Impact of HCV cure on depressive symptoms in the HIV-HCV co-infected population

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BACKGROUND

- Depression is common in people co-infected with HIV- HCV.
- Depression was a major side effect of the earlier interferon (IFN)-ribavirin-based HCV treatments, and thus current or past psychiatric illness was a relative contraindication.
- However, 2nd generation direct acting antiviral (DAA) regimens, introduced after 2013, have minimal side-effects and treatment guidelines have thus been updated.
- These changes in prescribing practices provide us with the opportunity to assess the potential impact of HCV treatment on depressive symptoms over time.
- We may expect lower depressive symptoms post-cure via biological pathways, but people continue to face challenges like stigma, discrimination and socioeconomic burdens.

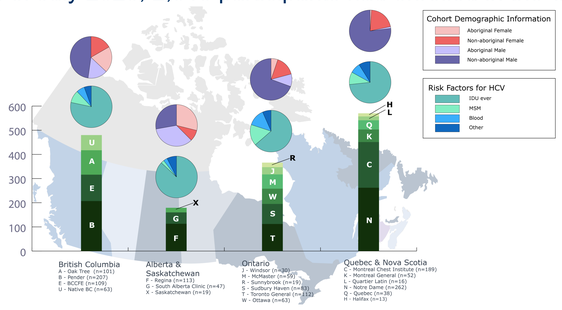
OBJECTIVE

To evaluate impact of sustained virologic response (SVR) on depressive symptoms in the HIV-HCV co-infected population in Canada during the 2nd generation DAA era (2013-2020).

DATA SOURCES

Canadian Co-infection Cohort (CCC)

- Multicenter prospective cohort study ongoing since 2003.
- As of July 2020, 2,018 participants had enrolled in the CCC.



Food Security (FS) sub-study

- 725 CCC participants were followed up for 5 CCC visits.
- Depression screening was performed using Center for Epidemiologic Studies Depression Scale-10 (CES-D-10).
- 10-item scale, score range of 0-30; ≥10 for depressive symptoms indicative of risk of clinical depression.

Following *SVR*, there was *gradual decline* in the *presence of depressive symptoms* in the HIV-HCV co-infected population. This indicates *health benefits* of SVR *beyond liver disease* and provides additional rationale for *treating HCV* in all *chronically infected persons*.

METHODS

- Outcome
  - Presence of depressive symptoms indicative of being at risk for clinical depression (CES-D-10 ≥10), which was predicted by a random forest classifier developed using the FS sub-study data.
  - We corrected for misclassification using a predictive value-based record-level correction method.
- Exposure
  - SVR, i.e., undetectable HCV viral load 12 weeks after end of treatment, in individuals treated with 2nd generation DAA regimens (post-November 2013).
- Time-varying confounders
  - Advanced fibrosis/cirrhosis, HIV viral load, CD4 cell count, current injection drug use, current alcohol use, recent incarceration and antidepressant use.
  - We conducted multiple imputation by chained equations (MICE) to address the missing data in the confounders.
- We included time from cohort entry to DAA initiation in the pre-exposure period and time after SVR in the post-exposure period.
- We used a segmented modified Poisson model with an interrupted time series design.
- We used Generalized Estimating Equations (GEEs) with robust standard errors, which account for correlation between repeated measurements on the same participant over time.

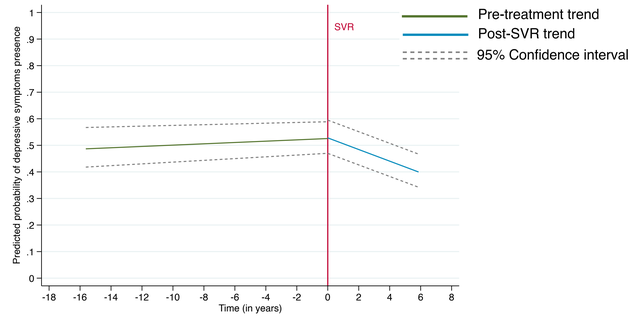
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RESULTS

- Of the 517 individuals treated in the DAA era, we included 482 participants who achieved SVR in the analysis.

Baseline characteristics	Participants (n = 482) n (%) or median (IQR)
Depressive symptoms	279 (58%)
Age in years	47 (41-52)
Sex - Male	331 (69%)
Race/ethnicity - White	331 (69%)
Education - High school or less	349 (72%)
Employment - Not employed	326 (70%)
Current injection drug use	173 (36%)
Recent incarceration	42 (9%)
Current antidepressant use	50 (10%)

- Median follow-up: Pre-SVR: 3 years (IQR:1.3-5.5) and post-SVR: 1.4 years (IQR: 0.6-2.5).
- No change in depressive symptoms before treatment and no immediate level change at SVR.
- Post-SVR trends indicate a decrease of 5% per year in depressive symptoms presence.



Adjusted risk ratios (95% CI)		
Pre-treatment trend	Level change at SVR	Post-SVR trend
1.01 (1.00-1.01)	1.00 (0.98-1.04)	0.95 (0.94-0.97)

CONCLUSIONS

- Our study suggests depressive symptoms declined over time following SVR in the 2nd generation DAA era.
- These improvements may reflect changes in biological pathways and better general health.
- Extended follow-up will allow us to evaluate the durability of this reduced depression.

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