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A cluster RCT of enhanced pharmacy services (EPS) to improve outcomes for patients on methadone maintenance therapy (MMT)

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Background

- 79% of pharmacies in Scotland dispense methadone for over 17,000 patients
- 57% consume it under pharmacist supervision in the pharmacy
- Pharmacists have been shown to increase smoking cessation rates **after behavioural change training**
- A pilot study found that pharmacy delivered **motivational interviewing (MI)** for methadone patients was feasible
- MI is a counselling technique grounded in the stages of change model (Miller, 2001)



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EPS Randomised Controlled Trial

(Nov 2007 – March 2010)

- **Aim:** To identify whether pharmacists trained in MI techniques can improve the outcomes of methadone treatment
- **Setting:** Six NHS areas across Scotland
- **Participants:**
 - Pharmacists dispensing for 10 or more patients on MMT
 - Patients on MMT for ≤ 24 months in this treatment episode
- **Intervention:** Pharmacists were trained in motivational interviewing skills (STRADA), provided with a sign-posting information pack & GP referral forms



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Methods

- Face to face interviews using a structured tool (MAP & treatment satisfaction)
- Primary outcome was **use of illicit heroin**
- Secondary outcomes were:
 - **Patient retention in treatment**
 - **Treatment satisfaction**
 - **Injecting behaviour and risky injecting practice (e.g. sharing needles)**
 - **Physical and psychological health**
 - **Pharmacist attitudes and belief in 'self-efficacy'**
- Six month follow-up (face to face if possible)
- Analysis: intention to treat, main outcomes and additional sub-group analysis



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Results: Patient Recruitment by area

Area	Intervention	Control	Total
Tayside	52	45	97
Ayr	44	20	64
Forth Valley	26	22	48
Lanarkshire	52	31	83
Grampian	61	87	148
Fife	60	42	102
Total	295	247	542



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Results: Patient baseline demographics (n=542)

All participants	Intervention N = 295	Control N = 247
Age in years, mean (SD)	32.3 (7.1)	32.6 (7.3)
Male, n (%)	189 (64.1)	156 (63.4)
Employment, n (%)		
Employed	20 (6.8)	22 (8.9)
Unemployed	273 (92.5)	222 (90.2)
Student	2 (0.7)	2 (0.8)
Length of treatment prior to recruitment in months, median (IQR)	8.9 (3.2, 17.4)	9.0 (3.2, 18.2)

Completed both Questionnaires	Intervention N = 182	Control N = 153
Age in years, mean (SD)	32.7 (7.0)	33.1 (7.0)
Male, n (%)	123 (67.6)	94 (61.4)
Employment, n (%)		
Employed	15 (8.2)	18 (11.8)
Unemployed	165 (90.7)	134 (87.6)
Student	2 (1.1)	1 (0.7)
Length of treatment prior to recruitment in months, median (IQR)	8.9 (3.1, 17.9)	11.0 (3.8, 21.3)



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Results: Primary outcome - Illicit heroin use

Outcome: Illicit heroin use (intention to treat analysis)		Intervention N=182	Control N=153	Crude ¹		Adjusted ²	
				OR (95% CI)	P-value	OR (95% CI)	P-value
Illicit heroin use, n (%)	Baseline Follow-up <i>P-value</i> ³	88 (48.4) 59 (32.4) <0.001	77 (50.3) 48 (31.4) <0.001	- 1.09 (0.67, 1.78)	- 0.73	- 1.06 (0.64, 1.76)	- 0.83
Days of illicit heroin use, median (IQR)	Baseline Follow-up <i>P-value</i> ³	0 (0, 4) 0 (0, 2) <0.001	1 (0, 6) 0 (0, 2) <0.001	-	-	-	-

1.Adjusted for pharmacy and baseline illicit heroin use.

2.Adjusted for pharmacy, baseline illicit heroin use, age, gender and length of treatment prior to recruitment.

3.Within group crude p-value from McNemar's or Wilcoxon signed rank test.

- There was a **significant reduction** in the proportion of patients in both groups using heroin in last 30 days;

Within both groups, there was also a significant reduction in the crude median days of illicit heroin use;

These did **not differ** significantly between the groups.



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Results: Primary outcome - Illicit heroin use

Effect of treatment by different subgroups on illicit heroin use (intention to treat analysis)		Intervention N=182	Control N=153	OR (95% CI) ¹	P-value
Treatment length, n (%)	≤9 months	33 (58.9)	18 (40.0)	1.49 (0.72, 3.10)	0.29
	>9 months	23 (41.1)	27 (60.0)	0.79 (0.39, 1.60)	0.51
Follow-up method, n (%)	Telephone	7 (11.9)	12 (25.0)	0.43 (0.14, 1.30)	0.13
	Face-to-face	40 (67.8)	28 (58.3)	0.97 (0.50, 1.89)	0.93
	Patient completed	12 (20.3)	8 (16.7)	2.67 (0.85, 8.41)	0.09
Length of follow-up, n (%)	≤7 months	34 (60.7)	27 (60.0)	0.99 (0.50, 1.97)	0.99
	>7 months	22 (39.3)	18 (40.0)	1.10 (0.51, 2.41)	0.80

1. Adjusted for pharmacy and baseline illicit heroin use.

- Sub group analysis by length of time in treatment, method of follow-up and length of follow-up revealed **no significant** differences between groups



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Results: Primary outcome – Use of other illicit drugs

Outcome: Other illicit drug use (intention to treat analysis)		Intervention N=182	Control N=153	Crude ¹		Adjusted ²	
				OR (95% CI)	P-value	OR (95% CI)	P-value
Other illicit drug use, n (%)	Baseline Follow-up <i>P-value</i> ³	133 (73.1) 123 (68.3) 0.13	115 (75.2) 101 (67.8) 0.06	- 1.10 (0.64, 1.87)	- 0.74	- 1.06 (0.61, 1.86)	- 0.83

1.Adjusted for pharmacy and baseline other illicit drug use.

2.Adjusted for pharmacy, baseline other illicit drug use, age, gender and length of treatment prior to recruitment.

3.Within group crude p-value from McNemar's test.

- Reduction over time in both groups but this was **not significant**;

No significant differences between groups;



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Results: Secondary outcome - Retention in treatment

Retention in treatment (i.e. on MMT) (<i>intention to treat analysis</i>) ³	Intervention N=285	Control N=240	Crude ¹		Adjusted ²	
			OR (95% CI)	P-value	OR (95% CI)	P-value
Yes	250 (87.7)	194 (80.8)	-	0.21	1.76 (0.55, 5.64)	0.34
No	9 (3.2)	16 (6.7)	2.04 (0.67, 6.22)			
Don't know ⁴	26 (9.1)	30 (12.5)				

1.Adjusted for pharmacy.

2.Adjusted for pharmacy, age, gender and length of treatment prior to recruitment.

3.Excluding 17 patients who died during follow-up or people who were discharged from service for unknown reason

4.'Don't know' category excluded from clustered analysis.

- Treatment retention was **high** overall (84%);
- This was **higher** in intervention group than in the control group but this did not reach statistical significance;
- Similar numbers in each group left or moved from their original pharmacy.



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Results: Primary outcome – Frequency of injecting

Outcome		Intervention N=182	Control N=153	Crude ¹		Adjusted ²	
				OR (95% CI)	P-value	OR (95% CI)	P-value
Injecting n (%)	Baseline	42 (23.1)	41 (27.0)	-	-	-	-
	Follow-up <i>P-value</i> ³	30 (16.5) 0.06	19 (12.4) <0.001	1.58 (0.82, 3.08)	0.17	1.55 (0.77, 3.10)	0.22
Frequency of injecting median (IQR)	Baseline	0 (0, 0)	0 (0, 1)	-	-	-	-
	Follow-up <i>P-value</i> ⁴	0 (0, 0) 0.18	0 (0, 0) <0.001				

1.Adjusted for pharmacy and baseline injecting behaviour.

2.Adjusted for pharmacy, baseline injecting behaviour, age, gender, and length of treatment prior to recruitment.

3.Within group crude p-value from McNemar's test.

4.Within group crude p-value from Wilcoxon signed rank test.

- Proportions injecting and frequency of injecting **decreased** in both groups but only reached significance in the control group;
- These **did not differ significantly** between groups at either time point.



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Results: Secondary outcomes – Physical health

Outcome (ITT analysis)		Intervention N=182	Control N=153	Crude ¹		Adjusted ²	
				Parameter Estimate (95% CI)	P- value	Parameter Estimate (95% CI)	P- value
Physical health, Mean (SD)	Baseline Follow- up <i>P-value</i> ³	12.8 (7.2) 13.9 (7.4) 0.02	12.7 (7.7) 12.9 (7.5) 0.99	1.17 (-0.16, 2.50)	0.08	1.39 (0.02, 2.75)	0.046

1. Adjusted for baseline outcome.

2. Adjusted for baseline outcome, age, gender, length of treatment prior to recruitment and pharmacy.

3. Within group crude p-value from Wilcoxon test.

Note: Higher physical and psychological health score indicates *poorer* health; Higher treatment satisfaction scores indicates *better* treatment satisfaction

- At follow-up, this was significantly **poorer** in the **intervention group** but remained unchanged in controls.



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Results: Secondary outcomes – Psychological health

Outcome (ITT analysis)		Intervention N=182	Control N=153	Crude ¹		Adjusted ²	
				Parameter Estimate (95% CI)	P- value	Parameter Estimate (95% CI)	P- value
Psychological health, mean (SD)	Baseline	14.6 (9.5)	15.0 (9.7)	0.76 (-1.11, 2.63)	0.42	0.68 (-1.26, 2.63)	0.49
	Follow-up <i>P-value</i> ³	16.2 (10.4) <i>0.01</i>	15.6 (10.4) <i>0.42</i>				

1. Adjusted for baseline outcome.

2. Adjusted for baseline outcome, age, gender, length of treatment prior to recruitment and pharmacy.

3. Within group crude p-value from Wilcoxon test.

Note: *Higher* physical and psychological health score indicates *poorer* health; *Higher* treatment satisfaction scores indicates *better* treatment satisfaction

- Did not differ between the groups at follow-up;

However, this **deteriorated** by follow-up in intervention patients.



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Results: Secondary outcomes – Treatment satisfaction

Outcome (ITT analysis)		Intervention N=182	Control N=153	Crude ¹		Adjusted ²	
				Parameter Estimate (95% CI)	P- value	Parameter Estimate (95% CI)	P- value
Treatment satisfaction, mean (SD)	Baseline Follow- up <i>P-value</i> ³	27.6 (5.0) 28.5 (4.9) <i>0.03</i>	28.7 (4.3) 28.4 (4.8) <i>0.26</i>	0.62 (-0.41, 1.66)	0.24	0.52 (-0.59, 1.64)	0.36

1. Adjusted for baseline outcome.

2. Adjusted for baseline outcome, age, gender, length of treatment prior to recruitment and pharmacy.

3. Within group crude p-value from Wilcoxon test.

Note: Higher physical and psychological health score indicates poorer health; Higher treatment satisfaction scores indicates better treatment satisfaction

- No significant difference between the groups at follow-up;
- Improvements evident for the intervention group at follow-up but no change for controls.



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Supplementary analysis

- Main outcomes by number of training sessions attended by pharmacists;
- Changes in methadone dose and supervision arrangements at follow-up;
- Treatment satisfaction by pharmacy;
- Per protocol analysis.



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Recap of the results

- There was a reduction in heroin and illicit drug use overall but no difference between groups;
- Retention in treatment was high overall but no difference between groups;
- Treatment satisfaction improved in intervention group but no change in controls;
- Physical and psychological health was poorer in the intervention group at follow-up.



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Discussion

- **Intervention had insufficient power to affect drug use outcomes. Possible reasons:**
 - difficulty recruiting target number of patients in treatment for less than 9 months;
 - limited pharmacist fidelity to the intervention;
 - differential rate of pharmacist recruitment across areas;
 - poorer than expected follow-up rate (62%).
- **However, it **did improve** treatment retention and satisfaction.**



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Discussion

- Deterioration in physical health in intervention group – increased awareness/sensitivity?;
- Deterioration mental health in intervention group – as above or related to stage in treatment?;
- Contrary to previous MMT research;
- In-line with other pharmacy intervention research;
- Increased treatment satisfaction in intervention group correlates with increased treatment retention.



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Implications of the results

- Results demonstrate that there is some benefit to the drug treatment sector if pharmacists provide an enhanced service;
- Further work is needed to:
 - explore why intervention patients were more satisfied and had higher rates of retention in treatment;
 - design a service which would result in improvements in clinical outcomes;
 - to explore why physical and psychological health deteriorated.



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