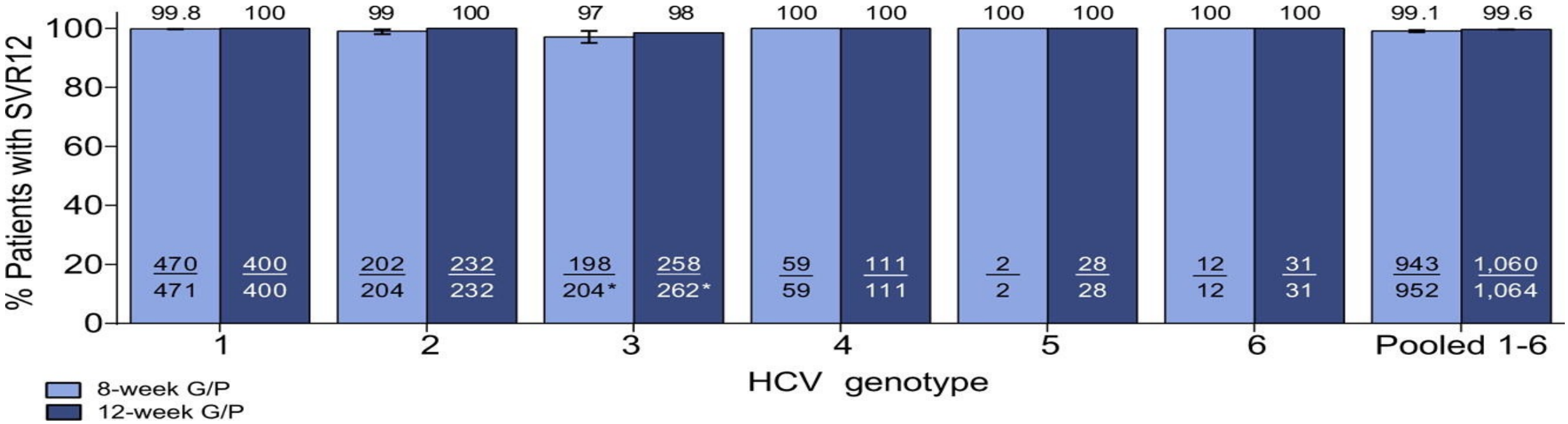
Sofosbuvir/Velpatasvir



Feld JJ et al. NEJM 2016; Foster G et al NEJM 2016

Persons with HCV genotype 1, 2, 3, 4, 5, or 6 infection can be effectively treated with 3 tablets daily for 8 weeks

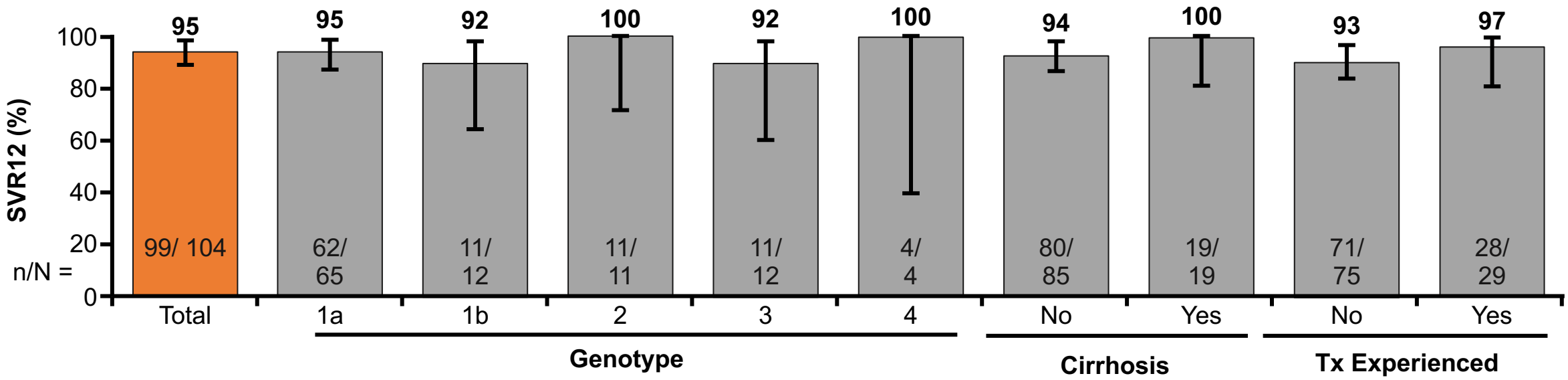
Glecaprevir/Pibrentasivir



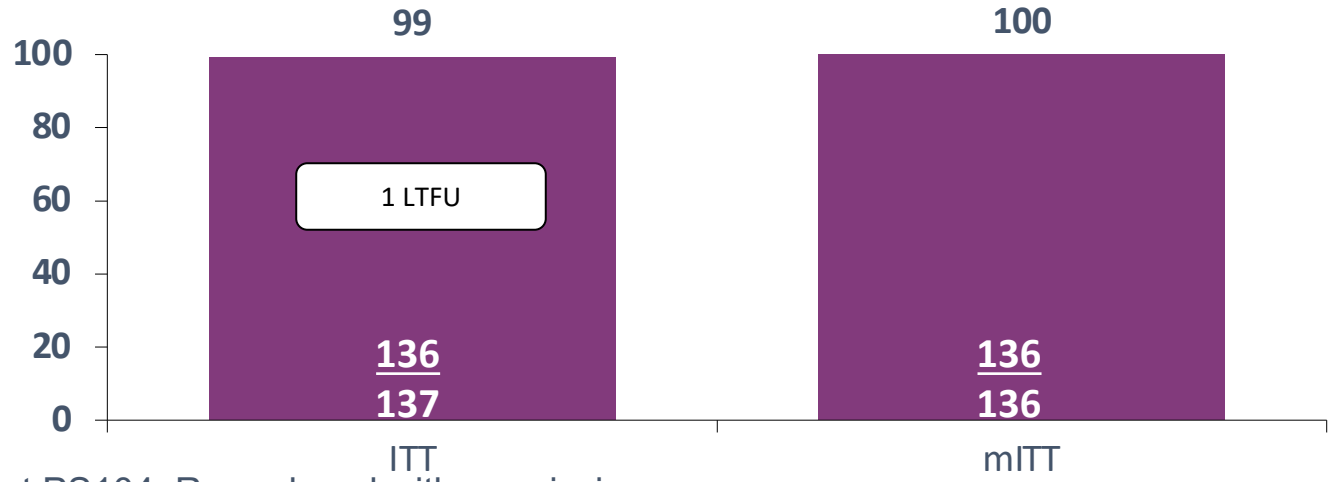
Puoti M et al. Journal of Hepatology (2018); Brown RS et al. Journal of Hepatology (2019)

HIV/HCV Coinfected Individuals Have Similar Cure Rates

Sofosbuvir/Velpatasvir x 12 weeks



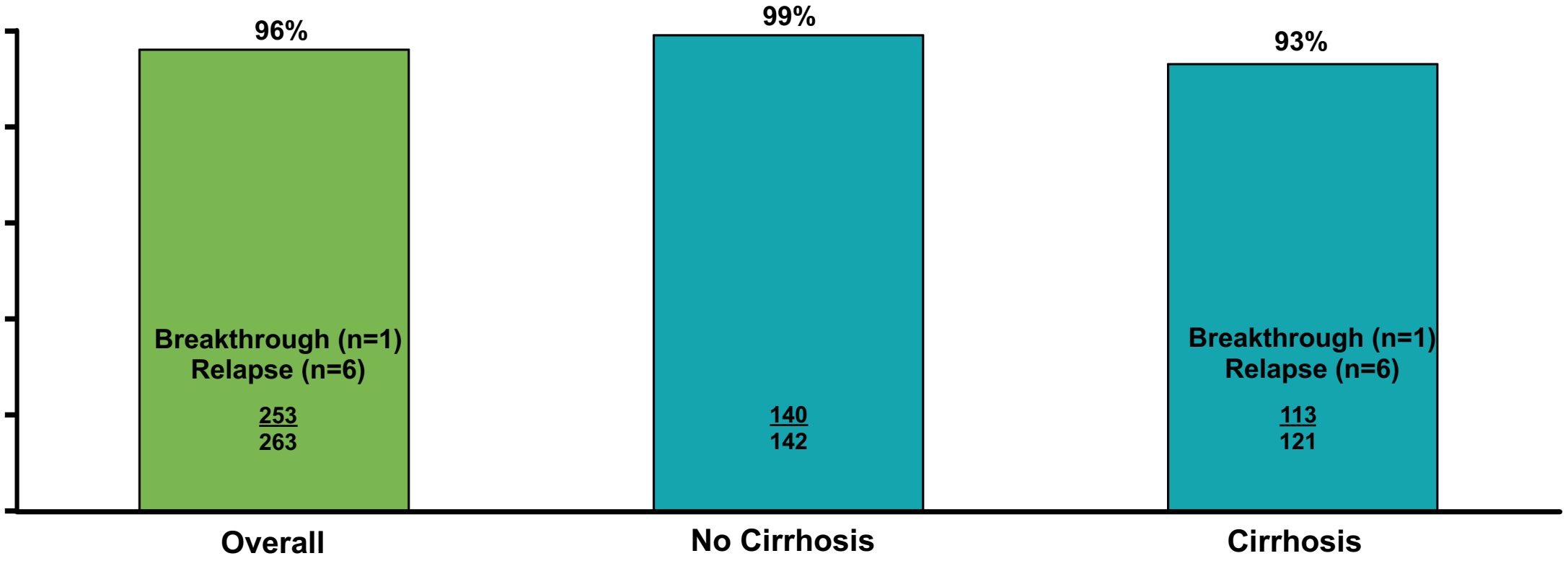
Glecaprevir/Pibrentasvir for 8 weeks



Wyles D, et al. EASL 2016. Abstract PS104. Reproduced with permission.

Overall Cure Rates in NS5A inhibitor – Experienced patients

Sofosbuvir/Velpatasvir/Voxilaprevir (Genotypes 1-6)



No placebo patients achieved an SVR12.

*P<0.001 for superiority versus pre-specified goal of 85% for sofosbuvir/velpatasvir/voxilaprevir.

Bourlière M, et al. Hepatology. 2016;64(suppl S1):102A. Abstract 194.

THE SAFETY AND EFFICACY OF EPCLUSA WERE STUDIED IN A PROSPECTIVE CLINICAL TRIAL IN PEOPLE WHO INJECT DRUGS

The Phase 4 SIMPLIFY clinical trial evaluated the efficacy and safety of EPCLUSA for 12 weeks in adults with HCV and recent injection drug use (within the past 6 months) who were naïve to NS5A-based HCV therapy.[1]

- SVR12 was the primary endpoint in SIMPLIFY and was defined as HCV RNA <12 IU/mL at 12 weeks after the end of treatment[1]
- **Patients were instructed to use EPCLUSA for 12 weeks as recommended in the EPCLUSA Prescribing Information and given weekly electronic blister packs[1]**
- Patients with HIV and/or decompensated liver disease were excluded[1]
- The study population was recruited from hospital-based and community-based clinics.

Study Limitations: Weekly clinic visits and weekly electronic blister packs, which patients were incentivized to return, may have led to improved adherence and treatment completion, which may not be generalizable to the larger HCV population.[1]

[a]Or those with a positive urine drug test at screening.[2]

1. Grebely J, et al. *Lancet Gastroenterol Hepatol*. 2018;3(3):153-161. 2. Grebely J, et al. *Clin Infect Dis*. 2016;63(11):1479-1481.

SIMPLIFY INCLUDED SUBJECTS WITH CHALLENGES THAT ARE COMMON AMONG PEOPLE WHO INJECT DRUGS

Baseline Characteristics		N=103
Mean age, years (SD)		48 (41-53)
Male sex, n (%)		74 (72)
GT, n (%)	1	36 (35)
	2	5 (5)
	3	60 (58)
	4	2 (2)
F4 (cirrhosis), n (%)		9 (9)
Any injection drug use in the past 6 months, n (%)		103 (100)
Any injection drug use in the past 30 days, n (%)		76 (74)
At least daily injection drug use in the past 30 days, n (%)		27 (26)
Alcohol use in the past 30 days, n (%)		62 (60)
History of MAT, n (%)		84 (82)
Current MAT, n (%)	Methadone	45 (44)
	Buprenorphine	4 (4)
	Buprenorphine–naloxone	12 (12)
Unstable housing, n (%)		24 (23)

94%

overall cure rate (ITT) in a clinical study in GT 1-4 NC/CC subjects[1]
(n=97/103; SIMPLIFY)

MAT=medication-assisted treatment.

Grebely J, et al. *Lancet Gastroenterol Hepatol*. 2018;3(3):153-161.

WMMG WEST MIDTOWN MEDICAL GROUP

ANCHOR STUDIED EPCLUSA IN PEOPLE WHO INJECT DRUGS WITH REAL CHALLENGES IN A REAL-WORLD SETTING

ANCHOR evaluated the efficacy of EPCLUSA for 12 weeks in adults with opioid use disorder and reported ongoing injection drug use (within 3 months of screening visit) treated at a harm-reduction center in Washington, DC (N=100)

- Primary endpoint was the proportion of participants with SVR12.
- Adherence was assessed by monthly pill count, HCV viral load, number of bottles completed, interruptions on treatment (3 or more days with subsequent resumption), and date of last pill taken relative to planned end-of-treatment date.
- Imperfect daily adherence was defined as finishing treatment >7 days after the anticipated treatment end date
- Patients with decompensated liver disease and those who were pregnant or breastfeeding were excluded
- Participants were offered optional buprenorphine initiation

Study Limitations: MAT status groups were non-randomized and self-selected. Factors associated with non-uptake or discontinuation of MAT may have been the same factors that led to HCV treatment failure or LTFU. Results may not be generalizable to the larger HCV population

IQR=interquartile range.

Rosenthal E, et al. *Clin Infect Dis.* 2020 Feb 3.

WMMG WEST MIDTOWN MEDICAL GROUP

ANCHOR STUDIED EPCLUSA IN PEOPLE WHO INJECT DRUGS WITH REAL CHALLENGES IN A REAL-WORLD SETTING

Select Baseline Characteristics	N=100
Median age, years (IQR)	58 (53-62)
Men, n (%)	76 (76)
Black race, n (%)	93 (93)
Cirrhosis, n (%)	33 (33)
Unstably housed, n (%)	51 (51)
Prior incarceration, n (%)	92 (92)

Baseline Drug Use Factors	N=100
Median age at first injection drug use, years (IQR)	21 (17-31)
Daily or more frequent injection drug use, n (%)	59 (59)
MAT, n (%)	33 (33)
Receptive sharing of injection drug use equipment within 3 months, n (%)	29 (29)
Hazardous drinking (AUDIT-C), n (%)	40 (40)

88%

overall cure rate (PP) in the real world

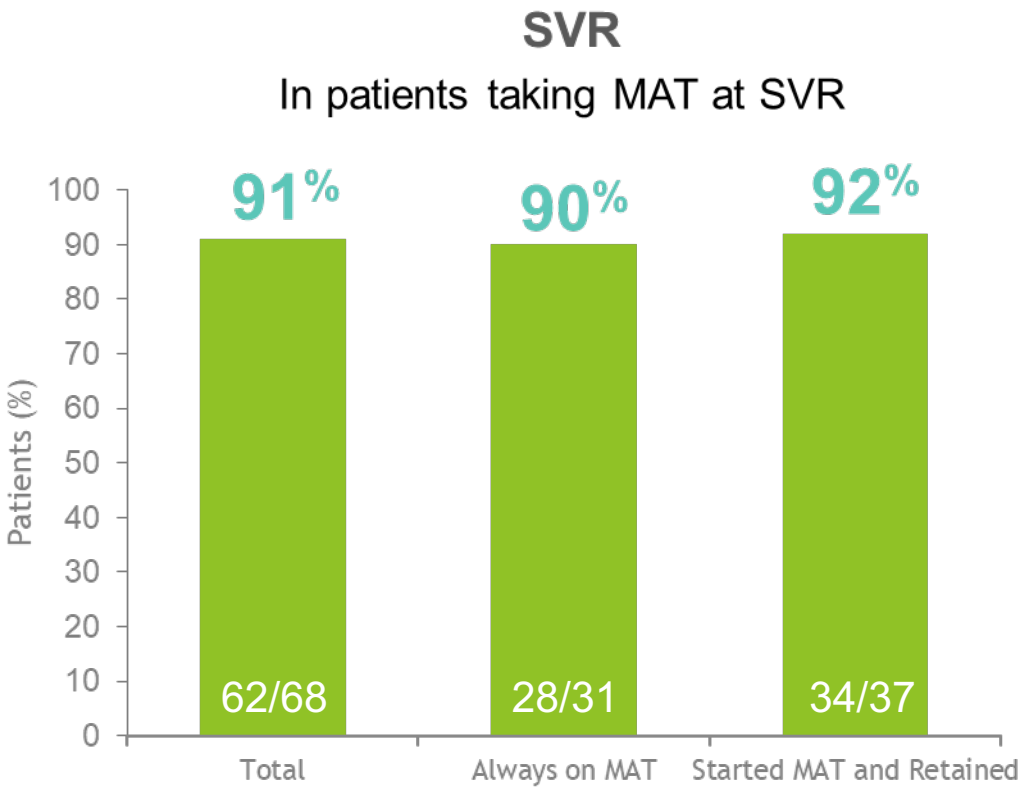
(n=82/93; ANCHOR)

For the total patient population, the cure rate was 82% (82/100).

Rosenthal ES, et al. *Clin Infect Dis.* 2020 Feb 3.

WMG WEST MIDTOWN MEDICAL GROUP

MAT AND CURE RATES IN ANCHOR



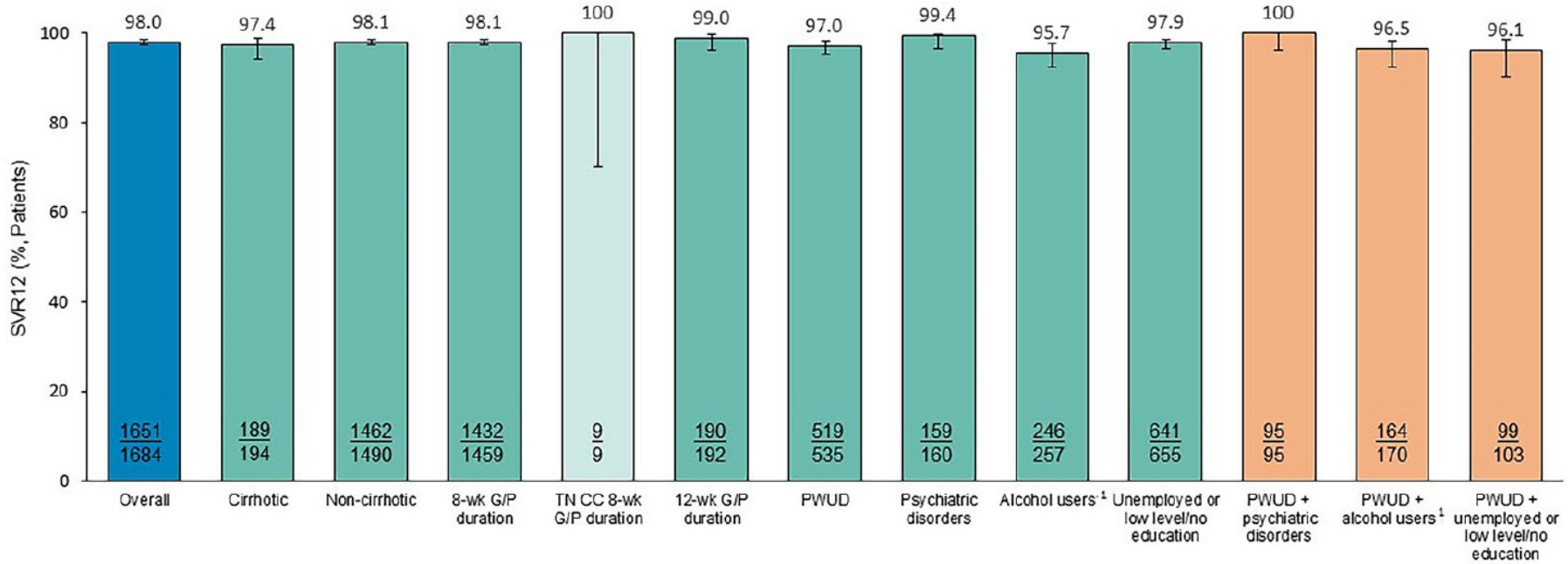
- At Week 24, 68 (68%) patients were on MAT
  - 31 patients were on MAT prior to and throughout the study period
  - 37 started and remained on MAT during the study
- Being on MAT was associated with higher rates of SVR

WMG WEST MIDTOWN MEDICAL GROUP

Rosenthal E, et al. *Clin Infect Dis.* 2020 Feb 3.

Real-World Outcomes in Historically Underserved Patients with Chronic Hepatitis C Infection Treated with Glecaprevir/Pibrentasvir

a



Reason for non-response, n													
On-treatment VF	6	0	6	6	0	0	1	1	2	3	0	1	1
Relapse	15	4	11	10	0	2	7	0	5	5	0	2	0
Premature G/P discontinuation	4	0	4	4	0	0	2	0	1	2	0	1	1
Missing SVR12	2	0	2	2	0	0	2	0	1	2	0	1	1
Other	6	1	5	5	0	0	4	0	2	2	0	1	1

WEST MIDTOWN MEDICAL GROUP

Aghemo A et al. *Infect Dis Ther*. 2021 Dec; 10(4): 2203–2222.

OPTIMIZING HCV TREATMENT IN A US CO-LOCATED HCV/OPIOID AGONIST THERAPY PROGRAM

- Retrospective chart review to determine SVR and reinfection rates at a Rhode Island MMTP (November 1, 2014 – October 31, 2019)

Simplified co-located test to treat OAT/HCV pathway

Enter care at OAT clinic:
- Universal (opt-out) HCV Ab screening with reflex RNA & GT
- HAV, HBV, HIV serologies
- Liver Panel
- CBC, Cr, PT/INR, RPR, urine GC/Chlamydia

↓

Nurse navigates patient to initial HCV physician visit

↓

1st visit: HCV physician evaluation, DAAs ordered, Prior Authorization submitted

↓

2nd visit: HCV treatment initiated

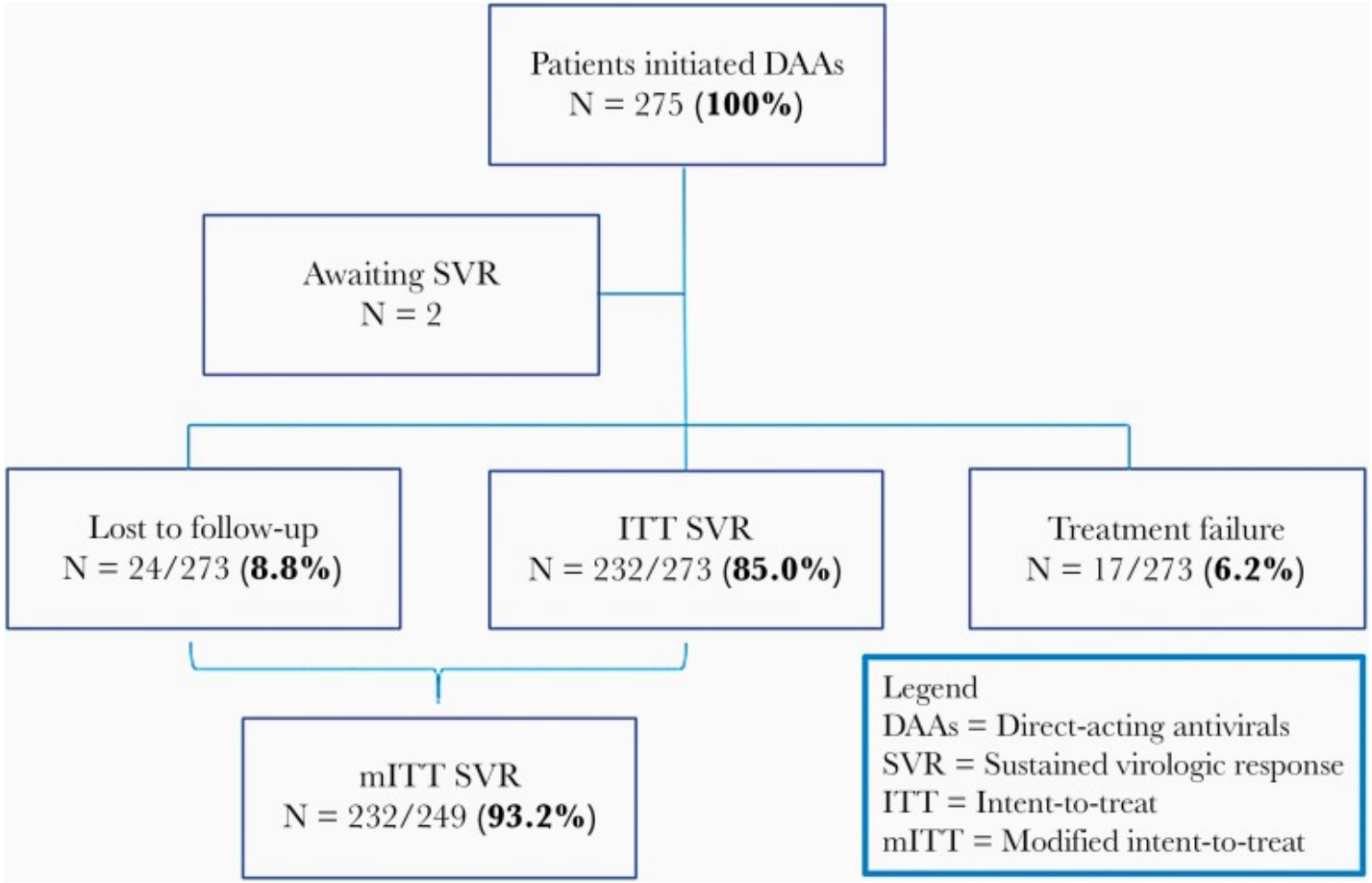
↓

SVR

WMMG WEST MIDTOWN MEDICAL GROUP

Habchi, J et al. *Open Forum Infect Dis*. Oct 2020

RESULTS: CO-LOCATED HCV/OAT TREATMENT



WMMG WEST MIDTOWN MEDICAL GROUP

Habchi, J et al. *Open Forum Infect Dis*. Oct 2020

Direct Acting Agents

- All oral medications
- Shorter course of therapy
- Pangenotypic
- Limited adverse events compared to previous treatments
- Access/coverage

Variable Adherence

Adherence is an EVERYONE issue, not unique to PWUD!

Variable Adherence

SOF/VEL - SIMPLIFY prospective in PWID)[1]

- >90% adherence (</= 8 dosages missed) = 96% SVR (69/103)
- <90% adherence (>8 doses missed) = 91% SVR (31/34)

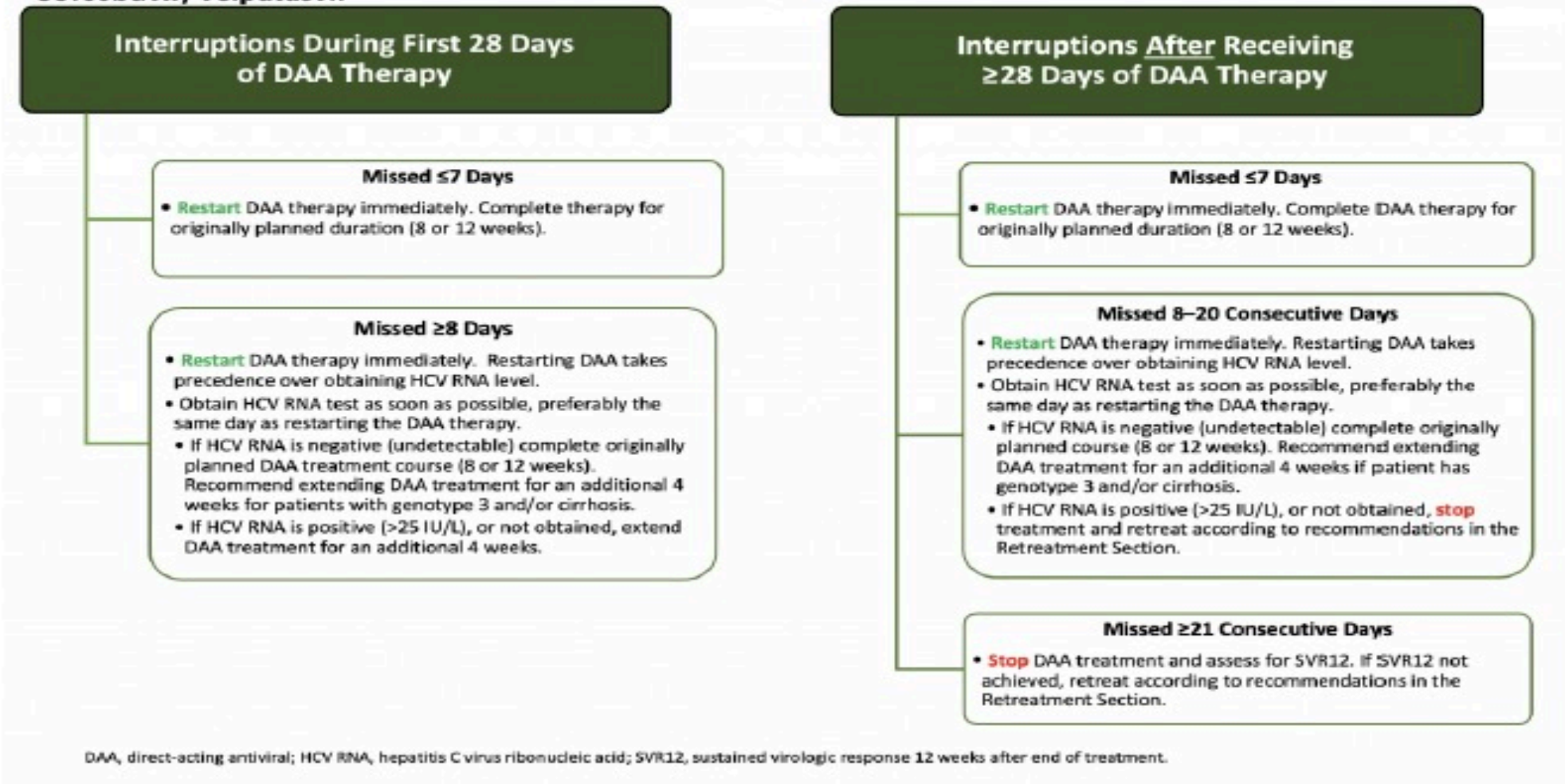
GLE/PIB- retrospective[2]

- Data on 8-week regimen from 10 phase 3 clinical trials
- <90% adherence = 100% SVR (weeks 0-4 n=21/21, weeks 5-8 n=76/76
- >90% adherence = 99% SVR (weeks 0-4 n=1155/1162, weeks 5-8 n=1136/1143)

1. Cunningham EB, et al. *Int J Drug Policy*. 2018; 62:14-23; 2. Zamor PJ, et al. *Am J Gastroenterol*. 2021; 116(9):1896-904.

Management of Missed Dosages

Figure 1. Recommended Management of DAA Treatment Interruptions for Treatment-Naive Patients, Without Cirrhosis or With Compensated Cirrhosis, Receiving Glecaprevir/Pibrentasvir or Sofosbuvir/Velpatasvir



DAA, direct-acting antiviral; HCV RNA, hepatitis C virus ribonucleic acid; SVR12, sustained virologic response 12 weeks after end of treatment.

https://www.hcvguidelines.org/evaluate/monitoring

HCV Re-Infection

Hepatitis C reinfection after successful antiviral treatment among people who inject drugs: A meta-analysis

- Thirty-six studies were included (6,311 person-years of follow-up)
- **Overall rate of HCV reinfection was 5.9/100 person-years (95% CI 4.1–8.5) among people with recent drug use (injecting or non-injecting)**
- 6.2/100 person-years (95% CI 4.3–9.0) among people recently injecting drugs
- 3.8/100 person-years (95% CI 2.5–5.8) among those receiving OAT

Stratified analysis

- **1.4/100 person-years (95% CI 0.8–2.6) among people receiving OAT with no recent drug use**
- 5.9/100 person-years (95% CI 4.0–8.6) among people receiving OAT with recent drug use
- 6.6/100 person-years (95% CI 3.4–12.7) among people with recent drug use not receiving OAT

Hajarizadeh B, et al. *J Hepatol*. 2020;72(4):643-57.

Clinical Models to Improve Linkages to HCV/Addiction Care and Treatment Uptake

Conventional referral

- System is difficult to navigate for many
- Transportation
- Need a multidisciplinary approach
- Utilization of case managers
- Peer navigators

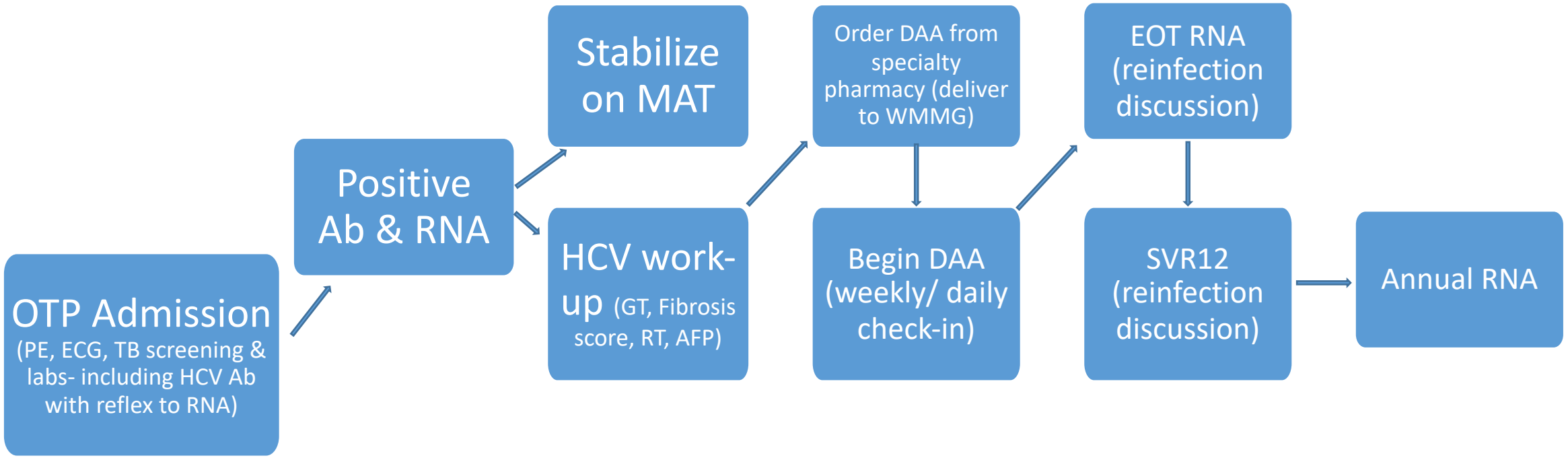
Telemedicine

- Useful to deliver services to any setting (prison, rural, substance abuse clinics)
- Provide specialty care where not otherwise available
- Supportive data in both addiction and HCV settings
- Slows cascade

Colocalization

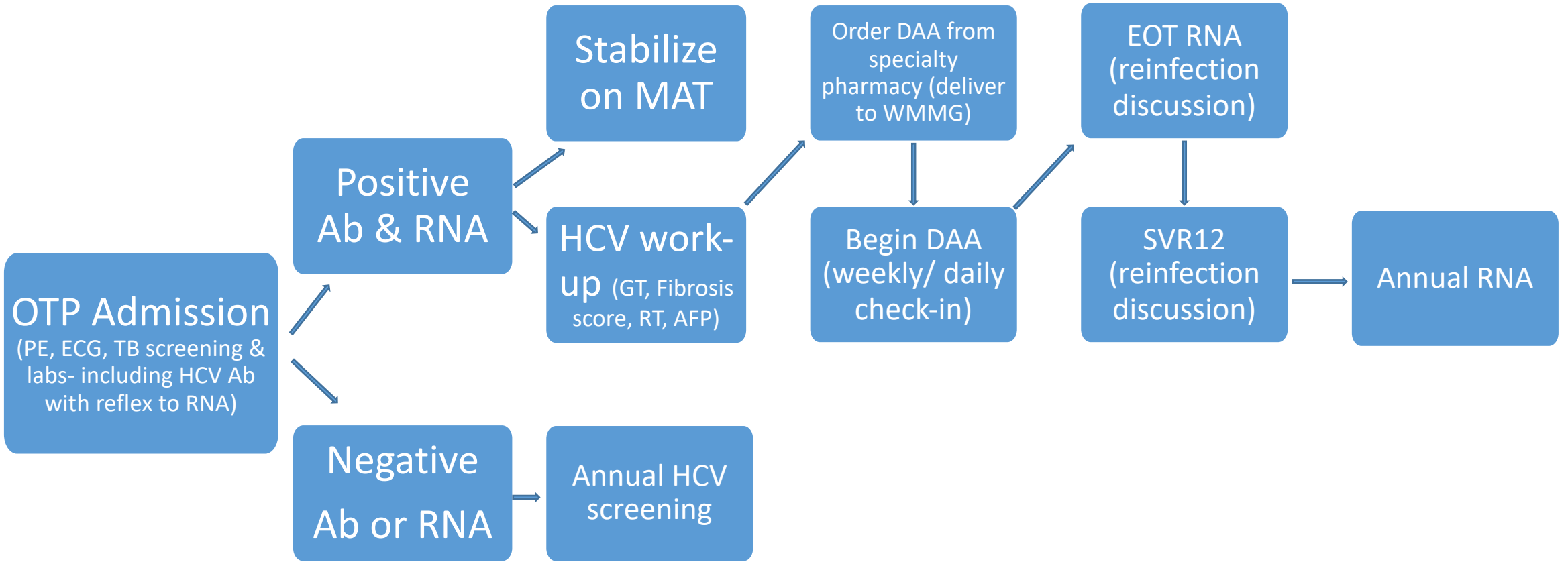
- One-stop shopping
- Multiple services offered in one location
- Minimizes loss to follow-up
- Streamlines care

West Midtown Medical Group Protocol



WMG WEST MIDTOWN MEDICAL GROUP

West Midtown Medical Group Protocol



WMG WEST MIDTOWN MEDICAL GROUP

Challenges & Supports

- Challenges
  - Patient readiness and agreement
  - Adherence to treatment
  - Housing
  - Food insecurities
- Supports
  - RN/LPN
  - Admin
  - Counseling staff
  - Support group
  - Specialty pharmacy

WMMG WEST MIDTOWN MEDICAL GROUP

Conclusions

Need to eliminate all restrictions- fibrosis, sobriety, provider type, re-Tx and PA process

Need more providers – NP, PA, pharmacists, community health workers etc

Reimbursement ability in the addiction setting is a must

To achieve 100% linkage to care and treatment initiation- need a mix-and-match approach, One size won't fit all.

HARM REDUCTION, HARM REDUCTION, HARM REDUCTION

WMG WEST MIDTOWN MEDICAL GROUP

WMG WEST MIDTOWN MEDICAL GROUP