

Supervised co-prescription of heroin to treatment-resistant heroin addicts is more effective than treatment with methadone alone

van den Brink W, Hendriks VM, Blanken P, *et al.* Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials. *BMJ* 2003;**327**:310.

Q Is supervised prescription of heroin successful in treating people addicted to heroin, who have not benefited from methadone maintenance treatment?

METHODS

-  **Design:** Two randomised controlled trials.
-  **Allocation:** Open.
-  **Blinding:** Open.
-  **Follow up period:** 12 months.
-  **Setting:** Methadone maintenance programmes in 6 cities in the Netherlands; recruitment from 15 July 1998 to 1 October 2000.
-  **Patients:** 549 people aged ≥25 years; using illicit heroin daily or almost daily, and not voluntarily abstaining from heroin for ≥2 months in the previous year. Participants must have regularly attended methadone maintenance programmes during the previous 6 months and used methadone at a dose of ≥50mg/day for the inhaling heroin RCT and at ≥60mg/day for the injecting heroin RCT for a minimum uninterrupted period of 4 weeks in the previous 5 years. People were allocated to the injecting RCT, or the inhaling RCT, depending on how they normally used heroin.
-  **Intervention:** Inhaling RCT: 375 people randomised to: 12 months of methadone alone (maximum 150 mg/day); 12 months of methadone plus inhalable heroin (maximum 1000 mg/day); or 6 months of methadone alone followed by 6 months of methadone plus inhalable heroin. Injecting RCT: 174 people randomised to: 12 months of methadone alone, or 12 months of methadone plus injectable heroin (maximum 1000 mg/day).
-  **Outcomes:** A positive treatment response defined as: a ≥40% improvement compared with baseline in at least 1 of the following 3 measures: physical functioning (defined according to the Maudsley addiction profile), mental health (defined according to the symptom checklist (SCL-90)), or social integration (based on the self reported number of days in the previous month in which the participant was involved in criminal activities, and had ≥30 minutes contact with a non-user), provided that any improvement was not associated either with a serious (≥40%) deterioration in function of either of the other outcome measures or a large (≥20%) increase in cocaine or amphetamines usage.
-  **Patient follow up:** 94%.

MAIN RESULTS

In both RCTs, treatment with methadone plus heroin produced more positive responses in at least one of the physical, mental, or social outcome measures compared with methadone alone (see table 1).

CONCLUSIONS

Supervised co-prescription of heroin to treatment-resistant heroin addicts was more effective than treatment with methadone alone.

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Commentary

Heroin dependence is a major public health problem and has high social costs. Prescribing pharmaceutical heroin (diamorphine) to heroin addicts has been seen in some countries as a way of reducing the associated harms. The most common form of substitution drug for heroin dependence is methadone. However, despite the benefits of oral methadone,¹ there are individuals who appear not to want it nor benefit from it. It has been suggested, therefore, that pharmaceutical heroin should be prescribed to these individuals.

The evidence base for the effectiveness of prescribing heroin is small. Previous research includes four small scale studies conducted in the UK,²⁻⁵ one large cohort study conducted in Switzerland,⁶ and one small randomised trial conducted in Geneva.⁷ While the results of these studies suggest that prescribing heroin is feasible, improves health, and reduces illicit drug use and crime, the lack of control groups limits interpretation. Only two studies used a randomised controlled design. Without suitable control groups, it is not known whether similar results might have been achieved with oral methadone or if the results are due to the additional psychosocial interventions, or both.

van den Brink and colleagues should be congratulated on using a scientifically rigorous design to examine the effectiveness of prescribing heroin. Furthermore, this is the first study of a non-injectable preparation of heroin and to use non-injecting drug users. They found that those receiving a co-prescription of heroin made significantly better improvements than those receiving methadone only.

These trials provide useful information, but, since the treatment context differs in other countries, it is unclear how far results from these trials are generalisable. Patient interest in receiving heroin will be influenced by the usual delivery of treatment (eg supervised consumption of prescription or dispensed daily for unsupervised consumption at home) and by the history, quality, accessibility, and availability of treatments in their particular country.

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NOTE

There were a number of methodological limitations that were identified by the authors, such as reliance on self reported outcome measures, and difference in settings between the treatment groups.

Table 1 Outcome measures in the inhaling and injecting RCT.

	Inhaling			Injecting		
	Methadone alone (n = 139)	Methadone plus heroin (n = 117)	ARR (95% CI)	Methadone alone (n = 98)	Methadone plus heroin (n = 76)	ARR (95% CI)
Completed 12 months treatment (%)	121 (87)	80 (68)	18.7 (8.8 to 28.6)	83 (85)	55 (72)	12.3 (0.2 to 24.5)
Response rated ITT (%)	37 (27)	58 (50)	22.8 (11.0 to 34.6)	31 (31)	42 (56)	24.3 (9.6 to 39.0)
Sustained* response at 12 months (%)	6 (4)	26 (22)	17.9 (9.7 to 26.1)	11 (12)	19 (25)	13.1 (1.5 to 24.7)

*Sustained responders were people who achieved a positive response before the 12 month assessment and remained responders throughout the trial.