

EPIToPe - HCV prevention Among People who Inject Drugs

Matt Hickman, Sharon Hutchinson, John Dillon



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- National Institute for Health Research (NIHR) Programme Grants for Applied Research programme (RP-PG-0616-20008) – EPIToPe – [Ethics:18/ES/0128; Trial Reg:ISRCTN72038467]
- NIHR Health Protection Research Unit in Behavioural Science and Evaluation of Interventions
- Public Health Scotland: HCV Action Plan
- European Commission Drug Prevention and Information Programme (DIPP) "Treatment as Prevention in Europe: Model Projections [JUST/2013/DPIP/AG/4812]
- NIHR (HS&DR) (12/3070/13) Assessing the impact and cost-effectiveness of NSP
- Extending HCV community care pathways in Tayside [ERADICATE C, ISRCTN27564683, Super DOT C Trial NCT02706223).
- MH received honoraria from Gilead and MSD in last 3 years

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Collaborators:- Sharon Hutchinson, Vivian Hope, Graham Foster, John Dillon, Sema Mandell, Mary Ramsay, Helen Harris, Ross Harris, Fiona Gordon, Stephen Ryder, David Goldberg, Daniela De Angelis, Will Irving, Noel Craine, Marion Lyons, Norah Palmateer, Esther Aspinall, Lucy Platt, Amy Master, Maria Prins, Bernd Schulte, Henrikki Bummer, Viktor Mravcik, Martin Kåberg, Anne Ovrehus, Geert Robaeys, Patrizia Varreiri, Marie Jauffret, Olav Dalgard, Majca Matičič, Hannah Fraser, Zoe Ward, Jason Grebely, Greg Dore, Margaret Hellard, Bristol Drug Project. Silvia Minozzi, Holly Hagan, Clare French, Louisa Degenhardt, bristol.ac.uk Lisa Maher, Sarah Larney, Adam Trickey, Peter Vickerman, Hannah Fraser, Natasha Martin





Cochrane Database of Systematic Reviews

Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs (Review)

Platt L, Minozzi S, Reed J, Vickerman P, Hagan H, French C, Jordan A, Degenhardt L, Hope V, Hutchinson S, Maher L, Palmateer N, Taylor A, Bruneau J, Hickman M

ADDICTION

HCV PREVENTION

University of

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doi:10.1111/add.14012

Needle and syringe programmes and opioid substitution therapy for preventing HCV transmission among people who inject drugs: findings from a Cochrane Review and meta-analysis

Lucy Platt¹ ^(D), Silvia Minozzi², Jennifer Reed³, Peter Vickerman⁴ ^(D), Holly Hagan³, Clare French⁴, Ashly Jordan³, Louisa Degenhardt⁵ ^(D), Vivian Hope⁶ ^(D), Sharon Hutchinson⁷, Lisa Maher⁸ ^(D), Norah Palmateer⁷ ^(D), Avril Taylor⁹, Julie Bruneau¹⁰ & Matthew Hickman⁴ ^(D)

University of BRISTOL Impact of current OST exposure (adjusted estimates)



- 12 studies:
- 6361 participants
- 1030 HCV cases
- 50% reduction in risk of HCV
- Little heterogeneity
- GRADE: Low Evidence.



Impact of high NSP by region (unadjusted analyses)

Reference	RR (95% CI)	% Weight
North America		
Bruneau, 2015	0.77 (0.50, 1.19)	16.10
Hagan, 1999	📥 1.42 (0.64, 3.14)	14.04
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
Europe		
Hope, 2011	0.11 (0.02, 0.54)	9.27
Hope, 2015 (1)	- 0.99 (0.21, 4.63)	9.31
Hope, 2015 (2)		4.42
Hope, 2015 (3)	- a 1 0.55 (0.05, 6.15)	5.59
Palmateer, 2014		11.37
Van Den Berg, 2007	0.62 (0.30, 1.29)	14.42
Subtotal (I-squared = 12.3%, p = 0.337)	0.44 (0.24, 0.80)	54.38
Overall (I-squared = 78.8%, p = 0.000)	0.77 (0.38, 1.54)	100.00
NOTE: Weights are from random effects	analysis	
	.01 1 5	

7 studies

 High heterogeneity (l²=79%)

 Weak evidence overall – RR 0.77

 In Europe NSP associated with 66% reduction in HCV

• Grade: very low evidence



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Impact of NSP and OST





High NSP with OST

- •4 studies
- •3356 participants
- •518 HCV cases Reduced HCV by 71%
- •moderate heterogeneity

Low NSP with OST

- •3 studies
- •3071 participants
- •449 HCV cases,
- •Reduced HCV by 24%

•GRADE: low evidence



MODELLING HCV TREATMENT AS PREVENTION





COMBINATION PREVENTION SCALE-UP: 10 YEAR RELATIVE PREVALENCE REDUCTIONS WITH NO BASELINE COVERAGE OF OST/NSP AND USING DAAs



- Dark red: modest (<20%) impact, high HCV
- Orange: ~50% impact
 - White: >80% impact
 - >40% reduction requires HCV treatment
 - OST&NSP increases benefit of HCV treatment

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Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, and Vickerman P. C. Clinical Infectious Diseases 2013



GENERAL SCENARIOS: COMBINATION INTERVENTION REQUIRED TO REDUCE INCIDENCE AMONG PWID BY 90%, 2017-2030

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60%



- Stable epidemics, 12 year injecting duration
- <60 per 1000 PWID treated annually without harm reduction
- With harm reduction. • could reduce to <40 per 1000 PWID annually

Preliminary work based on Martin NK et al. CID



Research Article





Prioritization of HCV treatment in the direct-acting antiviral era: An economic evaluation

Natasha K. Martin^{1,2,*}, Peter Vickerman², Gregory J. Dore³, Jason Grebely³, Alec Miners⁴, John Cairns⁴, Graham R. Foster⁵, Sharon J. Hutchinson^{6,7}, David J. Goldberg^{6,7}, Thomas C.S. Martin⁸, Mary Ramsay⁹, the STOP-HCV Consortium, Matthew Hickman²

¹Division of Global Public Health, University of California San Diego, San Diego, USA; ²School of Social and Community Medicine, University of Bristol, UK; ³Kirby Institute, UNSW Australia, Sydney, Australia; ⁴Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, UK; ⁵Queen Mary's University of London, UK; ⁶Glasgow Caledonian University, UK; ⁷Health Protection Scotland, UK; ⁸Guy's and St Thomas's NHS Foundation Trust, London, UK; ⁹Public Health England, UK







PWID, moderate
PWID, mild
Ex-non PWID moderate

*£20,000 willingness to pay. Martin NK et al. J Hepatol 2016: 65(1):17-25.

Economic modeling supports treatment for and prioritization of PWID – essential for achieving elimination targets





NUMBER OF NEW INFECTIONS AVERTED PER EARLY TREATMENT



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Martin NK et al. J Hepatology 2016



ARE CURRENT HCV TREATMENT RATES SUFFICIENT?





ARTICLE IN PRESS

Research Article Viral Hepatitis JOURNAL OF HEPATOLOGY

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Model projections on the impact of HCV treatment in the prevention of HCV transmission among people who inject drugs in Europe

Hannah Fraser^{1,*}, Natasha K. Martin^{2,1}, Henrikki Brummer-Korvenkontio³, Patrizia Carrieri^{4,5}, Olav Dalgard^{6,7}, John Dillon⁸, David Goldberg⁹, Sharon Hutchinson^{10,9}, Marie Jauffret-Roustide^{11,12}, Martin Kåberg¹³, Amy A. Matser^{14,15}, Mojca Matičič^{16,17}, Havard Midgard⁶, Viktor Mravcik^{18,19,20}, Anne Øvrehus²¹, Maria Prins^{14,22}, Jens Reimer^{23,24}, Geert Robaeys^{25,26,27}, Bernd Schulte²⁴, Daniela K. van Santen¹⁴, Ruth Zimmermann²⁸, Peter Vickerman^{1,†}, Matthew Hickman^{1,†}

With chronic infections treated BRISTOL at baseline (2015/16)



Fraser et al, (2017) Journal of Hepatology

BRISTOL Baseline chronic prevalence



Treatment needed per 1000 PWID to reduce BRISTOL HCV to 2 per 100pyrs by 2026



Fraser et al, (2017) Journal of Hepatology, In press

University of BRISTOL HCV to 2% by 2026 IF scale-up OST/NSP





NIHR Programme (Evaluating the Population Impact of Hepatitis C Direct Acting Antiviral Treatment as Prevention for **People Who Inject Drugs**)

Investigators and Collaborators

Matt Hickman, Sharon Hutchinson, John Dillon, Daniela De Angelis, Lawrie Elliott, Graham Foster, David Goldberg, Natasha Martin, Ann Eriksen, Peter Donnan, Sema Mandal, Peter Vickerman, William Hollingworth, David Liddell, Paul Flowers, Samreen iljaz, Magdalena Harris, Viv Hope, Zoe Ward, Ross Harris, Mary Ramsay, Anne Presanis, Ruth Simmons, Katy Sinka, Stephanie Migchelsen, Rachel Glass, Helen Harris, Chris Metcalfe, Athene Lane, David Whiteley, Andrew McAuley, Rebekah Moore, Norah Palmateer, Hamish Innes, Rory Gunson, Lesley Graham, Kate Drysdale, Hannah Fraser, Sarah Inglis, Jade Meadows, Gaby Vojt











Public Health England

Protocol **Open access BMJ Open** Evaluating the population impact of hepatitis C direct acting antiviral treatment as prevention for people who inject drugs (EPIToPe) - a natural experiment (protocol)

http://www.bristol.ac.uk/population-health-sciences/projects/epitope/







Universit University for the Common Good Bristol **Randomised Trials** Collaboration



EPITOPe Programme (Evaluating the Population Impact of Hepatitis C Direct Acting Antivral Treatment as Prevention for People Who Inject Drugs)



Trends in HCV antibody prevalence among PWID in Scotland and England 2010/2011 to 2016.



BMJ Open

Matthew Hickman et al. BMJ Open 2019;9:e029538

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Projected chronic HCV prevalence and incidence among PWID in Tayside with and without the intervention.

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Ho: Rapid-scale up - over 2 years from 2017/2018 of at least 500 HCV treatments in PWID will reduce chronic HCV prevalence to ~10% (>60% reduction) and reduce HCV incidence to ~1.4 p100py).



PWID defined as those who either (a) are currently injecting drugs, (b) have ever injected drugs and are currently on opioid substitute therapy, or (c) have ever injected drugs and are currently in prison

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DBS: dried blood spot; OST: opioid substitution therapies; PWID: people who inject drugs

Target Reached ahead of schedule:– 555 patients treated on 583 occasions by September 2019 and to date >730 HCV Rx

EMERGING EVIDENCE

Estimates of chronic and cleared HCV infection among PWID in Scotland*

(*missing Ab and RNA data have been imputed)

All PWID



Chronic HCV

Cleared HCV, with evidence of therapy

Cleared HCV, no evidence of therapy

Estimates of chronic and cleared HCV infection among PWID in Scotland*

All PWID

(*missing Ab and RNA data have been imputed)

Antibody positive PWID

30% decline 5% decline 100% 100% 15 90% 90% 29% decline 9% decline 24% 22% 24% 26% 32% 80% 80% 70% 6% 70% 16% 20% 19% 8% 42% 60% 60% 9% 50% 50% 14% 12% 15% 14% 18% 4% 40% 40% 9% 11% 11% E 0/ 24% 68% 30% 60% 60% 30% 58% 57% 42% 20% 20% 39% 35% 34% 32% 33% 24% 10% 10% 2017.18 2017.18 0% 2015,16 2013.14 2015.16 0% 2013.14 2013, 2015, 2017, 2013, 14 2015, 2017, 18 Tavside **Rest of Scotland Rest of Scotland** Tayside

Chronic HCVNorah Palmateer REDUCTION IN THE
POPULATION PREVALENCE OF HCV VIRAEMIACleared HCV, with evidence of therapyAMONG PWID.... : REAL WORLDCleared HCV, no evidence of therapyDATA (Addiction under review)

Causal impact synthetic control method (CIM) simulation and estimated intervention effects and 95% credible intervals for a range of assumed effects.

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A Bayesian multivariate factor analysis model for evaluating an intervention by using observational time series data on multiple outcomes. Pantelis Samartsidis et al. JRSSA 2020 doi.org/10.1111/rssa.12569; Evaluating the power of the causal impact method in natural experiments of HCV treatment as prevention. 'Statistical communications in infectious diseases': under review

Next Steps

- Evaluate HCV TasP in Tayside
 - Synthetic control analysis
 - Infectious Disease & Economic Model
 - Qualitative studies of scaling up manual
 - Qualitative accounts of opioid use disorder treatment outcomes post SVR
- Evaluate HCV TasP in England
 - New protocol emulate step wedge trial design

Modelling the impact of incarceration and prison-based hepatitis C virus (HCV) treatment on HCV transmission among people who inject drugs in Scotland

Jack Stone, Peter Vickerman, Sharon Hutchinson, Matt Hickman et al

Recent incarceration associated with increased risk of HCV/HIV acquisition among PWID

			Relative
Study	Location		Risk (95% CI)
Iversen 2013	Australia	-	2.84 (2.01, 4.02)
Maher (unpublished)	Australia		2.31 (0.86, 6.21)
Azim (unpublished)	Bangladesh		1.36 (0.60, 3.09)
Bruneau 2015	Canada	<u> </u>	0.94 (0.30, 3.10)
Milloy (unpublished)	Canada		2.61 (1.69, 4.04)
Milloy (unpublished)	Canada	÷	1.16 (0.81, 1.68)
Roy (unpublished)	Canada	-	1.08 (0.78, 1.49)
Sacks-Davis 2016	Canada		2.38 (1.43, 3.95)
Spittal 2012	Canada	 	1.25 (0.83, 1.89)
Aladashvili (unpublished)	Georgia	-	1.56 (0.57, 4.23)
Smyth 2003	Ireland	_ _ _	0.79 (0.42, 1.48)
Brunton 2000	New Zealand		- 2.75 (0.34, 21.99)
Havens (unpublished)	USA	÷ •	2.80 (1.36, 5.77)
Mehta (unpublished)	USA		1.60 (0.55, 4.68)
Craine 2009	United Kingdom		1.36 (0.48, 3.85)
Hutchinson (unpublished)	United Kingdom		2.02 (0.89, 4.61)
Platt, Hope and Hickman (unpublished)	United Kingdom		1.22 (0.48, 3.09)
Overall (l²=57.3% , p)=0.002)	1.	62 (1.28,2.05 <mark>)</mark>
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Impact of Scaling-up Prison Treatments



* 43% of incarcerated PWID have lengths > 16 weeks; 60% have sentence lengths > 12 weeks. sentence

26 October 2020

Preliminary logic model HCV treatment as prevention (EPIToPe).

Situating the Problem across five								
diverse settings		Intervention			Outcomes			
ces Level	F (C	Focus of Change in Implementation (Contexts, Antecedents & Behaviours)		Short Term Intermediate Long Ter				
For All Settings Busy stretched services Resistance to larger client groups Attrition in client pathway	Inputs Co-ordinated leadership at all levels Additional financial resource for testing and treatment	Settings Culture of settings Prioritisation of TasP Scale of patient population Systems processes Clarity of new patient pathways For HCV Nurse Facilitators Identify local HCW champions	Common intervention functions • Behaviour change wheel Education, Persuasion, Training, Environmental Restructuring, Modelling	New service culture	Immediate reduction in HCV prevalence and positive signal that HCV risk reduced. Cultural change within services – treating all	Reduce undiagnosed		
For Health Care Professionals (population target) Resistance to increased workload Lack of awareness and engagement with TasP Lack of "buy-in" to new pathway	Community HCV treatment Nurse Facilitator (key opinion leaders)	within settings Work with PWID champions and potential client key opinion leaders For HCPs Embedding new TasP into existing services Endorsement of TasP to	Enablement.	New systems, processes Larger client group Less chaotic client group	and prioritising TasP Increased uptake of HCV treatment among PWID New systems to manage	infection Reduced onwards transmission Reduced reinfection Reduced spend on liv health		
PWID (target population) Recognising risk of HCV Stigma associated with HCV Lack of knowledge of TasP Fear of older HCV treatments Culture of treatment suspicion	Scaling up the settings. Treatment in the community where PWID is: drug treatment facilities (Inc. OST); new TP in key NSP; Prisons; Pharmacies; NHS Hep-C treatment centres.	colleagues Engagement with TasP Increased offer of test to new clients Increased offer of treatment to all clients For PWID Awareness of TasP adherence to TasP patient pathway Changing descriptive and injunctive norms to saturate the population	Common Mechanisms of Action within intervention *TDF domains Social influence, Environment, context and resource, Beliefs about Consequences, Behavioural regulation, Professional/social role and identity, Knowledge.	New norms for HCW New norms for PWID	patient flow across pathway Better understanding of new HCV treatments Demand for new HCV treatments	Increases in Quality of Life Reductions in HCV morbidity/Improve public health		

Matthew Hickman et al. BMJ Open 2019;9:e029538

BMJ Open