Costs of Addressing Heroin Addiction in Malaysia and 32 Comparable Countries Worldwide

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Objective. Develop and apply new costing methodologies to estimate costs of opioid dependence treatment in countries worldwide.

Data Sources/Study Setting. Micro-costing methodology developed and data collected during randomized controlled trial (RCT) involving 126 patients (July 2003–May 2005) in Malaysia. Gross-costing methodology developed to estimate costs of treatment replication in 32 countries with data collected from publicly available sources.

Study Design. Fixed, variable, and societal cost components of Malaysian RCT micro-costed and analytical framework created and employed for gross-costing in 32 countries selected by three criteria relative to Malaysia: major heroin problem, geographic proximity, and comparable gross domestic product (GDP) per capita.

Principal Findings. Medication, and urine and blood testing accounted for the greatest percentage of total costs for both naltrexone (29–53 percent) and buprenorphine (33–72 percent) interventions. In 13 countries, buprenorphine treatment could be provided for under \$2,000 per patient. For all countries except United Kingdom and Singapore, incremental costs per person were below \$1,000 when comparing buprenorphine to naltrexone. An estimated 100 percent of opiate users in Cambodia and Lao People's Democratic Republic could be treated for \$8 and \$30 million, respectively.

Conclusions. Buprenorphine treatment can be provided at low cost in countries across the world. This study's new costing methodologies provide tools for health systems worldwide to determine the feasibility and cost of similar interventions.

Key Words. Malaysia, micro-costing, gross-costing, heroin treatment, international comparison, health systems

There are an estimated 13–22 million opiate users globally, with more than half residing in Asia (United Nations Office on Drugs and Crime [UNODC] 2010). Heroin use in Malaysia has reached significant levels, with 234,000

official heroin users or heroin-dependent individuals in the government registry at the end of 2004; other estimates reach as high as 500,000 in a population of roughly 24 million (2 percent) (Mazlan, Schottenfeld, and Chawarski 2006). Moreover, three quarters of all Malaysian HIV/AIDS cases stem from injection drug use (Ministry of Health of Malaysia/World Health Organization [WHO] 2004; WHO Representative Office of Malaysia 2006–2008). In many countries, injection drug users (IDUs) have a 40 percent or higher HIV prevalence rate (UNODC 2009). Treating and ending opioid dependence, then, is an important public health aim in Malaysia and around the world.

Naltrexone has been approved by the U.S. Food and Drug Administration for treating opioid dependence since 1984 (Schottenfeld, Chawarski, and Mazlan 2008), and buprenorphine with counseling has proven effective in treating opioid dependence and addiction as well as reducing HIV risk behavior (Barnett, Zaric, and Brandeau 2001; Chawarski, Mazlan, and Schottenfeld 2008). The cost of providing opioid maintenance treatment and concurrent group and individual therapy, however, can be a major concern, especially for governments that send arrested drug users to mandatory drug treatment centers, such as Cambodia, China, Indonesia, Lao People's Democratic Republic (PDR), Malaysia, Myanmar, Thailand, and Vietnam (WHO 2009). This study develops and applies novel costing methodologies to estimate the cost of opioid dependence treatment in countries around the world.

We conducted a cost study of buprenorphine and naltrexone maintenance treatment with counseling for opiate addiction in a three-arm randomized controlled trial (RCT) in Malaysia. The interventions have demonstrated efficacy in improving abstinence and retention, and reducing relapse (Schottenfeld, Chawarski, and Mazlan 2008). Grounded in economic theory, we developed a micro-costing methodology, a bottom-up approach to data collection that produces precise estimates by directly accounting for the units and costs of each input consumed by participants in a given intervention. Micro-

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costing is often used to study a given intervention in a particular setting, with the “implicit assumption” that the “mix of inputs and the quality of the product or service will generalize to the next application of the approach in a new setting” (Gold et al. 1996, p. 189).

Based upon this micro-costing methodology, we created an analytical framework and methodology for extrapolating our results through gross-costing to estimate the costs of treatment replication in 32 other countries, selected based on their heroin problem, geographical proximity, or comparable gross domestic product (GDP) per capita to Malaysia. Compared to micro-costing, gross-costing is top down; rather than measuring costs directly, this method uses more general cost data, such as national average wages or reimbursement rates (Gold et al. 1996). Gross-costing is simpler and less expensive to undertake than micro-costing, but it may lack sensitivity and precision. It is an appropriate costing method when a high degree of precision is not necessary or not possible, or when researchers can expect large differences in costs (McBride and Hessel 2008), which we do when estimating treatment replication costs in 32 countries spanning widely different levels of development.

To our knowledge, this type of multipart study has yet to be done and offers promise as a new way to take advantage of the precision and accuracy gained from micro-costing for health system analysis and for extrapolation through gross-costing on a global scale.

METHODS

Intervention Overview

Details of the Malaysian RCT can be found in Schottenfeld, Chawarski, and Mazlan (2008). Briefly, 126 patients were enrolled between July 2003 and May 2005, all completing a 14-day detoxification protocol before being randomly assigned to placebo ($N = 39$), naltrexone ($N = 43$), or buprenorphine ($N = 44$) treatment. Patients were given one 8-mg tablet of buprenorphine (or matching placebo) or one 50-mg tablet of naltrexone (or placebo) each day for the first week, and two tablets of the same doses every Monday and Wednesday and three tablets every Friday in subsequent weeks, adjusting for craving and withdrawal symptoms. Each patient also received weekly 45-minute manual-guided individual and group counseling at an outpatient clinic in Muar, Malaysia.

The mean age of study participants ranged from 36 in the buprenorphine arm to 38 in the naltrexone arm. About two-thirds of participants in

each arm were of Malay ethnic origin. Very few attained a high-school level of education or above (a low of 5 percent in the buprenorphine arm and a high of 13 percent in the placebo arm), and between a third to a half of the participants in each arm were unemployed. The mean number of years of lifetime heroin use was approximately 15, and the average participant used heroin almost daily in the past 30 days. At least 75 percent of participants had injected drugs at some point, and between 37 and 46 percent were current IDUs. Participants who were HIV positive accounted for 26 percent of the buprenorphine arm, 26 percent of the naltrexone arm, and 13 percent of the placebo arm.

Micro-Costing Methodology

Based on the recommendations of the Panel on Cost-Effectiveness in Health and Medicine (Gold et al. 1996), we developed a micro-costing methodology and conducted cost analyses of all three treatment arms by identifying, measuring, and valuing resources used from a provider and societal perspective. Our methodology was based on previous studies (Ruger et al. 2009; Ruger, Ben Abdallah, and Cottler 2010). Data were collected from the investigators, staff, and project records on the number and type of resources used and unit costs. Total costs and cost per participant by arm as well as incremental costs—the additional cost per participant compared to the next least costly intervention—were calculated. Costs accrued solely for research purposes, such as recruitment, mouthwash used to mask slight taste differences in medication, RCT management and oversight, and activities to record data that would not be used in a clinical setting, were excluded. We categorized costs according to fixed, variable, and societal costs (Table 1).

Fixed costs, which do not necessarily change with the number of participants, included costs for buildings and facilities, detoxification, training, and quality assurance. We conservatively estimated conference calls and tape reviews with nurses, psychiatrist, and/or investigators as approximations for the quality assurance that would take place in a typical clinical setting. For example, we included one half of the time in weekly conference calls because half of the time was spent addressing research-specific issues. Variable costs, which vary by the number of participants, included costs for materials and testing, medications, and personnel for therapy and administration of tests and medications. Costs of finding and recruiting study participants and maintaining their participation were excluded. While the RCT received its buprenorphine supply free of charge, for this

Table 1: Micro-Costing Components by Cost Category

<i>Fixed Costs</i>	<i>Variable Costs</i>	<i>Societal Costs</i>
Building and facilities	Materials and testing costs	Participant's time
Clinic overhead (rent, utilities, maintenance)	Therapy materials	Detoxification
Detoxification	Individual therapy (40 pages/patient)	Time in detox center (2 weeks)
Detoxification	Testing materials	Physical exam (30 minutes/patient)
Buprenorphine during detoxification; 14 mg/patient	Gloves (2/blood and 2/liver)	Travel time for detox (20 minutes/patient)
Naltrexone during detoxification; 87.5 mg/patient	Wipes (2/blood and 2/liver)	Travel costs (motorcycle)
Psychiatrist time for physical exam	Testing	
Training	Urine, 1-panel	
Training manuals (10 total)	EKG	Tests
Nurse trainer (individual and group therapy training)	X-ray	Urine (5 minutes/test)
Nurse trainee (individual therapy training; five nurses)	Blood (FBC, blood sugar, renal, liver, VDRL/TPHA, Hep B/C, HIV; 2/patient)	EKG (10 minutes/test)
Nurse trainee (group therapy training; five nurses)	Additional liver tests	X-ray (10 minutes/test)
Quality assurance	Nurse time to administer tests	X-ray waiting time (1 hour/test)
Monthly conference (25 total, 1 hour each)	Urine (5 minutes/test)	Blood (10 minutes/test)
Nurse counselors (three nurses, for period I)	EKG (10 minutes/test)	Additional liver tests (10 minutes/test)
Nurse counselors (five nurses, for period II)	X-ray (10 minutes/test)	Therapy session
Advisor (co-investigator)	Blood (10 minutes/test)	Individual therapy
Monthly tape review (25 total, 1 hour each)	Additional liver tests (10 minutes/test)	Group therapy
Nurse counselors (three nurses, for period I)	Personnel costs	Family therapy
Nurse counselors (five nurses, for period II)	Individual therapy (1×/week, nurse only)	
Psychiatrist	Nurse time for therapy session (45 minutes/session)	
Weekly conference calls (109 total; 1 hour each, 1/2 clinical)	Nurse time for admin and scheduling (10 minutes/session)	Time for medication
Advisor (investigator)	Group therapy (1×/week per arm; 109 weeks total; psychiatrist/nurse)	Time for dosage and testing (15 minutes/visit)
Advisor (co-investigator)	Psychiatrist time for therapy session (45 minutes/session)	Travel
Advisor (psychiatrist)	Psychiatrist time for admin (15 minutes/session)	Travel time (20 minutes/visit)
Research assistants (4 total)	Nurse time for therapy session (45 minutes/session)	Travel cost (motorcycle)
	Nurse time for admin (10 minutes/session)	Travel time, X-ray (10 minutes/visit)

continued

Table 1. Continued

Fixed Costs	Variable Costs	Societal Costs
	Family therapy (1 ×/week, Nurse only)	Family member's time, family therapy
	Nurse time for therapy session (45 minutes/session)	(2/session) Time in therapy
	Nurse time for admin and scheduling (10 minutes/ session)	Travel time (20 minutes/session)
	Appointment scheduling time	Travel cost (motorcycle)
	RA time calling for appointments (1 minute/missed visit)*	
	Administration of medication treatment	
	Naltrexone	
	Clinical nurse time to greet/ log in/administer/log out (15 minutes/dose)	
	Dose of naltrexone	
	Pharmacist time (15 minutes/ dose)	
	Buprenorphine	
	Clinical nurse time to greet/ log in/administer/log out (15 minutes/dose)	
	Dose of buprenorphine	
	Pharmacist time (15 minutes/ dose)	

Notes. EKG, electrocardiogram; FBC, full blood count; TPHA, treponema pallidum hemagglutination assays; VDRL, venereal disease research laboratory test.
*Missed visits are estimated to be the difference between total actual visits and 3 visits per week per patient, which equals 3,998 visits, distributed proportionally across interventions.

study's purposes we used the market price in Malaysia. Societal costs included time spent by the participant in detoxification, testing, therapy, taking medication, and travel, as well as the family's time in family therapy and their travel costs. We estimated the participant's and family's costs using Malaysia's minimum wage.

Gross-Costing Methodology

Extrapolating from the methodology developed in our micro-costing analysis, we created an analytical framework and methodology for gross-costing the

intervention for replication in 32 relevant countries and estimated costs. We varied all cost categories (aside from pharmacist wage, placebo medication cost, motorcycle costs to get to clinic, and training manuals cost) identified in the micro-costing study employing country-specific data (Table 2), keeping constant the number of resources used. To vary detoxification and building fixed costs as well as testing and materials in variable costs, we used 2005 World Bank (WB) data (closest to 2004) on the price level index (PLI) in health, which is the ratio of a purchasing power parity to a corresponding market exchange rate (IBRD/WB 2008). The PLI indicates the number of common currency units needed to purchase the same good or service in each country, thereby providing the differences in price levels between countries (World Bank n.d.). Advisor costs were kept constant to account for the possible need of an international consultant.

We estimated costs for three groups of countries, according to (1) significant heroin use—including the three largest heroin producers in the world (Myanmar, Afghanistan, Lao PDR) plus the largest heroin users of the major regions (Brazil, Iran, India, the Russian Federation, the United Kingdom, and the United States) (UNODC 2009); (2) geographical proximity to Malaysia (Australia, Bangladesh, Cambodia, China, Indonesia, New Zealand, Philippines, Singapore, Thailand, and Vietnam); or (3) a comparable GDP per capita in 2004 to Malaysia (in increasing order: Botswana, Panama, Mauritius, Costa Rica, Turkey, Lithuania, Latvia, Venezuela, Poland, Lebanon, Chile, and Hungary) (2004 GDP per capita data in constant 2000 USD, World DataBank). For the last group, we further compared their Human Development Index (HDI) world ranking (United Nations Development Programme [UNDP] 2006). Myanmar, Lao PDR, and India were also included in the regional analyses.

To obtain national-level results, we scaled up the buprenorphine intervention to treat larger numbers of persons, according to opiate use prevalence rates from the UNODC (2009) and certain benchmarks of government expenditures on health (WHO National Health Accounts [NHA]). To allow for the most accurate comparison to the Malaysian study, we converted all costs to 2004 USD.

We conducted sensitivity analyses varying significant cost drivers such as medication, and urine and blood tests; we also varied costs of advisors and wages of doctors, nurses, and pharmacists. These alternative cost scenarios are presented for Malaysia (the base case), and the two countries with the lowest and highest costs from each of the three country groupings.

Table 2: Gross-Costing Values and Sources

Country	Values and Sources										PLI, Relative to Malaysia	
	Hourly Rates			Medication Costs								
	Nurse		Physician	Min Wage		Bup (\$/mg)		Nalt (\$/50 mg)		Value	Source	
	Rate	Source		Rate	Source	Cost	Source	Cost	Source			
Heroin problem group												
Myanmar	0.09	ILO	0.14	ILO	0.01	US	0.59	1	2.13	1	0.04	2
Afghanistan	0.91	3	1.40	3	0.15	4	0.64	1	2.34	1	0.22	2
Lao PDR	0.12	5	0.14	5	0.05	US	0.87	1	3.16	1	0.34	6
Brazil	5.10	ILO	9.46	ILO	0.58	US	0.80	7	3.19	1	1.72	6
Egypt	0.38	ILO	0.40	ILO	0.04	8	0.57	1	2.06	1	0.47	6
India	1.88	9	2.86	10	0.91	11	0.75	1	2.74	1	0.41	6
Iran	0.57	12 (ratio-M)	1.70	12	0.67	13	0.16	14	1.01	1	0.41	6
Russia	0.33	ILO	1.74	ILO	0.16	US	0.50	1	1.83	1	0.97	6
UK	23.48	ILO	54.93	ILO	8.82	US	0.87	15	2.80	16	4.56	6
US	25.62	ILO	69.06	ILO	5.15	17	0.50	18	3.72	1	5.81	6
Region group												
Australia	19.83	ILO	28.69	ILO	8.78	US	0.42	19	2.93	20	4.63	6
Bangladesh	0.90	21	1.97	21	0.30	US	0.74	1	2.69	1	0.59	6
Cambodia	0.05	ILO	0.06	ILO	0.04	ILO	0.65	1	2.38	1	0.41	6
China	0.99	ILO	2.20	22	0.63	23	1.02	1	3.71	1	0.50	6
Indonesia	0.79	ILO	20.83	24	0.46	US	0.69	14	2.39	1	1.06	6
New Zealand	13.80	25	43.82	26	5.46	US	0.41	19	3.31	20	4.19	6
Philippines	0.97	ILO	1.90	ILO	0.67	US	0.83	1	3.03	1	0.97	6
Singapore	9.56	ILO	28.30	ILO	2.88	ILO	1.05	1	3.83	1	1.94	6

continued

Table 2. *Continued*

Values and Sources												
Hourly Rates				Medication Costs						PLI, Relative to Malaysia		
Nurse		Physician		Min Wage		Bup (\$/mg)		Nalt (\$/50 mg)				
	Rate	Source	Rate	Source	Rate	Source	Cost	Source	Cost	Source	Value	Source
Thailand	2.47	ILO	5.75	ILO	0.53	US	0.99	1	3.59	1	0.81	6
Vietnam	0.25	27	0.50	27	0.25	US	0.54	1	1.97	1	0.41	6
GDP per capita group												
Botswana	3.58	28	7.69	29	0.64	US	0.61	1	2.22	1	2.09	6
Panama	3.90	30	8.48	31	1.56	US	0.93	1	3.39	1	1.34	32
Mauritius	3.09	ILO	8.28	ILO	0.44	US	0.76	1	2.78	1	1.34	6
Costa Rica	3.86	ILO	8.57	ILO	0.83	US	0.52	1	1.89	1	0.96	32
Turkey	4.20	ILO	7.91	ILO	1.82	US	0.67	1	2.42	1	2.38	6
Lithuania	4.29	ILO	6.03	ILO	1.11	US	0.85	1	3.10	1	1.56	6
Latvia	2.50	ILO	5.04	ILO	0.91	US	0.68	1	2.47	1	1.47	6
Venezuela	1.31	ILO	1.10	ILO	1.16	US	0.57	1	2.08	1	1.69	6
Poland 33	9.16	ILO	4.86	ILO	1.72	US	1.02	1	3.71	1	1.59	6
Lebanon	3.10	34	13.44	35	1.43	US	0.93	1	3.38	1	1.69	6
Chile	3.82	ILO	10.69	ILO	1.02	US	0.92	1	3.36	1	2.13	6
Hungary	5.50	ILO	8.20	ILO	1.63	US	0.87	1	3.18	1	1.97	6

Notes. All costs are in 2004 USD, using the annual average of U.S. Treasury quarterly exchange rates from *Treasury Reporting Rates of Exchange*. For minimum wage data citing non-ILO and non-U.S. sources, the highest available minimum wage is used for a conservative cost estimate. Where applicable, wages and prices are adjusted to 2004 levels using annual percent change in consumer prices as reported by IMF World Economic Outlook (Tables A6 and A7), April 2003, April 2005, and April 2010.

References can be found in Appendix S1.

Bup, buprenorphine; ILO, International Labour Organization database of wages (<http://laborsta.ilo.org/>); Min, minimum; Nalt, naltrexone; PLI, price level index (for the health category); Where it is referenced for minimum wage, it indicates the lowest wage listed; US, United States State Department Human Rights reports (<http://www.state.gov/g/drl/rts/hrpt/2004/index.htm>).

RESULTS

Malaysian Micro-Costing

Tables S1–4 report detailed variable, fixed, societal, and total costs. Direct costs (fixed and variable) accounted for approximately 90 percent of the total cost for the placebo, naltrexone, and buprenorphine treatment arms; the remaining 10 percent for each arm was attributable to societal costs (Table S4). While fixed and variable costs each made up 44 percent of the total cost of the placebo arm, variable costs—which included medication cost—constituted over half of the total cost of naltrexone, and almost 65 percent that of buprenorphine. Medication costs accounted for the greatest percentage of total costs for both buprenorphine (27 percent) and naltrexone (12 percent) arms (Table 3). This was highlighted by the incremental variable costs, which were \$29,527 comparing buprenorphine to naltrexone, while the total incremental costs were only marginally higher—\$32,460 (Table S4). Total incremental costs per participant were \$699 comparing buprenorphine to naltrexone.

The separate cost components of urine and blood testing made up a combined 18 percent of total costs for naltrexone and 16 percent for buprenorphine (Table 3). Nurse time to administer medication—15 minutes each dose to greet participants, log them in, administer the drug, and log out—was more costly for buprenorphine (\$8,162) than for naltrexone (\$5,146) (Table S1). Nurse and psychiatrist time spent in individual and group therapy combined was also higher for buprenorphine (\$6,500, buprenorphine; \$5,335, naltrexone) (Table S1).

Table 3: Selected Malaysia Micro-Costing Components as Percentage of Total Costs for Naltrexone and Buprenorphine Interventions

	<i>Naltrexone (%)</i>	<i>Buprenorphine (%)</i>
Patient time for individual therapy	0.32	0.32
Patient time for dosage	0.62	0.68
Patient time for group therapy	0.68	0.77
Pharmacist time for medication administration	0.74	0.82
Psychiatrist time for group therapy	3.30	2.29
Nurse time for individual therapy	3.63	3.62
Nurse time for medication administration	7.04	7.74
Blood testing	8.52	6.04
Urine testing	9.68	10.00
Medication costs	11.61	27.43

Notes. Costs do not add to 100% of total costs because only selected costs are being reported; costs not shown include fixed costs and all other variable and societal costs (Tables S1–3).

Gross-Costing

Because gross-costing lacks the same precision as micro-costing, we report extrapolated costs to the nearest \$10. For buprenorphine treatment in all countries, variable costs accounted for the highest costs, followed by fixed and societal costs (Table S5).

Heroin Group

Myanmar—one of the three largest producers of heroin in the world—and Iran yielded the lowest buprenorphine treatment costs (\$36,710; \$830/person), followed by Afghanistan (\$48,010; \$1,090/person). The United Kingdom (\$316,900; \$7,200/person) and United States (\$329,980; \$7,500/person) yielded the highest (Table 4). Myanmar's costs proved exceedingly low due to its low estimated PLI and minimum wage. India and the Russian Federation yielded similar total cost estimates for buprenorphine, ranging from \$66,520 to 69,880 or \$1,510–1,590 per person (Table 4). Medication-only costs for buprenorphine ranged from \$7,020 (Iran) to \$38,150 (United Kingdom and Lao PDR) (Table S6). Comparing cost categories within buprenorphine treatment, in all countries, variable costs accounted for the highest costs, followed by fixed and societal costs (Table S5). The variation in societal costs for buprenorphine treatment (\$3,450–59,000) proved dependent upon the country's minimum wage (Table S5).

Incremental costs comparing buprenorphine to naltrexone treatment also varied. Compared to naltrexone, the buprenorphine intervention would cost an additional \$420 in Myanmar, \$480 in Afghanistan, and \$720 in Brazil (Tables 4 and S5). The United Kingdom had the highest incremental costs for buprenorphine treatment (\$1,360); in the United States this cost was \$940.

Of the estimated 288,000 and 331,000 opiate users in Myanmar and Afghanistan, 10 percent could be treated with this buprenorphine intervention at costs of \$24 and \$36 million, respectively (Table S7).

Regional Group

Excluding Myanmar (also included in the regional analysis), Vietnam had the lowest buprenorphine intervention costs (\$50,460); Australia reported the highest (\$291,280) (Table 4; Figure S1a). Neighboring countries Cambodia, Vietnam, and Lao PDR had average costs per person for buprenorphine treatment of \$1,220, \$1,150, and \$1,390, respectively. Bangladesh,

Table 4: Total Costs of Buprenorphine and Naltrexone Treatments for Heroin Dependence in Malaysia and Thirty-Two Countries

	<i>Naltrexone</i>		<i>Buprenorphine</i>		<i>Incremental Costs/pp B-N</i>
	<i>Total</i>	<i>Total/pp</i>	<i>Total</i>	<i>Total/pp</i>	
Heroin problem					
<i>Malaysia</i>	<i>73,042.29</i>	<i>1,698.66</i>	<i>105,502.08</i>	<i>2,397.77</i>	<i>699.12</i>
Myanmar	17,580	410	36,710	830	420
Afghanistan	26,340	610	48,010	1,090	480
Lao PDR	32,510	760	61,060	1,390	630
Brazil	88,700	2,060	122,220	2,780	720
Egypt	32,500	760	52,950	1,200	440
India	39,700	920	66,520	1,510	590
Iran	29,530	690	36,710	830	140
Russian Fed	49,390	1,150	69,880	1,590	440
UK	251,310	5,840	316,900	7,200	1,360
US	282,130	6,560	329,980	7,500	940
Region					
Australia	247,150	5,750	291,280	6,620	870
Bangladesh	41,370	960	67,710	1,540	580
Cambodia	31,440	730	53,730	1,220	490
China	44,500	1,040	79,010	1,800	760
Indonesia	59,130	1,380	86,550	1,970	590
New Zealand	211,910	4,930	246,490	5,600	670
Philippines	57,860	1,350	88,750	2,020	670
Singapore	117,710	2,740	164,670	3,740	1,000
Thailand	55,960	1,300	91,390	2,080	780
Vietnam	31,050	720	50,460	1,150	430
GDP per capita (increasing order)					
Botswana	95,890	2,230	126,000	2,860	630
Panama	80,430	1,870	117,840	2,680	810
Mauritius	71,100	1,650	102,040	2,320	670
Costa Rica	57,100	1,330	80,240	1,820	490
Turkey	113,550	2,640	148,140	3,370	730
Lithuania	84,470	1,960	120,130	2,730	770
Latvia	75,760	1,760	105,220	2,390	630
Venezuela	81,320	1,890	108,240	2,460	570
Poland	95,980	2,230	139,290	3,170	940
Lebanon	91,500	2,130	129,940	2,950	820
Chile	104,720	2,440	144,490	3,280	840
Hungary	103,050	2,400	141,960	3,230	830

Notes. All amounts in 2004 USD; exchange rates from U.S. Treasury, averaged over the four quarters of 2004. Costs for countries other than Malaysia are gross-costed and reported to the nearest \$10. Italic type indicates micro-costed values for Malaysia; all other values are gross-costed and extrapolated based on Malaysian values.

B, buprenorphine; N, naltrexone; pp, per person.

with costs per person of \$1,540, presented costs more similar to those of India (\$1,510) and China (\$1,800) (Table 4). Medication-only costs for buprenorphine ranged from \$17,980 (New Zealand) to \$44,730 (China) (Table S6), while societal costs spanned from \$3,640 (Cambodia) to \$58,750 (Australia) (Table S5).

All countries' incremental costs (B-N) were within a range of \$420 (Myanmar) to \$1,000 (Singapore). Although Australia had the highest total buprenorphine costs, its incremental (B-N) costs (\$870) were lower than Singapore's. New Zealand and Philippines reported very different buprenorphine costs (\$246,490 and \$88,750, respectively), but they had the same incremental (B-N) cost of \$670 (Table 4). Administering the buprenorphine intervention in China would cost an estimated \$79,010 (\$1,800/person), or an additional \$760 per person compared to naltrexone, whereas in Indonesia the average cost per person was \$1,970, but incremental costs were \$590 (Table 4).

It would cost an estimated \$26–27 million to treat 10 percent of opiate users with the buprenorphine intervention in Vietnam and Thailand, while an estimated 100 percent of opiate users in Cambodia and Lao PDR could be treated for \$8 and \$30 million, respectively (Table S7).

GDP per Capita Group

Of the countries similar to Malaysia in GDP per capita, Costa Rica had the lowest buprenorphine intervention cost at \$80,240 (\$1,820/person), whereas Turkey had the highest at \$148,140 (\$3,370/person) (Table 4). Costa Rica's low cost was due to its low minimum wage and relatively inexpensive medication cost. Medication-only costs of the buprenorphine intervention ranged from \$22,800 (Costa Rica) to \$44,730 (Poland) (Table S6); societal costs varied from \$6,160 (Mauritius) to \$14,860 (Turkey) (Table S5).

Intervention costs did not necessarily correlate with HDI rankings. Although Botswana had the lowest ranking HDI in 2004 (131) as well as the smallest GDP per capita of this group (\$3,941), its buprenorphine intervention costs were \$2,860 per person, which was more expensive than Mauritius (\$2,320/person; HDI—63), Costa Rica (\$1,820/person; HDI—48), and Venezuela (\$2,460/person; HDI—72) (Table 4). Hungary (35) and Chile (38) ranked highest in HDI as well as GDP per capita and incurred per person costs of \$3,230 and \$3,280, respectively.

The naltrexone intervention was least expensive in Costa Rica (\$1,330/person), Mauritius (\$1,650/person), and Latvia (\$1,760/person). Costa Rica

had the smallest incremental (B-N) cost (\$490), whereas Poland had the largest (\$940) (Table 4).

For an estimated \$2 million, 10 percent of opiate users could be treated with the buprenorphine intervention in Botswana or Panama. In Lithuania, an estimated 100 percent of opiate users could be treated at a cost of <\$10 million (Table S7).

Sensitivity Analyses

The results of sensitivity analyses show that total costs of each treatment may be sensitive to variations in costs of different inputs, even within the same country (Table S8). In countries with relatively higher incomes, such as the United States, Australia, and Turkey, changes in urine and blood test costs made the greatest difference to the total cost of all three treatment arms, compared to costs of advisors, medication, and wages. Interventions with more expensive medications—especially buprenorphine but also naltrexone—tended to be most sensitive to variations in medication costs, as shown in Myanmar, Malaysia, Vietnam, and Costa Rica. The total costs of the placebo and naltrexone arms—which were cheaper relative to the buprenorphine arm—tended to be more responsive to other factors: for the placebo and naltrexone arms, total costs in Malaysia were most sensitive to doctor, nurse, and pharmacist wages. In Myanmar, the country with the lowest costs in our study, the total cost of the cheapest arm—the placebo arm—proved most sensitive to advisor costs, which accounted for 20 percent of all costs.

DISCUSSION

We developed and employed a micro-costing methodology, the gold standard for economic analyses of clinical trials, to estimate the costs of interventions for heroin dependence in Malaysia as well as created an analytical framework and methodology for gross-costing the interventions for replication in other countries. Costs of medication and urine and blood testing were significant drivers of intervention costs in Malaysia, while personnel costs for time in therapy and administering medication made up a smaller percentage of total costs.

Through gross-costing for the other 32 countries, we found that urine and blood testing and medication costs continued to account for large portions of intervention costs, ranging from 33 percent (Australia) to 72 percent (Myan-

mar, Lao PDR) of the total buprenorphine intervention costs, with an average of 54 percent (Table S6). Incremental costs comparing buprenorphine to naltrexone treatment proved low; they were estimated to be under \$1,000 for all countries except the United Kingdom and Singapore, driven partly by medication costs.

We further found that the buprenorphine intervention could be implemented in the three largest heroin-producing countries in the world with relatively low expense, and at <\$2,000 per person in 13 countries. Per person costs of the buprenorphine intervention were 54 percent of GDP per capita in Malaysia and spanned from 20 percent (United States) to over 300 percent in Afghanistan, Lao PDR, Bangladesh, and Cambodia (Table S9). By this standard the costs may seem high in very low-income countries, but they are arguably worthwhile investments when compared to the costs of long-term HIV/AIDS treatment and drug abuse. Take Cambodia, for example, where the buprenorphine intervention was estimated to be \$1,220 per person or 330 percent GDP per capita (Table S9). A 2002 study funded by USAID estimated the costs of providing generic versions of highly active antiretroviral therapy (HAART) (with lab costs) in Cambodia to be \$532 per person *per year* (144 percent GDP per capita) (Forsythe 2002). If the buprenorphine intervention delayed drug-related HIV infection in one opiate user for 2.3 years, the savings from obviated HIV treatment would pay for the intervention costs. The intervention would pay for itself even more quickly if savings from the burdens of drug-related crimes, morbidity, accidents, and lost productivity were factored in as well.

Scaling up the buprenorphine intervention (assuming no economies of scale) according to certain benchmarks of government expenditures on health (WHO NHA) and opiate use prevalence rates from the UNODC provided policy-relevant results (UNODC 2009). Excluding the costs of finding and recruiting opiate users and maintaining their participation in treatment, an increase of <1 percent of government expenditure on health could be used to treat at least 10 percent of the opiate-using population in the following countries: the United Kingdom, United States, Australia, Cambodia, New Zealand, Philippines, Singapore, Thailand, Botswana, Panama, Turkey, Lithuania, Venezuela, Poland, Lebanon, Chile, and Hungary. Myanmar could treat 10 percent of its estimated 288,000 opiate users at a cost of \$24 million. Afghanistan, Thailand, and Vietnam could treat 10 percent of their opiate-using population with costs between \$26 and \$36 million, and 100 percent of estimated opiate users could be treated in Cambodia and Lao PDR at a cost of \$8 and \$30 million, respectively (Table S7). In 2005, the Vietnamese government

invested \$70 million in compulsory drug treatment centers (WHO 2009). This amount could treat an estimated 60,870 heroin users in that country with this buprenorphine intervention. It would cost an estimated \$6 million to treat 10 percent of primary heroin users arrested in Malaysia in 2004 (estimated to be 2,495, based on data provided by Chawarski, Mazlan, and Schottenfeld 2006).

In addition to the principal findings above, gross-costing analyses in the heroin and regional groups according to each country's 2004 GDP per capita and HDI also revealed important results (HDI for Afghanistan was unavailable). Intervention costs were not well correlated with HDI ranking. For example, India, Cambodia, Myanmar, Lao PDR, and Bangladesh ranked lowest in HDI, ranging from 126 to 137, respectively, but reported dissimilar intervention costs. Myanmar (\$36,710; \$830/person) had just over half the buprenorphine intervention cost of Bangladesh (\$67,710; \$1,540/person), while Cambodia (\$53,730; \$1,220/person), Lao PDR (\$61,060; \$1,390/person), and India (\$66,520; \$1,510/person) yielded costs closer to—but still less than—those of Bangladesh. This was due to Bangladesh's high PLI relative to this group (Table 2). Other examples were Indonesia and Vietnam, respectively, 108 and 109 on the HDI, but each showed fairly different buprenorphine costs (\$86,550, or \$1,970/person; and \$50,460, or \$1,150/person). These differences were accounted for by the higher PLI and salaries in Indonesia relative to Vietnam (Table 2). Total intervention costs, however, were closer than what one might expect given the large disparities in costs and salaries, partly due to comparable costs of buprenorphine, the main cost driver. We determined another significant difference in costs in the Russian Federation, whose HDI ranking was 65, better than that of Brazil (69), but whose costs were significantly lower (\$69,880; \$1,590/person) than Brazil's (\$122,220; \$2,780/person). All values we varied were lower in Russia than in Brazil.

Buprenorphine treatment costs and GDP per capita were correlated for the very high-income countries such as the United States, United Kingdom, Australia, and New Zealand. For example, the United States had a significantly higher GDP per capita (\$36,920) than Australia (\$23,563), as well as higher buprenorphine intervention costs (\$329,980 for the United States, \$291,280 for Australia). For less wealthy countries, however, the correlation weakened. Egypt (GDP per capita \$1,501) had a total buprenorphine treatment cost of \$52,950 or \$1,200 per person, lower than in Bangladesh, Cambodia, China, Indonesia, India, Lao PDR, and the Philippines, all countries with lower GDP per capita. Egypt's salaries—\$0.38/hour for nurses, \$0.40/hour for physicians, and \$0.04/hour for the minimum wage—were exceedingly

low (Table 2). Only Lao PDR, Cambodia, Myanmar, Vietnam, and Russian Federation had lower nurse salary estimates; only Myanmar, Lao PDR, and Cambodia had lower physician salary estimates; and only Myanmar had a lower minimum wage.

Complex economic and political issues beyond those of cost and efficacy affect the implementation and potential effectiveness of drug treatment programs. Heroin production is an important part of the economy in several countries. In 2002, it was estimated that Afghanistan's opium production constituted 27 percent of its total GDP, although that figure has since dropped to 4 percent in 2009 (UNODC/Ministry of Counter Narcotics 2009). Farmers in Afghanistan in 2009 were able to earn over three times more by producing opium (\$3,562/ha) than wheat (\$1,101/ha) (UNODC/Ministry of Counter Narcotics 2009). Afghanistan not only supplies more than 90 percent of the world's illicit opium (UNODC 2010), but the major supply routes originating in Afghanistan also pass through other countries in this study—Russian Federation, Iran, and Turkey. Myanmar continues to be the main opium supplier for Southeast Asia and China, although production decreased by 59 percent from 2003 to 2008 (UNODC 2010). The formulation and implementation of drug treatment and policy may be more difficult and less effective in countries in which heroin is economically significant and widely available.

Government's approach toward heroin dependence is also consequential for the implementation of treatment programs, as demonstrated in Malaysia. Prior to 2005, treatment of heroin dependence was considered a security and social deviancy concern under the purview of the Ministry of Internal Security (Scorzelli 1992; Mazlan, Schottenfeld, and Chawarski 2006). The Malaysian government, however, realized it was progressing toward all of the Millennium Development Goals except for the spread of HIV/AIDS, leading it to consider injection drug use as a public health and medical issue and giving authority for its treatment to the Ministry of Health (Reid, Kamarulzaman, and Sran 2007; WHO 2009). The securitization and restriction of heroin dependence treatment was not unique to Malaysia. In Cambodia, for example, buprenorphine remains a restricted substance (WHO 2009), while in Kyrgyzstan, Cambodia, Malaysia, and Indonesia patients at methadone clinics and needle and syringe program centers continue to be subject to arrest (Open Society Institute 2008; WHO 2009). Nonetheless, the Open Society Institute reports that methadone and buprenorphine programs in China and Iran are planned to dramatically increase, the Global Fund to Fight AIDS, Tuberculosis and Malaria has given support to methadone or buprenorphine treatment projects in countries including China and Indonesia, and Vietnam has

received international grants to begin pilot projects (Open Society Institute 2008). Cost analyses are a necessary input for policy analysis and planning, and for the generation of political will to support such programs (Ruger 2009).

To our knowledge, this is the first study that both develops a methodology and micro-costs heroin treatment interventions and creates and expands an analytical framework and methodology to estimate implementation costs for health systems in other countries. We located one study that estimated treatment costs for IDUs in a developing country, analyzing hospital-based methadone maintenance in Indonesia for 129 clients (Afriandi et al. 2010). They estimated annual societal costs to equal \$123,672 (\$959/client) in 2007 USD, although it is unclear whether the counseling was as extensive as in our study. More research on the costs and feasibility of opioid substitution therapy is desirable, as this therapy has been shown to be effective for treatment retention in China, Indonesia, Thailand, Lithuania, and Poland (using methadone) (Lawrinson et al. 2008). We emphasize the costs of buprenorphine treatment in reporting results because this treatment is promising; it has been shown to be cost-effective in Australia (Harris, Gospodarevskaya, and Ritter 2005; Shanahan et al. 2006), the United Kingdom (Connock et al. 2007), and the United States (Barnett, Zaric, and Brandeau 2001). The cost estimates yielded by this study further suggest that buprenorphine treatment can be provided at low cost in other countries.

Treating heroin use has also been shown to reduce HIV risk behaviors (Chawarski, Mazlan, and Schottenfeld 2008). Of the countries studied, four have HIV prevalence above 40 percent among IDUs: Brazil (48 percent), Myanmar (43 percent), Thailand (43 percent), and Indonesia (43 percent). The Russian Federation, Vietnam, and Cambodia have high HIV prevalence among IDUs as well—37 percent, 34 percent, and 23 percent, respectively (UNODC 2009). Although cost-effectiveness is not assessed here, taking into account the costs to society of HIV infections is likely to indicate that such interventions are cost-effective, if not cost-saving. Of 14 studies located in a systematic review for HIV prevention in Thailand (Pattanaphesaj and Teerawattananon 2010), one targeted injecting drug users and three evaluated cost-effectiveness. Further work on the costs of HIV/AIDS among IDUs is needed. The costing framework developed in this study would facilitate the analysis of IDU HIV/AIDS prevention and treatment costs and savings at individual and societal levels, in future studies conducted within a given country or internationally.

To maximize the usefulness of our costing methodology, more international research is required to better specify medication and personnel costs globally. While the Management Sciences for Health publishes an “International Drug Price Indicator Guide” (Management Sciences for Health n.d.), buprenorphine and naltrexone are not included. Moreover, we estimated detoxification, testing, and overhead costs according to broad economic indices, suggesting additional need for country-specific research.

Our study has several limitations. First, gross-costing estimates lack the accuracy of micro-costing due to the nature of price weights (Polsky and Glick 2009). National-level data (e.g., national average wages from the International Labour Organization [ILO] and consumer price indices from the International Monetary Fund [IMF]) may not address directly the specific inputs and services that would be used in treatment replication; this problem is exacerbated in countries for which major sources provide no data and alternative (and potentially less reliable) information had to be substituted (Table 2). Second, due to limitations in data availability, we did not vary the pharmacist wage. Since it was very low in Malaysia, a country like the United States with high pharmacist salaries would incur higher personnel costs. In all other variations, however, we chose high-cost values to provide conservative cost estimates. Third, we did not take into account the infrastructure and personnel necessary to start up such interventions, which could be a major factor in countries where resources and health care workforce are limited. Fourth, variations in costs and salaries within a country could be significant, especially in developing or war-torn countries (Newbrander, Yoder, and Debevoise 2007). Fifth, although we included participants’ and family costs, we did not expand the societal perspective to include possible future cost savings. Strengths and weaknesses of micro-costing are discussed elsewhere (Ruger et al. 2009; Ruger, Ben Abdallah, and Cottler 2010).

Our study estimates the costs required to provide maintenance treatment and therapy for heroin dependence in Malaysia using a micro-costing framework and extrapolates its costs if implemented by health systems in 32 other countries through gross-costing. Depending on the cultural and political context, providing similar interventions could be inexpensive and may prove cost-effective. Understanding the cost implications of such treatments is an essential step in addressing heroin addiction in Malaysia and comparable countries worldwide.

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REFERENCES

- Afriandi, I., A. Y. Siregar, F. Meheus, T. Hidayat, A. van der Ven, R. van Crevel, and R. Baltussen. 2010. "Costs of Hospital-Based Methadone Maintenance Treatment in HIV/AIDS Control among Injecting Drug Users in Indonesia." *Health Policy* 95 (1): 69–73.
- Barnett, P. G., G. S. Zaric, and M. L. Brandeau. 2001. "The Cost-Effectiveness of Buprenorphine Maintenance Therapy for Opiate Addiction in the United States." *Addiction* 96 (9): 1267–78.
- Chawarski, M. C., M. Mazlan, and R. S. Schottenfeld. 2006. "Heroin Dependence and HIV Infection in Malaysia." *Drug and Alcohol Dependence* 82 (suppl 1): S39–42.
- . 2008. "Behavioral Drug and HIV Risk Reduction Counseling (BDRC) with Abstinence-Contingent Take-Home Buprenorphine: A Pilot Randomized Clinical Trial." *Drug and Alcohol Dependence* 94: 281–4.
- Connock, M., A. Juarez-Garcia, S. Jowett, E. Frew, Z. Liu, R. J. Taylor, A. Fry-Smith, E. Day, N. Lintzeris, T. Roberts, A. Burls, and R. S. Taylor. 2007. "Methadone and Buprenorphine for the Management of Opioid Dependence: A Systematic Review and Economic Evaluation." *Health Technology Assessment* 11 (9): 1–171.
- Forsythe, S. 2002. *Resource Requirements for Cambodia's 2001–2005 HIV/AIDS National Strategic Plan*. The POLICY Project/Future Group [accessed on June 20, 2011]. Available at http://www.policyproject.com/pubs/countryreports/CAM_costing.pdf.
- Gold, M. R., J. E. Siegel, L. B. Russell, and M. C. Weinstein, eds. 1996. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press.
- Harris, A. H., E. Gospodarevskaya, and A. J. Ritter. 2005. "A Randomised Trial of the Cost Effectiveness of Buprenorphine as an Alternative to Methadone Maintenance."

- nance Treatment for Heroin Dependence in a Primary Care Setting." *Pharmacoeconomics* 23 (1): 77–91.
- International Bank for Reconstruction and Development/The World Bank. 2008. *Global Purchasing Power Parities and Real Expenditures: 2005 International Comparison Program* [accessed on June 22, 2010]. Available at <http://siteresources.worldbank.org/ICPINT/Resources/icp-final.pdf>.
- International Monetary Fund. 2010. "World Economic Outlook Database" [accessed on January 12, 2011]. Available at <http://www.imf.org/external/pubs/ft/weo/2010/01/weodata/index.aspx>.
- Lawrinson, P., R. Ali, A. Buavirat, S. Chiamwongpaet, S. Dvoryak, B. Habrat, S. Jie, R. Mardiaty, A. Mokri, J. Moskalewicz, D. Newcombe, V. Poznyak, E. Subata, A. Uchtenhagen, D. S. Utami, R. Vial, and C. Zhao. 2008. "Key Findings from the WHO Collaborative Study on Substitution Therapy for Opioid Dependence and HIV/AIDS." *Addiction* 103 (9): 1484–92.
- Management Sciences for Health. n.d. "International Drug Price Indicator Guide" [accessed on June 18, 2010]. Available at <http://erc.msh.org/mainpage.cfm?file=1.0.htm&id=1&temptitle=Introduction&module=DMP&language=English>.
- Mazlan, M., R. S. Schottenfeld, and M. C. Chawarski. 2006. "New Challenges and Opportunities in Managing Substance Abuse in Malaysia." *Drug and Alcohol Review* 25 (5): 473–8.
- McBride, D., and F. Hessel. 2008. "Economic Measures." In *Encyclopedia of Public Health*, edited by W. Kirch, pp. 316–9. New York: Springer Science + Business Media.
- Ministry of Health of Malaysia/World Health Organization. 2004. *Consensus Report on HIV and AIDS: Epidemiology in 2004: Malaysia* [accessed on October 18, 2010]. Available at http://www.wpro.who.int/NR/rdonlyres/47E92EB0-3F10-45D9-BF7A-AEDCBF4A5E22/0/Consensus_Report_MAA_2004.pdf.
- Newbrander, W., R. Yoder, and A. B. Debevoise. 2007. "Rebuilding Health Systems in Post-Conflict Countries: Estimating the Costs of Basic Services." *International Journal of Health Planning and Management* 22 (4): 319–36.
- Open Society Institute. 2008. *Barriers to Access: Medication-Assisted Treatment and Injection-Driven HIV Epidemics. Public Health Fact Sheet*. Public Health Program, International Harm Reduction Development Program.
- Pattanaphesaj, J., and Y. Teerawattananon. 2010. "Reviewing the Evidence on Effectiveness and Cost-Effectiveness of HIV Prevention Strategies in Thailand." *BMC Public Health* 10: 401 [Epub ahead of print].
- Polsky, D., and H. Glick. 2009. "Costing and Cost Analysis in Randomised Trials: Caveat Emptor." *Pharmacoeconomics* 27 (3): 179–88.
- Reid, G., A. Kamarulzaman, and S. K. Sran. 2007. "Malaysia and Harm Reduction: The Challenges and Responses." *International Journal on Drug Policy* 18 (2): 136–40.
- Ruger, J. P. 2009. *Health and Social Justice*. Oxford, England: Clarendon Press.
- Ruger, J. P., A. Ben Abdallah, and L. Cottler. 2010. "Costs of HIV Prevention among Out-of-Treatment Drug-Using Women: Results of a Randomized Controlled Trial." *Public Health Reports* 125 (suppl 1): 83–94.

- Ruger, J. P., K. M. Emmons, M. H. Kearney, and M. C. Weinstein. 2009. "Measuring the Costs of Outreach Motivational Interviewing for Smoking Cessation and Relapse Prevention among Low-Income Pregnant Women." *BMC Pregnancy and Childbirth* 9: 46.
- Schottenfeld, R. S., M. C. Chawarski, and M. Mazlan. 2008. "Maintenance Treatment with Buprenorphine and Naltrexone for Heroin Dependence in Malaysia: A Randomised, Double-Blind, Placebo-Controlled Trial." *Lancet* 371 (9631): 2192–200.
- Scorzelli, J. F. 1992. "Has Malaysia's Antidrug Effort Been Effective?" *Journal of Substance Abuse Treatment* 9 (2): 171–6.
- Shanahan, M. D., C. M. Doran, E. Digiusto, J. Bell, N. Lintzeris, J. White, R. Ali, J. B. Saunders, R. P. Mattick, and S. Gilmour. 2006. "A Cost-Effectiveness Analysis of Heroin Detoxification Methods in the Australian National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD)." *Addictive Behaviors* 31 (3): 371–87.
- United Nations Development Programme. 2006. *Human Development Report*. New York: Palgrave MacMillan.
- United Nations Office on Drugs and Crime. 2009. *World Drug Report*. Vienna. E.09. XI.12 [accessed on October 18, 2010]. Available at http://www.unodc.org/documents/wdr/WDR_2009/WDR2009_eng_web.pdf.
- United Nations Office on Drugs and Crime. 2010. *World Drug Report*. Vienna. E.10. XI.13 [accessed on October 18, 2010]. Available at http://www.unodc.org/documents/wdr/WDR_2010/World_Drug_Report_2010_lo-res.pdf.
- United Nations Office on Drugs and Crime/Ministry of Counter Narcotics. 2009. *Afghanistan Opium Survey 2009: Summary Findings*. Kabul, Afghanistan: U.N. Office on Drugs and Crime/Ministry of Counter Narcotics [accessed on October 18, 2010]. Available at http://www.unodc.org/documents/crop-monitoring/Afghanistan/Afghanistan_opium_survey_2009_summary.pdf.
- World Bank. n.d. "International Comparison Program. Price and Volume Measures" [accessed on June 23, 2010]. Available at <http://go.worldbank.org/L65J0VWOC0>.
- World DataBank. "GDP Per Capita (Constant 2000 US\$), 2004" [accessed June 17, 2011]. Available at <http://data.worldbank.org/indicator>.
- World Health Organization. 2009. *Assessment of Compulsory Treatment of People Who Use Drugs in Cambodia, China, Malaysia and Viet Nam: An Application of Selected Human Rights Principles*. Office for the Western Pacific Region [accessed on October 18, 2010]. Available at http://www.who.int/hiv/topics/idu/drug_dependence/compulsory_treatment_wpro.pdf.
- World Health Organization. "National Health Accounts" [accessed on September 10, 2011]. Available at <http://www.who.int/nha/country>.
- World Health Organization Representative Office in Malaysia. 2006–2008. *WHO Country Cooperation Strategy, Malaysia* [accessed on October 18, 2010]. Available at http://www.who.int/countryfocus/cooperation_strategy/countries/ccs_mys_final_en.pdf.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

Appendix SA1: Author Matrix.

Appendix S1: Technical Appendix.

Table S1: Variable Costs, Malaysia Micro-Costing Study.

Table S2: Fixed Costs, Malaysia Micro-Costing Study.

Table S3: Societal Costs, Malaysia Micro-Costing Study.

Table S4: Total Average and Incremental Costs, Malaysia Micro-Costing Study.

Table S5: Total and Incremental Costs for Thirty-Two Countries.

Table S6: Urine and Blood Testing and Medication Costs as Percentage of Total Costs of Naltrexone and Buprenorphine Treatments for Thirty-Two Countries.

Table S7: Nationwide Cost Estimates of Reaching Targeted Population with Buprenorphine Intervention.

Table S8: Sensitivity Analyses Varying Costs of Advisors, Medication Costs, Urine and Blood Test Costs, and Doctor, Nurse, and Pharmacist Wages.

Table S9: Naltrexone and Buprenorphine Costs per Person as Percentage of GDP per Capita for Malaysia and Thirty-Two Countries.

Figure S1: (a) Regional Group: Total Costs for Buprenorphine and (b) Regional Group: Total Costs for Naltrexone.

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