ClinicoEconomics and Outcomes Research

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ORIGINAL RESEARCH

Budget Impact Analysis of the Introduction of Injectable Prolonged-Release Buprenorphine on Opioid Use Disorder Care Resource Requirements

This article was published in the following Dove Press journal:
ClinicoEconomics and Outcomes Research

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Objective: To assess budget impact of the introduction of prolonged-release buprenorphine (PRB) for care of opioid use disorder (OUD) over 1 year in a defined population.

Materials and Methods: A healthcare perspective, decision-tree model analysis of the cost of OUD care for a standard population was prepared to compare two scenarios: treatment of a population under the existing standard of care, or with the addition of PRB. The model assessed OUD-related direct costs (medication, delivery, psychosocial treatment), other services costs (harm reduction, general healthcare, social and justice services) and the impact of behaviors such as engaging with treatment and electing to use additional opioids "on top" of treatment regimens, and "dropping out" from treatment.

Results: Standard population definition (persons offered OUD care services) is based on a typical administrative region in England with general population of 400,000 citizens, 1,777 high-risk opioid users requiring treatment and 909 patients initiating treatment in a year. The cost to provide OUD care for 1 year under the current scenario (70% treated with methadone, 30% sublingual buprenorphine) is £19.7M. In scenarios with increased PRB adoption/reduced sublingual buprenorphine or oral methadone use, the cost reduction ranges from £0.2M to 0.7M.

Conclusion: The assessment showed a reduction of overall costs after introduction of PRB.

Keywords: opioid use disorder, budget impact, pharmacotherapy, buprenorphine, methadone, injectable prolonged-release buprenorphine

Introduction

Opioid use disorder (OUD) is an important individual and public health issue.[1] Adverse health outcomes include risk of death due to overdose, infectious diseases, comorbidities, trauma, and suicide;[2] negative social impacts include unemployment, homelessness, family disruption, loss of economic productivity, social instability, criminal activities, and economic burden.[3–5]

Integrated treatment with pharmacotherapy and psychosocial support is effective and well-evidenced.[6] Standard care commonly includes medication choices of oral methadone or sublingual buprenorphine. OUD care programs are effective but associated with significant burdens and risks. Obligatory daily attendance at a clinic or pharmacy for supervised consumption of medication is common, especially at the start of therapy as provision of oral medication has a serious risk of diversion.[7]

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http://doi.org/10.2147/CEOR.S242984

Daily attendance for supervised therapy can limit the ability to work, lead to discrimination, and perceived loss of social equity or agency. Therapy is marginalizing for some people. Engaging with therapy whether collecting medication regularly at a pharmacy or visiting a treatment center – may be associated with its own limits and create stigma, which can make adherence difficult, leading to suboptimal dosing, "on top" use of illicitly sourced opioids and other drugs.[8,9] Innovation can address limitations of OUD treatment.

Prolonged-release buprenorphine (PRB)[10,11] is approved for management of opioid dependence. Different doses of the PRB product are given by weekly or monthly subcutaneous injections. Evidence including comparison to sublingual buprenorphine treatment[12–15] demonstrates efficacy and safety in treating patients with OUD.[16] The product has the potential to overcome the limits, burdens and risks of daily observed medication administration.[17–19]

In England, there are an estimated 250–300,000 people with a history of OUD who may require treatment;[20] approximately 140,000 engaged with treatment services.[21] OUD care is planned and commissioned by Public Health departments responsible for drug and alcohol services within 152 administrative regions/municipal "Local Authorities" (LA) in England.[22,23] This work assessed the budget impact of including PRB therapy in the standard of care.

Materials and Methods

Budget impact was assessed using a decision-tree model from a healthcare system perspective based on previous work.[24–26] The model was prepared to compare direct costs and indirect costs of OUD care for a standard population in two scenarios: existing standard of care, or with the introduction of PRB.

Direct costs were modelled for the provision of OUD care, including medication, delivery, and psychosocial treatment (Table 1). Medication cost was estimated based on daily treatment dose recommended in national guidelines.[27,28] Distribution costs included item fees, applicable for each methadone prescription, and fees charged for each patient interaction at pharmacy visits[29,30] for dispensing and controlled drug handling. Supervised consumption payment was based on the normal agreement with pharmacies. Costs of clinical interventions included monthly counselling services often led by key workers or other healthcare professionals.[31]

Indirect costs were assessed for the subpopulations: 1) engaged in treatment but electing to use additional opioids "on top" of the recommended treatment regimen; and 2) those electing to cease or "drop out" of the recommended treatment regimen, or never engaging with such during the period of assessment. Indirect costs include harm reduction, general healthcare, criminal justice and child safeguarding (Table 2). Evidence describing costs was identified from published sources or local records.[24,26]

Costs to provide care at weekly intervals were calculated and summed for the year based on distributions of subpopulations. Subpopulations were defined according to behavior, persons who were: 1) engaged with treatment, no additional opioid use; 2) engaged with treatment, additional opioid use present; and 3) never in or no longer engaged with treatment, other opioid use continues. The relative changes over the year of the distribution between subpopulations were simulated in the model, based on clinical outcomes and subgroup analysis of a Phase III trial.[16,32,33]

One-way sensitivity analyses assessed the impact of variance in: 1) the proportion of population living rurally; 2) the percentage of estimated high-risk opioid users in treatment; 3) the percentage of people on buprenorphine at baseline; 4) the unit costs for supervised consumption of oral methadone and sublingual buprenorphine; and 5) the level of adoption of PRB.

Results

A theoretical standard region of 400,000 citizens (85% urban residents; 15% living in rural areas) was defined for the purpose of this analysis, based on the average of six identified regions in England (population range for the six regions: 195,700–741,209). The estimated number of people using opioids in the region was 1,777 (based on an average number in the six identified regions; value range, 628–3,245), with an estimated 909 engaged in OUD care (based on the average number in the six regions; value range 238–1,958).

The overall costs to provide OUD care and associated services under each scenario are summarized in Table 3. Costs to provide OUD care for 1 year in the current scenario (scenario 1, 70% treated with oral methadone, 30% sublingual buprenorphine): £19.7M. For a future scenario (scenario 2) in which 10% receive injectable PRB, 20% sublingual buprenorphine, 70% methadone, costs were £19.4M (Figure 1), a reduction of £0.2M in costs (direct (£89,420), indirect healthcare (£24,220) and indirect non-healthcare (£93,915)) (Table 3).

One-way sensitivity analyses completed show further reduction in costs of care of £0.3–0.7M (assuming higher

Table 1 Direct Costs Associated with Delivering OUD Care

Cost		Utilization	Unit Cost, £	Source
Medication cost			Per week	
	Methadone	Daily dose 80 mg	4.54	Drug Tariff Apr 2019[27]
	Buprenorphine	Daily dose 16 mg	50.80[a]	Drug Tariff Apr 2019[27]
	Prolonged-release buprenorphine	Weekly strengths of 8, 16, 24, 32 mg (Price irrespective of the strength)	55.62	NICE Evidence review[37]
Drug dispensing			Per interaction	
Prescription item fee	Methadone	Every 14 days[38]	2.50	PSNC 2018[39]
Dispensing activity fee	Methadone	Number of interactions depends on dispensing schedule[b]	1.25	PSNC 2018[39]
	Buprenorphine		1.25	
	Prolonged-release buprenorphine		1.25	
Controlled drug fee	Methadone		1.28	PSNC 2018[40]
	Buprenorphine		0.43	
	Prolonged-release buprenorphine		0.43	
Supervised consumption	Methadone		1.44	Local records/ LA data
	Buprenorphine		2.83	
	Prolonged-release buprenorphine		0	
Clinical intervention			Per session	
Counselling/clinic	Methadone	Every 4 weeks	30	Local records/ LA data
	Buprenorphine			
	Prolonged-release buprenorphine	Every 8 weeks		
Urine testing	Methadone	Every 4 weeks	2.71	Local records/ LA data
	Buprenorphine			
	Prolonged-release buprenorphine	Every 6 months		
Satellite service/mobile consultation[c]	Methadone	Every 2 weeks	20	Local records/ LA data
	Buprenorphine			
	Prolonged-release buprenorphine	Every 10 weeks		

Notes: [a]Price indicated for branded buprenorphine because of current shortage of supply of generic buprenorphine; [b]Dispensing schedule for methadone and buprenorphine for patients: 1) engaged with treatment, no additional opioid use: 6 days per week in weeks 1–24, 3 days per week in weeks 25–52; and 2) engaged with treatment, additional opioid use present: 6 days per week in weeks 1–52; Dispensing schedule for flexible dose, subcutaneous injectable buprenorphine is 1 day per week in weeks 1–24, 1 day per month in week 25–52. [c]Only applies to patients living in rural areas.

levels of treatment engagement, higher rates of supervised consumption frequency, greater fraction of rural population (Table 4), higher level of adoption for PRB (Table 5).

Discussion

Introduction of injectable PRB directly addresses limitations[7] of current medication choices in OUD care. This analysis

Table 2 Indirect Healthcare and Non-healthcare Costs Associated with Delivering OUD Care

Cost	Frequency per Week by Health Status		Unit Cost, £	Source
	Engaged with treatment, additional opioid use present	Never in or no longer engaged with treatment, other opioid use continues		
Harm reduction				
Needle equipment program[a]	0.50	1.0	3.85	NICE costing 2014[40]
Take-home naloxone	0.14	0.14	23.80	Langham et al 2018[41]
Take-home naloxone training	0.036	0.036	124.00	Langham et al 2018[41]
Indirect healthcare				
Additional GP visits	0.108	0.069	36.00	Kenworthy et al, 2017[26]
A&E visits	0.015	0.014	163.24	
Inpatient hospital visits	0.054	0.034	470.21	
Outpatient mental health visits	0.015	0.025	101.46	
Inpatient mental health visits	0.008	0.029	429.00	
Indirect non-healthcare				
Arrest for drug crime	0.015	0.006	5592.11	Kenworthy et al, 2017[26]
Arrest for acquisitive crime	0.031	0.026	2199.68	
Court appearance	0.027	0.042	1100.78	
Child safeguarding				
Child safeguarding[b]	0	7%	50,000.00	Expert interview
Child in care	0	40%[c]	4036	Curtis et al 2017[42]

Notes: [a]Extrapolated from a full cost of £200 for patients who are never in or no longer engaged with treatment, other opioid use continues and half cost of £100 per annum for patients engaged in treatment, additional use present, [b]7% patients have parental responsibility for one or more children at a risk of removal. Average number of children at risk of removal per parent is 1.25. [c]40% of reviews result in children being taken into care.

assessed the cost impact of introducing PRB for a standard population. For a scenario with 10% patients on PRB, the total resources for direct OUD care and other related health, social and justice services were lower: 43.1% (£89,420) of the reduction comes from direct costs associated with frequent drug dispensing (prescription and dispensing, controlled drug handling, and supervised consumption), and requirement of clinical interventions (counselling/clinic, urine testing, satellite services); 45.2% (£93,915) from reduced indirect non-healthcare costs associated with drug and acquisitive crimes and court appearances; 11.6% (£24,220) from indirect healthcare costs (harm reduction GP, A&E, inpatient care, and mental health care). The medication costs increased by £16,459. Results are consistent with other work.[34,35] An analysis in the UK using a 5-state Markov model suggested that PRB accrued lower annual total per-patient costs compared to sublingual buprenorphine/naloxone.[34] Cost savings were attributed to lower crime rate, reduced supervised self-administration, prescription/controlled drug fees, avoided HIV/HCV infections. One study in Sweden highlighted reduced criminality/victimization costs and lower direct medical costs driven by reduced emergency and hospital services.[35]

This analytical method was consistent with a previously validated approach[24,26] based on two subpopulations (engaged in treatment, never in or no longer engaged with treatment). This study included a subdivision of the "engaged in treatment" subpopulation, based on choice to use additional opioids "on top" of treatment regimens (as defined by positive urine drug results). The decision-tree model did not include a scenario in which a population discontinued any form of treatment and also did not revert to additional opioid use (for example, injected heroin use).

Important assumptions determine the results; it was assumed, scenarios including both the use of additional opioids "on-top" while engaged in treatment and also "dropping out from treatment" (often measured by "retention") increased the need for additional resources in care. Retention was determined from different sources. For patients treated with methadone, retention was estimated from a previous study.[32] Evidence for retention with PRB and sublingual buprenorphine was estimated from a subgroup analysis of a phase III clinical study using data on file;[16,33] this subgroup represented subjects with recorded use of primarily illicit drugs, mainly injected heroin, and accounted for 71% of the

Table 3 Budget Impact of Prolonged-Release Buprenorphine Adoption

Scenario Comparison	Scenario 1	Scenario 2	Impact
Number of People by Therapy Choice When Treatment Initiated[a], n (%)			
Methadone	636 (70)	636 (70)	0
Buprenorphine	273 (30)	182 (20)	−91(−10)
Prolonged-release buprenorphine	0	91(10)	91(10)
Total	909 (100)	909 (100)	
Cost, £			
Medication	619,931	636,390	16,459
Drug Dispensing			
Prescription and dispensing	262,363	239,566	−22,797
Controlled drug handling	189,774	181,932	−7,842
Supervised consumption	353,724	297,344	−56,380
Clinical Intervention			
Counselling/clinic	241,381	228,576	−12,805
Urine testing	21,805	19,847	−1,958
Satellite services	48,276	44,179	−4,098
Total direct service	1,744,945	1655,525	−89,420
Harm reduction	1,003,334	997,845	−5,489
Indirect Healthcare			
GP visits	258,641	256,655	−1,986
A&E	202,650	201,364	−1,286
Inpatient hospital stays	1,661,879	1,648,910	−12,969
Outpatient mental health	196,454	195,654	−800
Inpatient mental health	837,621	835,931	−1,690
Total indirect healthcare	4,160,579	4,136,359	−24,220
Indirect non-healthcare			
Drug crime arrests	4,351,752	4,307,685	−44,067
Acquisitive crime	5,334,103	5,299,435	−34,668
Court appearances	3,634,351	3,619,170	−15,180
Child safeguarding/children in care	425,333	425,333	0
Total indirect non-healthcare	13,745,538	13,651,623	−93,915
Total	19,651,062	19,443,506	−207,555

Notes: [a]Based on a theoretical region with 400,000 population, 1,777 high-risk opioid users, 909 patients initiating treatment in a year.

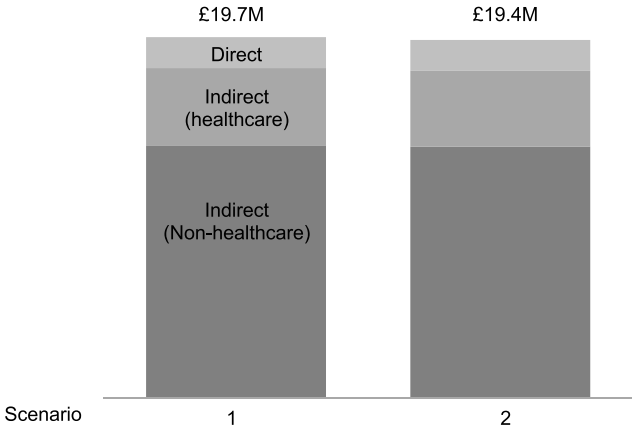

Figure 1 Budget impact of prolonged-release buprenorphine adoption. The overall cost to provide OUD care and associated services under two scenarios were calculated: current scenario (scenario 1, 70% treated with oral methadone, 30% sublingual buprenorphine), a future scenario (scenario 2, 10% receive injectable prolonged-release buprenorphine, 20% sublingual buprenorphine, 70% methadone). Analysis is based on a theoretical region with 400,000 population, 1,777 high-risk opioid users, 909 patients initiating treatment in a year.

total study population, consistent with the profile of patients with OUD in England.[36] These sources of evidence describing retention are different (observational vs phase III study): they represent the best known evidence for assumptions.

It was assumed in this work that no additional incremental cost (indirect and non-healthcare costs) are required for the group in treatment with no additional opioid use. Direct costs to provide OUD treatment services were considered for this group only. This work assumed that PRB is administered in the normal course of contact with healthcare services, and that this does not incur additional cost. For the subpopulation that is engaged with treatment with additional opioid use present, it was assumed that additional costs are needed to provide full supervision, based on clinical experience. Treatment dose in the standard-of-care arm of the analysis determined cost; assumptions were based on a typical dose in national guidance (oral methadone 80 mg, guidance 60–120 mg; sublingual buprenorphine 16 mg (12–32 mg).[31] PRB listed cost does not vary with dose.

This work identified the budget impact and reduction in cost following introduction of PRB over 1 year: it does not attempt to capture all possible benefits and does not count future benefits beyond 1 year. This analysis was based on current approach to services build up around daily, observed oral medication; weekly or monthly treatment may potentially change the current model of treatment delivery significantly and allow for further reallocation of current resources.

It is likely that the realization of benefits from improved treatment in family status and reduction in resources needed for child safeguarding are not fully captured in this analysis. Benefit to families and children could be greater than stated because analysis linked potential benefit to engagement in treatment which was unchanged for the subpopulations treated on PRB/sublingual buprenorphine. This is likely to lead to an underestimate of benefit: analysis shows that as novel product adoption level increases, reduced costs associated with a reduction in need for child safeguarding are observed. In the situation where collection of medications or attendance for daily observed therapy is not possible or is not desirable because of association with major limiting risk, the benefits of PRB are likely significantly greater.

Table 4 Sensitivity Analysis on Parameters with Local Variations

Parameter Modified	Range[a]		Scenario 1: Baseline Scenario, £	Scenario 2: Prolonged-Released Buprenorphine Adoption (10%), £	Impact, £
Cost for supervision	Higher	Buprenorphine: £4.00 Methadone: £1.60	19,733,807	19,502,943	−230,865
	Lower	Buprenorphine: £2.05 Methadone: £1.20	19,565,989	19,373,973	−192,016
Proportion of population rurally based	Higher Lower	70% 0%	19,820,384 19,595,095	19,597,803 19,391,637	−222,580 −203,458
Percentage of patients in treatment	Higher Lower	60% 35%	20,002,499 18,987,596	19,759,049 18,845,584	−243,450 −142,012
Percentage of patients on buprenorphine	Higher Lower	35% 15%	19,732,451 19,376,132	19,524,895 19,168,577	−207,555 −207,555

Note: [a]Range defined based on data collected from six local authorities in England.

Table 5 Sensitivity Test of Level of Adoption of Prolonged-Release Buprenorphine

Budget Impact (£)	PRB adoption in patients on buprenorphine				
		0%	10%	20%	30%
PRB adoption in patients on methadone	0% 10% 20% 30%	– −30,495 −60,990 −91,485	−207,556 −238,051 −268,545 −299,040	−415,111 −445,606 −476,101 −506,596	−622,667 −653,162 −683,656 −714,151

Conclusion

This analysis shows that introduction of PRB to treatment choices was associated with a decrease in costs required for care of a population with OUD.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

This work was funded by Camurus AB. Camurus had no influence on the research nor content of this work. The authors declare no conflicts of interest in this work.

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