

Evaluating the impact of opiate substitution treatment on drug related deaths in the population: a natural experiment using primary care, other drug treatment databases & model projections (NIHR OST DRD Project)

Patient Participation and Involvement – Bristol and Blackpool June – August 2016

Method

PPI was conducted by 2 members of staff at Bristol Drugs Project during August 2015. Staff and service users were interviewed in small groups each by two facilitators. Service users were reimbursed £15 cash for their time. Each focus group lasted approximately 1 hour.

Bristol – Members of staff from BDPs Shared Care service were interviewed in two groups and members of DHI (Developing Health and Independence) Peer Support group were interviewed in 1 group.

Blackpool – 3 groups of current service users and staff from Horizon Drug and Alcohol Service were interviewed at the premises; 49-55 Cookson Street, Blackpool FY1 3DR. Groups were arranged by staff from ADS Addiction Dependency Solutions

Rationale for approach used:

Outcomes data taken from a Lay Summary provided by M Hickman was presented to the staff groups in Bristol (Appendix I). The complexity of the data lead us to present data to subsequent groups in a further simplified PowerPoint, in agreement with MH (Appendix II).

Three reports are presented:

1. 2 staff groups from Bristol Drugs Project, Bristol (combined data),
2. 1 group of Peers, DHI, Bristol
3. 3 groups of service users and staff, from Blackpool (combined data).

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27 June 2016

Shared Care practitioners x 2 groups combined answers (18 staff)

Question 1

What other important differences could there be between people starting OST with Methadone or Buprenorphine?

- More 'On top' use possible with Methadone
- Cultural differences around attitudes to taking Methadone / Buprenorphine e.g. social group uses Methadone therefore client also wants to use Methadone
- Buprenorphine has an Anti-depressant element which could help stabilise clients mood
- Clients who choose Buprenorphine are less ambivalent about making changes to their illicit using
- Clients who choose Buprenorphine are more stable with less historic trauma
- The data should look at supervised vs unsupervised consumption
- Would expect B to be provided to more unstable/chaotic clients
- Chaotic meaning mental health problems
- Mental health must be looked at
- Sedating effect of methadone is seen to be more helpful for complex clients
- Clients saying "I'm not ready to stop – unlikely to be prescribed B" Need to know about continued 'on top' use to understand this data
- Missing data:
 - continued I/V use
 - co-existing Mental health problems
 - Co-morbidity index mainly physical - - no mention of mental health
 - Looking at how much people are using at Assessment is important
 - Has length of using history been looked at (not just age)
 - If clients are seeking oblivion – they are more likely to seek Methadone
 - More comfort in Methadone
 - Victims of Sexual abuse or trauma more likely to want methadone
 - People with family history of drug use will want methadone
 - Looked at geographical but should look at socio-economic grouping
 - Can we look at who is initiating the PX GP or drugs worker – feeling that GP more likely to initiate onto methadone
 - Should look at how much support client is getting in first 4 weeks
 - Should look at co-use of Crack
 - Should look at illicit use of benzos – more erratic

Question 2

What do you think of the findings? (with particular reference to the 1st four weeks on treatment and 1st four weeks after treatment has ended)

- 1st four weeks safer on Buprenorphine but Methadone safer 1st four weeks after treatment
- What psycho social treatment had patients done and was this taken into account?
- Had past trauma been taken into account?
- Practitioners tended to express that clients who had chosen to be on Buprenorphine were likely to be more stable and more ready to make changes to their drug use
- Totally not surprised at results
- Clients on B tend to be more stable
- Circular argument – more stable clients – less like complications
- B is safer anyway – did anyone in the study die from B overdose?
- Thought the data might have shown even bigger differences
- 1st 4 weeks off (*noticing slight increased risk from Overdose with B*) clients on B may experience increased expectations of success from professionals and self and find it more difficult to return to treatment. May be relapse and failure and fear of judgements – more likely to relapse and not seek help?
- Easy to disappear and keep coping if ending/ or falling off a Buprenorphine script.
- Is being on a methadone script still safer than not being on OST if you are an injecting opiate user? (despite this data)

Question 3

What needs to be done to test the hypothesis that Buprenorphine is safer than Methadone?

- Does this data include multiple presentations of same patients? Conduct a long term study of patients of 1-2 years Is being on anything safer than being on nothing?
- Must look at the length of time in (and out) of treatment (not just age) Look at number of episodes

Question 4

Your views on the proposed study

- Unethical as it reduces choice for the client
- Possibility of clients opting out of OST treatment completely
- Would need to measure OD rate of clients not in OST treatment at all
- Despite the evidence of this data, the practitioner can make a better, more experienced decision about OST which enhances better/safer outcome

Cluster trial

- If you do this – must compare similar socio economic groups, Bristol and Liverpool (i.e. not Bristol and Herefordshire)
- Is a cluster trial ethical now we know this data?

- Worried about unintended consequences of a trial – forcing people onto buprenorphine knowing they can't manage this regime
- Cluster trial – people would walk away and not get treatment
- No Treatment as Usual for those opting not to have buprenorphine for first 4 weeks
- I would feel uncomfortable being a shared care worker in a Buprenorphine only cluster (1 experienced worker)
- I would be happy to initiate everyone onto buprenorphine (1 experienced S/C worker)
- I can't think of anyone I have thought are Inappropriate for buprenorphine who has asked for it (experienced S/C worker)

RCT

- People who opt for the trial may have an interest in doing better (*because they don't mind being in the trial*)
- People would withdraw from the trial after randomisation if they didn't get the treatment they wanted (*based on knowledge that patients consenting to trials can withdraw at any point*)
- RCT would self select people who are already OK with buprenorphine

Question 5

Other views / comments

- Clients who choose not to be part of the cluster trial – how will their outcome be measured
- Clients who accept trial more likely to be more engaged and therefore likely to have better outcomes
- Is cluster trial ethical now we have the data
- Is there data on OD deaths for people who never access OST

27th June 2016

DHI Peer Support Workers (9)

Question 1 What do you think of the findings? (with particular reference to the 1st four weeks on treatment and 1st four weeks after treatment has ended)

- It makes sense. The mind set on Buprenorphine is that you want to stop
 - If you aren't in the fellowship etc., even if you are on Buprenorphine you might use again
 - Buprenorphine needs more support because it (using) gets less euphoric – when you have life issues, it's scary
 - Methadone gives warm comfy feeling so prefer it
 - If you use Buprenorphine in prison (sniff it) get a buzz – could want that in the community and be disappointed
 - Some people do prefer Buprenorphine – If I sniffed or injected it I would get a buzz
 - People who choose Buprenorphine initially are wanting to stop – but they need more support to cope on it
 - It's clearly obvious that Buprenorphine is safer because of the mind set of the people on it
 - Motivation to be on Buprenorphine in the first 4 weeks is high but can go off as time goes by
 - Some people get what they need from Buprenorphine (clarity)
 - 1st 4 weeks after treatment on Buprenorphine is really hard – psychologically – if you have been on Buprenorphine for a long time
 - If you've been on Methadone a long time, you want the effect of heroin when you come off
- Did you look at what treatment (psycho social support) people were in around their OST?
- 1st 4 weeks off treatment are crucial – we need (support) or we will stray
 - If you are on Methadone, you will have been on it for a very long time

Question 2

What other important differences could there be between people starting OST with Methadone or Buprenorphine?

- Different services tell you that Buprenorphine blocks at different doses – I would just smoke (heroin) until I overcame the blocking

- When homeless I didn't care which OST I had, I would take anything
- I didn't want Buprenorphine because it would mess with my using
- I chose Methadone when I didn't want to stop using
- Only chose Buprenorphine when I wanted to stop using
- When I wanted to stop I stopped
- If you are on a whack of methadone, it didn't do anything if you used on top I was on Buprenorphine because I wanted to stop

Question 3

What needs to be done to test the hypothesis that Buprenorphine is safer than Methadone?

- Why not put people on Buprenorphine in 1st 4 weeks?
- How long were people on Buprenorphine / Methadone?
- My money is on people on Methadone will have been in (OST) treatment for much longer
- Must find out length of (OST) treatment
- What about the people on long term Methadone being put on Buprenorphine?
- Could put everyone on Buprenorphine but they would need masses of support

Question 4 Your views on the proposed study

- If clustered in Bristol – people will move surgery
- RCT people who want Methadone will decline the trial
- If a trial is 'enforced' people will leave it i.e. if randomised to Methadone when you want Buprenorphine – you would leave the trial
- Has the Mortality Rate in people not on a script been measured?

10th August 2016

Blackpool Horizon Drug and Alcohol Service

3 focus groups

Group 1

2 staff (1 outreach, 1 HR)

5 service users (1 recently drug free, 1 Buprenorphine, 3 Methadone) 2 women 3 men **Group 2**

2 Staff (Addaction Navigator Service)

1 service user (Methadone) Male

Group 3

2 Staff (1 Delphi prescribing service, 1 ADS Horizon Outreach)

4 service users (3 Methadone, 1 recently drug free) all men

Question 1

What do you think of the findings? (With particular reference to the 1st four weeks on treatment & 1st four weeks after treatment)

Service User Comments:

- Chaos doesn't stop just because you start a 30 ml Methadone script
- Difficult on provide a clean urine (using Methadone), Lifestyle doesn't change I was using on top of Methadone
- Given Methadone script and nothing else is looked at (*no psycho social interventions*)
- Keep upping dose until you provide a clean sample (*i.e. keep on using on Methadone at the beginning*)
- If starting dose is low i.e. 30 ml, which it is in Blackpool and you have £ 70-80 heroin habit you know it won't hold you so go and use on top
- If you had a machine that could measure amount of heroin (*rather than presence or absence*) in your system it would reduce on top use (*i.e. you could have an accurate amount of Methadone prescribed*)
- Prescribers need to be braver and titrate up quicker
- Start on a higher dose (use a blood test)
- Buprenorphine is more expensive you have to work harder to get it – I was lucky and had a good key worker so I got it (9 years ago)
- I had to beg to get off Methadone and on Buprenorphine – was stable and stuck on Methadone for 6 years
- Best key workers are ex users
- Now its easier to get on Buprenorphine (*all service users felt that until recently it had been very difficult to get PX for Buprenorphine in their area*)

- I'm on medication for MH problems & 80mls Methadone
- When people come off scripts they are not given enough support to manage. If support not there, people will use
- People are often depressed after they stop their script – it's a dangerous time – same if coming off Buprenorphine or Methadone
- No point in using on Buprenorphine
- Less chance of OD because Buprenorphine is a partial blocker – they say that but...
- When I first went on Buprenorphine it made me cheerful / chirpy and I had an appetite – didn't want to use
- People I know who have died on Methadone were using lots of other things too; Pregabalin & alcohol
- Subutex (not Buprenorphine) made you want to do things – be more active
- I don't think its right (the data), I think it is safer if you're on Methadone script and using on top
- I can see why Methadone is higher risk (because) people use on top
- Lots of people have their hit first and then Methadone on top to get the buzz

Staff Comments:

- Looking back, people (clients) didn't have much of a say – people were reduced against their will. (They) may not have had a choice of Buprenorphine or Methadone either
- Not surprised at the findings
- It's been easier to get Buprenorphine since the Recovery model came in
- Response to first 4 weeks off: may be because people have other health issues Data didn't look at MH issues

Response to increased risk from Methadone in weeks 1-4 off script Service User

Comments:

- People on Methadone have other health issues (*implication that these have not been treated during using/scripting time and come on top when you detox*)
- They (*researchers*) didn't look at mental health problems – I am on medication for MH problems and script 80 ml Methadone.
- When people come off script and are not given enough support (*psychosocial*) then people will use
- People are often depressed when they come off scripts it's a dangerous time – same for Methadone and Buprenorphine

Question 2

What important differences could there be between people starting OST with Methadone or Buprenorphine?

Service User Comments:

- Buprenorphine is a lot 'cleaner' drug to come off when on Buprenorphine you don't feel lost
- I started on Buprenorphine once – it made me feel sick so I asked to change to Methadone – wish I had stayed on Buprenorphine because Methadone dragged me down.
- Methadone made me feel embarrassed /stigma in pharmacy, people know what I am in for. Self esteem goes down on Methadone (*Methadone is for people who don't have much hope and makes you feel like that*)
- If your self esteem is quite good you would want Buprenorphine
- If you are clear and want to move forward you would ask for Buprenorphine
- If you don't want stop you would go for Methadone
- Methadone took me a step back, made me think about how I'm a heroin user
- People on Buprenorphine probably don't use on top
- People on Methadone know that you can use on top so will do
- I know lots of people on Buprenorphine – they stop using
- Most people I know on Methadone are still using
- People would prefer to withdraw from Buprenorphine
- Having had a negative experience of Methadone withdrawal would choose to withdraw on Buprenorphine
- Best to give up on top use in order to swop to Buprenorphine for easier withdrawal
- Binge / Giro using: If you are on Methadone you don't have to plan it – can just do it. If you are on B you have to plan it – might just continue the pattern of planned using after detox – may explain slightly increased risk for Buprenorphine in first 4 weeks off script
- People on Buprenorphine have lost relationship with Heroin, a lapse will have more consequences – don't know local strength etc.,
- People who ask for Methadone may be people without much else going on. I know on Methadone I can choose to use on top
- If I wanted to sort my life out I would ask for Buprenorphine
- Subutex – can detox without noticing – could be risky

Staff Comments:

- More people on Methadone mix with other drugs. People on Methadone less fearful of OD'ing – people think they can use a lot. People on Buprenorphine more fearful – less on top use
- Anyone using significantly more street opiates will be prescribed Methadone to stabilise them – then will be switched to Buprenorphine
- If someone is using 10 bags a day, difficult to get them started on Buprenorphine

Question 3

Should everyone be started on Buprenorphine and then offered a choice of Methadone or Buprenorphine after 4 weeks?

Service User Comments

- You should be offered a choice at the very beginning – “What do you (client) want”
- I don't think Keyworkers are listening – SU's must have a choice
- People have to be put on Methadone if they are injecting – lots can't start on Buprenorphine
- Assessment is a tick box and then you are told you need to start on Methadone “I'll start you on Methadone, then if you give a clean sample you can move to Buprenorphine”
- I went on Suboxone first and opiates went out of my head, then got put on Methadone (because Suboxone too expensive) and I started using
- No – should have a choice but doctors will have the final choice
- I would really try to understand / find out how much people are using then give them a choice
- People should be seen more often by keyworkers
- Individuals must have a choice
- Yes they should be started on Buprenorphine but Buprenorphine is not the same as old Subutex – doesn't perk you up
- I reckon Buprenorphine is a better choice – Methadone is bad for you – it's nasty but you can use on top – it's (a trial) a good idea
- Sometimes people come off Buprenorphine too quickly – feels easy, so think they can just use gear again
- Precipitated withdrawal 10-14 days after stopping Buprenorphine – can get withdrawal symptoms again and panic and use and OD

Staff Comments:

- “I think everyone should be given a choice despite the evidence”
- “I'm an evidence girl” – I'd go with starting on Buprenorphine
- We agree – especially for treatment naïve people
- I think Buprenorphine is safer, so probably a good idea

Question 4

Should there be more studies to test the observation that Buprenorphine is safer than Methadone? What do you think of these 2 options for a study?

Service User Comments:

- I like the second option – but don't see the point of randomisation – if people want to join (the trial) it's because people want Buprenorphine anyway
- I'd accept a trial, but a lot of people wouldn't want a trial
- The risk of a cluster trial is that people will opt out of OST altogether
- Yes, it (the data) should be tested further

- Trials – I wouldn't like to be randomised / If I knew what I wanted I wouldn't want a trial
- People are scared of coming off – wouldn't accept Buprenorphine if they were randomised to it if that's not what they wanted
- I have heard that people on Methadone then changed to Buprenorphine have had problems with their hearts

Staff Comments:

- Anything that will help should be researched – but should look at regional differences in how px are started and compare OD & all cause mortality rates across the country
- RCT would be difficult because of regional differences
- There may be an age difference with younger people preferring to start on Buprenorphine and older people starting on Methadone
- I think they automatically start you on Methadone in Blackpool
- Problem for people collecting OST from specialist prescribers – centralised, it's very hard to get them to attend GP for other health issues – a lot of untreated illnesses – festering e.g. leg ulcers not treated at specialist providers COPD, embolisms, DVT
- Look at link between HOW OST is provided across regions
- Go with RCT because there is a choice
- If there is no choice there will be no engagement with treatment
- Very difficult if the doctor makes the decision (of Buprenorphine or Methadone) regardless of what you want as a keyworker says the client wants – ruins the relationship & the client disengages

Question 5

Any other views or comments on the study?

- What's missing is the psycho social support whilst on scripts – doesn't matter what you are on
- Genuine clients were penalised because of others messing around i.e. Methadone on the streets and doctors insisting on supervised (scripts) all the time so people dropped out (*explanation for increased deaths immediately after treatment with Methadone*)

Facilitators Observations:

Have regional differences in patterns of prescribing been correlated with outcomes NB. Difference between Bristol & Blackpool – In Blackpool reports that more or less everyone starts on Methadone and then switched to Buprenorphine if client insists

Staff at Addiction Dependency Solutions (ADS) Blackpool: Impression that Methadone is 1st line of treatment provided by Delphi which is a private prescribing organisation – no more key working – seen by doctors

Horizons (Blackpool) has contract with 21 day turnaround to start OST – 7 day to start alcohol treatment

Lay Summary and Discussion (provided by MH)

- People who inject drugs (PWID) such as heroin have a risk of death >10 times higher than the general population. Overdose is the most common cause of death among PWID.
- Opioid substitution treatment is the most effective treatment for heroin injectors, most commonly methadone or buprenorphine. Several recent studies have highlighted that there is a period of very high mortality risk in the first few months immediately after treatment cessation – and there may be an elevated risk also in the first few weeks of OST.
- In the UK despite an increase in OST the number of drug related deaths has not fallen and is cause of public health concern.
- We have conducted a series of analyses of patients prescribed OST in primary care to consider how OST might be changed to be more protective and reduce drug related deaths in the population.
- We compare the mortality risk for people prescribed buprenorphine or methadone.

Summary Results

- We analysed data from primary care on 11,033 patients and 26,546 OST episodes – 17,373 methadone and 9173 buprenorphine.
- There were a total of 587 all cause deaths during or within 1 year of finishing OST – giving an overall mortality rate of 1.93 deaths per 100 person-years (nearly 2% annually).
- Information on overdose deaths was available for 5935 patients (54%), 15,600 episodes (9550 methadone and 6050 buprenorphine and involved 87 deaths – mortality rate 0.53 deaths per 100 person-years (0.5% per year).
- There were differences in the mortality risk during periods on and off treatment as shown in the two tables below:-

Period	All cause mortality				Overdose Deaths mortality			
	Deaths	Interval	MR	p	Deaths	Interval	MR	p
On 1-4 weeks OST	48	1541	3.11	<0.0001	8	897	0.89	<0.0001
On rest of time OST	179	18240	0.98		27	9165	0.29	
Off OST 1-4 weeks	165	1730	9.54		18	1044	1.72	
Off OST rest of time	195	8900	2.19		34	5257	0.65	

Interval: person-years at risk; MR mortality rate (deaths/100 person-years – like a %)

Period	All cause				Overdose			
	IRR	95% CI		p	IRR	95% CI		P
On 1-4w	3.17	2.31	4.37	<0.0001	3.03	1.38	6.66	<0.0001
On rest	1 (ref)				1 (ref)			
Off 1-4w	9.72	7.85	12.03		5.85	3.22	10.63	
Off rest	2.23	1.82	2.74		2.20	1.33	3.64	

IRR – incidence rate ratio – relative measure of risk of all cause or OD death compared to being on OST from 4 weeks.

- The lowest risk period is on OST after the first month of OST – compared to this period the risk of OD is 3 times higher in first month, nearly 6 times higher in first month off treatment, and twice as high in the rest of time off OST. Similarly the risk of all cause mortality is 3 times higher in the first month on treatment, nearly 10 times higher the month after OST drop out or discharge, and 2 times higher the rest of the time in the community – compared to the lower risk period during OST from week 4 onwards.
- There are important differences in mortality risk between people on buprenorphine and methadone shown in the tables below:-

Period	OST drug	All cause mortality				Drug related mortality			
		Deaths	Interval	MR	p	Deaths	Interval	MR	p
On 1-4w	Methadone	46	1036	4.44	0.0001	7	563	1.24	0.2561
	Buprenorphine	2	505	0.40	0.0144	1	334	0.30	0.5583
On rest (ref)	Methadone	157	14639	1.07		23	6924	0.33	
	Buprenorphine	22	3601	0.61	n/a	4	2242	0.18	n/a
Off 1-4w	Methadone	150	1091	13.75		10	620	1.61	
	Buprenorphine	15	639	2.35	0.0007	8	424	1.89	0.2084
Off rest	Methadone	153	6054	2.53		28	3379	0.83	
	Buprenorphine	42	2846	1.48	0.9309	6	1878	0.32	0.7011

Period	OST drug	All Cause				Overdose			
		IRR	95% CI		p	IRR	95% CI		P
On 1-4w	Methadone	1 (ref)				0.0001			
	Buprenorp.	0.09	0.02	0.37	0.0144	0.24	0.03	1.96	0.5035
On rest (ref)	Methadone	1 (ref)				1 (ref)			
	Buprenorp.	0.57	0.36	0.89	n/a	0.54	0.19	1.56	n/a
Off 1-4w	Methadone	1 (ref)				1 (ref)			
	Buprenorp.	0.17	0.10	0.29	0.0007	1.17	0.46	2.98	0.2805
Off rest	Methadone	1 (ref)				1 (ref)			
	Buprenorp.	0.58	0.41	0.82	0.9309	0.39	0.16	0.93	0.6382

P values in bold reflect the interaction effect with 3 dfs. Other p values compare IRR at one time with IRR for on rest.

- There is evidence that the risk of overdose and all cause mortality is lower in the first 4 weeks of treatment on buprenorphine compared to methadone. And some evidence that risk of all cause mortality is lower for patients on buprenorphine at other periods as well.
- These mortality rates and measures of difference (IRR) have not been adjusted for differences in patient characteristics and so must be interpreted very cautiously.
- There are many different factors between methadone and buprenorphine treatment.

Duration of Treatment:- The durations of treatment episodes were highly skewed with methadone having longer durations on average than buprenorphine.

Duration	Methadone	Buprenorphine
≥3 weeks	76.30	65.55
≥3 months	53.71	33.44
≥6 months	39.43	21.08
≥1 year	26.71	12.22
Mean (days)	360	173
Median (days)	110	40
N (episodes)	17373	9173

Other Factors:- There are differences also in patient characteristics and GP prescribing habits by:- sex, age, calendar year, co-morbidity, region, co-prescription of benzodiazepines, co-prescription of Gabapentin/Pregabalin, history of self-harm, overdose, alcohol problems, prison or homelessness reported in GP notes, number of OST patients per practice and size of practice.

- We do not have other important information on the patients – such as severity of addiction, recent imprisonment, current housing status, reason for OST.
- However, after adjusting for these factors the differences between methadone and buprenorphine are not removed – if anything they are strengthened for all cause mortality (see table below).

9Period	OST Type	All Cause				Overdose			
		Adjusted IRR	95% CI		p	Adjusted IRR	95% CI		P
On 1-4w	Methadone	1 (ref)			0.0002	1 (ref)			0.2631
	Buprenorp.	0.04	0.01	0.16	0.0136	0.27	0.03	2.07	0.5599
On rest (ref)	Methadone	1 (ref)				1 (ref)			
	Buprenorp.	0.26	0.16	0.43	n/a	0.53	0.18	1.59	n/a
Off 1-4w	Methadone	1 (ref)				1 (ref)			
	Buprenorp.	0.07	0.04	0.12	0.0002	1.32	0.48	3.64	0.2076
Off rest	Methadone	1 (ref)				1 (ref)			
	Buprenorp.	0.21	0.14	0.32	0.5225	0.41	0.16	1.05	0.7174

IRR Incident rate ratio. Adjusted for gender, age, year, comorbidity, region, treatment period and OST type.

- We have less data on OD and so the analyses are slightly underpowered. The differences in mortality risk between Buprenorphine and Methadone follow similar pattern to all cause mortality except for the comparison between methadone and Buprenorphine in first 4 weeks after treatment. However, some of the differences between Buprenorphine and Methadone also may be due to unmeasured confounding - so we need to be careful when interpreting these findings.

We would like to consult with users and drug workers on these findings:-

1. What other important differences could there be between people starting Buprenorphine vs Methadone?
2. What do you think of the findings? What else needs to be done to support hypothesis that Buprenorphine is safer than Methadone?
3. Would you participate, support and be interested in a study that induces all patients in a research study onto Buprenorphine then from 4 weeks allows patients to choose to continue with Buprenorphine or switch to Methadone?
4. What interventions / communication is needed to support such a study with users and drug workers?
5. How do we ensure people in Buprenorphine or Methadone are retained in treatment?
6. Other views/comments