# A PRECISION RANDOMIZED TRIAL OF HEPATITIS C TREATMENT ADHERENCE SUPPORT AMONG 3000 PWID IN INDIA

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697

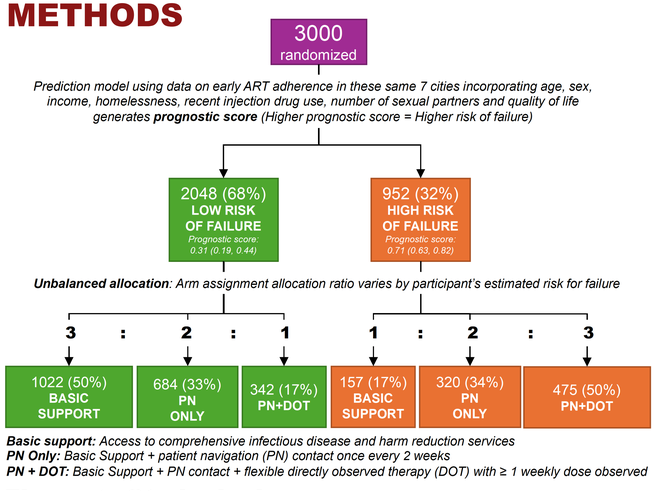
## BACKGROUND

- HCV elimination is unlikely without curing people who inject drugs (PWID)
- Many PWID will need additional support to achieve HCV cure, but resources are limited
- A precision medicine approach could improve the efficiency of intervention delivery

## OBJECTIVE

- The **STOP-C** trial evaluated whether HCV treatment outcomes could be optimized by *tailoring* adherence support to *PWID need* across community-based HIV prevention and treatment centers in 7 cities across India

## METHODS




***Basic support:*** *Access to comprehensive infectious disease and harm reduction services*
***PN Only:*** *Basic Support + patient navigation (PN) contact once every 2 weeks*
***PN + DOT:*** *Basic Support + PN contact + flexible directly observed therapy (DOT) with ≥ 1 weekly dose observed*

**Figure 1. Study design**

- Precision-randomized trial: arm assignment probabilities varied by estimated probability of treatment failure (*Fig 1)*
- Eligibility criteria included history of injection and no prior HCV treatment; decompensated cirrhosis were excluded
- Primary outcome = sustained virologic response (SVR), HCV RNA<LLOQ (12 weeks post treatment), Poisson regression adjusted for site (intention to treat [ITT]) generated adjusted relative risks (aRR)
- Per protocol (PP) analysis excluded those who died, discontinued treatment or were LTFU before SVR visit
- Exploratory analyses examined the aRR of SVR by the prognostic score

**In this high burden setting, intensive HCV treatment support only impacted cure in PWID at low risk for failure; radical approaches to treatment and harm reduction are needed to eliminate HCV in this population**

## RESULTS

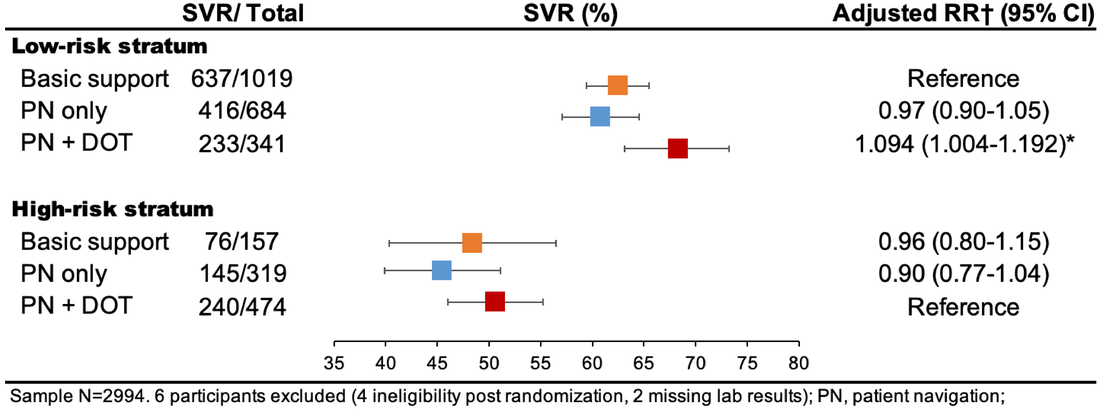
- 2798/3000 (93%) completed SVR assessment

| | Low risk % (N) | High risk % (N) |
|---|---|---|
| | *n=2044* | *n=952* |
| Median age (IQR) | 31 (26-36) | 27 (23-30) |
| Cis-gender male | 98 (2002) | 100 (950) |
| Never married | 43 (883) | 70 (660) |
| Median annual income USD (IQR) | 72 (0-120) | 97 (66-121) |
| < High school education | 70 (1436) | 85 (804) |
| Experiencing homelessness* | 6 (117) | 26 (247) |
| Ever incarcerated | 17 (353) | 29 (271) |
| Injection drug use* | 42 (865) | 89 (848) |
| Shared injection paraphernalia* | 4 (84) | 21 (198) |
| MOUD** | 41 (837) | 49 (464) |
| Harmful/hazardous alcohol use | 76 (1559) | 75 (711) |
| Living with HIV | 17 (356) | 30 (285) |
| On antiretroviral therapy | 92 (327) | 73 (208) |

Of 3000 randomized, 6 excluded from analytical sample
*in the prior 3 months; **in the prior 6 months

**Table. Characteristics by risk stratum**

- **ITT analysis for SVR** (*Fig 2*)**:**
  - *Overall SVR:* 49% high risk; 63% low risk
  - No difference by arm in high risk
  - Significantly higher SVR for PN+DOT vs. basic support in low risk (**aRR: 1.10, p=0.04**)
- **PP analysis for SVR**
  - *Overall SVR*: 60% low risk; 70% high risk
  - No difference by arm in high risk
  - Significantly higher SVR for PN+DOT vs. basic support in low risk (**aRR: 1.11, p=0.02**)
- SVR increased from **36.1%** in the highest risk quartile receiving PN only to **76.5%** in the lowest risk quartile receiving PN+DOT (*Fig 3*)
- Overall SVR increased with better prognostic score, *aRR per 10% decrease in score*:
  - low risk: **1.04** (95% CI: 1.01 – 1.06)
  - high risk: **1.10** (95% CI: 1.03 – 1.19)




Sample N=2994. 6 participants excluded (4 ineligibility post randomization, 2 missing lab results); PN, patient navigation; DOT, directly observed therapy; RR, relative risk† Adjusted for site; * p<0.05

**Figure 2. Sustained virologic response (SVR) by risk stratum and arm**

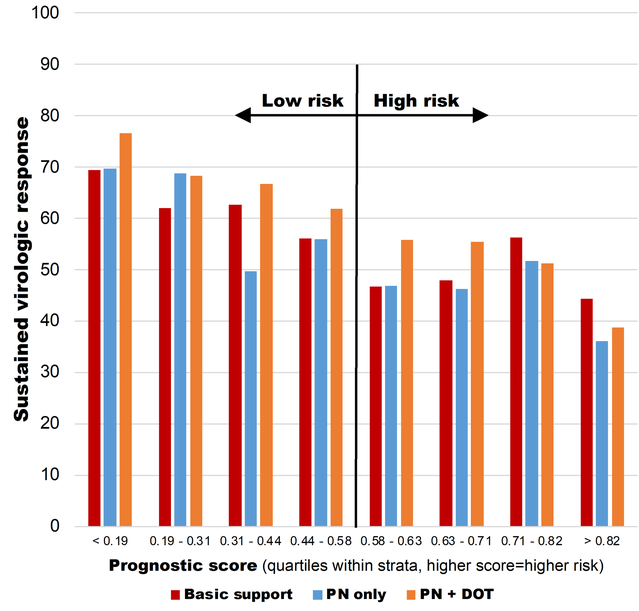



**Figure 3. SVR by prognostic score and arm**

## LIMITATIONS

- No data yet to distinguish between treatment failure and reinfection among those viremic at the SVR visit

## CONCLUSIONS

- SVR in this population of PWID who were young and actively injecting was low
- Among those at *lowest* risk of failure, highly intensive adherence support improved outcomes
- Among those at *highest* risk of failure, none of the adherence support interventions had any impact
- Additional interventions beyond adherence support (e.g., housing support, long-acting MOUD) may be needed to achieve optimal SVR in this group
- In the meantime, programs should consider using prognostic scores to target interventions more efficiently and proactively to address barriers to treatment adherence and improve outcomes

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