Enhancing the HCV care cascade among people who inject drugs: a systematic review and considerations from an expert panel

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Disclosure statement

I have no potential conflict of interest in relation to this presentation

Background & Aim

ECDC/EMCDDA stakeholders survey in 2018:

- linkage to care and adherence to treatment ⇒ priority areas for inclusion in the updated guidance

Systematic review commissioned by ECDC to GOEG that:

- **aims** to support the guidance update process by identifying interventions that can improve HCV linkage to care and adherence to DAA treatment among people who inject drugs
- Part of a larger review on hepatitis B and C, HIV, and tuberculosis
- considerably larger body of evidence identified for HCV

<u>Research question</u>

"What interventions are associated with improved linkage to care and adherence to treatment regimens for HCV among people who inject drugs?"

PICO

Population	PWID or ≥50% of study sample composed of people who reported ever injection drug use *or* people receiving OAT; with chronic HCV infection
Intervention	Intervention(s) aimed at improving engagement at any (or combination) of the following stages along the HCV care cascade: a) linkage to care – defined as clinical assessment of HCV infection/liver disease b) adherence to treatment (regimens combining interferon/DAA or DAA only)
Comparator	RCTs: Participants **receiving care as usual or routine care** as defined by study authors; Non-randomized studies: before and after intervention comparison
Outcomes	a) For linkage to care: • % study population that came in contact with a care provider i.e., **"visit"** and/or, • % study population initiating HCV treatment i.e., **"treatment initiation"** as defined by the study authors b) For adherence to treatment: • % study population **adherent** to HCV treatment and/or **completing** HCV treatment • **SVR12 or SVR24**

Information sources & eligibility criteria

Databases	Time period	Geographical considerations	Exclusion of
PubMed, EMBASE, PsycINFO, Clinical Trials Registry, CDSR	from 01/01/2011 to 08/07/2020	EU/EEA/EFTA countries, EU candidate countries, the UK, US, Canada, Australia and NZ	non-peer-reviewed scientific articles or conference abstracts, study protocols, review articles including systematic reviews and non-comparative studies

Results

7 318 records screened → 7 067 excluded

251 for full text review → 226 excluded

HCV studies*

(n = 14)

DAA=11; DAA+IFN = 3

- Risk of bias assessment: EPHPP
- Quality of evidence: GRADE system
- Synthesis of results: individual studies were grouped in **intervention categories**

*six HCV studies reporting interventions in interferon only era were excluded

Expert Panel consultation

Before the expert panel meeting

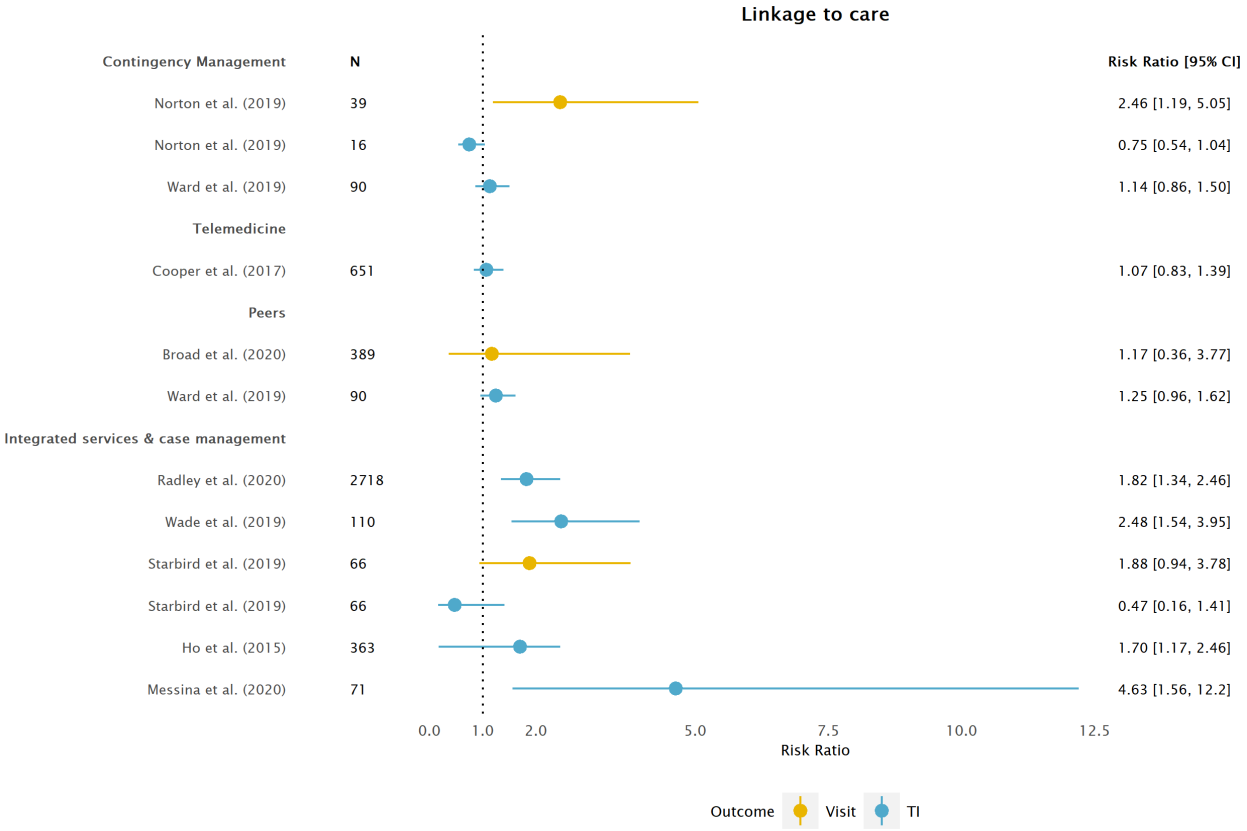
- Pre-filled Evidence to Decision tables were submitted to the experts
- Summary of Expert's feedback and comments on recommendation

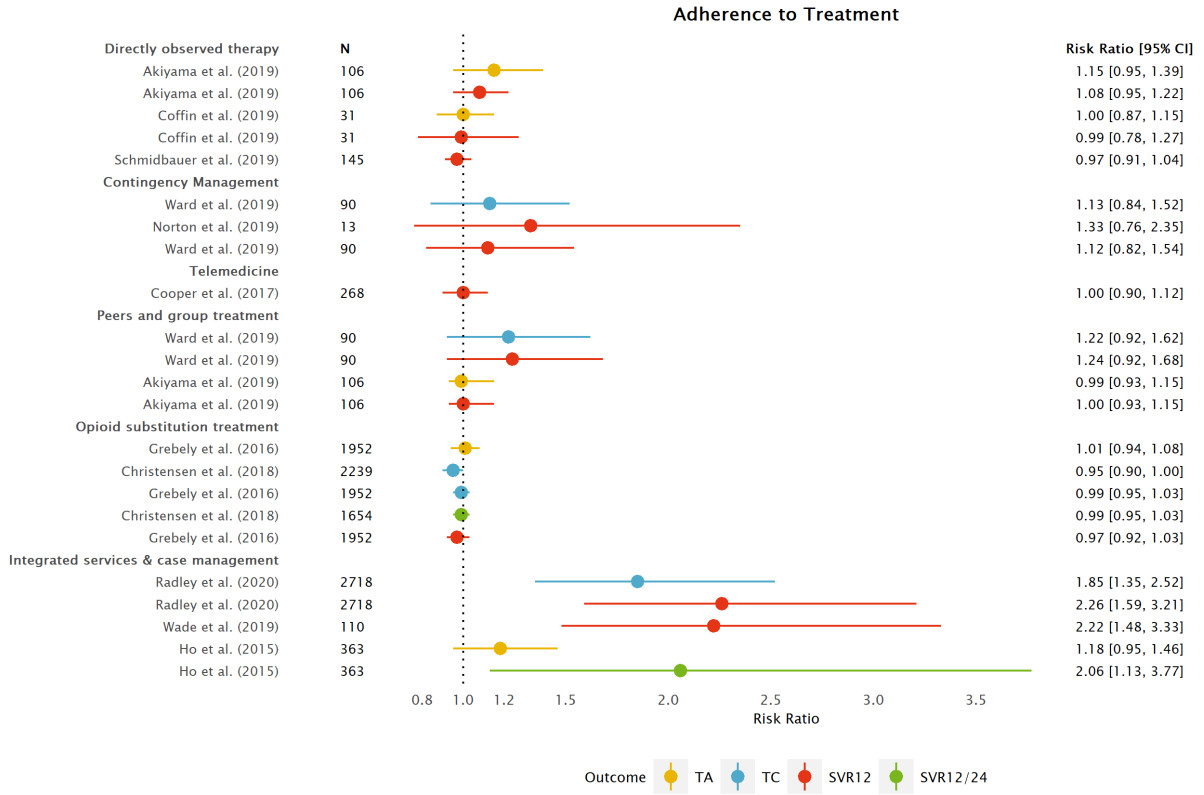
2-days virtual meeting (March 2021)

During the meeting, the Expert Panel members:

- examined the evidence gathered and the identified gaps
- discussed the evidence tables and the draft recommendations (including practice considerations);
- commented and formulated expert opinions, suggested revisions/edits; and
- gave direction for final recommendations

Results: forest plots





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Results (1)

	Contingency management ⊕ Not sign.	Telemedicine ⊕ Not sign.	Peer interventions ⊕ Not sign.	Directly observed therapy (DOT) ± Not sign.
Settings	• NSPs, other service providers for PWID	• Limited/remote access to healthcare • Prisons • Drug treatment centres	• Closed informal social networks • High stigma	• Close to daily lives of PWID, e.g., pharmacy, NSP, OAT, DCR, emergency centres, prisons
PWID sub-populations (where specified)	• Vulnerable groups (incentives may reduce barriers)	• Marginalised PWID	• Hidden and hard to reach PWID (e.g., migrants, illiterates)	
Practice considerations	• In addition to peer-lead interventions, harm-reduction, OAT, NSP education, community campaigns etc. • **Consider legal framework** • **Avoid inequalities**	• More effective for adherence to treatment (SVR) than linkage to care • Can be challenged by lack of equipment • COVID-19 context	• **Training of peers as pre-condition** • Raise awareness on peer work • Consider legal framework	• Enable link to specialised HCV care • Consider healthcare system characteristics and legal requirements • **DOT should not be a condition to receive DAA** • Linking DOT with OAT can be a major success factor

Outcome indicators for *linkage to care* - visit, treatment initiation and *adherence to treatment* - treatment adherence, treatment completion, SRV12
Comparator - usual care (for most, hospital)

Results (2)

	Opioid agonist treatment ± Not sign.	Primary care ⊕ Sign.	Integrated services and case management ⊕ Sign.
Practice considerations	• OAT not directly impacted treatment completion, SVR12 or safety - OAT should therefore not be a barrier/prerequisite to treatment access • Integration OAT & HCV treatment beneficial; **OAT provides a fixed setting, regular meeting point during therapy.** • High benefits for PWID with underlying psychiatric comorbidities.	Familiar environment, easy to access, however, consider organisation of healthcare system e.g., • GPs offer DAA & OAT? • GPs trained and allowed to prescribe DAA? • GPs perform first pre-treatment visit and handle complex patients (comorbidities)?	Integrated care approach combining: • addiction, • infectious diseases, • mental health therapy, **could increase accessibility and facilitate treatment success** by covering various needs of PWID population. High benefits for PWID with underlying comorbidities. • Between: harm reduction services, mobile units and HCV care providers, • Preferably located in same geographic area, • Should **reduce barriers by actively accompanying clients in the referral to other services.** • Cooperation between drug addiction services and institutions providing treatment

Outcome indicators for *linkage to care* - visit, treatment initiation and *adherence to treatment* - treatment adherence, treatment completion, SRV12
Comparator - usual care (for most, hospital)

Gaps & Limitations

Gaps in research

- **Lack of well-powered RCTs** or comparative studies evaluating interventions to enhance LtC and AtT for HCV in PWID
- **Most studies on HCV**: no studies evaluating interventions to enhance linkage to HBV and TB care addressing PWID and only one study assessing adherence to TB treatment for PWID
- Gap between **science and practice**: Lack of information on actual practice and implementation

Limitations

- **Meta-analysis not feasible** due to the diversity of interventions, included participants, settings, comparators and study designs
- **Limited quality** of studies with one third of all studies included being non-randomized studies
- Most studies **small in sample size** with high risk of bias and confounding
- **Geographical bias:** scarcity of research from countries in the EU/EEA and the Eastern European region

Conclusions

(1) Low to moderate quality evidence that integrated, people-centered approaches may improve engagement

(2) Critical success factors for interventions:

- Implemented in settings close to target population (e.g., harm reduction services, OAT)
- Adequate funding and coverage
- Recent drug use should not be an exclusion criteria for DAA treatment
- Testing and treatment free of costs for PWID
- Interventions tailored to and integrated in existing national strategies

(3) Enabling factors, e. g. peer involvement, trustful environment, low-threshold approaches are rarely measured in RCTs require attention in future research agenda

Take home messages

To improve the HCV cascade of care among PWID, interventions should be implemented **in cooperation** with harm reduction services, drug treatment and consider the **healthcare system characteristics and legal framework.**

Call for more qualitative research on **implementation characteristics** and overarching **enabling factors** in implementation practice to complement literature with practice-based evidence.

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