Reducing overdose and drug-related deaths

plus

Impact

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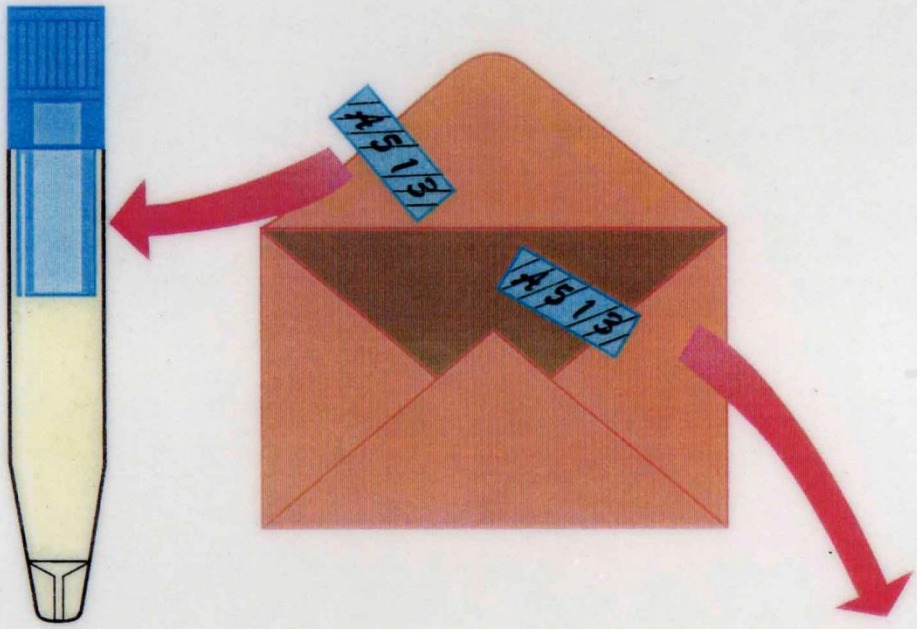


Anonymous HIV surveillance in HM Prison Glenochil

Thank you for your help in this study which will enable us to plan better HIV care in prisons. We do not need to know your name nor any other form of identification when you complete this questionnaire. It goes to the Medical Research Council for analysis. No results will be reported which relate to fewer than 50 prisoners.

Please tick (√) the box beside the answer that applies to you

1 How old are you?
- under 26 years ☐
- 26-30 years ☐
- 31-35 years ☐
- 36-40 years ☐
- over 40 ☐

2 Where did you live before coming into Glenochil Prison?
- Glasgow : Springburn, Maryhill, Possilpark, Ruchill ☐
- Glasgow : Easterhouse ☐
- Glasgow : Castlemilk ☐
- Glasgow : Garbals, Govan, Nitshill, Pollock ☐
- rest of Glasgow ☐
- Edinburgh ☐
- Dundee ☐
- Fife ☐
- elsewhere ☐

3 How long is your present sentence?
- less than 1 year ☐
- between 1 and 3 years ☐
- more than 3 years ☐

4 When did your present sentence begin?
- in 1994 ☐
- in 1993 ☐
- in 1991 or 1992 ☐
- in 1990 or 1989 or 1988 or 1987 ☐
- in 1986 or 1985 or 1984 or 1983 ☐
- before 1983 ☐

5 Were you in Glenochil Prison at any time during January to June last year (1993)?
- yes ☐
- no ☐

6 How many times have you been inside before this sentence?
- never ☐
- once ☐
- 2 or 3 or 4 times ☐
- 5 or more times ☐

7 Have you been in a borstal or young offenders' institution?
- yes ☐
- no ☐

8 Have you ever been charged with a drugs-related offence?
- yes ☐
- no ☐

9 How much time have you done inside since January 1983?
- less than 6 months ☐
- between 7 and 12 months ☐
- between 1 and 3 years ☐
- more than 3 years ☐

A 5 1 3

Please fix sealed label here.

MRC
Medical Research Council
Biostatistics Unit
Cambridge

10 In which year did you first inject drugs (excluding insulin)?
- NEVER INJECTED ☐
- 1982 or earlier ☐
- 1983-1985 ☐
- 1986-1988 ☐
- 1989-1991 ☐
- 1992 or later ☐

11 In which year did you last inject?
- NEVER INJECTED ☐
- 1982 or earlier ☐
- 1983-1985 ☐
- 1986-1988 ☐
- 1989-1991 ☐
- 1992 or later ☐

12 Have you ever injected while inside?
- yes ☐
- no ☐

13 Did you start injecting while inside?
- yes ☐
- no ☐

14 Did you inject in Glenochil Prison during January to June last year (1993)?
- yes ☐
- no ☐

15 Have you ever taken the blood test for HIV?
- yes ☐
- no ☐

16 Did you have an HIV blood test in Glenochil Prison during January to June last year (1993)?
- yes ☐
- no ☐

17 Have you had an acute attack of hepatitis or yellow jaundice?
- yes ☐
- no ☐

18 In the last year before this sentence, how many women did you have sex with?
- none ☐
- 1 ☐
- 2 - 5 ☐
- 6 - 10 ☐
- 11 or more ☐

19 In the last year before this sentence, how many men did you have sex with?
- none ☐
- 1 ☐
- 2 - 5 ☐
- 6 - 10 ☐
- 11 or more ☐

20 Have you ever accepted money (or goods) for sex?
- yes ☐
- no ☐

21 Have you ever paid for sex?
- yes ☐
- no ☐

22 Have you ever been treated for a sexually transmitted disease?
- yes ☐
- no ☐

23 Have you ever had anal sex with another man in prison?
- yes ☐
- no ☐

Thank you for answering this confidential questionnaire.

"Bespoke questionnaire"

Have you ever injected? **One third {still}**

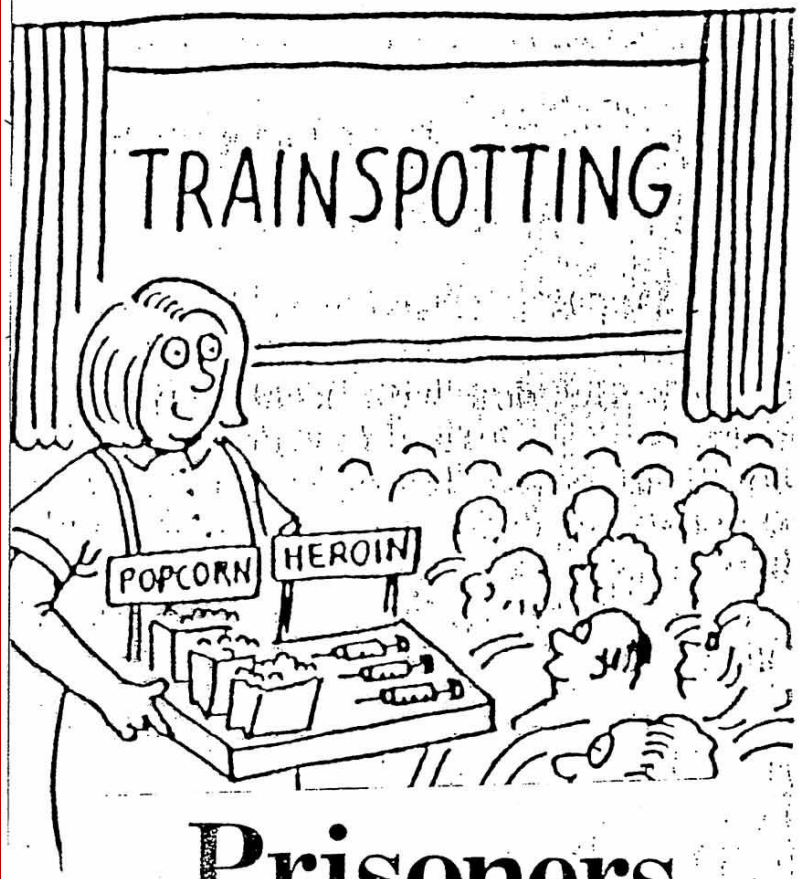
When did you start to inject?

Ever injected inside prison? **50%** {now **25%**}

Did you **start** to inject **inside prison**? **10%**

Have you ever had an HIV test? 75%

Ever had anal sex with another man inside prison?



Prisoners use heroin to thwart drug tests

JASON BENNETTO
Crime Correspondent

country said they were finding a similar trend." He added that

HMP Edinburgh

Quantified mortality of **HIV-infected** injectors soon **after** release from Edinburgh Prison in 1983-94.

Seaman et al, BMJ 1998

Bird & **H**utchinson: **Method**

BH set eligibility criteria: male, 15-35 @ release, served 14+ days, 1st release in July-Dec of 1996-1999.

SPS applied the criteria

⇔ **RGS** file had prisoners' name, date of birth, full postcode, release date & **prisoner number**

⇔ **BH** file had birth-year, 1st part postcode, reception and release date & **prisoner number** + alive/dead on release.

Using **prisoner number**, **RGS** informed **BH** about deaths in 12 weeks after prison-release.

Drugs-related deaths in fortnight after prison: *19 486 male ex-prisoners, aged 15-35 years, released after 14+days' incarceration*

DEATHS	1st 2 weeks	subsequent 5 fortnights	**RELATIVE RISK** (95% CI)
Drugs-related	34*	23 (11 in 2nd fortnight +12 in next 8 wks)	**7** (3 to 16)
Other causes	3	18	0.8 (0.2 to 2.4)

WASH: 1 in 200 adult injectors dead within 2 weeks after prison

Judges aware?

Prison-based interventions

a) **Information leaflet**: how to avoid overdose risk after release

b) **Naloxone on release RCT**: heroin antidote.

Addiction 2003; 98: 185-190

Pilot N-ALIVE Trial: RCT on effectiveness of Naloxone-on-release for reducing **opiate-overdose deaths** soon after release of prisoners who ever injected heroin

Three musketeers

Drugs-related death soon after release from prison + **HMP Edinburgh (Bird)**

Peers' willingness to intervene & Naloxone-training of users **(Strang)**

RCT-challenge **(Parmar)**

Design assumptions: N-ALIVE Trial

Eligibility: 18+years, history of heroin injection, 7+ days incarceration.

1. **Some-one else present: @ 80% overdoses.**
2. **Naloxone carriage: 75% in 1st 4-weeks, 50% in next 8 weeks.**
3. **50% chance: that Naloxone is administered by present other.**

⇔ Effectiveness

in 1st 4-weeks @ 30%; in weeks 5-12 @ 20%

4. **One overdose death in 1st 4-weeks per 200 controls.**

Prison-based, with-consent **RCT** for 56,000 pre-release adult IDUs

Expected drugs deaths	1st 4 weeks after release	Next 8 weeks after release
Controls [28,000 IDUs]	140	35
Naloxone [28,000 IDUs]	98	28

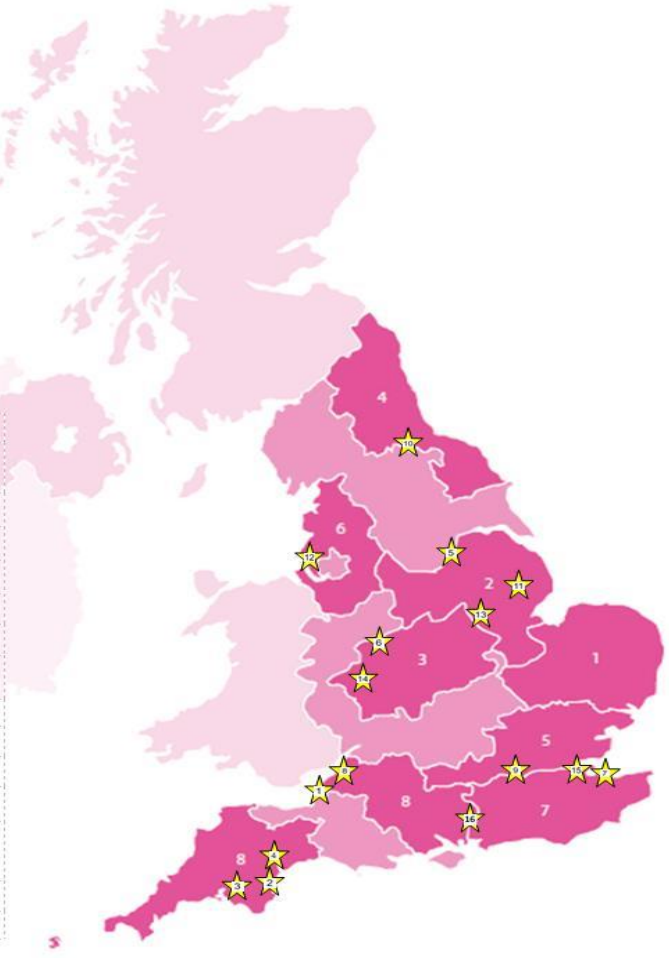
MHRN Networks & N-ALIVE Sites

NIHR Mental Health Research Network (MHRN)

Mental Health Local Research Networks:

1. East Anglia
2. East Midlands
3. Heart of England
4. North East
5. North London
6. North West
7. South London and South East
8. West

For more information contact
mhrn@iop.kcl.ac.uk



N-ALIVE Sites	
1	HMP Bristol
2	HMP Devon: Channings Wood
3	HMP Devon: Dartmoor
4	HMP Devon: Exeter
5	HMP Doncaster
6	HMP Dovegate
7	HMP Elmley
8	HMP Gloucester (Now Closed)
9	HMP Holloway
10	HMP Leeds
11	HMP Lincoln
12	HMP Liverpool
13	HMP Nottingham
14	HMP Oakwood
15	HMP Rochester
16	HMP Winchester

Scotland's Ministerial Decision National Naloxone Policy: 2011

?

Primary outcome

Secondary outcome

NOT number of opioid-related deaths. WHY?

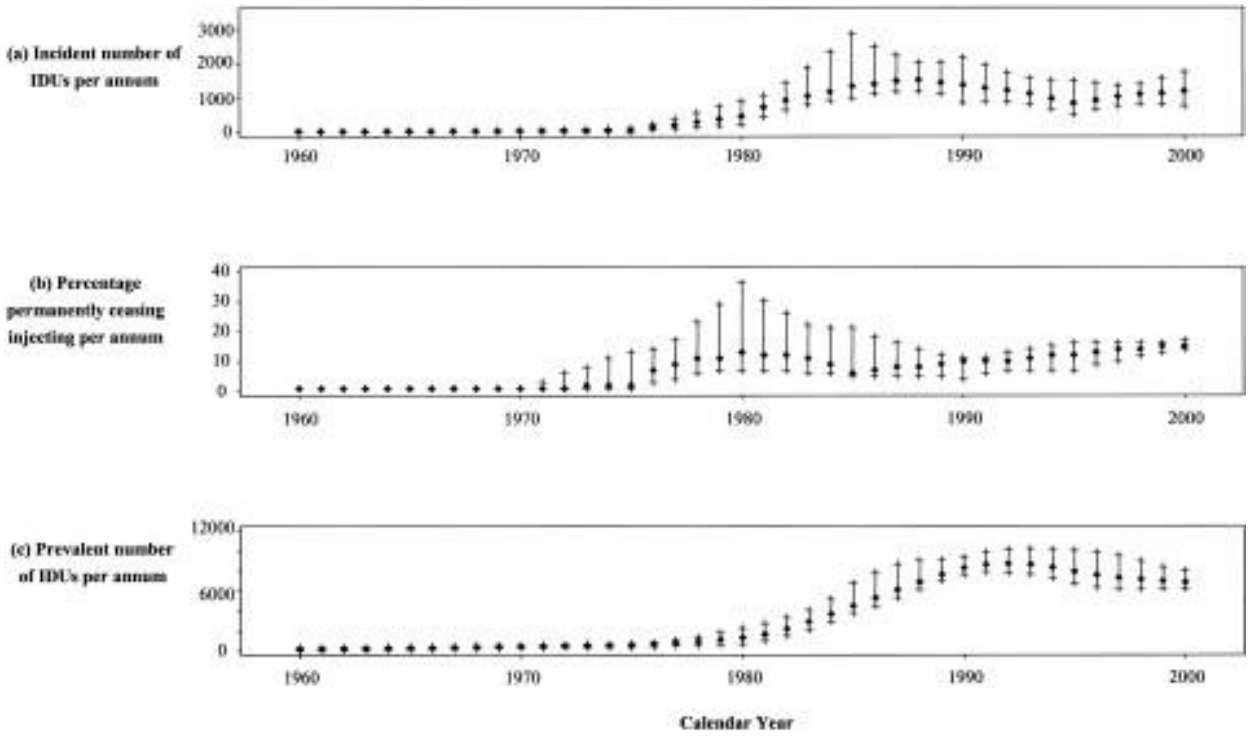
Scotland's rising tide of opioid-related DRDs: demography

Subgroup	female	MALES	MALES ONLY: by age at death			
			<25	25-34	35-44	45+years
4 years of 2006-09: 1,994 DRDs (1,571 opioids)						
Opioid-DRDs *per annum*	***70***	***323***	***53***	***123***	***104***	***43***
6 years of 2000-05: 2,018 DRDs (1,554 opioids)						
Opioid-DRDs *per annum*	***40***	***219***	***51***	***93***	***59***	***17***

Modelling the current and future disease burden of hepatitis C among injection drug users in Scotland.

Hutchinson SJ, Bird SM, Goldberg DJ. **Hepatology 2005; 42: 711-23**

4-fold (incident) or 8-fold (prevalent) increase from 1980 to 1990?



Before/after evaluation of Effectiveness for Scotland's National Naloxone Policy (NNP)

Pre-NNP outcomes (ie during 2006-2010)

Primary: 10% of 1970 ORDs with 4-week antecedent of prison-release

Secondary: 20% of 1970 ORDs with 4-week antecedent of prison-release **or hospital-discharge.**

Power for NNP-evaluation: outcome, target & duration

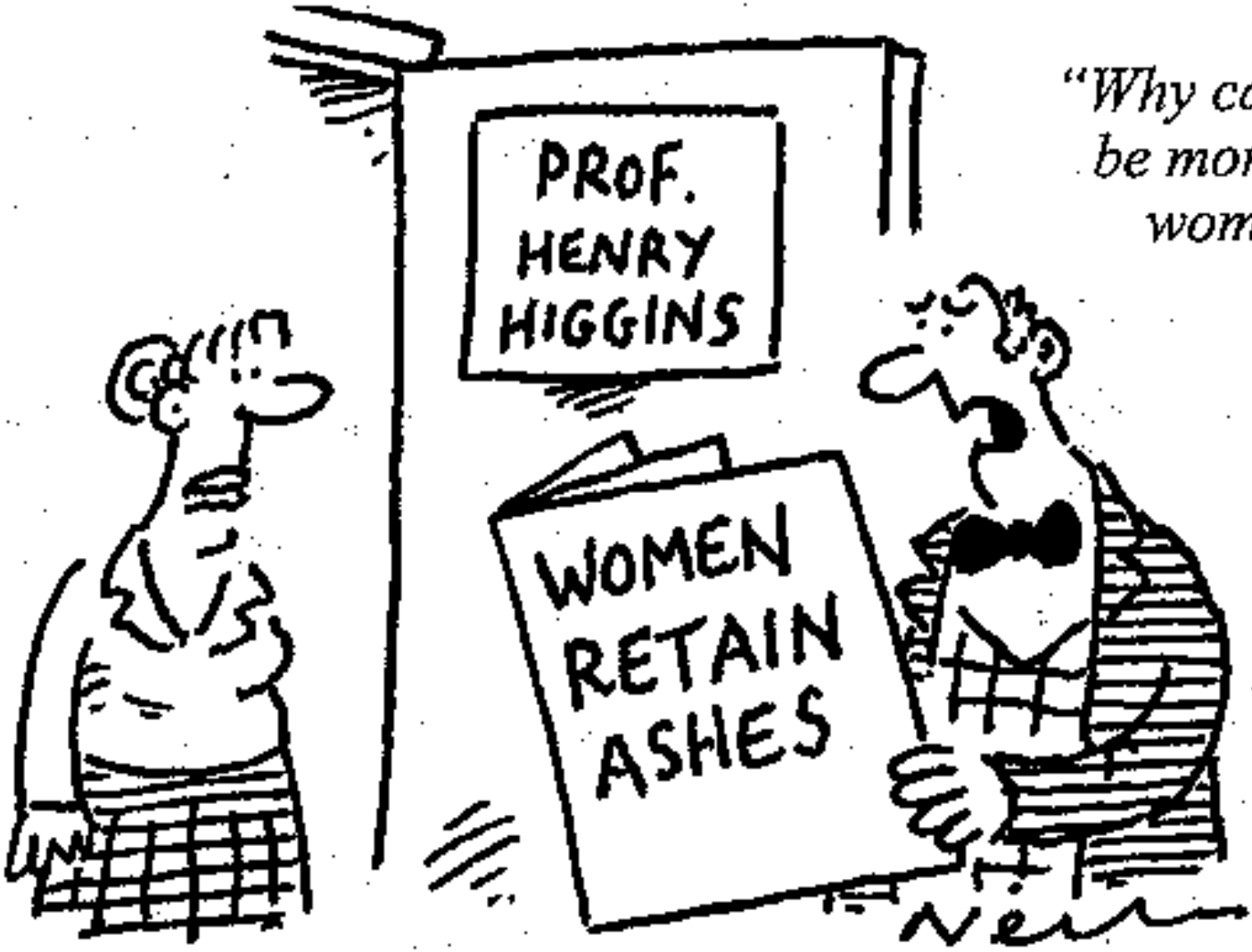
Primary: 80% power for **30%** target (10% to 7%) in 3-years

Secondary: 80% power for **20%** target (20% to 16%) in 3-years (ie 2011-2013).

Before/after evaluation of Scotland's National Naloxone Programme (NNP)

PERIOD	Naloxone-kits issued in Scotland (including by prisons)	% (CI) of Scotland's opioid-related deaths (ORDs) with 4-week antecedent:	
		Prison-release **PRIMARY OUTCOME**	Prison or hospital discharge **SECONDARY OUTCOME**
2006-10: baseline Before NNP		**193/1970: 9.8% (8.5- 11)**	**374/1970: 19% (17.2-21)**
NNP 2011-13	**11 900** (2 300)	**76/1212: 6.3% (4.9-7.6)**	**181/1212: 15% (12.9-17)**

Implications for England: Naloxone-kits annually should be 20 times England's annual number of opioid-related deaths: ie **over 40,000**



"Why can't a man be more like a woman?"

Scotland's DRD-rate in 2009-2013 per 1000 problem drug users: gender * age-group

Demography	CaptureRC central estimate for PDUs in 2009/10	2009-2013 Scotland's DRDs	DRDs per annum per 1000 PDUs (95% CI)
Male: 15-24	7 900	209	**5.3** (4.6 to 6.0)
Male: 25-34	16 000	647	**8.1** (7.4 to 8.7)
Male: 35+ yrs	18 200	1158	**12.7** (12.0 to 13.5)
Female: 15-24	3 200	63	**3.9** (3.0 to 4.9)
Female: 25-34	7 100	184	**5.2** (4.4 to 5.9)
Female: 35+yrs	7 000	460	**13.1** (11.9 to 14.3)

E&W Drug Data Warehouse, 2005-09: opiate users, Pierce et al. DAD 2015; 146: 17-23.

Age-group time-updated	**Person-years in '000s [DRDs]**	**DRD-rate** per 1000 pys **(95% CI)**	**Male DRD**-rate per 1000 pys **(95% CI)**	**Female DRD**-rate per 1000 pys **(95% CI)**
18 - 24	63K [119]	**1.9** **(1.6, 2.3)**	**2.9** **(2.6, 3.1)** [580 DRDs]	**1.5** **(1.3, 1.8)** [141 DRDs]
25 - 34	236K [602]	**2.6** **(2.4, 2.8)**		
35 - 44	175K [686]	**3.9** **(3.6, 4.2)**	**4.2** **(3.8, 4.5)**	**3.2** **(2.8, 3.8)**
45 - 64	68K [308]	**4.5** **(4.0, 5.0)**	**4.7** **(4.1, 5.3)**	**4.0** **(3.2, 5.1)**

“Methadone deaths”

Scotland's CHI-identified methadone-prescription cohort for 2009-15: 36,347 clients.

26,533 (73%) clients with actual or recovered daily-dose at 1st CHI-identified prescription:

2 342 deaths,

include 995 DRDs (42%),

include 420 methadone-specific DRDs (42%)

Impact Summary

WASH design: acceptable to prisoners (> 80% volunteered)

\+ Record-linkage for injector-prisoners' benefit

N-ALIVE's plausible effect-size . . .

Ministerial decision in Scotland (& Wales) . . .

Before/after evaluation-design: science-led

Late sequelae of UK's heroin injector epidemics: **methadone-specific DRDs** (sex=f; dose; co-morbidities; SAE)

Scotland's ageing epidemic injector-wave, 2006-2018

ORDs (ERA mean)

ERA	Under 25 years	25-34 years	35-44 years	45+ years
2006-2008	207 **(69)**	432 **(144)**	359 **(120)**	145 **(48)**
2009-2011	154 **(51)**	432 **(144)**	451 **(150)**	220 **(73)**
2012-2014	72 **(24)**	362 **(121)**	459 **(153)**	338 **(113)**
2015-2017	58 **(19)**	422 **(141)**	750 **(250)**	622 **(207)**
2018	**32**	**165**	**365**	**334**

Ageing epidemic injector-wave: **England & Wales**

Any opiate mentioned-DRM$_{isuse}$s (ERA mean): E&W

ERA	Under 25 years	25-34 years	35-44 years	45+ years
2006-2008	498 **(166)**	1441 **(480)**	1480 **(493)**	1075 **(358)**
2009-2011	327 **(109)**	1181 **(394)**	1568 **(523)**	1439 **(480)**
2012-2014	237 **(79)**	1047 **(349)**	1695 **(565)**	1846 **(615)**
2015-2017	269 **(90)**	1169 **(390)**	2124 **(708)**	2633 **(878)**
2018				
Change since 2006-2008	**46% decrease**	**19% decrease**	**44% increase**	**More than doubled**
Scotland's ORD-change	**72% decrease**	**2% decrease**	**At least doubled**	**At least quadrupled**

Ageing epidemic injector-wave: England & Wales

DRP$_{oisoning}$-DRM$_{isuse}$s (ERA mean) by death-year: E&W

ERA	Under 25 years	25-34 years	35-44 years	45+ years
2006-2008	205 **(68)**	396 **(132)**	659 **(220)**	1496 **(499)**
2009-2011	189 **(63)**	389 **(130)**	656 **(219)**	1460 **(487)**
2012-2014	171 **(57)**	445 **(148)**	782 **(391)**	1711 **(570)**
2015-2017	195 **(65)**	536 **(179)**	911 **(304)**	2086 **(695)**
Change since 2006-2008	**5% decrease**	**35% increase**	**38% increase**	**39% increase**

Ageing epidemic injector-wave: **England & Wales**

ORD-mentions as % of DRM$_{isuse}$s in E&W (95% confidence interval)

ERA	Under 25 years	25-34 years	35-44 years	45+ years
2006-2008	**65%** [420/650] **(61% to 68%)**	**66%** [1208/1817] **(64.3% to 68.7%)**	**62%** [1150/1851] **(59.9% to 64.3%)**	**44%** [624/1414] **(41.5% to 46.7%)**
2009-2011	**63%** [258/410]	**67%** [958/1434]	**62%** [1183/1897]	**45%** [805/1787]
2012-2014	**44%** [170/390]	**58%** [799/1389]	**64%** [1292/2014]	**49%** [1093/2248]
2015-2017	**40%** [175/439] **(35% to 44%)**	**56%** [882/1570] (53.7% to 58.6%)	**64%** [1667/2617] (61.8% to 65.5%)	**55%** [1754/3201] (53.1% to 56.5%)

Scotland's National Naloxone Programme

Calendar Period: naloxone kits issued, including by prisons	Number of opioid-related deaths, ORDs	PRIMARY: ORDs within 4-weeks of Prison-release	TERTIARY: ORDs within 4-weeks of Hospital-discharge	SECONDARY: ORDs within 4-weeks of Prison-release and/or Hospital-discharge
2006-10 (5 years)	1970	193 (**9.8%**; 8.5 -11.1)	191 (9.7%; 8.4 -11.0)	374 (19%; 17.2 - 20.7)
2011-13 (1st 3 years): **12,000**	**1212**	76 (**6.3%**; 4.9 - 7.6)	111 (9.2%; 7.5 –10.8)	181 (15%; 12.9 - 16.9)
2014-16 (2nd 3 years): **24,000**	**1592**	60 (**3.8%**; 2.8 - 4.7)	151 (9.5%; 7.7 – 11.4)	204 (13%; 11.2 – 14.5)
2011-16 (6 years): **36,000**	2804	136 (**4.9%**; 4.1 – 5.6)	262 (9.3%; 8.2 – 10.4)	385 (14%; 12.4 – 15.0)

1991 **WASH**

Willing ***[ethical]***

Anonymous

[no deductive disclosure]

Saliva & linked self-Q

[high volunteer rate]

HIV surveillance

Linked to self-Q on risks

[frank answers]

1996: new WASH questions

Injected inside in past 4 weeks?

(mean ~ 6 times, also sd = 6)

Used sterilization tablets to clean needles/works in past 4 weeks?

(mean ~ 6 times)

Random Mandatory Drugs Testing

BMJ 1997; 315: 21-24.

I'm

gonna

WASH

that

wo(e)-man

right

outta

my

hair

Design assumptions by **BH**

1. **~ 20,000 eligible releases**
2. **WASH: 40% adult male & 20% young offender index releases would be injectors [IDUs]**
3. **Drugs-related deaths [DRDs] mainly in IDUs**
4. **One DRD per 3000 recently-released IDU-days, not 1 per 1000, as in Seaman.**
5. **DRD Relative Risk in 1st fortnight of 4, not 8.**

Scottish Drug Misuse Database Cohort, 1996-2010

Ever-injectors' DRD risk in 1st 4-weeks after hospital-discharge {White et al.}

2.4 DRDs per 1,000 hospital-discharges

Hospital-doctors

FAX to GP/drug tx. team

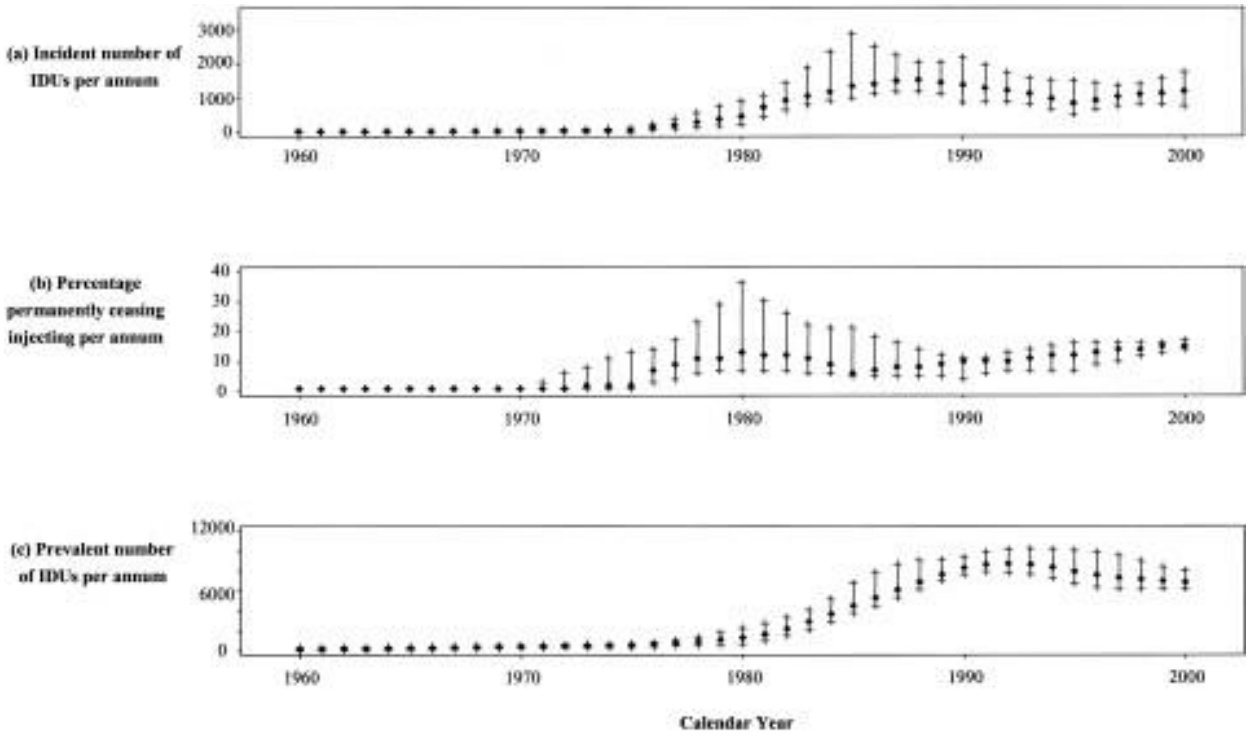
CONSIDER take-home Naloxone

Public health policy in Scotland & Wales

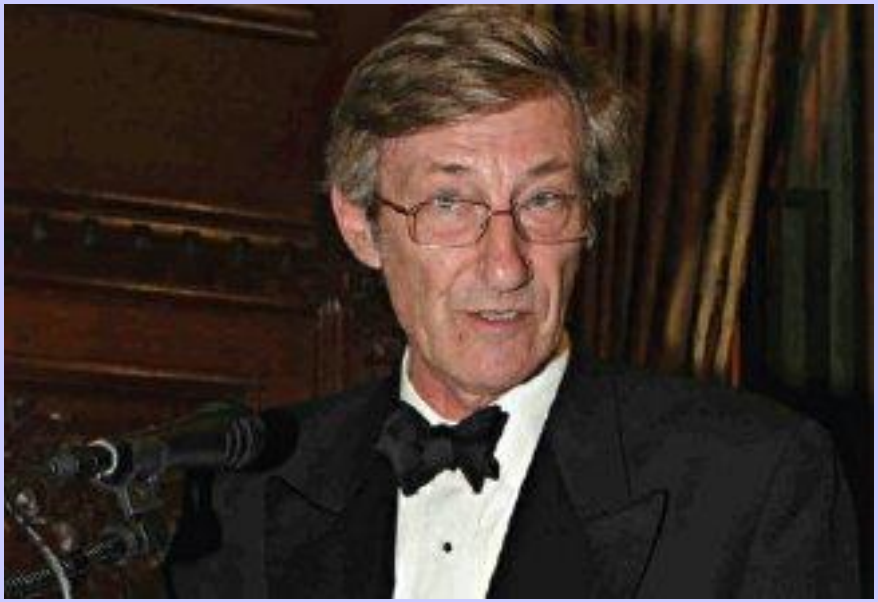
3. Modelling the current and future disease burden of hepatitis C among injection drug users in Scotland.

Hutchinson SJ, Bird SM, Goldberg DJ. Hepatology 2005; 42: 711-23

4-fold (incident) or 8-fold (prevalent) increase from 1980 to 1990?



Advisory Council on Misuse of Drugs



2005

Naloxone

was added to exempt list of Prescription Only Medicines for administration by anyone in an emergency to save life


MRC
Trials Unit
This card is to notify that
is authorised to carry an emergency dose of Naloxone as an antidote to heroin overdose. They have been given this by the N-Alive trial.
For further details on the trial, contact
Freephone: 08x0 xxx xxxx
ACTIONS
call ambulance
Problems with Naloxone
Today

What did N-ALIVE pilot Trial's Data Monitoring Committee decide?

1. Cease randomization on 8 Dec. 2014.

N-ALIVE & Scotland's data show that naloxone-on-release is twice as likely to be administered to someone other than the ex-prisoner.

Individually-randomized trial now infeasible: ie wrong design.

2. Offer naloxone-on-release to those already-randomized but not released by 8 Dec. 2014.

Based on Scotland's strong before/after comparisons.

As judged by Hill's criteria for causality.

3. Mortality follow-up continues to 8 March 2015.

But will be incomplete before March 2017.

Due to late-registration of deaths in England . . .

See Bird et al. *DEPP* 2014; Parmar et al. *Addiction* 2017; Bird et al. *Contemporary Clin. Trials Communications,* 2017; Meade et al. *Drug & Alcohol Review* 2017 (eprint).

Advocate for evaluated Naloxone Policy in England!

Hill's criteria for appraising causality

strength, consistency, specificity, temporality; biological gradient, plausibility, coherence; experiment, analogy.

Scotland's methadone-DRD-rate per 1000 client-years had risen. Why?

Age-related [1]: DRD-rate increases with age.

Should we expect **methadone-DRD rate to increase as methadone-clients age?**

Age-related or gender-related daily-dose [2]:

Does prescribed daily-dose of methadone increase with clients' age; or differ by gender? **Find out!**

Methadone-DRD [3]: Does **not** imply that the deceased had been prescribed methadone **. . .**

Scotland has toxicology protocol @ forensic autopsy

Scotland's ageing epidemic injector-wave, 1997-2018

DRDs (ERA mean)

ERA	Under 25 years	25-34 years	35-44 years	45+ years
1997-1999	258 **(86)**	310 **(103)**	130 **(43)**	66 **(22)**
2000-2002	253 **(84)**	419 **(140)**	231 **(77)**	104 **(35)**
2003-2005	207 **(69)**	365 **(122)**	299 **(100)**	140 **(47)**
2006-2008	255 **(85)**	514 **(171)**	450 **(150)**	230 **(77)**
2009-2011	194 **(65)**	523 **(174)**	559 **(186)**	338 **(103)**
2012-2014	125 **(42)**	465 **(155)**	596 **(199)**	534 **(178)**
2015-2017	111 **(37)**	547 **(182)**	936 **(312)**	913 **(304)**
2018	**65**	**217**	**442**	**463**

Ageing epidemic injector-wave: **England & Wales**

DRM$_{isuse}$s (ERA mean) by death-year: E&W

ERA	Under 25 years	25-34 years	35-44 years	45+ years
2006-2008	650 **(217)**	1817 **(606)**	1851 **(617)**	1414 **(471)**
2009-2011	410 **(137)**	1434 **(478)**	1897 **(632)**	1787 **(596)**
2012-2014	390 **(130)**	1389 **(463)**	2014 **(671)**	2248 **(749)**
2015-2017	439 **(146)**	1570 **(523)**	2617 **(872)**	3201 **(1067)**
2018				
Change since 2006-2008	**32% decrease**	**14% decrease**	**41% increase**	**At least doubled**
Scotland's DRD-change	**56% decrease**	**6% increase**	**At least doubled**	**Quadrupled**