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UK Public Health England Data

University of BRISTOL

Nelson PK et al. Lancet 2011:378:571-83

K INTERVENTION EFFECTIVENESS

- Needle and syringe provision (NSP) and Opiate substitution therapy (OST) effective in reducing selfreported injecting risk behaviour
- · BUT on HCV transmission
 - Insufficient review level evidence that NSP is effective
 - · Weak evidence that OST is effective
 - · No review level evidence for other interventions

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Palmateer et al Addiction 2010 105: 844-59 Hagan JID 2011

Emerging epidemiological evidence for impact of harm reduction on IDU's HCV incidence

- First evidence came from Amsterdam cohort
- Pooled survey data from England, Wales and Scotland²
- Looked at impact of <u>OST</u> and/or <u>exchanging more syringes than</u> <u>you inject</u> (defined as '100%NSP' from now on) on an individual's risk of recent infection

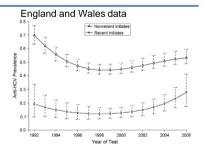
Effect Estimates	AOR*	95% CI		
Currently on 100%NSP	0.48	0.3	0.9	
Currently on OST	0.41	0.2	0.8	
On both OST and 100%NSP	0.21	0.1	0.5	

- * adjusted for: gender, crack injecting, homelessness, injecting duration
- Further data adding to evidence base suggesting OST decreases risk of HCV acquisition by 71-87%^{3,4} and also 100%NSP⁵

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1. Van den Berg Addiction 2007; 2. Turner et al. Addiction 2011; 3. Page INHSU 2013; 4. Edlin INHSU 2013; 5. Aller IJDP 2012

- HCV transmission has decreased over time in some settings¹⁻⁵
- But none have decreased HCV to low levels
- Data from England/Wales suggests might be increasing⁶

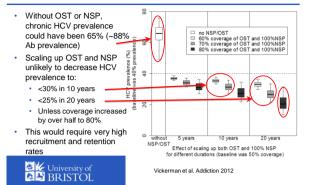




Mehta JID 2011; 2. Grebely Plos one 2014; 3. Van den Berg Etr J E 2007; 4. Des Jarlais AIDS 2005; 5. Roy Epid Inf 2007; 6. Sweeting; V et al., American Journal Epidemiology, 2009. 170; p. 352-60

⊮ Aims	
Can scaling up the coverage of OST and high intensity NSP (100%NSP) reduce HCV prevalence in the UK?	
Can HCV antiviral treatment for IDUs reduce HCV prevalence, is it cost-effective, and how should we case find?	
How will new direct acting antivirals (DAAs) change the situation and are they affordable?	
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Can scaling up the coverage of OST and	
NSP reduce HCV prevalence in the UK?	
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Deterministic HCV transmission modelCalibrated to UK current HCV prevalence and	
intervention coverage:Stable 40% chronic prevalence	
 50% current coverage of both OST and 100%NSP OST and 100%NSP efficacy estimates from UK analysis 	
 Model impact of scaling up OST and 100%NSP to 60, 70 or 80% coverage for each intervention 	
University of Vickerman et al. Addiction 2012	

(assume current UK chronic HCV prevalence is 40%)





Other prevention options are needed:

Could HCV treatment have an impact?



★ HCV ANTIVIRAL TREATMENT: BARRIERS AMONG ACTIVE INJECTING DRUG USERS **THE CONTROL OF THE CONTROL OF THE

- Existing antiviral treatment effective (45-80% with pegIFN+ribavirin)
- ...but few (<1%) IDU currently treated

Why?

 Ongoing concern over potential non-compliance and re-infection



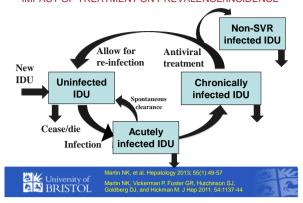
- What does the evidence say?
- IDU achieve similar SVR and compliance rates as non- or ex-IDU [1,2,3]
- Small scale studies report low reinfection rates after treatment in first few years[1,4,5].



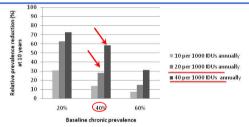
J Aspinall et al. Clin Infec Dis 2013;57(suppl 2):580-5 Dimova et al. Clin Infec Dis 2013;56:806-816. Hellard, M., et al. Clin Infec Dis 2009;49(4):561-57. Dalgard, O., Clin Infect Dis 2005;40(55):5336-5338.



NEED DYNAMIC TRANSMISSION MODEL TO ASSESS IMPACT OF TREATMENT ON PREVALENCE/INCIDENCE



✓ PREVENTION IMPACT RESULTS: PREVALENCE REDUCTIONS AT 10 YEARS



Population of 4000 IDUs, 1600 chronic infections (40% chronic, $^{\sim}55\%$ Ab+)

- 80 treated yearly (20 per 1000 IDUs) 30% decrease in 10 yrs (40% → 28%)
- 160 treated yearly (40 per 1000 IDUs) 58% reduction in 10 yrs(40% \rightarrow 17%)



Martin et al. J Hep 2011



Is treating IDU with pegIFN+RBV costeffective?



MATHEMATICAL MODEL

- · Extend previously used dynamic transmission model
 - · Incorporates the prevention benefits of treating IDUs
- · Track ex-IDU after permanent cessation of injecting
 - Ex-IDU have no reinfection risk, but no prevention benefit of treatment
- Expand model to incorporate HCV disease progression



INCREMENTAL COST PER QALY GAINED (compared to treating ex/non-IDUs)

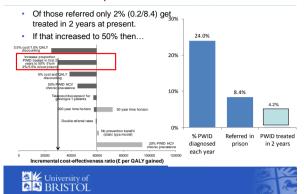
At low to moderate HCV chronic prevalence: Treating IDUs cheaper per QALY saved because: Mean incremental costeffectiveness ratio, Averts infections ICER(cost per QALY gained) QALYs saved from averting infections greater than from treating infections IDU Ex/non IDU At high HCV prevalence: 20% prevalence £521 Dominated Cheaper to treat ex/non-PWID 40% prevalence £2,359 Dominated Rapid re-infection €6,803 60% prevalence Always below UK threshold (£20-30,000 per QALY) <u>BUT never</u> <u>cost saving</u>



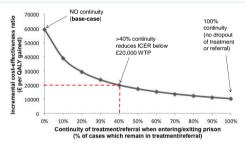
Intervention location	Discounted Costs (2011 £) [95% interval]	Discounted QALYs [95% interval]	Incremental costs [95% interval]	Incremental QALYs [95% interval]	ICER (£ per QALY gained)
Addiction services Baseline	37,181,582 [19,384,816–67,271,249]	5,354,331 [4,867,168-5,960,766]	-	-	-
Intervention	38,099,060 [20,140,578–68,378,488]	5,354,393 [4,867,206-5,960,853]	917,478 [481,174–1,664,430]	63 [19–153]	14,632
Prison Baseline	37,181,582 [19,384,816–67,271,249]	5,354,331 [4,867,168–5,960,766]	-	-	-
Intervention	38,245,293 [19,852,634–68,601,970]	5,354,349 [4,867,184-5,960,823]	1,063,710 [-225,101 –	18 [-12 – 75]	59,418

- · Compared to £20,000-30,000 WTP threshold:
 - · Cost-effective in addiction services
 - Not cost-effective in prison due to...





Reason 2: Short sentence length (4 months) and poor continuity of treatment/referral on prison entry/exit





rtin NK, Hickman M, Miners A, Hutchinson SJ, Taylor A, and Vickerman P. Cost citiveness of HCV case-finding for people who inject drugs via dried blood epot ling in specialist addiction services and prisons. BMJ Open 2013



How could things change with the new direct acting antiviral treatments?

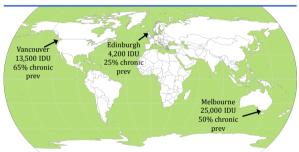


W FUTURE DIRECT-ACTING ANTIVIRAL THERAPY

- Future IFN-free DAA treatment regimes could substantially increase impact and feasibility of treatment as prevention:
 - Enhanced efficacy for all genotypes (likely >90% all genotypes)
 - Once/twice-daily oral-only dosing
 - Reduced toxicity
 - · High barrier to resistance
 - Shortened treatment duration (<12 weeks)
- May lead to:
 - Higher uptake/adherence/completion
 - · More treatment capacity



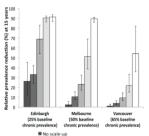
GLOBAL SETTINGS



Baseline treatment rates 3-8 per 1000 IDU annually



IFN-FREE DAA THERAPY COULD HALVE PREVALENCE IN 15 YEARS, BUT IS IT AFFORDABLE?



■ Scale-up to 10/1000 PWID annually
■ Scale-up to 20/1000 PWID annually
□ Scale-up to 40/1000 PWID annually
□ Scale-up to 80/1000 PWID annually

Treatment rates required to halve chronic prevalence within 15 years: Edinburgh: 1.5% IDU annually (2-fold increase)

Melbourne: 4% IDU annually (13-fold increase)

Vancouver: 7.6% IDU annually (15-fold increase)

If future treatments cost \$50,000 USD per course, halving prevalence within 15 years would require:

- Edinburgh: \$3.2 million USD annually
- Melbourne & Vancouver:
 ~\$50 million USD annually

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Martin NK, Vickerman P, Grebely J, Hellard M, Hutchinson SJ, Lima VD, Fosfer GR, Dillon J, Goldberg DJ, Dore G, and Hickman M. HCV treatment for prevention among people who inject drugs: modeling treatment scale-up in the age of direct

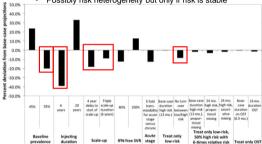
Extrapolate costs to worldwide IDU

- 16 million IDU and 10 million anti-HCV positive
- Equates to average chronic prevalence of 47% similar to Melbourne
- SO back of envelope calculation suggests need to treat 4% of all IDU per year for 15 years to halve prevalence:
 - · 640,000 infected IDU need to be treated per year
- Estimated cost per year, just for drugs
 - At \$50,000 per course → \$32 billion per year
 - 25% at \$50,000 (HICs) and 75% at \$900 (cost in Egypt) then \$8 billion for Western Countries and \$432 million for LMIC countries
- Compares well to \$19 billion spent on HIV programmes in LMIC in 2012, about \$10 billion of which was care/treatment
- However, 150 million other non-IDU with HCV

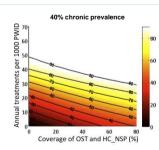


What can hinder impact?

- · Higher HCV prevalence
- · Shorter injecting duration
- · Delay in scale up or slower scale up
- Possibly risk heterogeneity but only if risk is stable



COMBINATION PREVENTION SCALE-UP (OST/NSP/DAAS): 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

Scale-up of harm reduction reduces numbers needed to treat AND prevents transmission/reinfection



artin NK, Hickman M, Hurchinson SJ, Goldberg DJ, and Vickerman P. Combination erventions to prevent HGV transmission among people who inject drugs: modelling the pact of antiviral treatment, needle and syringe programmes, and opiate substitution thempy.



★ CONCLUSIONS – new DAAs

- Potential to halve prevalence within 15 years with IFN-free DAAs, but much harder in high prevalence settings
- Such scale-up has been achieved for HIV treatment in both resource rich and poor settings¹, and even amongst IDUs^{2,3}
- Programs designed to address barriers to care among IDU have achieved yearly HCV treatment rates of 4-8% of IDU with PEG-IFN+RBV in Australia, Canada, Europe, and US⁴⁻⁷.
- · Scale-up may be achievable, BUT will it be affordable?
 - Will likely require drug-price reform, especially for lower and middle income settings, as occurred for HIV
 - · But could be possible for PWID if this occurs



1)WHO/JUNIDS/UNIDES (folial HIV/JUDS Response, Epidemic update and health region becomes under University (1) (2) Mathers et al. Lancet 375(9719):1014-28 (3) Woods (3) 2009, 338. (4) Grebely et al. Eur | Gastroentrol Hepathol 2010, 22(3):2707-. (5) Hallmann et al. 2010; 3016 Depend 2007, 88(1):49-53. (6) Undershung Cet et al. Eur | Gastroenterol Hepathol 2010; 23(3):273-17, 17 Herris Ket al. Juliod Med. 2010, 4(1):20-6.



ACKNOWLEDGEMENTS

Bristol: Prof. Matthew Hickman, Dr. Natasha Martin, Dr. Katy Turner, Dr Christinah Chiyaka

LSHTM: Dr. Alec Miners

Health Protection Scotland: Prof. Sharon Hutchinson, Prof. David Goldberg, Dr. John Dillon

Queen Mary's London: Prof. Graham Foster

Burnet Institute: Prof. Margaret Hellard

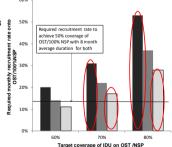
University of New South Wales: Prof. Greg Dore, Dr. Jason Grebely

FUNDERS: National Institute for Health Research (NIHR) Postdoctoral Fellowship Health Protection Scotland, Medical Research Council (MRC), NICE, BMGF,



What increases in OST/NSP recruitment are needed?

- If OST duration remains at 8 months, then monthly recruitment needs to be:
 - 30% to get 70% coverage55% to get 80% coverage
- If OST duration doubles to 16 months then increase in recruitment is much smaller
 - 18% for 70% coverage - 30% for 80% coverage
- Emphasises need to increase duration on OST/NSP



Target coverage of IDU on OST /NSP

Duration on OST/NSP ■8 months ■12 months ■16 months



Vickerman et al. Addiction 2012

W LIMITATIONS & NEXT STEPS

· Theoretical modelling projections

- NO empirical data on effectiveness of treatment as prevention!
- · Neglect programmatic issues around scale-up of interventions
- Do not include other benefits of harm reduction interventions
- Parameter uncertainty

Next steps

- Model how to best allocate resources with combination interventions
- Empirical studies showing treatment of PWID can prevent onwards transmission and reduce prevalence in the population!



