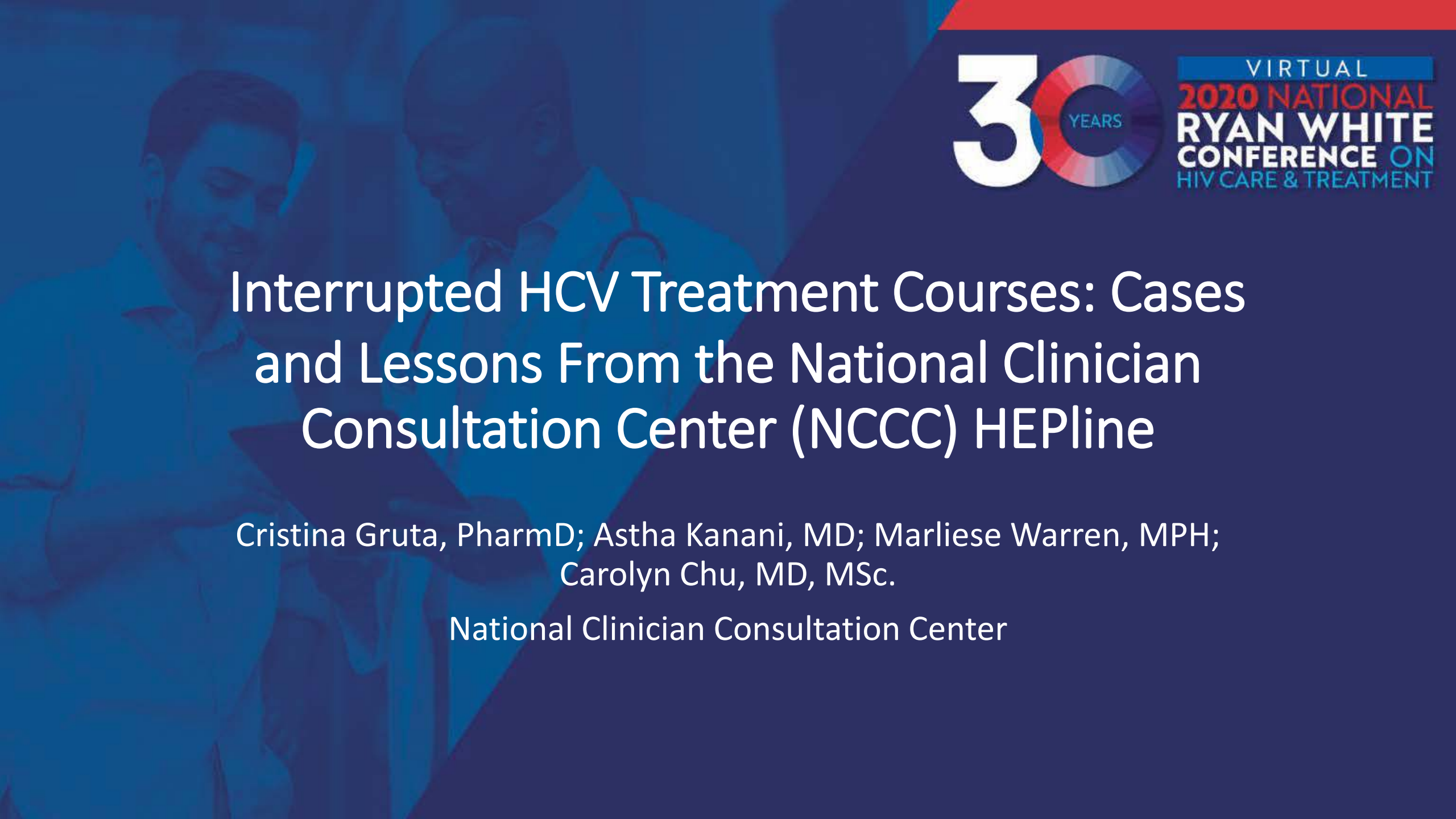


Interrupted HCV Treatment Courses: Cases and Lessons From the National Clinician Consultation Center (NCCC) HEPline

Cristina Gruta, PharmD; Astha Kanani, MD; Marliese Warren, MPH; Carolyn Chu, MD, MSc.

National Clinician Consultation Center

Disclosures

- Presenters have nothing to disclose

Objectives

- Explain the role the HCV Consultation Line (HEPline) can play in providing clinical support to HCV providers
- Discuss the different types of HCV treatment lapse scenarios
- Describe factors that lead to interruptions in HCV treatment
- Discuss pre-emptive or real-time interventions that HCV treaters can make to avoid or minimize treatment interruptions

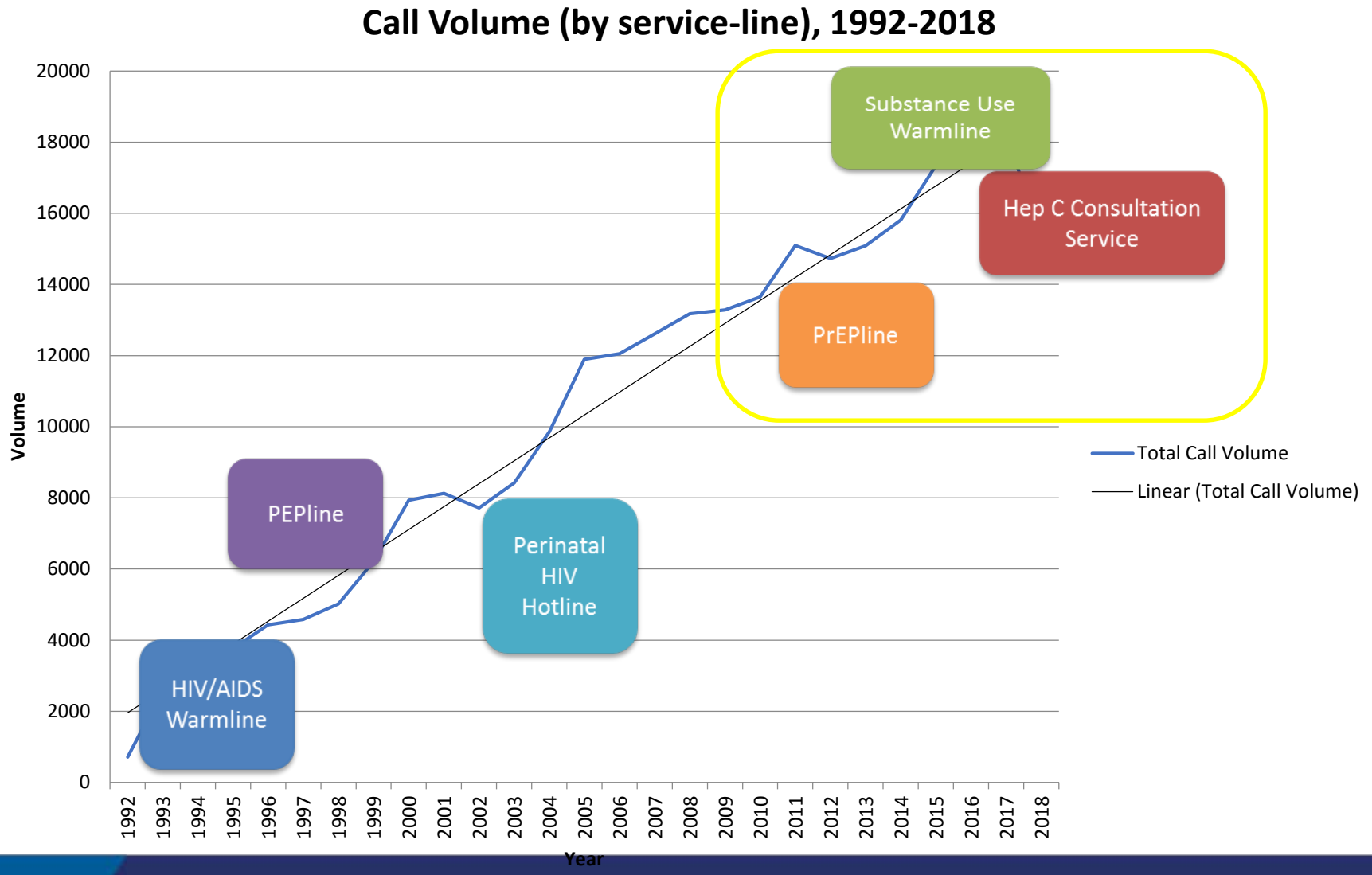
Who is the NCCC?

Our mission is to improve health outcomes by building the capacity of healthcare providers through expert clinical consultation and education.

- National tele-consultation/education arm of AETC Program: have offered **free clinical decision support** to health care providers for 25+ years
- **Multi-disciplinary, inter-professional teams** → 500+ years of collective experience on viral hepatitis, HIV, and substance use
- **Point-of-care/"one-stop" resource** individually-tailored consultation
- **Practical, compassionate** assistance (*"options, not answers"*)

AETC AIDS Education & Training Center Program

What does the NCCC do?



How do you reach the HCV Warmline (HEPline)?

(844) HEP-INFO, 9am-8pm EST | Mon-Fri

- Leave voicemail during evenings/weekends/holidays: call-back within 1 business day
- Online case submission available via nccc.ucsf.edu: same-day response if received during standard program hours, otherwise response w/in 1 business day

- Brief caller registration process to collect caller/practice information: *no PHI involved*

HCV Warmline ("HEPline")

My patient's HCV antibody test just came back positive and she is 5 months pregnant. What should I do?

I'm not sure if my patient has cirrhosis: what regimen should I select and how many weeks of treatment do I give?

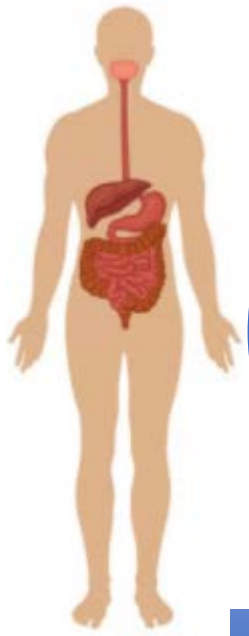
My patient has HBV serologies of someone with recovered infection (HBsAb+, HBcAb+). How should I follow them once we start DAA treatment?

Can the HCV Warmline team serve as the "consulting specialist" since my state's insurance program requires review by a specialist?

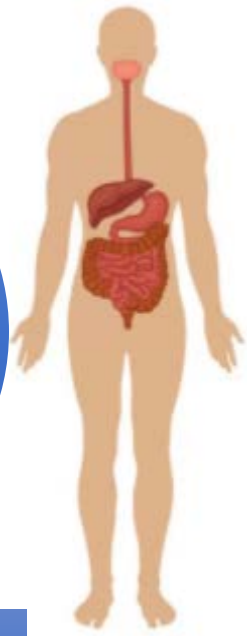
Anatomy of an HCV Warmline Consultation

Pharmacy review: potential drug interactions between HCV medications, prescribed, and non-prescribed therapies

Share **updated treatment guidelines** and other clinical/educational resources



Which DAA regimen should I select for a previously-treated 63yo with GT1a? He also has diabetes and acid reflux.



Explore whether there is a "**question behind the question**": does this patient have cirrhosis? How can I make that assessment?

Help determine whether **additional input from hepatologist or other specialist** could be beneficial

HEPline- Case “A”

- Consult requested by PharmD in Arizona in May 2019
- Pt is 25 yo Native American male with GT1a infection, tx-naïve, F0
- Treated with ELB/GRZ from January to April 2019 but finished 12-week course over 13 weeks (break b/w weeks 5 and 6)

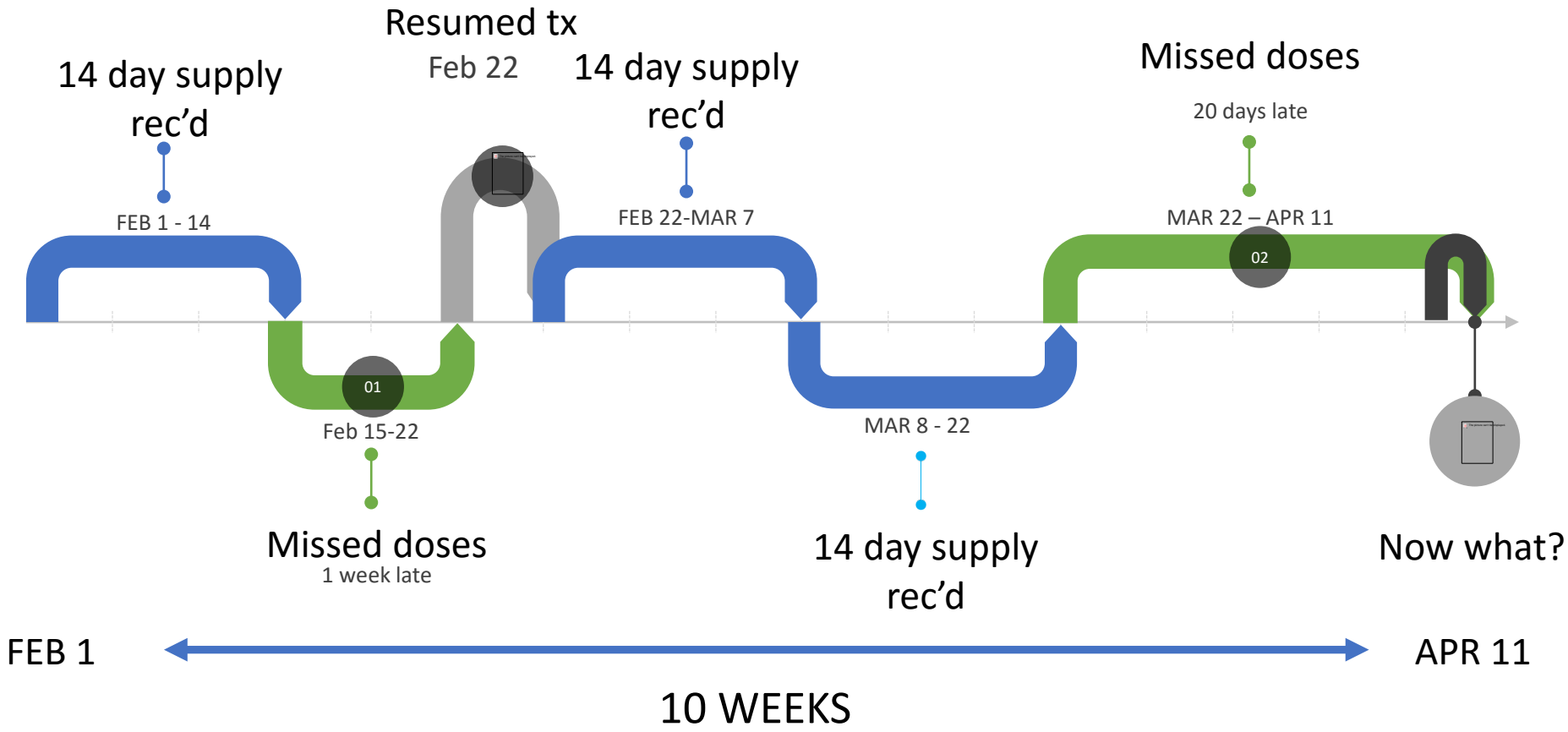
Week #	HCV RNA PCR
4	undetectable
8	217,000
12	BLQ

QUESTION:
How do you explain the HCV viral load trend? Could the interruption in treatment be a factor?

HEPline Case "B"

- Caller is NP in Northern California FQHC→ not the pt's PCP but is the HCV "treater" in the clinic
- Pt is 28 yo male with GT 1a infection, tx-naïve; VL 94,230; FIB-4→ 0.92
- Pt still actively using IV drugs
- Decision was to tx pt with GLE/PIB x 8 weeks starting Feb 2019
- Caller saw pt in urgent care in mid-March 2019 (for non-HCV related reasons) and at that visit reported missed doses of G/P
- Pt reportedly went to rehab sometime in late March/early April– missed G/P doses x 1 week

HEPline Case B – Treatment interruption timeline



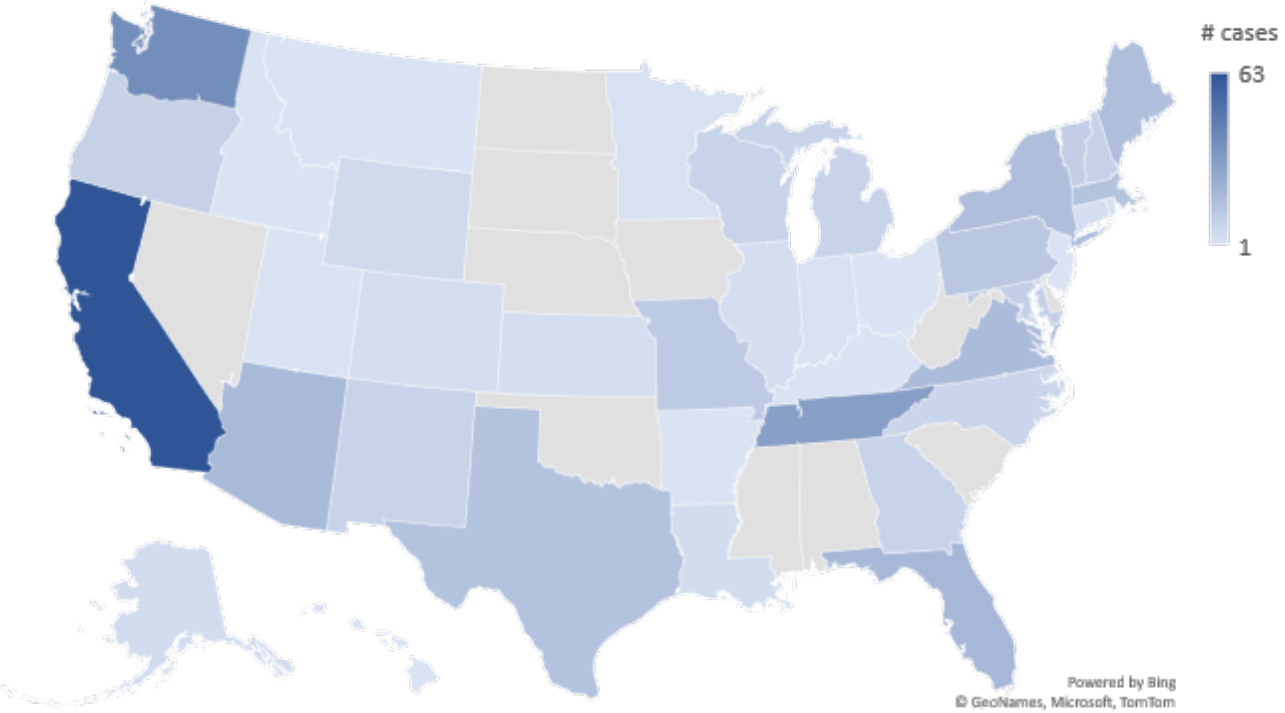
QUESTION→ What is best approach?

Methods

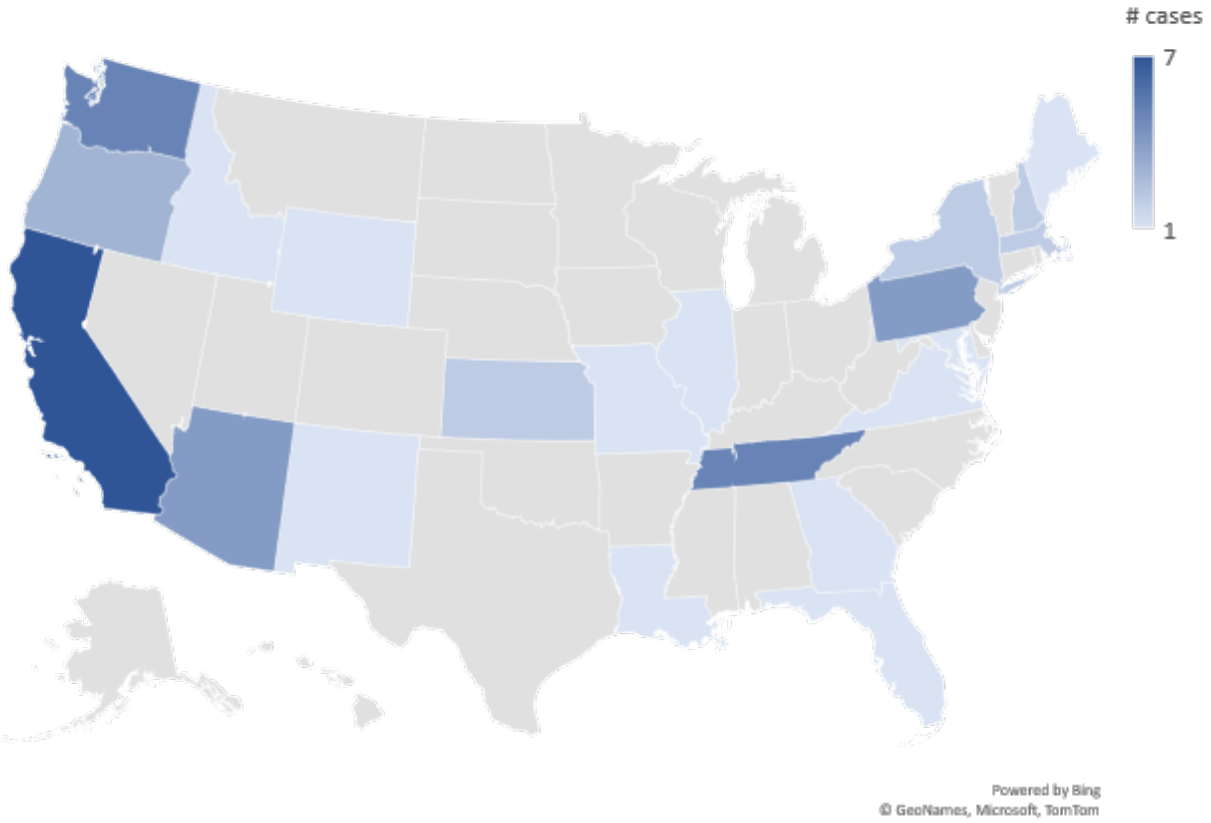
- Reviewed HepLine calls 11/1/18 through 4/30/20
- Identified calls that pertained to interrupted or lapsed HCV treatment
- Excluded calls if not patient-specific, i.e. posing general question
- Excluded calls involving pregnant patients
- Collected both caller and patient demographics
- Identified situational themes for the context of interruptions

Results- cases reviewed

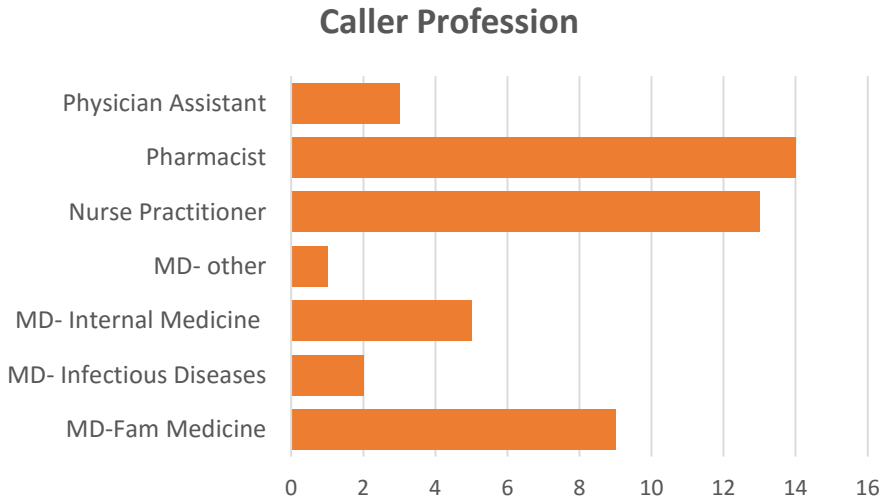
Cases by state N = 395

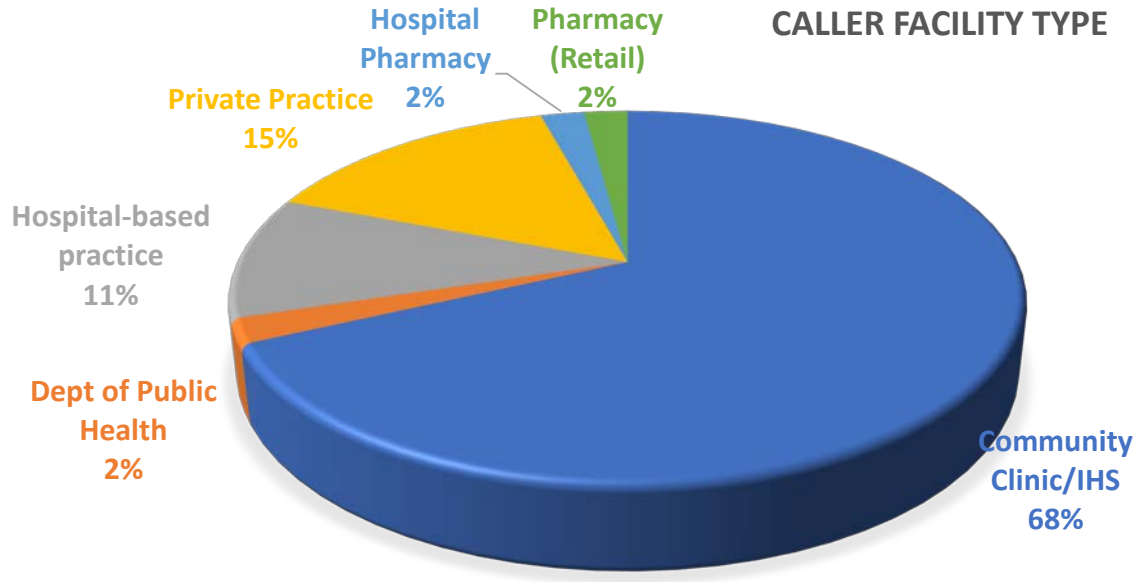


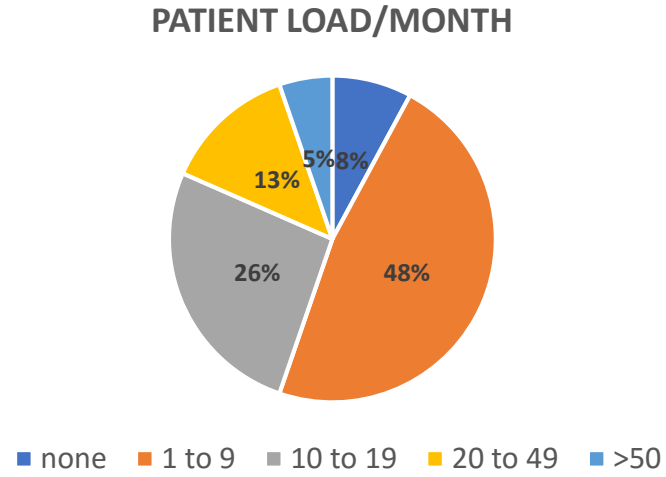
Cases with lapsed treatment N=47



Caller Demographics





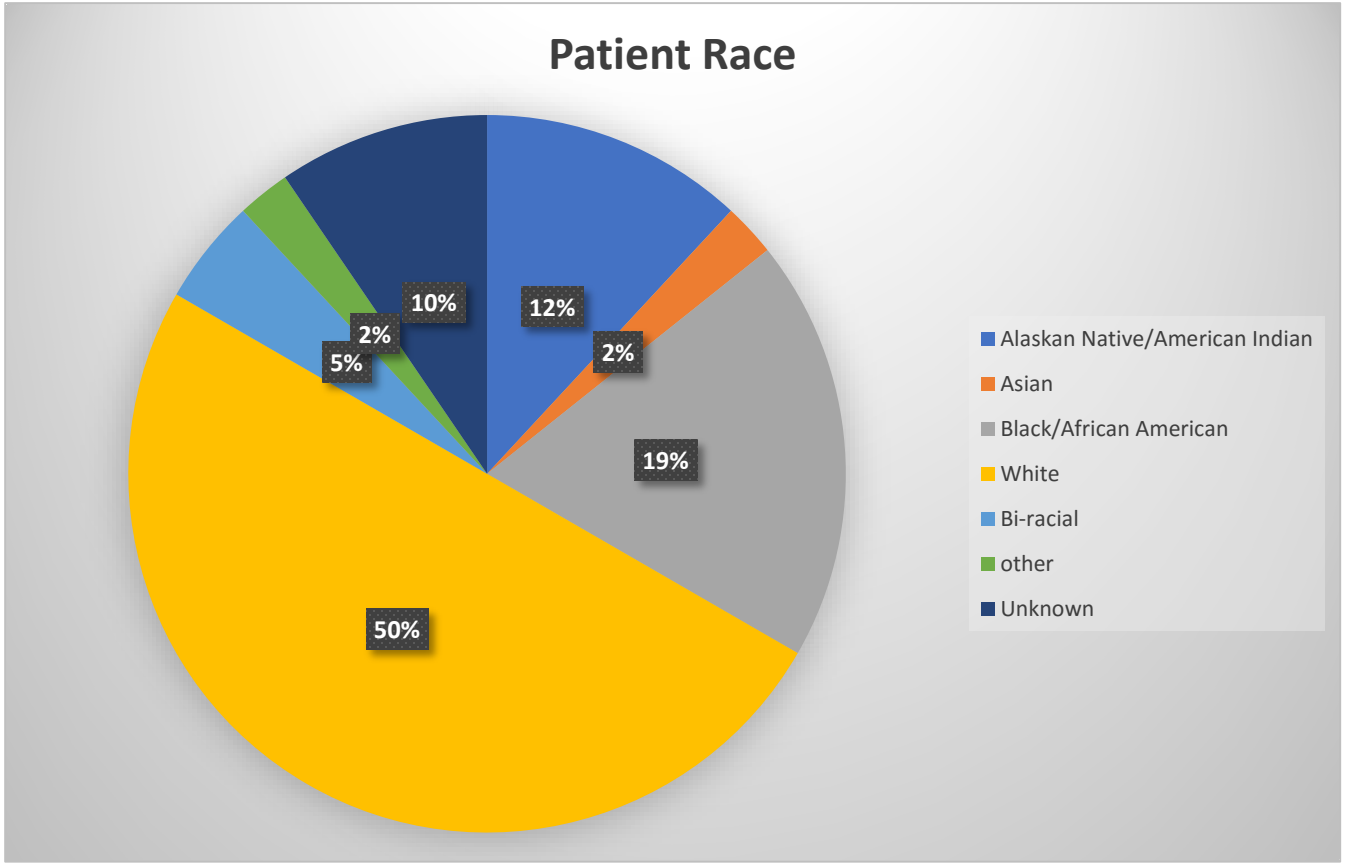


Years HCV Experience	
range	<1 to 25
average	3.25
median	1.50

Patient Demographics

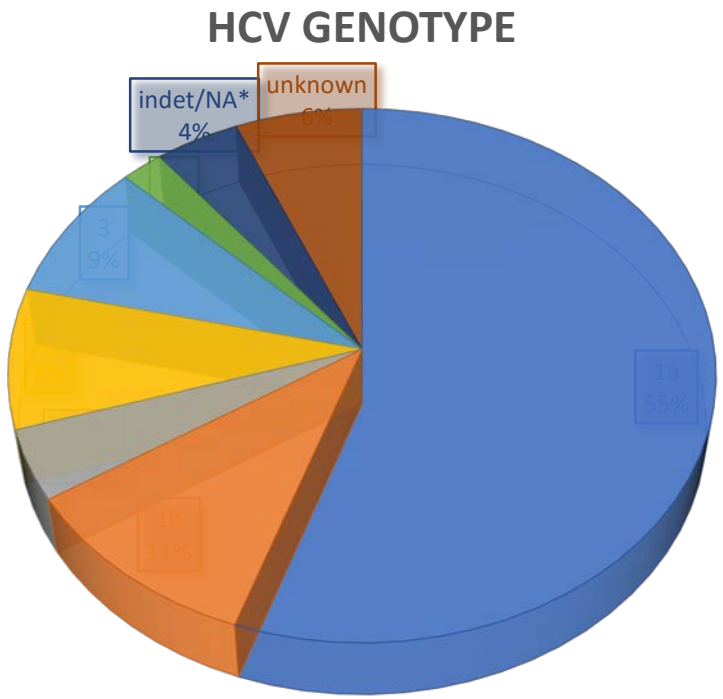
Patient Gender	
Female	15
Male	31
DNA/NA	1

Patient Age	Years
Range	23-70
Average	47.068
Median	48

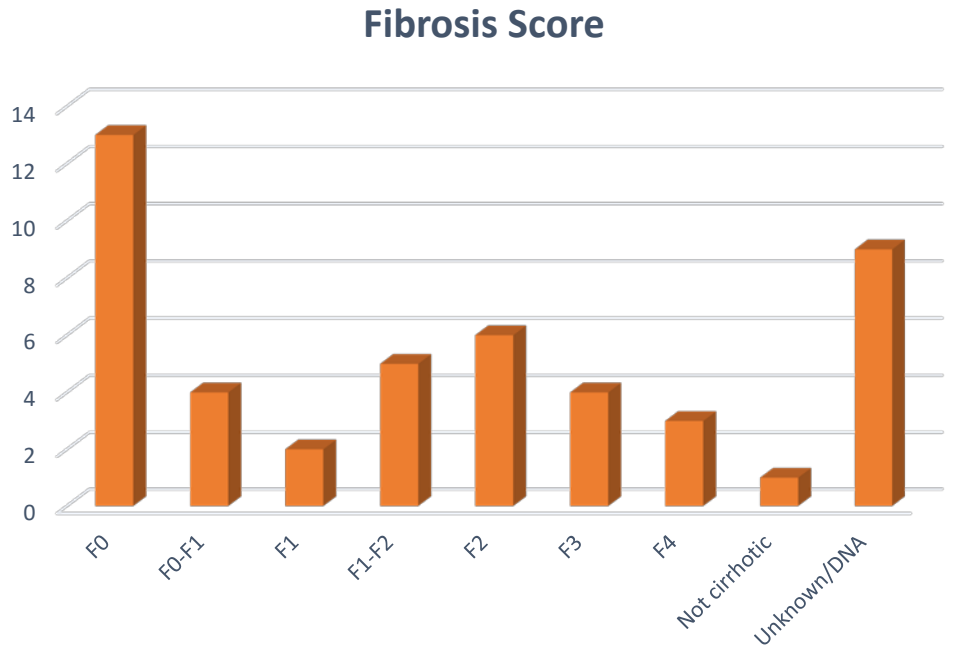


Patient HCV demographics

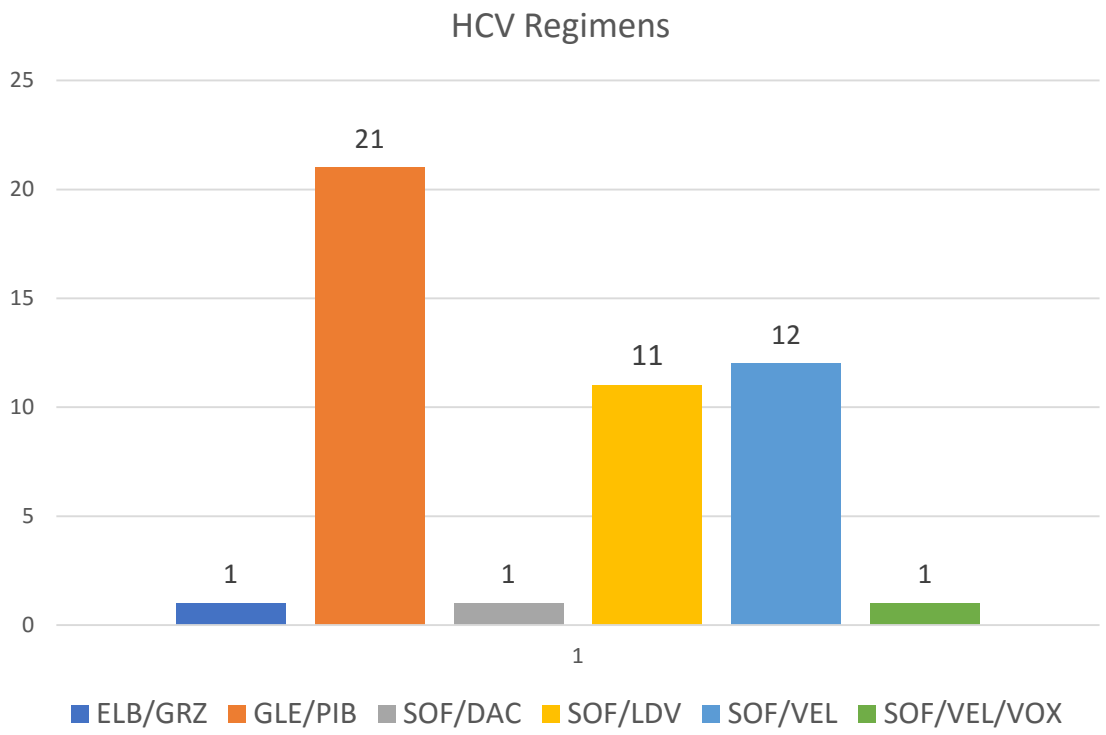
Tx Naïve or Experienced	
Experienced	3
Naïve	42
Unknown	2

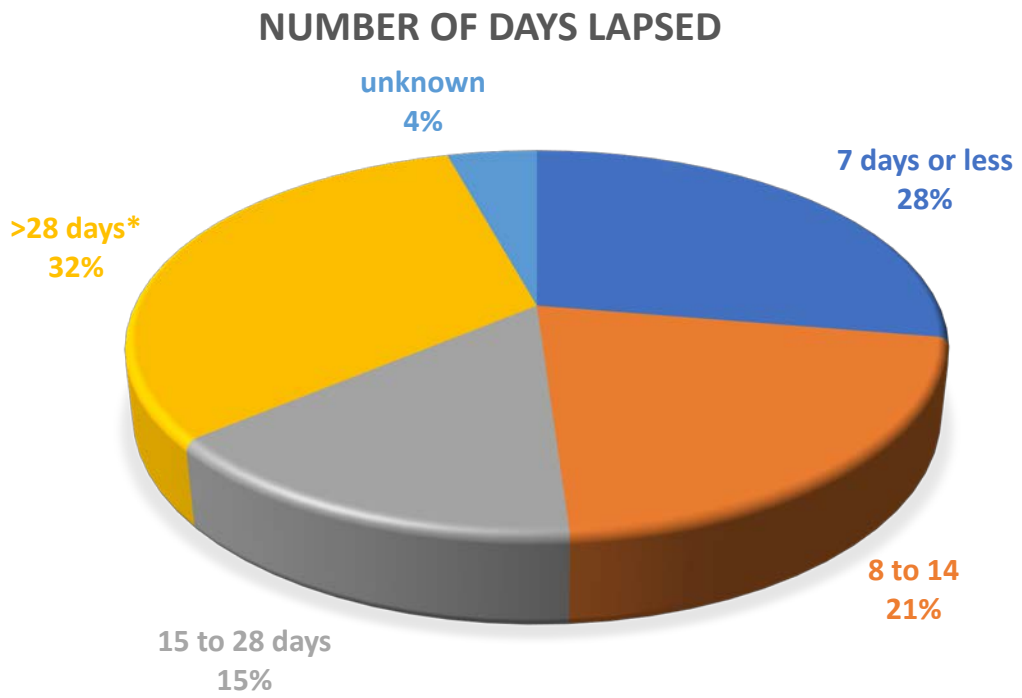


*For "indet/NA" category, genotyping not covered by HCV treatment funds



HCV Treatment Course





*For >28 days lapsed, range >4 weeks to 2 years

What level of adherence to DAAs is needed to achieve SVR12?

SIMPLIFY study

- SIMPLIFY international open-label, single arm study recruited subjects with recent IDU (last 6 months) with chronic HCV infection
- Participants given SOF/VEL x 12 weeks in one-week electronic blister packs
- 61% on opioid substitution
- Of an N=103 recruited, 100 finished treatment (2 LTFU, one died from overdose)
- 97/100 achieved SVR12

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

SIMPLIFY study- adherence

Table 2
Treatment adherence and dosing patterns among all participants in the SIMPLIFY study.

Variable	Overall (n = 103) n (%)
Treatment completion	100 (97)
Missed doses of sofosbuvir/velpatasvir as measured by electronic blister-pack, n (%)	
No missed doses (100%)	12 (12)
1-4 missed doses (95- < 100%)	36 (35)
5-8 missed doses (90- < 95%)	20 (19)
9-17 missed doses (80- < 90%)	17 (17)
≥18 missed doses (< 80%)	18 (17)
Longest episode of non-adherence[a]	
1 day	44 (43)
2 days	19 (18)
3 days	3 (3)
4 days	9 (9)
5 days	2 (2)
6 days	3 (3)
≥7 days	11 (11)

- Adherence defined as taking ≥90% of doses
- Median adherence 94%
- 32% were non-adherent (took <90%of doses)
- SVR12 similar between adherent (94%, 66/70) and non-adherent (94%, 31/33) participants (p = 0.944)
- Of 11 patients who had one episode of missing ≥7 consecutive days of SOF/VEL, 9 finished treatment and had no virologic failure

E.B. Cunningham et al. International Journal of Drug Policy 62 (2018) 14–23

ANCHOR: Pilot Study of HCV Treatment at Drop-in Harm Reduction Organization in Washington, DC

- Single-center study
  - 76% men, 93% black, 33% cirrhotic, 58% injected drugs at least daily, 33% receiving medication-assisted therapy for drug use

Patients with chronic HCV infection, opioid use disorder, and opioid injection in last 3 mos; no decompensated cirrhosis or contraindicated DDIs
(N = 100)

→

SOF/VEL* QD

Concurrent buprenorphine and HIV PrEP offered as indicated

*Dispensed in 28-day increments at Day 1, Wk 4, Wk 8 (ie, 3 bottles).

- Primary endpoint: SVR12

Kattakuzhy. AASLD 2018. Abstr 18.

Slide credit: clinicaloptions.com

ANCHOR: HCV Treatment at Harm Reduction Organization

- 93 patients in ITT analysis
  - Lost to follow-up: n = 8
  - Deceased: n = 3
  - Virologic failure: n = 9
  - **SVR12: n = 73 (78%)**
- Per protocol SVR12: 89% (73/82)
- Virologic success unaffected by baseline demographics such as drug use frequency, housing stability, medication-assisted therapy

Adherence Measure in ITT Population		SVR12, %	*P* Value
Wk 4 HCV RNA < 200 IU/mL	▪ Yes (n = 80) ▪ No (n = 8)	86 25	.0005
No treatment interruptions	▪ Yes (n = 76) ▪ No (n = 12)	86 67	.22
Completed 2 or 3 of 3 SOF/VEL bottles	▪ Yes (n = 87) ▪ No (n = 6)	84 0	.0001
Finished SOF/VEL on time (vs late)	▪ Yes (n = 20) ▪ No (n = 43)	95 88	.65

Kattakuzhy. AASLD 2018. Abstr 18.

Slide credit: clinicaloptions.com

ANCHOR study– additional observations

- 59 pts completed 12 weeks of treatment but not all on time

Number (%) of pts completing 12 week course	# days completed beyond expected completion date
28 (48%)	1-7
9 (16%)	8-14
9 (16%)	>14

- Of 58 pts who reached week 24 follow-up, 52 (90%) attained SVR

What are the limits of imperfect adherence?

- Studies are small
- Show encouraging success if SOF/VEL regimen completed 1-2 weeks beyond intended end-of-treatment
- Do other DAA options offer similar forgiveness?
- But what about those who miss more than 1-2 weeks of treatment?

HCV treatment lapse- multiple types of scenarios

My patient didn't know to call the pharmacy to refill his SOF/VEL and it's been 10 days. Is it okay to continue?

Our patient received her first month of HCV treatment, started using meth again and was LTFU. Now she is back after a 3 week lapse. Do we stop?

A new patient to us says they took a month of SOF/LDV a year ago but stopped. Now they are ready to be treated. Should we start over or give rescue therapy?

What circumstances lead to treatment gaps?

Reported reasons for lapses

"Pt was lost to follow-up"

"Pharmacy delivery didn't reach pt, maybe it was intercepted? "

"Pt relapsed and ended up being incarcerated"

"There was clinic miscommunication"

"Pt could not get to clinic to pick up her meds"

"Pt didn't know to pick up the 2nd month of GLE/PIB; it's now 7 months later"

"Pt has had adherence issues in past; just forgets to take meds"

"Pt is unstably housed– lives in a car"

"Care team did not catch missed refill"

"Pt relapsed and ended up in rehab– may have run out of meds during stay"

"Pt suffering from bad Crohns, had to be hospitalized"

Reported reasons for lapses

OVERALL	
Unknown	10
Lost to Follow-Up	2
Substance Involvement/Relapse	9
Unstable Housing/Homelessness	2
Pharmacy Issues (Delivery)	5
Patient Confusion- med access	5
Incarceration	3
Insurance lapse/issues	2
Patient could not get to clinic	3
Patient acutely sick/hospitalized	6
Adverse effect (suspected)	3
Clinic miscommunication	1
Immigration from other country	1
Patient adherence issues/forgets	2

Most Common Identified Reasons:

1) Substance Involvement/Relapse
2) Medication access issues
   - Pick-up confusion
   - Lost deliveries
   - Insurance lapses/issues
3) Acute illness or exacerbated chronic illness

Models of HCV care in patients with substance involvement

Integrated HCV/MAT Care

Clin Infect Dis. 2019 Jul 2;69(2):323-331. doi: 10.1093/cid/ciy899.

Integrated, Co-located, Telemedicine-based Treatment Approaches for Hepatitis C Virus Management in Opioid Use Disorder Patients on Methadone

Andrew H Talal [1 2], Phyllis Andrews [2], Anthony Mcleod [2], Yang Chen [3], Clewert Sylvester [2], Marianthi Markatou [3], Lawrence S Brown [2]

Affiliations + expand

PMID: 30329042 DOI: 10.1093/cid/ciy899

- Investigated effectiveness of HCV care via telemedicine in OST program
- OUD patients on methadone underwent biweekly telemedicine sessions between a hepatologist and physician assistant during the entire HCV treatment course
- DAAs administered with methadone using modified DOT
- Of the 45 treated patients, 42 (93.3%) achieved viral eradication
- Marriage and mental health diagnosis other than depression highly associated with HCV treatment pursuit

Conclusions: HCV management via telemedicine integrated into an OST program is a feasible model with excellent virologic effectiveness. Psychosocial and demographic variables can assist in identification of subgroups with a propensity or aversion to pursue HCV treatment.

Integrated HCV/MAT Care

Drug Alcohol Depend. 2020 Jun 12;213:108116. doi: 10.1016/j.drugalcdep.2020.108116. Online ahead of print.

Co-Located Hepatitis C Virus Infection Treatment Within an Opioid Treatment Program Promotes Opioid Agonist Treatment Retention

Brooke Severe [1], Jeanette M Tetrault [2], Lynn Madden [2], Robert Heimer [3]

Affiliations + expand

PMID: 32599493 DOI: 10.1016/j.drugalcdep.2020.108116

- Patients (n = 89) treated for OUD and chronic HCV infection were compared to control patients (n = 199) being treated for OUD and diagnosed with but not treated for HCV
- Patients who completed HCV treatment had 2.22 (95 % CI: 1.11, 4.45) increased likelihood of remaining in the OTP compared to patients in the control group

Conclusion: Results indicate that a co-located model of care is associated with improved OTP treatment retention following HCV treatment, and suggest that co-locating HCV and OUD treatment has a secondary impact on keeping patients engaged in OAT.

Is it better to treat HCV in primary care setting?

HCV in primary care settings

› Infect Dis (Auckl). 2019 Apr 28;12:1178633719841381. doi: 10.1177/1178633719841381. eCollection 2019.

Integration of Hepatitis C Treatment in a Primary Care Federally Qualified Health Center; Philadelphia, Pennsylvania, 2015–2017

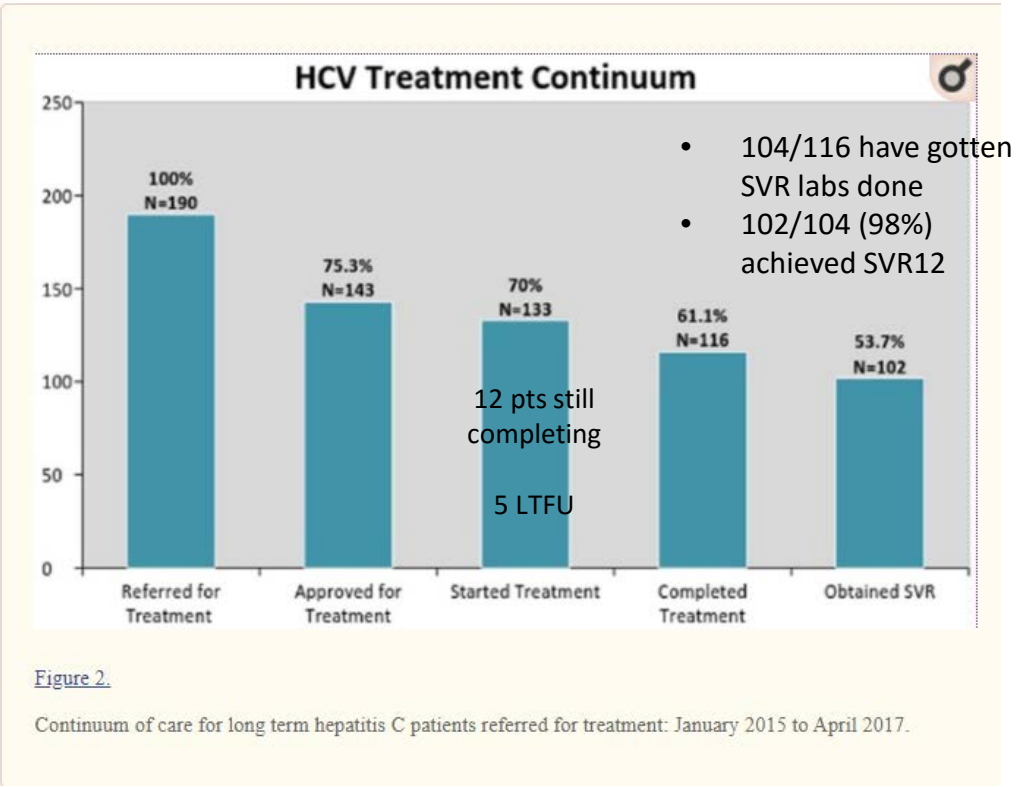
Tyler S Bartholomew [1 2], Kaitlin Grosgebauer [2], Katherine Huynh [3], Travis Cos [3 4]

Affiliations + expand

PMID: 31065216 PMCID: PMC6488784 DOI: 10.1177/1178633719841381

Free PMC article

- FQHC in Philadelphia with high burden of underserved population with high rates of mental illness and/or substance involvement
- HCV treatment team lead by physician assistants and NPs (supervised by 2 PCPs) but no onsite GI/hepatologist
- Rest of team included
  - Behavioral health consultants (BHCs)
  - HCV treatment coordinator
  - 340B pharmacy which processes prior authorizations, assess for drug interactions, provides medication refills



- 104/116 have gotten SVR labs done
- 102/104 (98%) achieved SVR12

Figure 2.

Continuum of care for long term hepatitis C patients referred for treatment: January 2015 to April 2017.

CONCLUSION:
"With the proper support and integrated BHCs, treating HCV in a primary care setting with high rates of substance abuse and mental health illness is possible and effective."

Pharmacist role in HCV treatment

J Prim Care Community Health. Jan-Dec 2018;9:2150132718807520.
doi: 10.1177/2150132718807520.

A Regional Analysis of Hepatitis C Virus Collaborative Care With Pharmacists in Indian Health Service Facilities

Rebecca Geiger [1], Jessica Steinert [2], Grant McElwee [3], Jennifer Carver [4], Robert Montanez [5], Julie Niewoehner [6], Cassandra Clark [7], Brigg Reilley [8]

Affiliations + expand

PMID: 30348039 PMCID: PMC6201170 DOI: 10.1177/2150132718807520
Free PMC article

"These data indicate that rural clinics using collaborative practice agreements with pharmacists can be instrumental in HCV services at the primary care level and have strong outcomes in HCV treatment/SVR12. "

- IHS facilities treated pts with HCV using pharmacists as point of contact
- Utilized collaborative practice agreement and HCV telehealth to external specialists
- Pharmacists provide comprehensive HCV care under MD supervision
- Analysis of collaborative practice looked at charts for proportion of pts with HCV Ab status, confirmatory testing, liver staging, treatment and SVR rate.
- Biggest gap was step between staging and initiation of treatment
- Concluded feasibility of treating HCV in rural settings

Patient Navigation

Clin Infect Dis. 2017 Mar 1;64(5):685-691. doi: 10.1093/cid/ciw806. Epub 2016 Dec 10.

From Care to Cure: Demonstrating a Model of Clinical Patient Navigation for Hepatitis C Care and Treatment in High-Need Patients

Mary M Ford [1], Nirah Johnson [1], Payal Desai [1], Eric Rude [1], Fabienne Laraque [1]

Affiliations + expand

PMID: 27940945 DOI: 10.1093/cid/ciw806

- Check Hep C→ NYC DOHMH patient navigation program
- Program based in either FQHCs (where care was "onsite") or harm reduction/needle exchanges (pts linked to "offsite providers")
- Patient navigators provided risk assessment, health education, treatment readiness and medication adherence counseling, and medication coordination

- Of 388 participants, 129 (33%) initiated treatment, and 119 (91% of initiators) had sustained virologic response (SVR)

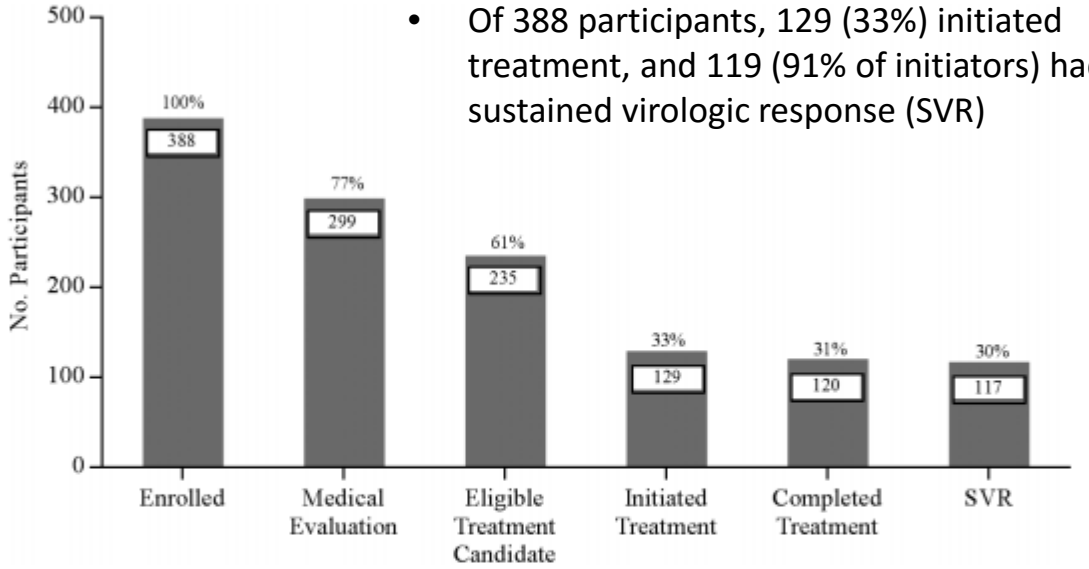


Figure 1. Check Hep C program hepatitis C virus care continuum. Abbreviation: SVR, sustained virologic response.

CONCLUSION- Check Hep C successfully supported high-need participants through HCV care and treatment, and SVR rates demonstrate the real-world ability of achieving high cure rates using patient navigation care models.

Lessons learned- how do we prevent HCV treatment gaps?

Preventing HCV treatment lapses/gaps- Patient factors

- Motivation/readiness
  - Educate about health benefits and prevention of forward transmission
  - No need to be abstinent to be treated
- If ready, do they have ready access to
  - Insurance coverage and if not special programs
  - Medical visits, including specialist access if HCV treatment not done in primary care
  - Labs
  - Pharmacy
- Are there co-occurring issues/social determinants that may potentially affect adherence?
  - Housing/place to store meds safely
  - Transportation
  - Substance involvement– where are they with this?
- Patient understanding of medication regimen before and during treatment
  - Dosing/administration/side effects
  - Consequences of suboptimal adherence
  - When/how to pick up meds or setting up delivery at appropriate timeframe
  - How to communicate with clinic staff

Preventing HCV treatment lapses/gaps- Medical system factors

- Structure of HCV treatment team (other than the provider)
  - Who coordinates care? Is there HCV panel management?
  - Does community have HCV patient navigation program?
  - What is the system for reminding patients of visits, labs, pharmacy pickups?
  - Who takes care of prior authorizations or insurance issues?
- Addressing patient's substance involvement and mental health needs
  - Are social services and mental/behavioral health support available?
  - Is MAT co-located in clinic or coordinated with another clinic?
  - Is HIV PrEP offered for those with ongoing risk?
- Optimize communications with the patient, the pharmacy, within the clinic
  - What is follow-up protocol (phone calls, in-person visit, labs)?
  - What is best mode of communication with pt– text, phone, email, EMR portal

Preventing HCV treatment lapses/gaps- Pharmacy factors

- How comfortable is patient/clinic with chosen pharmacy?
- Does the pharmacy have reliable patient reminder systems?
- Does pharmacy contact prescriber for missed prescription pick-ups?
- What is role of specialty pharmacies if available?
  - May be able to do prior authorizations
  - Should have specialized pharmacists/staff with HCV training
  - 340B pricing?
- Dispensing of 14-day vs 28-day supplies of HCV regimen
  - Is it better?
  - Payor/PBM determines this
- If mail order is mandated by health plan
  - How will plan coordinate delivery with patient?
  - If pt homeless, is there option to mail to clinic or local pharmacy

HEPline- Case "A"

- Consult requested by PharmD in Arizona in May 2019
- Pt is 25 yo Native American male with GT1a infection, tx-naïve, F0
- Treated with ELB/GRZ from January to April 2019 but finished 12-week course over 13 weeks (break b/w weeks 5 and 6)

Week #	HCV RNA PCR
4	undetectable
8	217,000
12	BLQ

HEPline input→ there is a good chance that SVR12 can be achieved, so just check then

QUESTION:
How do you explain the HCV viral load trend? Could the interruption in treatment be a factor?

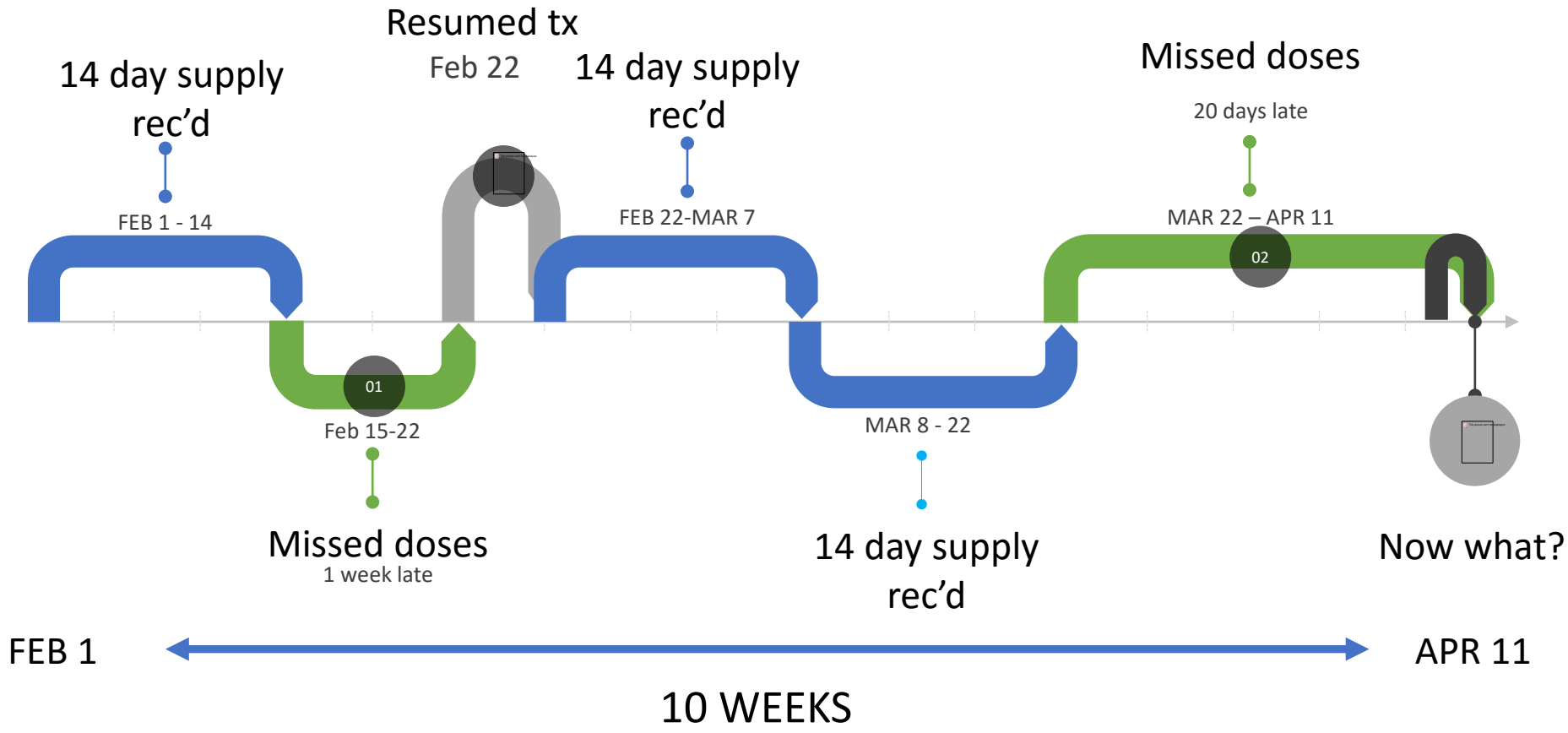
HEPline- Case "A" (part 2)

- Same caller called back October 2019
- Unclear if treatment interruption b/w weeks 5 and 6 contributed to treatment failure
- Perhaps ELB/GRZ is not as forgiving with suboptimal adherence
- Advice→ give SOF/VEL/VOX

Week #	HCV RNA PCR
4	undetectable
8	217,000
12	undetectable
12 weeks post treatment	14,000

QUESTION:
What should we treat pt with now?

Hepline Case "B" – Treatment interruption timeline



QUESTION→ What is best approach?

HEPline Case “B”- Advice

- Discussed with our team’s hepatologist, ID physician, a senior PharmD (very experienced in HCV care)
- Acknowledged to caller than there is no clear evidenced-based answer for “next steps”→ recall pt took about 6 weeks worth of GLE/PIB over a 10-11 week timespan
- Advised to check VL now, consider doing resistance testing and gave option to 1) complete last 2 weeks of GLE/PIB or 2) wait to see if pt cleared and if not can offer rescue therapy with SOF/VEL/VOX

OUTCOME→ pt achieved SVR12!

SUMMARY

- Treatment lapses/gaps appear to be common (>1/10 cases) in HEPline calls received
- Best approaches to HCV treatment interruptions are not addressed in current HCV treatment guidance
- SIMPLIFY and ANCHOR studies suggest perfect adherence not needed to achieve SVR12 but need to identify outer bounds of missed doses
- Reasons for treatment lapses varied but most commonly involved substance involvement/relapse and medication access/supply issues
- Gaps in care coordination evident among patient, provider(s), pharmacy, case management, etc.
- To minimize treatment gaps, consider optimizing:
  - Treatment of substance involvement, e.g. co-location of treatment or use telemedicine for co-management
  - Care coordination (panel management, treatment navigators, case management) in primary care settings
  - Linkage to dispensing pharmacy for prescription coordination

HCV, HIV/PrEP, and Substance Use Warmlines operate 6am-5pm PT, Mon-Fri

Perinatal HIV Hotline available 24/7, 365 days/year

Substance Use Warmline 855-300-3595
Substance use evaluation and management

HEPline 844-HEP-INFO
HCV testing, staging, monitoring, treatment

HIV/AIDS Warmline 800-933-3413
HIV testing, ARV decisions, complications, and co-morbidities

PrEPline 855-HIV-PrEP
Pre-exposure prophylaxis for persons at risk for HIV

Perinatal HIV Hotline 888-448-8765
Pregnant/postpartum women with HIV (or at-risk for HIV) & their infants

PEPline 888-448-4911
Occupational & non-occupational exposure management