## Treatment of Hepatitis C in People Who Use Drugs (PWUD)

Andrew Seaman, MD Oregon HCV Update Meeting December, 2018

## Conflicts of interest

2016 received <8% of my salary from an investigator initiated, Merck funded trial (makers of elbasvir/grazoprevir)

I am highly influenced by the opinions, life experience, and knowledge my patients bring to the table (many of whom inject drugs)

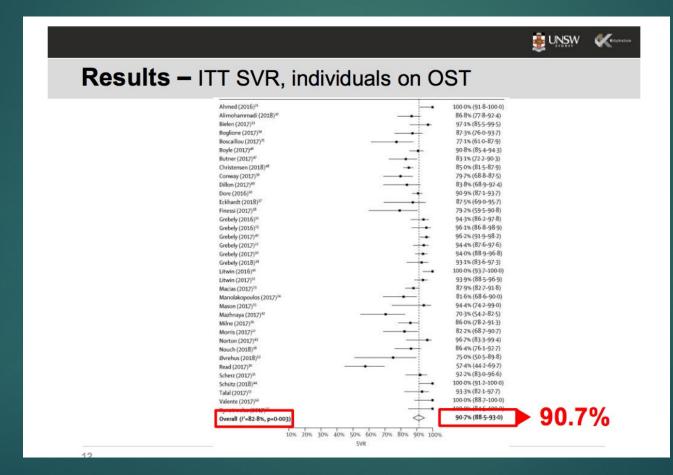
## Objectives

Brief update literature treatment of PWIDs for HCV

Brief review of the Old Town Clinic / Outside In / OHSU pilot trial for HCV treatment in People Who Inject Drugs

Brief discussion of the Old Town Clinic treatment program (if time)

## Meta-analysis 3,634 PWUD treated with DAAs



Hajarizadeh, The Lancet Gastroenterology & Hepatology 2018. Adapted INHSU 2018 with permission.

## Strongly biased by 75% observational studies

|                                    |                               | ISW 帐 |  |  |  |
|------------------------------------|-------------------------------|-------|--|--|--|
| Results – Meta-regression, ITT SVR |                               |       |  |  |  |
|                                    | Adjusted model<br>OR (95% CI) | Ρ     |  |  |  |
| Participants with recent drug use  |                               |       |  |  |  |
| Participants receiving OST         | 1.04 (0.96-1.12)              | 0.364 |  |  |  |
| Men                                | 1.07 (0.82-1.39)              | 0.612 |  |  |  |
| Median/mean age                    | 1.07 (1.02-1.12)              | 0.008 |  |  |  |
| Participants with HIV co-infection | 0.96 (0.86-1.07)              | 0.427 |  |  |  |
| Study design                       |                               |       |  |  |  |
| Observational                      | 1.00                          |       |  |  |  |
| Clinical Trial                     | 2.18 (1.27-3.75)              | 0.006 |  |  |  |

Hajarizadeh, The Lancet Gastroenterology & Hepatology 2018. Adapted INHSU 2018 with permission.

## OTC – OI – OHSU Pilot Study

- Prospective, non-randomized real world clinical trial using elb/graz to treat people who inject drugs with GT 1 or 4 HCV and an APRI <0.7 who:</p>
  - Arm 1: engage with Medication Assisted Therapy (Methadone/Bupe), n=25, Old Town Clinic
  - Arm 2: are actively using and engage with needle exchange program, n=25, Outside In
  - Arm 3: matched cohort in OHSU hepatology clinic, n=50

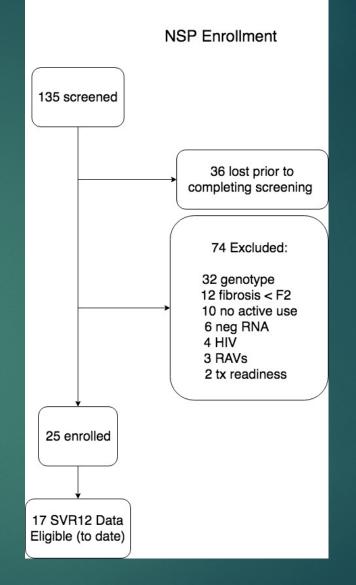
### NSP vs OAT HCV Pilot Study

|   | OAT             | NSP                                 | PWID<br>Standar<br>d | Com.<br>Standar<br>d |
|---|-----------------|-------------------------------------|----------------------|----------------------|
| SVR 12, ITT<br>% / (N)                      | <u>96% (24)</u> | <u><b>59% (10)</b></u><br>(p<0.001) | <u>89% (32)</u>      | <u>94% (47)</u>      |
| SVR12, Per<br>Protocol<br>% / (N)           | 100% (24)       | 90% (10)                            | 100% (32)            | 100% (47)            |
| Treatment<br>Failures<br>% / (N)            | 0%              | 6%* (1)                             | 0%                   | 0%                   |
| <b>Adherence</b><br>(% ≤ 7 pills<br>missed) | 92%             | 65%                                 | 81%                  | 98%                  |



Seaman et al. INHSU. 2018.

Many barriers to HCV treatment in harm reduction environments.



# Small difference in SVR, partially explained by trial type, LTFU

Meta-analysis of 38 studies of PWUDs, n=3,634 included

|              | <b>Treatment Completion</b> | Svr12 |
|--------------|-----------------------------|-------|
| All PWUDs    | 98%                         | 8.8%  |
| PWUDs on OAT | 97%                         | 91%   |
| Recent IDU   | 97%                         | 87.5% |

Meta-Regression Analysis: Clinical trials associated with OR 2.2 (1.27-3.75) of achieving SVR12

#### ► ITT analysis

Hajarizadeh B. Lance Gastro & Hepatology. V3 (11), Nov 2018.

## Old Town Clinic Treatment Program

#### Multidisciplinary

- Medical director + two providers
- ► HCV coordinator
- Clinical pharmacist
- CADC as indicated
- Weekly committee meetings
  - Decision made on need for treatment candidacy, Substance Used Disorder support, adherence support
  - Drug, labs ordered and PA process started by coordinator
  - First, last, and SVR visit by provider, remainder by pharmacist

### We treat... everyone

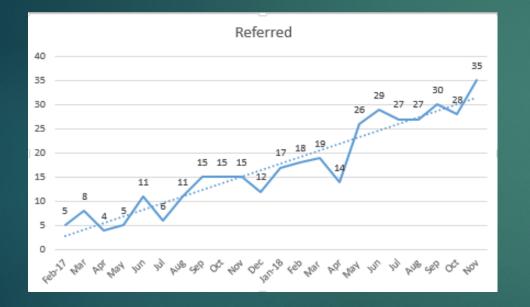
#### Treatment candidacy

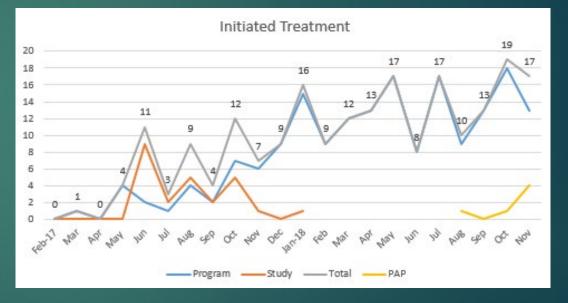
- Made 2/3 last appointments <u>or</u> subjective adherence measure (whichever lower barrier)
- Desires treatment
- Any engagement in treatment for substance use disorder, usually in primary care setting

## HCV Tx at OTC: ~2 years in

#### Patients Referred

#### Patients Initiating Tx



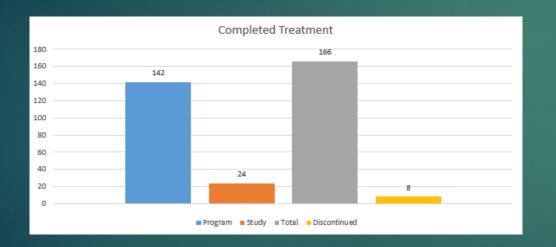


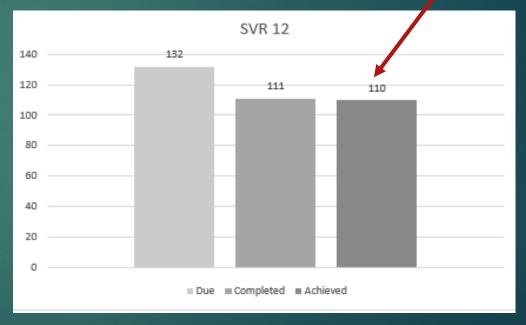
## HCV Tx at OTC: SVR12

#### Patients Completing Tx

#### Patients Achieving SVR12

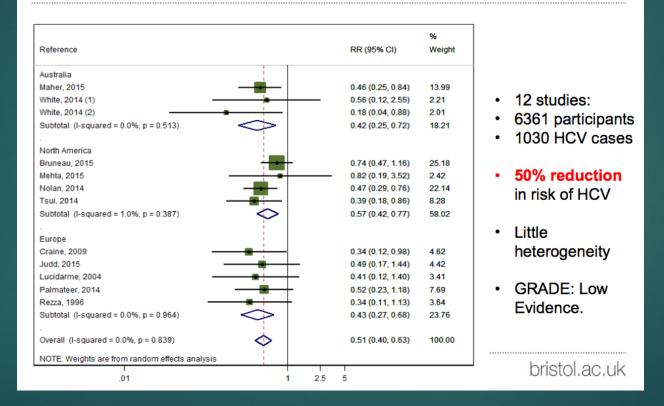
#### 1 tx failure





## OAT associated with 50% reduction HCV transmission

Impact of current OST BRISTOL exposure (adjusted estimates)



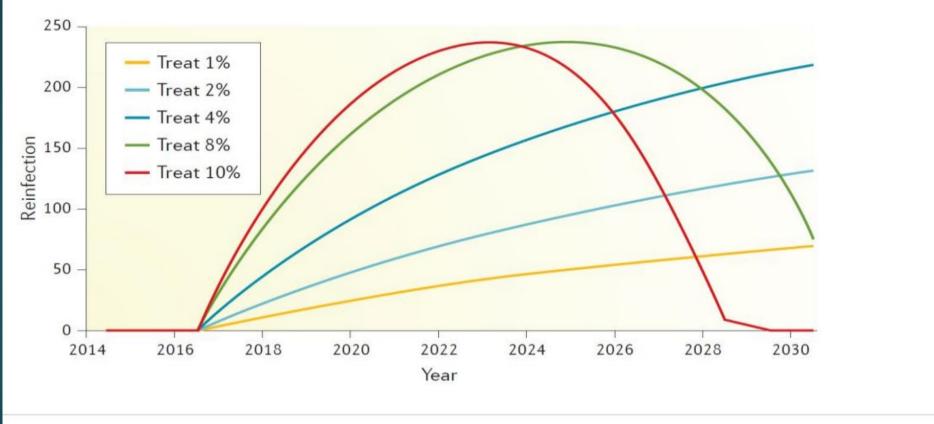
Hickman et al. Lancet Global Health. Vol 5 (2): e1192-e1207.

## NSP associated with 20% reduction HCV transmission

| Reference                               | RR (95% CI)                  | %<br>Weight | 7 studies  |
|---|------------------------------|-------------|--|
| North America                           |                              |             |  |
| Bruneau, 2015                           | 0.77 (0.50, 1.19)            | 16.10       | High heterogeneit                                |
| Hagan, 1999                             | 1.42 (0.64, 3.14)            | 14.04       | (l <sup>2</sup> =79%)                            |
| Patrick, 2001                           | 3.69 (2.12, 6.43)            | 15.48       |  |
| Subtotal (I-squared = 89.5%, p = 0.000) | 1.58 (0.57, 4.42)            | 45.62       | Weak evidence     overall – RR 0.77              |
| Europe                                  |                              |             |  |
| Hope, 2011                              | 0.11 (0.02, 0.54)            | 9.27        | <ul> <li>In Europe NSP</li> </ul>                |
| Hope, 2015 (1)                          |                              | 9.31        | associated with                                  |
| Hope, 2015 (2)                          |                              | 4.42        | 66% reduction in                                 |
| Hope, 2015 (3)                          | - <b>1</b> 0.55 (0.05, 6.15) | 5.59        | HCV  |
| Palmateer, 2014                         | 0.26 (0.08, 0.86)            | 11.37       | 1101   |
| Van Den Berg, 2007                      | <b>0.62 (0.30, 1.29)</b>     | 14.42       | Condex and the                                   |
| Subtotal (I-squared = 12.3%, p = 0.337) | 0.44 (0.24, 0.80)            | 54.38       | <ul> <li>Grade: very low<br/>evidence</li> </ul> |

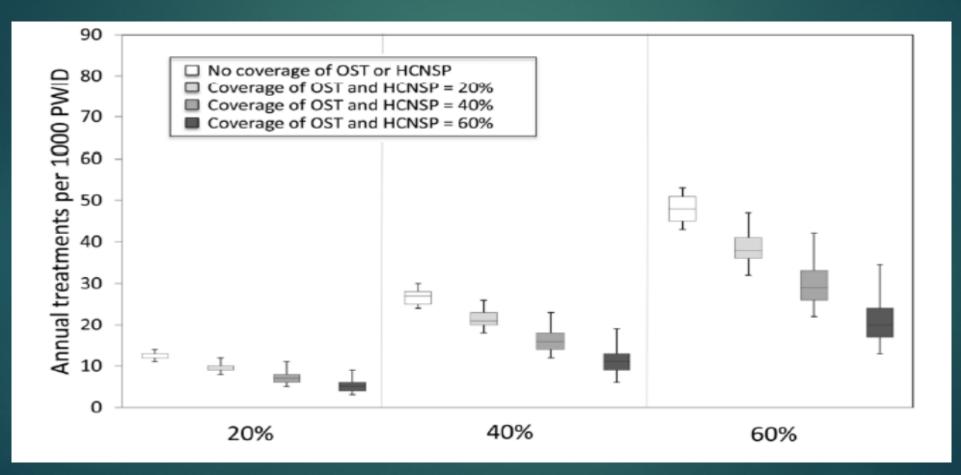
Hickman et al. Lancet Global Health. Vol 5 (2): e1192-e1207.

## Treat more high risk pts, end HCV sooner



Grebely J, Hajarizadeh B, Dore GJ. Nature Reviews Gastro Hepatol 2017

## DAA tx rates to half chronic prevalence in 10 years with HR.



Martin, et al Clinical Inf Diseases 2013. Adapted from Hickman, INHSU 2018.

## References

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