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Cost Effectiveness of Emergency Department-Initiated Treatment for Opioid Dependence

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Abstract

Background and Aims—In a recent randomized trial, patients with opioid dependence receiving brief intervention, Emergency Department (ED)-initiated buprenorphine, and ongoing follow up in primary care with buprenorphine (buprenorphine) were twice as likely to be engaged in addiction treatment compared with referral to community-based treatment (referral) or brief intervention and referral (brief intervention). Our aim was to evaluate the relative cost effectiveness of these 3 methods of intervening on opioid dependence in the ED.

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Trial Registration Information: Models of screening, brief intervention with a facilitated referral to treatment (SBIRT) for opioid patients in the emergency department; ClinicalTrials.gov Identifier: NCT00913770.

Dr Fiellin reported that he has received honoraria from Pinney Associates for serving on an external advisory board monitoring the diversion and abuse of buprenorphine. The authors have no other competing interests to report.

Design—Measured healthcare use was converted to dollar values. We considered a health care system perspective and constructed cost effectiveness acceptability curves that indicate the probability each treatment is cost effective under different thresholds of willingness-to-pay for outcomes studied.

Setting—An urban ED in the USA.

Participants—Opioid-dependent patients 18 years or older.

Measurements—Self-reported 30-day assessment data were used to construct cost effectiveness acceptability curves for patient engagement in formal addiction treatment at 30 days and the number of days illicit opioid free in the past week.

Findings—Considering only health care system costs, cost effectiveness acceptability curves indicate that at all positive willingness-to-pay values, ED-initiated buprenorphine treatment was more cost-effective than brief intervention or referral. For example, at a willingness-to-pay threshold of $1000 for 30-day treatment engagement, we are 79 percent certain ED-initiated buprenorphine is most cost effective compared with other studied treatments. Similar results were found for days illicit opioid free in the past week. Results were robust to secondary analyses that included patients with missing cost data, included crime and patient time costs in the numerator, and to changes in unit price estimates.

Conclusion—In the United States, emergency department-initiated buprenorphine intervention for patients with opioid dependence provides high value compared with referral to community-based treatment or combined brief intervention and referral.

In 2014 close to 2 million Americans had prescription opioid use disorder and 435,000 were current heroin users(1), with a record 28,647 overdose deaths attributed to either prescription opioid or heroin overdose(2). Emergency department use is common among these groups; In 2011, there were an estimated 420,000 prescription opioid related emergency department visits and 258,482 heroin related visits (3). This epidemic has significant health consequences and burden on individuals, family members and society. Although multiple effective treatments are available, survey research indicates less than 10% of individuals needing treatment related to drug or alcohol use received treatment in a specialty facility (4). Limited access to the most effective form of treatment - pharmacotherapy - and a fragmented delivery system are often cited as barriers to individuals receiving treatment (5,6). The relative costs and benefits of potential strategies to engage untreated patients is of importance to insurers, providers and society as more individuals need these services.

In a recent clinical trial emergency department (ED) patients with a DSM-IV diagnosis of opioid dependence were randomized to one of three treatment groups: brief intervention combined with ED-initiated buprenorphine/naloxone and ongoing primary care-based buprenorphine/naloxone; brief intervention along with referral to community-based treatment; and referral alone (7). The group receiving ED-initiated buprenorphine/naloxone had improved outcomes compared to the other two treatments studied. Yet, ED-initiated buprenorphine has yet to become common practice in the ED. To further inform ED managers, physicians and policy makers about the value of ED-initiated buprenorphine, we evaluated the costs and effects observed in this trial. Base-case analysis considered only

health care system costs and assessed the cost effectiveness of two clinical benefits considered in the trial 30-day post-baseline: whether the patient was engaged in formal addiction treatment on the 30th day after randomization and the number of days illicit opioid free in the past week at 30 days.

Methods

Design

The randomized clinical trial on which this study is based compared the efficacy of three interventions among 329 opioid dependent patients treated at an urban teaching hospital ED. These interventions were: 1) screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral to primary care for 10-week follow-up (herein referred to as buprenorphine); 2) screening, brief intervention, and facilitated referral to community-based treatment services (brief intervention); and 3) screening and referral to treatment (referral). Detailed information on the clinical trial design, treatment protocols and substance use outcomes has been published(7). In this study we limited base case analyses to 244 (74%) patients who completed the 30-day assessment where self-report of health care utilization, crimes committed and self-reported number of days of illicit opioid use in the past 7 days were collected.

Costs

The trial tested outcomes among three interventions, all of which included screening for opioid dependence. Because we conducted an incremental cost effectiveness analysis, comparing the incremental cost and incremental benefit across groups, the cost of screening was not included. This is most useful to an ED or health care payer committed to screening for opioid dependence in ED patients.

Costs for individual interventions performed during the enrollment ED visit were not collected prospectively. These costs include time for the brief intervention, activities related to referral to treatment, support activities, and, where relevant, buprenorphine administration. The Brief Interventions were audiotaped and the mean (SD) duration for the ED-initiated buprenorphine, brief intervention and referral group were 10.2(4.1), 11.0(4.5) and 2.0(1.3) minutes respectively. In the case of ED-initiated buprenorphine and brief intervention this made reference to the patient's motivation to use the provided referral services and in the case of the referral group it included distribution of a handout listing providers in the area. Although we did not measure staff activities related to referral to treatment or other support activities (e.g., record keeping, reading the patient's chart, locating patients), Bray et al. examined time spent on these activities in a small number of observations from seven screening, brief intervention, and referral to treatment (SBIRT) studies(8). They found mean staff time spent on referral to treatment in the outpatient or ED setting was 5–18 minutes and time spent on support activities for brief intervention was 7–10 minutes. We assumed a duration for both arranging referrals and support activities of approximately 19–20 minutes for the ED-initiated buprenorphine and brief intervention group, and 13 minutes for the referral group. We assumed the ED-initiated buprenorphine group required an additional 15 minutes to administer buprenorphine in the ED and 5

minutes for related patient education (for a total of 20 additional minutes, compared to the brief intervention group). The above assumptions yielded an intervention duration of 50 minutes, 30 minutes and 15 minutes for ED-initiated buprenorphine, brief intervention and referral respectively. Bureau of Labor Statistics' wage plus fringe benefit(9) estimates for healthcare social workers were multiplied by intervention duration to calculate costs, except for the 15 minutes allocated to buprenorphine/naloxone administration, where physician wages were used (10; see electronic-only appendix for more detail). Here and when calculating office-based use of buprenorphine/naloxone, we used the actual 2015 hospital drug acquisition price for generic buprenorphine/naloxone, although we varied this price in sensitivity analyses(11).

Health care utilization data included self-report of all inpatient, outpatient, addiction-related medication, and ED-based services used at any point between study enrollment and the 30th day following randomization(12). Crimes studied in sensitivity analyses included self-reports of assault, robbery, theft, burglary, shoplifting/vandalism and fraud. Although there is no gold standard to assess the validity of self-report of criminal behavior, studies have found relatively high correlation between self-reported arrest information and police contact(13). Health care price weights(14,15,16) were based on published estimates, as were the per-offense costs of specific crimes(17). All price weights are noted in electronic-only appendix.

Patient time costs were based on individual self-reported travel time to providers and, based on times reported in national surveys, assumed treatment duration of 0.5 hours, 0.25 hours and 4 hours for office-based, addiction treatment center and ED visits respectively(18,19). For each inpatient and residential treatment night, we assumed treatment duration of eight hours, but did not include travel time. Because about half of enrollees reported no or part time work hours in the previous 30 days during the baseline interview, we conservatively used the minimum wage in Connecticut to convert times to patient time costs. In all cases prices were converted to real 2013 dollars using the Consumer Price Index (CPI-U).

Effects

The primary study outcome, enrollment in and receiving formal addiction treatment on the 30th day after randomization, was assessed by direct contact with the facility, clinician, or both. A secondary clinical endpoint, change in number of days of illicit opioid use in the past 7 days based on self-report, was also evaluated(20). Data on all outcomes were collected by research associates not involved in the patients' ED care.

Analysis

We calculated average health care costs, crime costs and patient time costs for each treatment group. Due to highly skewed cost data, to test for cost differences between groups we used nonparametric bootstrap with 1000 resamples and rank ordered differences in mean costs and calculated nonparametric 95% confidence intervals. We derived p-values using the nonparametric percentile method and determined the percent of bootstrap estimates where the difference in means was less than zero, and doubled to conduct a two-sided test(21,22,23). To test for differences in non-economic effects between groups, traditional parametric t-tests were used.

To illustrate the uncertainty around costs and effects, we used nonparametric bootstrap methods to construct cost effectiveness acceptability curves, which allow us to simultaneously evaluate the relative cost effectiveness of the three treatment groups while varying assumptions about a decision maker's maximum willingness-to-pay to achieve the reported outcome (24,25). This is useful when the willingness-to-pay is unknown or differs among decision makers. At each willingness-to-pay value considered we calculated the net monetary benefit for each treatment equal to (W*E)-C, where W represents the relevant willingness-to-pay, E the effect and C the cost. For each treatment, we report the share of 1000 bootstrap replicates for which that treatment had the maximum net benefit (shares for the three treatments sum to unity). Thus, the cost effectiveness acceptability curve provides estimates of the probability each treatment is the most cost effective at different willingness-to-pay values.

In base case analyses only health care treatment costs were included when constructing cost effectiveness acceptability curves. Although we calculated crime costs and patient time costs, we did not include these in our base case analyses. Decision makers may already implicitly consider crime costs when determining their maximum willingness-to-pay for the outcome studied. A second reason we excluded crime costs from our base case analysis is it is likely to be underestimated in self-reports. Related to patient time costs, although they should be considered when evaluating cost effectiveness of competing treatments, decision makers may find an analysis that considers these costs less useful when choosing among treatments. We take a conservative approach and exclude these from our base case cost calculations. In secondary analysis we incorporate both crime costs and patient time costs in the numerator.

Secondary analyses also address concerns regarding missing cost data. For 327(99.4%) of randomized patients, verified information regarding treatment engagement is available. Although 83 patients had missing cost data, the reason for failing to complete the 30-day assessment is known for half of these patients: 32(38.6%) were in inpatient treatment and 10(12.1%) were incarcerated. In a robustness check we assumed incarcerated patients used no health care services in the past 30 days, and that patients in inpatient treatment used 14 days residential treatment in the past 30 days, with no other health care use. Although incarcerated patients may have used health care, we assumed no health care use because we had no information on these patient's treatment, and this was the most conservative assumption since fewer individuals were incarcerated in the ED-initiated buprenorphine group compared to the other groups(7). For the remaining 41 patients, we assumed mean, within group, health care costs.

Sensitivity analyses related to unit price assumptions included changes to addiction specialty treatment price (+20%; −20%), general health care treatment price (+20%; −20%), and buprenorphine price (+50%; −50%).

Finally, although all three of the interventions studied included screening, some emergency departments may not currently screen for opioid dependence and thus the cost of screening may be of interest. We take a post-hoc service delivery approach and retrospectively estimate the cost of screening per enrollee.

The Yale University School of Medicine Institutional Review Board approved this study. This trial was registered, with no data analysis conducted, after 11 patients had been enrolled due to administrative delay. Analyses were conducted using SAS 9 and STATA 11.2.

Results

Study population

A review of baseline characteristics is in the electronic-only appendix. The only significant difference between groups was in intravenous drug use, which was higher in the brief intervention compared to the referral group.

Resource use and costs

Use and costs of health care services, patient time and crimes committed are presented in Table 1. Generally, the ED-initiated buprenorphine group used more drug addiction-specific office-based services, while the referral and brief intervention group used more addiction treatment center-based resources (both outpatient and residential treatment). Use of non-addiction specific (general medical) services were similar among groups.

Table 2 notes summary cost and outcome measures. Intervention costs occurring during the enrollment ED visit were low in all treatment groups (ranging from $8 to $83). Although the types of treatments received following ED discharge differed considerably by treatment group (Table 1), there were small nonsignificant differences in total health care costs across the groups, with point estimates indicating costs were lowest in the ED-initiated buprenorphine group. As reported in the original reports from the clinical trial the ED-initiated buprenorphine group had significantly improved effects compared to the other two groups on both studied outcomes (7).The Incremental cost effectiveness ratios indicate that under both outcomes studied, referral and brief intervention were dominated by ED-initiated buprenorphine (i.e., the two other treatments studied each cost more than ED-initiated buprenorphine, with fewer benefits).Figure 1a presents the cost effectiveness acceptability curve for engagement in formal addiction treatment on the 30^{th} day post randomization. The x-axis indicates threshold willingness-to-pay values for a one percentage point increase in the probability a patient is engaged in formal addiction treatment, while the y-axis indicates the probability each of the treatment groups has the highest net benefit at each willingness-to-pay value. For example, if a decision maker determined they were willing to pay $10 for each one percentage point increase in the probability a patient would be engaged in treatment at 30-days, the estimated probability that ED-initiated buprenorphine, brief intervention and referral have the highest net benefit is 79%, 16% and 5%, respectively. Because at all positive willingness-to-pay values the ED-initiated buprenorphine curve is above both the brief intervention curve and the referral curve, ED-initiated buprenorphine is the treatment estimated *most likely* to be cost-effective. When the distribution of net benefit is skewed, the treatment with the highest probability of having the highest net benefit may not be the treatment with the highest expected net benefit (i.e., the optimal treatment) (24). To consider this possibility, we calculated expected net benefit and found results consistent with those presented here.

Figure 1b presents the cost effectiveness acceptability curve related to the second outcome studied: change in opioid-free days. Similar to treatment engagement, the ED-initiated buprenorphine curve is above the brief intervention and referral arm at all willingness-to-pay levels.

Secondary analyses to determine whether these results were robust to including patients with missing health care data, or including crime and patient time costs in the numerator indicate both are consistent with the results in the base case analysis (see Figure 2 and electronic-only appendix). Patient time costs were significantly lower in the ED-initiated buprenorphine group compared to the referral group ($97 versus $283; $p<.01$) or the brief intervention group ($97 versus $322; $p<.01$). Additional sensitivity analyses suggest these results are robust to changes to unit prices (see electronic-only appendix).

Discussion

Even under the most conservative assumptions about willingness-to-pay (i.e., that willingness-to-pay is zero), we find ED-initiated buprenorphine is *most likely* to be cost effective among treatments studied. A willingness-to-pay threshold of zero is equivalent to requiring that a treatment be cost neutral or cost saving; Our point estimates indicate that ED-initiated buprenorphine is cost-saving, compared to brief intervention or referral. This suggests that an ED currently screening individuals for opioid dependence should provide care consistent with that received by the ED-initiated buprenorphine group rather than referral or brief intervention alone. These findings are robust in a range of secondary analyses.

Estimates of intervention costs occurring during the enrollment ED visit were remarkably low ($8–$83), reflecting the minimal health care resources used in the ED-based component of the intervention. The initial investment for EDs may require that emergency physicians be waivered to prescribe (but not to dispense) buprenorphine/naloxone, but the ongoing investment for EDs to provide the ED-initiated buprenorphine strategy would be small. Differences in the distribution of health care service use among the three groups is informative. The most common medication received in all three groups was buprenorphine/naloxone, although use of buprenorphine/naloxone was much higher in the ED-initiated buprenorphine group (72% versus 20%–24%). While 15–18 percent of patients in the referral and brief intervention groups received methadone treatment, almost no patients in the ED-initiated buprenorphine group reported treatment with methadone.

Like previous research, we find the crime costs associated with substance use disorders are large(26; see electronic-only appendix). The prices assigned to these crimes included only tangible costs (including crime victim, criminal justice system, and crime career costs), suggesting these are an underestimate of true crime costs. In addition, the use of self-reported data is likely to underestimate crimes committed. Estimates of crime costs were lower in the ED-initiated buprenorphine group ($2566) compared to those in the brief intervention ($3743) and referral group ($5357), although these were not statistically significantly different.

The ED-initiated buprenorphine group had significantly lower patient time costs compared to the other two groups ($97 versus $283–$322; p<.001 for both comparisons). Although we did not include crime or patient time costs when constructing base-case cost effectiveness acceptability curves, that these are lowest in the ED-initiated buprenorphine group indicates it is more likely policymakers with a societal perspective will find the treatment provided in the ED-initiated buprenorphine group to be valuable enough to be funded. To the extent private decision makers (e.g., private insurers, health system administrators) do not consider these costs because they are borne by others, there may be a role for government to incentivize providers to use treatments associated with lower crime.

While differences in effects are statistically significant among the three groups, differences in costs are not. This is because, like other studies of health care costs, there is considerable variation in our cost estimates.

We only consider clinical endpoints, making it difficult to compare to quality adjusted life years or funded interventions for other health disorders. Since stakeholders may have different thresholds for the value of the clinical endpoints studied, we present acceptability curves for multiple willingness-to-pay values.

A recent study derived standard gamble utilities for opioid misuse and initiation stage buprenorphine therapy(27). Using a threshold of $100,000 per quality adjusted life year, differences in these utilities suggest a willingness-to-pay of approximately $1000 per individual engaged in buprenorphine treatment for 30 days, or $10 per 1 percentage point increase in probability of treatment engagement (see electronic-only appendix). To the extent there are further cost savings from ED-initiated buprenorphine not included in the numerator such as improved labor market outcomes, benefits to family members, or reduced infectious disease transmission, this is an underestimate of the threshold willingness-to-pay.

A secondary analysis including crime and patient time costs is informative. Both of these costs would be important when taking a societal view, the appropriate viewpoint for cost effectiveness studies(28). Thus, a decision maker taking a societal viewpoint might include these estimates when considering the adoption decision. Even if this decision maker required the intervention be cost saving in 66% of iterations the ED-initiated buprenorphine treatment strategy was the treatment with the highest net benefit(see electronic only appendix).

It would be useful to compare results presented here to other cost studies of treatment for opioid dependence. Although in different settings and using different comparator treatments than those in this study, one recent review of 43 economic evaluations of treatment for opioid use disorders found that of the eight cost-benefit or cost-effectiveness studies that include buprenorphine-naloxone, half indicated buprenorphine-naloxone maintenance therapy was cost effective relative to the other studied interventions(29). The authors of this review concluded that there was a need for more high quality research in this area.

One potential problem with outcomes of short time horizons such as those used in this study is it is often difficult to evaluate the relative value of the clinical benefits measured. In this study, this is less of a problem. Our results indicate that unless health care, crime, or time costs diverge in such a way to favor referral or brief intervention, ED-initiated

buprenorphine is most likely cost effective, even if there are no additional clinical benefits beyond 30-days.

The clinical trial on which this study is based was designed with the assumption that the ED was currently screening patients for opioid dependence, due to difficulties including a 'no screening' arm in the trial. An ED not currently screening for opioid dependence should consider these costs. We conducted a retrospective direct service cost calculation of screening assuming medical assistants would administer screening instruments, which indicated a cost of $214 per treated patient (see electronic-only appendix). *As in prior cost studies, this indicates that screening costs are substantially less than downstream health care costs.* It is likely the costs of screening have declined substantially since the start of this trial, due to the widespread availability of inexpensive local area wireless computer networking (WiFi). One study of a 24-question tablet-based screener for opioid prescription abuse potential in an urban ED found 100% of patients were able to complete the screener, 95% completed it in under five minutes, and 93% percent rated ease of completion as 'very easy' – the highest rating available(30). In addition, from 2006 to 2011 the share of EDs with an electronic health record increased from 46% to 84%(31), making it easier for information to be transferred among staff and providers within the ED, including as part of the electronic triage system(32).

These findings are particularly relevant in the current addiction treatment financing environment. Historically, addiction treatment financing has been fragmented, with a mix of health insurance (private and public), state agencies, and patients financing care, which was delivered in both traditional health care venues as well as addiction treatment-specific venues. Addiction treatment is now required to be covered as an essential health benefit in ACA Marketplace plans and Medicaid, and must be covered at parity, if offered, in almost all private health insurance plans. This has the potential to greatly increase the generosity of coverage for addiction treatments. If insurers are responsible for addiction treatment delivered in all settings, it increases their incentive to promote treatments that are cost effective (33).

Essential to the success of ED-initiated buprenorphine is the availability of a primary care or other physicians to provide follow-up care for patients who initiate buprenorphine in the ED. These findings suggest that integrated models, such as Accountable Care Organizations (ACOs) or other global or bundled payment arrangements, where organizations may bear responsibility for the full costs of an episode of care may encourage provider organizations to ensure that cost-effective downstream treatments are available. For example, ACOs may contract with a primary care group to accept referrals from an ED, with short waiting time to appointments. National efforts to increase access to buprenorphine treatment including expanding the treatment capacity of selected providers to 275 patients and expanding prescribing to PAs and nurse practitioners should make it easier for EDs to provide this treatment.

Limitations

Although these results strongly suggest ED-initiated buprenorphine/naloxone treatment is cost effective relative to brief Intervention and referral alone, there are several limitations to

this study. First, the measurement of effects as clinical endpoints (rather than a common metric such as the quality adjusted life year) makes it difficult to compare to health outcomes unrelated to opioid dependence. Second, we only follow patients for 30-days post randomization, although this is a time frame appropriate for ED-based interventions. Third, both health care utilization and crime may be reported with error since both are assessed by self-report, although there is little reason to believe this error would systematically differ among groups. Other limitations of this analyses include that costs were estimated retrospectively without a formalized cost estimation instrument, the relatively high proportion of missing cost data, and that we are only able to measure a subset of societal costs. Finally, these results may not be generalizable to all US EDs. The ED studied had access to a primary care clinic that regularly provided buprenorphine/naloxone treatment and access to near-term appointments. Some EDs may not have similar primary care providers with appointments available in their vicinity (34) although provisions in the Affordable Care Act related to patient-centered medical homes and accountable care organizations may increase the availability of these providers. Likewise, some EDs may not have additional trained staff available at all times to provide brief interventions. However, medical schools and hospitals are including brief interventions in their training programs. In our prior work, we have trained frontline ED clinicians (physicians, physician assistants) to perform the Brief Negotiation Interview (35).

Conclusion

Among patients identified as opioid-dependent via ED-based screening, ED-initiated treatment with buprenorphine/naloxone is most likely to be cost-effective relative to brief intervention or referral. Further implementation and evaluation in other EDs is warranted to provide policy makers and other purchasers of health care robust data about this practice.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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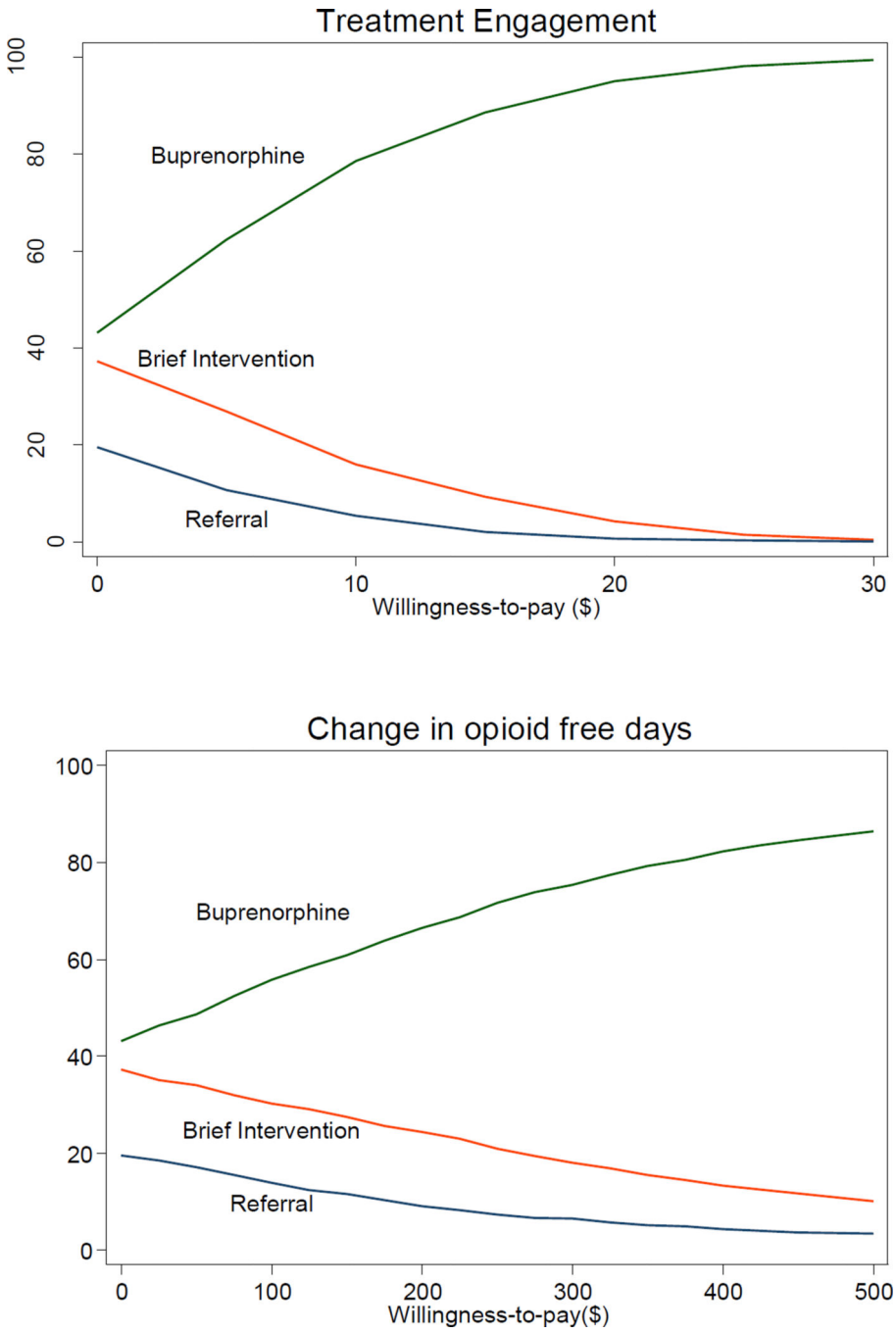

Figure 1.

Cost-effective Acceptability Curve: Base case analysis

Notes: Willingness-to-pay in panel (a) indicates willingness-to-pay for a one percentage point increase in the probability a patient is engaged in treatment 30-days post enrollment. In panel (b) willingness-to-pay indicates willingness-to-pay for one additional opioid free day in the past seven days.

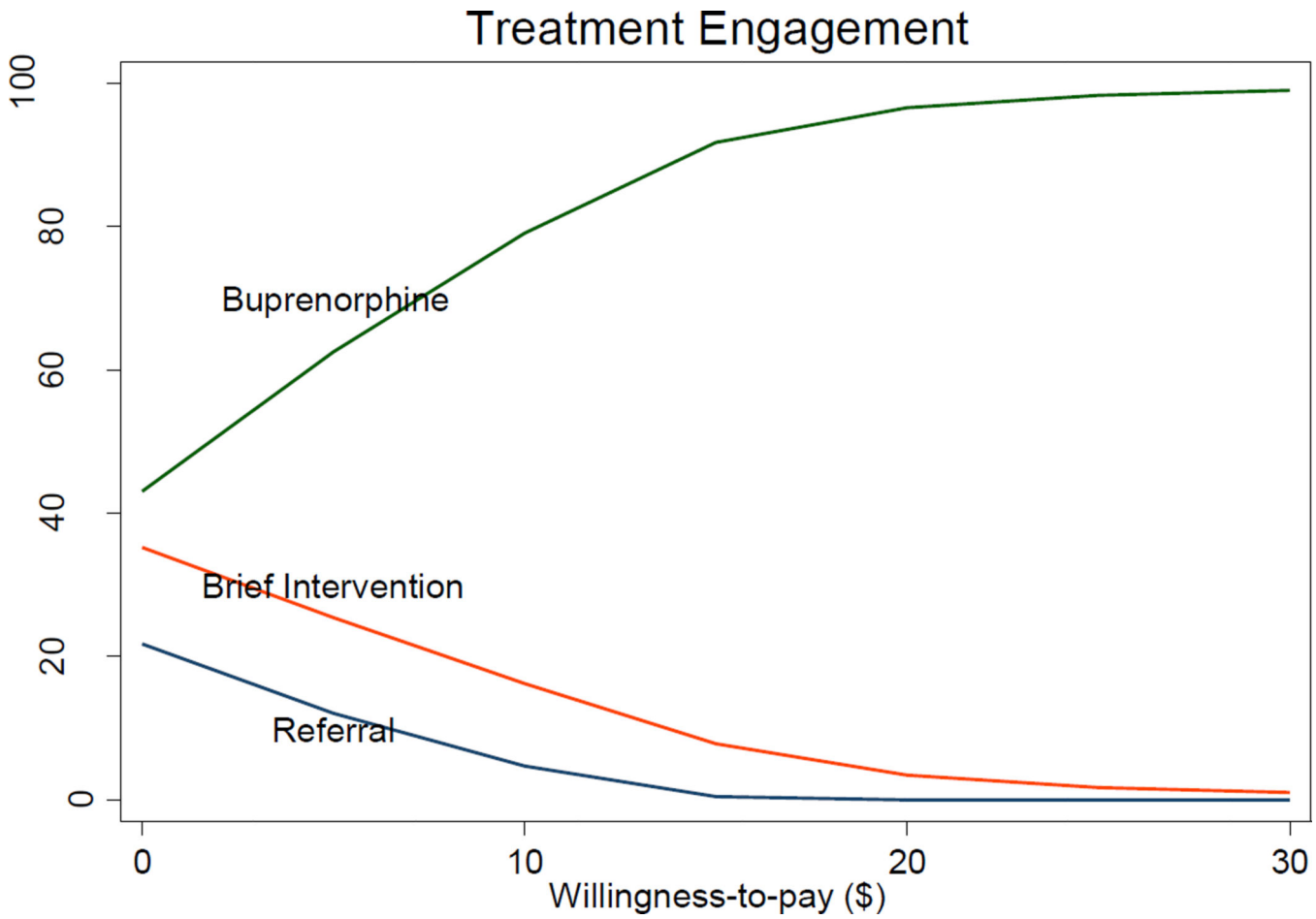

Figure 2.

Secondary Analysis: Including patients with missing cost information (N=327)

Notes: Willingness-to-pay in panel indicates willingness-to-pay for a one percentage point increase in the probability a patient is engaged in treatment 30-days post enrollment.

Table 1

Health Care Use, Patient Time and Crime

	Referral (N=69)			Brief intervention (N=82)			ED-initiated Buprenorphine* (N=93)		
	Any (%)	Average Quantity †	Average Cost † ($)	Any (%)	Average Quantity †	Average Cost † ($)	Any (%)	Average Quantity †	Average Cost † ($)
Health care									
Office-based (visits)									
Addiction-specific ‡									
Office-based (visits)	10	.38	52	12	.38	52	70	3.49	482
Addiction treatment center (visits)	30	4.72	95	37	5.29	107	4	.22	4
Non-addiction									
Office-based (visits)	17	.36	76	18	.43	89	19	.45	94
Hospital-based care									
Emergency Department (visits)	28	.42	429	22	.23	237	32	.36	373
Addiction-specific ‡									
Hospital (admissions)	3	.03	144	2	.02	121	1	.01	53
Residential treatment (nights)	20	1.81	237	27	2.84	372	3	.26	34
Non-addiction									
Hospital (admissions)	9	.09	873	6	.07	735	3	.04	432
Receipt of opioid use medication									
Methadone (days) §	15	2.62	0	18	4.0	0	1	.32	0
Buprenorphine (days)	20	5.34	64	24	6.27	75	72	16.54	198
Naltrexone (days)	0	0	0	1	.01	.01	0	0	0

† Average quantity and costs reflects average across all patients (i.e., users and non-users).

‡ Addiction treatment does not include treatment for alcohol addiction.

§ Methadone costs were included in the cost of addiction treatment center visits.

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Table 2

Mean Costs and Outcomes (N=244)

	Mean (SD) [IQR]			Differences between groups * (95% confidence interval) (p-value)		
	ED-initiated Buprenorphine (N=93)	**Brief Intervention (N=82)**	**Referral (N=69)**	**ED-initiated Buprenorphine versus Brief Intervention**	**Brief Intervention versus Referral**	**ED-initiated Buprenorphine versus Referral**
Health care costs						
Intervention costs occurring during enrollment ED visit †	83	16	8	66	8	74
All other health care costs (US $)	1670 (2947) [498,1933]	1788 (3467) [0,1545]	1969 (3142) [0,1914]	−117 (−1096,913) p=.80	−166 (−1232,895) p=.76	−284 (−1174,666) p=.56
Total (US $)	1752 (2948) [5801,2015]	1805 (3467) [16,1561]	1977 (3142) [8,1923]	−51 (−1030,979) p=.90	−158 (−1224,903) p=76	−209 (−1100,740) p=.66
Effects						
Enrolled and receiving formal addiction treatment at 30 days	86% (35)	45% (50)	39% (49)	41% (28, 54) p<.001	6% (−10, 22) p=.46	47% (34, 60) p<.001
Change in days of self-reported illicit opioid use in the past 7 days (days)	4.43 (2.37) [3, 6]	3.23 (.50) [0, 6]	3.01 (2.94) [1, 6]	1.20 (.38, 2.01) p=.0044	.21 (−.76, 1.20) p=.66	1.42 (.59, 2.24) p=.0009
Incremental cost effectiveness ratios (ICERs)						
Cost per enrollment in formal addiction treatment at 30 days (%)				Brief intervention dominated. (Costs more/ fewer benefits)	Referral dominated. (Costs more/ fewer benefits)	Referral dominated. (Costs more/ fewer benefits)
Cost per change in days of self-reported illicit opioid use in the past 7 days (days)				Brief intervention dominated. (Costs more/ fewer benefits)	Referral dominated. (Costs more/ fewer benefits)	Referral dominated. (Costs more/ fewer benefits)

Negative numbers indicate first group favored (i.e., lower cost); Cost differences and 95 percent ranges between groups were tested among 1000 bootstrap replicates. Differences are based on differences of bootstrap estimates so may not equal observed mean differences. For effects, differences were tested using t-tests.

† For intervention costs occurring in the ED there is no variation within sample because estimated costs for individuals were based on average use of intervention components.