

this protection comes from exposure to common infections.

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Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials

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Abstract

Objective To determine the cost utility of medical co-prescription of heroin compared with methadone maintenance treatment for chronic, treatment resistant heroin addicts.

Design Cost utility analysis of two pooled open label randomised controlled trials.

Setting Methadone maintenance programmes in six cities in the Netherlands.

Participants 430 heroin addicts.

Interventions Inhalable or injectable heroin prescribed over 12 months. Methadone (maximum 150 mg a day) plus heroin (maximum 1000 mg a day) compared with methadone alone (maximum 150 mg a day).

Psychosocial treatment was offered throughout.

Main outcome measures One year costs estimated from a societal perspective. Quality adjusted life years

(QALYs) based on responses to the EuroQol EQ-5D at baseline and during the treatment period.

Results Co-prescription of heroin was associated with 0.058 more QALYs per patient per year (95% confidence interval 0.016 to 0.099) and a mean saving of €12 793 (£8793, \$16 122) (€1083 to €25 229) per patient per year. The higher programme costs (€16 222; lower 95% confidence limit €15 084) were compensated for by lower costs of law enforcement (-€4129; upper 95% confidence limit -€486) and damage to victims of crime (-€25 374; upper 95% confidence limit -€16 625). The results were robust for the use of national EQ-5D tariffs and for the exclusion of the initial implementation costs of heroin treatment. Completion of treatment is essential;

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having participated in any abstinence treatment in the past is not.

Conclusions Co-prescription of heroin is cost effective compared with treatment with methadone alone for chronic, treatment resistant heroin addicts.

Introduction

Though treatment supplemented with heroin improves the physical, mental, and social functioning of heroin addicts,¹⁻³ we do not know whether this practice is efficient from a societal perspective. Costly daily practice guidelines and safety procedures must be followed to enable the prescription of heroin,³ yet costs savings may result from reduced use of health care and less criminal behaviour. We therefore performed a cost utility analysis alongside two Dutch trials comparing medical co-prescription of heroin with prescription of oral methadone alone.

Methods

Design of the clinical studies

Full details of the two Dutch heroin trials have been reported.³ Eligible patients were recruited from existing methadone maintenance programmes in six cities between July 1998 and October 2000 and randomised to treatment with methadone plus heroin (experimental group) or with methadone alone (control group). Participants in the experimental group received their methadone before the first administration of heroin and were allowed a maximum of 400 mg heroin each visit and 1000 mg a day. At baseline and every two months during the treatment period trained interviewers assessed physical functioning, mental health, and social integration.

We performed the economic analysis with data from 430 patients who were intended to receive the experimental or control treatment for a full year. We analysed the data from a societal perspective because the cost consequences of this intervention may well extend beyond the domain of health care.

Health outcomes

We used quality adjusted life years (QALYs) as our primary outcome measure, based on the EuroQol EQ-5D

questionnaire, completed at baseline and at months 6, 10, and 12 during treatment. The utility of each observed health score profile on the EQ-5D is based on the time trade-off elicitation technique from interviews with adults from the UK general population. Utilities range from -0.594, indicating serious health problems to unity, indicating no problems at all. Death takes the value of zero.

We derived QALYs from multiplying the utility of each health state by the time in between the actual observation and the previous one and summing the results over the 12 month treatment period.

Use of resources, programme related travel, and crime

We used clinical report forms and the European version of the addiction severity index (EuropASI)⁴ to collect follow-up data on the use of healthcare resources, travel related to the programme, and illegal activities. The EuropASI was completed at the same intervals as the EQ-5D. We measured travel by multiplying the number of visits with twice the standardised distances to the relevant locations.

The EuropASI identifies the number of illegal activities resulting in law enforcement and the number of days of illegal activity by type of crime. However, it does not provide data on the number, type, and victims of illegal activities needed to estimate the potential damage to civilians or companies. Therefore, we performed a substudy using similar EuropASI interview conditions during February and March 2004 in 51 new patients. The patients matched the inclusion criteria of the original trials, were also in their first year of experimental treatment, and reported at least one day of acquisitive crime in the month before participating in the programme.

Unit costing and costs

The costs included the direct medical costs of health care within the programme and elsewhere. The programme costs cover the costs of healthcare staff, security personnel, materials, overheads, and the depreciations (over 30 years, including interest) of initial rebuilding costs of the heroin dispensation facility. Furthermore, the direct personal costs of health related travel and the indirect costs of police investi-

Table 1 Comparison of per patient costs (€) between treatment groups. Figures are means; medians (interquartile ranges)

Type of costs	Methadone plus heroin (n=193)	Methadone alone (n=237)
Medical costs:		
Maintenance programme:		
Methadone	207; 200 (152-263)	216; 213 (146-274)
Heroin	559; 358 (265-818)	—
Intakes and additional care	16 868; 18 798 (11 036-23 422)	1196; 1318 (1072-1476)
Total programme costs	17 634; 19 600 (11 550-24 558)	1412; 1534 (1195-1748)
Out of institution consultations	39; 0 (0-35)	52; 0 (0-35)
Institutional, outpatient consultations	387; 0 (0-177)	259; 0 (0-227)
Institutional, inpatient stays	734; 0 (0-0)	816; 0 (0-0)
Total other healthcare costs	1160; 52 (0-308)	1126; 52 (0-377)
Law enforcement costs:		
Police investigations	5091; 0 (0-7314)	6748; 0 (0-7314)
Prosecution and adjudication	1946; 0 (0-0)	4172; 0 (0-0)
Imprisonment and resettlement	1719; 0 (0-0)	1965; 0 (0-580)
Total law enforcement costs	8756; 0 (0-9752)	12 885; 2438 (0-14 628)
Costs of damage to victims	9617; 0 (0-0)	34 991; 0 (0-28 007)
Health related travel	600; 637 (428-788)	146; 161 (131-181)
Total costs	37 767; 26 104 (18 544-39 554)	50 560; 11 847 (1987-51 530)

gations, prosecution, adjudication, imprisonment, resettlement, and damage to victims were included. See bmj.com for details.

Statistical analysis

Volume and costs data for the first year after randomisation were averaged per patient. With a one year treatment period no discounting of costs and effects was performed. We hypothesised that in the experimental group, programme costs and related out-of-pocket expenses would be higher and other healthcare costs and costs related to crime would be lower. Because of skewed distributions, we assessed mean differences between groups based on bias-corrected and accelerated non-parametric bootstrapping (see bmj.com). Point estimates of mean total costs and mean QALYs were used to calculate the incremental cost effectiveness ratio for experimental versus control treatment, again accounting for sampling variability. We performed multi-way sensitivity analyses to investigate the robustness of the cost acceptability of experimental treatment (for willingness to pay values up to €50 000) to plausible changes in key unit costs and to a Dutch time trade-off based health utility algorithm. We performed a subgroup analysis for patients with or without participation in abstinence-oriented treatment before baseline as such participation seemed to predict treatment effect.⁵ Another subgroup analysis was performed for patients who did or did not complete the 12 month treatment schedule.

Results

Patients' characteristics and health outcomes

Experimental (n = 193) and control (n = 237) patients were similar at baseline. Major sources of income were social welfare (47.5%), disability benefit or pension (11.7%), and illegal activities or prostitution (28.3%). Sixty one per cent had previously attempted at least one treatment based on abstinence. On average, they spent €900 (£610; \$1133) a month on drugs. About once every three days, patients engaged in illegal activities to acquire money or drugs.

One hundred and thirty five (70%) in the experimental group and 204 (86%) in the control group completed the full year of treatment. One hundred (51.8%) participants in the experimental group responded to treatment compared with 68 (28.7%) in the control group. Two deaths occurred, one in each group, both unrelated to treatment. Over one year, mean QALYs per patient were significantly higher for experimental than control patients with a mean difference of 0.058 (95% confidence interval 0.016 to 0.099) (see bmj.com).

Use of resources and illegal activity

Methadone intake was similar in both groups, at about 19 g a year. Experimental patients received 143 g heroin on average. The use of healthcare resources outside the programme was low with 8.6 and 7.4 consultations on average a year for experimental and control patients, respectively, and with each patient spending less than half a week as an inpatient (see bmj.com).

Participants in the experimental group engaged in criminal activities less often than those in the control group. They reported fewer days with crime against

Table 2 Differential costs per patient (€) in treatment groups (methadone plus heroin v methadone alone). Figures are differential mean costs (95% confidence limit or interval based on bias corrected and accelerated non-parametric bootstrapping; one or two tailed, depending on hypothesis)

	Cost (€)
Total programme costs	16 222 (lower limit 15 084; P<0.0001)
Total other healthcare costs	34 (upper limit 659)
Total law enforcement costs	-4129 (upper limit -486; P=0.03)
Costs of damage to victims	-25 374 (upper limit -16 625; P<0.0001)
Health related travel	456 (lower limit 417; P<0.0001)
Total costs	-12 793 (-25 229 to -1 083; P=0.032)

property (10.3 v 37.5), were arrested less often (2.1 v 2.8 times a year), were less frequently convicted (0.25 v 0.54 times), and stayed in prison almost one day less (11.7 v 12.5 days).

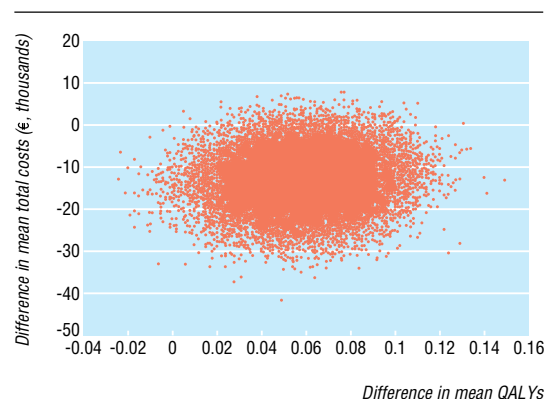
After we excluded patients with missing data or with more than 200 illegal activities a month (n = 47 remaining), the mean number of crimes against property per day of illegal activity with possible damage to third parties amounted to 3.4, with 2.5 (74%) crimes against companies and 0.9 (26%) against civilians.

Costs and cost utility

Tables 1 and 2 show the mean and median costs per patient. Mean cost differences between the groups resulted from the maintenance programme, law enforcement, victim damage, and travel. The mean total net savings amounted to €12 793. With these net savings and the higher mean QALYs, the experimental treatment was superior to the control treatment (figure).

Sensitivity and subgroup analyses

The dominance of the experimental treatment persisted when we used Dutch time trade-off based health utility values rather than UK values, and also when we excluded the costs of rebuilding existing treatment centres from the costs of experimental treatment. Having participated in any abstinence-oriented treatment in the past did not substantially influence the effectiveness of the experimental treatment, and completion of treatment strongly influenced the programme's efficiency. See bmj.com for details of sensitivity and subgroup analyses.



Cost effectiveness plane, showing differences between experimental treatment (methadone plus heroin) and control treatment (methadone alone) after 25 000 bootstrap replications. Vertical axis shows differences in mean total costs, horizontal axis shows differences in mean QALYs. The experimental treatment generated lower costs and more QALYs than the control treatment in 98% of all replications

What is already known on this topic

Supervised medical prescription of methadone plus heroin is feasible, safe, and effective with clinically relevant improvements in physical health, mental status, and social functioning (including substantial reductions in criminal behaviour) in chronic, treatment resistant heroin addicts

What this study adds

From a societal perspective supervised medical prescription of methadone plus heroin is less costly than methadone maintenance treatment

The medical co-prescription of heroin is beneficial in terms of quality adjusted life years (QALYs)

Medical co-prescription of heroin is cost effective in patients who have previously failed to respond to methadone treatment

Discussion

The costs of methadone plus heroin were higher than with methadone alone, but these higher costs were offset by savings for law enforcement and victim damage. The cost utility results are strikingly in favour of the experimental treatment at acceptable willingness-to-pay values per QALY. Others have found similar offsets of the higher costs of medical care by reduced costs of law enforcement and reduced costs of crime against property.^{6,7} However, potential savings from reduced crime might not always turn into actual savings—for instance, due to labour contracts. Our results cannot be generalised to heroin addicts who have not previously received methadone maintenance treatment.

This economic evaluation of heroin treatment was part of a randomised trial rather than within a single group before and after study.⁶ Compared with other addiction studies that included methadone maintenance treatment as reference care, we used a long observation period of 12 months rather than a potentially suboptimal⁸ six months.⁹ Furthermore, we took a societal rather than provider perspective,^{9,10} thereby paying attention to outcomes such as reductions in crime that also matter to policy makers.^{11,12}

Most patients need lifetime treatment with methadone plus heroin,³ which is consistent with the chosen depreciation period for the initial rebuilding costs. In the long run, however, these rebuilding costs might have a larger impact on the costs per visit because the yearly number of visits may decrease. To limit the future impact of the capital costs, the unit should in time develop into a multifunctional care facility including, for instance, treatment of patients with HIV.

Limitations

The EQ-5D is generally accepted as an instrument of choice in economic evaluations. Little is known, however, about its reliability and validity in drug addicts. Although our conclusions may be robust, further study is needed into the use of the EQ-5D in such patients. The estimate of cost effectiveness of the

experimental treatment is conservative as we used UK time trade-off based health utility values.

The modest difference in costs of law enforcement between experimental and control patients compared with the difference in costs of damage to victims may result from law enforcement related to offences committed before study inclusion. If so, the real economic benefit from avoided crime in case of experimental treatment is underestimated.

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Endpiece

The road to fame

There is not a more expeditious road to fame than to speak or write unintelligibly, but with plausibility; nor a more certain mode of doing so, than by a person's not understanding his own meaning, since with the vulgar, the conclusion will ever appear valid, that he who is above their comprehension must be a great man. For this reason we have heard of late, irritability, sensibility, spasm, incitement, and collapse suggested as the causes of most disorders, with all the parade of affected knowledge, but real ignorance.

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