RESEARCH PAPER

The cost effectiveness of pharmacological smoking cessation therapies in developing countries: a case study in the Seychelles

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Objective: To examine the incremental cost effectiveness of the five first line pharmacological smoking cessation therapies in the Seychelles and other developing countries.
Design: A Markov chain cohort simulation.
Subjects: Two simulated cohorts of smokers: (1) a reference cohort given physician counselling only; (2) a treatment cohort given counselling plus cessation therapy.
Intervention: Addition of each of the five pharmacological cessation therapies to physician provided smoking cessation counselling.
Main outcome measures: Cost per life-year saved (LYS) associated with the five pharmacotherapies. Effectiveness expressed as odds ratios for quitting associated with pharmacotherapies. Costs based on the additional physician time required and retail prices of the medications.
Results: Based on prices for currently available generic medications on the global market, the incremental cost per LYS for a 45 year old in the Seychelles was US$599 for gum and $227 for bupropion. Assuming US treatment prices as a conservative estimate, the incremental cost per LYS was significantly higher, though still favourable in comparison to other common medical interventions: $3712 for nicotine gum, $1982 for nicotine patch, $4597 for nicotine spray, $4291 for nicotine inhaler, and $1324 for bupropion. Cost per LYS increased significantly upon application of higher discount rates, which may be used to reflect relatively high opportunity costs for health expenditures in developing countries with highly constrained resources and high overall mortality.
Conclusion: Pharmacological cessation therapy can be highly cost effective as compared to other common medical interventions in low mortality, middle income countries, particularly if medications can be procured at low prices.

Tobacco use claims four million lives in the world each year, and this figure is expected to rise to 10 million by 2030.[1] The tobacco epidemic is particularly devastating in developing countries, where rates of tobacco use and tobacco related morbidity and mortality are rising steadily. By 2030 an estimated 70% of all tobacco deaths—half of which will occur during middle age (35–69 years old)—will be accounted for in developing countries.[1]

Smokers who quit before the onset of illness will avoid most of the added mortality risk from smoking within a few years of cessation.[2 3] Therefore increased cessation rates would avert millions of tobacco caused deaths over the next 50 years.[1 4] Quit rates are low, and only 2–3% of smokers who make unaided quit attempts have long term success. Quit rates are even lower in developing countries—ex-smokers comprise an estimated 5–10% of the population versus 30–40% in many developed nations.[5]

Pharmacological smoking cessation therapies—nicotine gum, nicotine patch, nicotine nasal spray, nicotine inhaler, and bupropion, an anti-depressant that reduces symptoms of withdrawal and depression associated with quitting—have been shown to approximately double a smoker's odds of quitting successfully when used in adjunction to brief physician counselling[6–8] (table 1). Furthermore, pharmacological cessation therapies (henceforth called ''pharmacotherapy'' or ''treatment'') have been demonstrated to be cost effective in developed country settings as compared to other common preventive drug treatments.[9–13]

The purpose of this analysis is to estimate the cost effectiveness of pharmacotherapy given in adjunct to physician counselling to smokers in the Seychelles, a rapidly developing middle income country in the Indian Ocean, as well as to provide a broad range of cost effectiveness estimates, via sensitivity analysis, that could mimic conditions in other developing country settings.

Smoking prevalence among Seychellois men and women aged 25–64 years is 37% and 6.9%, respectively, and approximately 55% among middle aged and older adult men.[14 15] In parallel with the country's rapid economic development, behaviour related health risks for cardiovascular disease, including hypertension, hypercholesterolaemia, and obesity, are increasingly prevalent,[14–16] and may be compounded by smoking.

METHODS

Calculation of cost effectiveness

We calculated the incremental cost per life-year saved of pharmacotherapy as provided by Seychellois general practitioners (GPs), assuming it is given in association with brief cessation counselling. We conducted the analysis from a third party payer perspective, assuming the Ministry of Health (versus individual smokers) would finance the medical and non-medical costs of the intervention as the sole payer. Indeed, all medications are provided free of charge to patients in the Seychelles by the National Health Service (NHS), so a

Abbreviations: CPSII, cancer prevention study II; GP, general practitioner; LYS, life-year saved; NHA, National Health Service; NRT, nicotine replacement therapy; QALY, quality adjusted life-year

Table 1 Variables used in the analysis

Variable	Base case (range for sensitivity analysis)
Natural cessation rate among all smokers (%)	2.5 (1–4)
OR†* counselling only	1.73 (1.46–2.03)
OR†** nicotine gum	1.66 (1.52–1.82)
OR†** nicotine patch	1.80 (1.61–2.01)
OR†** nicotine spray	2.35 (1.63–3.38)
OR†** nicotine inhaler	2.14 (1.44–3.18)
OR†** bupropion	2.51 (1.5–3.0)
Smokers who stop treatment after first month (%)	50 (40–60)
Smokers who stop treatment after second month (%)	20 (15–25)
Lifetime probability of relapse after one year of abstinence (%)	35 (10–50)
Time required for counselling (minutes)	10 (5–15)
Additional physician time required for treatment (minutes)	90 (75–105)
Cost of pharmacological treatments	US prices (12.5–100%)
Cost per hour of physicians' time for counselling (US$)	11.11 (1.40–22.22)
Discount rate (%)	3 (0–10)

95% confidence intervals used for sensitivity analysis range for treatment odds ratios.
*Odds ratio for continued cessation after one year, as compared to no intervention.
**Incremental odds ratio for continued cessation after one year, as compared to counselling only.
†Sources: Silagy,[6] Silagy *et al*,[7] Fiore MC *et al*.[8]

third party payer perspective has the advantage of presenting the results in a most practical context for policymakers.

We used a validated Markov-chain computer simulation to synthesise two cohorts of identical smokers.[17] We characterised the two cohorts according to a set of base case assumptions (table 1) and used the Markov design to account for smoking relapse among a subset of patients who started pharmacotherapy. The reference cohort received only cessation counselling from a physician. The second cohort received the same counselling plus each of the five pharmacotherapies. We expressed the cost effectiveness of the interventions as the incremental cost per life-year saved that is attributable to the offer, use, and follow up of each of the five treatments.

Natural cessation rates and risk of relapse

Data on natural (unassisted) quit rates are not available for the Seychelles. Therefore, based on data extracted from the existing literature, we assumed a natural quit rate among smokers of 2.5%.[18 19] The long term risk of relapse for former smokers is not well documented in developing countries, so we adopted the conservative assumption of a 35% lifetime probability of relapse after one year of abstinence.[9 11 20 21] Based on available evidence and theory, we assumed that only 25% of current smokers are truly prepared to make a serious quit attempt.[22 23] Each of these variables was subjected to sensitivity analysis.

Mortality effects of smoking cessation

We based the mortality effects of smoking cessation on the results of the American Cancer Society cancer prevention study II (CPSII), which compared mortality rates for smokers and non-smokers according to five year age ranges up to age 75.[20] According to this and other studies the excess mortality risk declines significantly within the first few years after cessation, and the mortality rate of former smokers finally rejoins that of never smokers approximately 20 years after quitting.[2 3 20 24] Based on the findings of the CPSII we extrapolated the mortality curves to age 90 and supposed a phase-in period of 25 years for former smokers' mortality risk to return to that of non-smokers.[20]

Cost of pharmacotherapy

We calculated the total cost of pharmacotherapy by summing the cost of the additional time spent by GPs and the respective prices for each treatment. Pharmacotherapy is not yet available in the Seychelles, so we used 2003 US retail prices as a conservative base case assumption (CVS, Chapel Hill, North Carolina, USA; RiteAid, Los Angeles, California, January 2003). Because treatment prices can vary significantly across countries (table 2),[25–28] we conducted sensitivity analysis including prices as low as 12.5% of US prices (current prices of locally manufactured nicotine gum and bupropion in India). Current US clinical guidelines recommend that treatment usually last 1–6 months.[8] To reflect an average course of treatment, we assumed that treatment lasts three months. In the analysis we assumed that all patients who start pharmacotherapy use at least one month's supply of treatment.

We based the cost of health care providers' time in the Seychelles on 2002 wages in the NHS, which employs more than 95% of the country's practising physicians. Average monthly wages including all allowances and benefits were approximately $3000 to $4000 (15 000 to 20 000 Seychelles rupees) for consultants and medical officers, $2000 (~10 000 SRs) for GPs (used as base case assumption), and $1000 (~5000 SRs) for senior nurses. We also calculated the cost effectiveness of pharmacotherapies assuming monthly provider wages of $500 and $250 to reflect lower physician salaries that may be representative in many other middle and lower income developing countries. We assumed that initial cessation counselling would last 10 minutes for all patients, and that patients who agree to undergo pharmacotherapy would receive six additional 15 minute follow up sessions.

Table 2 Total price (US$) for three months* of smoking cessation therapy

	Gum (4 mg)		Patch (7 mg–21 mg)		Spray (10 ml)		Bupropion (150 mg)	
	Price	Ratio	Price	Ratio	Price	Ratio	Price	Ratio
USA†	475	1.00	321	1.00	1145	1.00	410	1.00
Switzerland[25]	362	0.76	362	1.13	756	0.66	354	0.86
UK[26]	254	0.53	321	1.00	649	0.57	193	0.47
Canada†	251	0.53	303	0.94	NA	–	120	0.29
Spain[27]	237	0.50	235	0.73	432	0.38	219	0.53
France[28]	214	0.45	259	0.81	N/A	–	242	0.59
Sweden†	153	0.32	157	0.49	364	0.32	189	0.46
India‡	63	0.13					48	0.12

*Average daily dose: gum, 10 pieces/day; patch, 1/day; spray, 24 applications/day; bupropion, 2 pills/day.
†Prices based on original survey of local pharmacies, December 2002.
‡Prices indicated by a local manufacturer, April 2003.

Currency exchange rates as published in the Seychelles currently range from 4.8:1 (Seychelles rupees:US$) to 5.2:1. To facilitate easy use of the study results, we applied a currency exchange rate of 5.0:1 to all cost data.

Sensitivity analysis

Sensitivity analysis accounts for real life variations in input values that could have important effects on cost effectiveness. In this study, we conducted multi-way sensitivity analysis to show the independent and interactive effects of a wide range of possible values in health care provider salary, treatment price, and discount rate. The approach not only highlights the relative influences of these variables on cost effectiveness, but also extends the relevance of the results to other generalised developing country settings.

Discounting

To account for the time gap between the costs of the intervention and the benefits in life-years saved, it is common practice to calculate the present discounted value of the earlier incurred costs and the later realised benefits, thereby measuring their value on the same relative scale.[29 30] We used a 3% discount rate in our base case analysis, which adheres to current guidelines for cost effectiveness analysis.[31] However, to present the results in their ''raw'' form and to acknowledge other discounting rationales, we included rates of 0%, 5%, and 10% in our sensitivity analysis.

RESULTS

Cost per LYS for all treatments should be interpreted in incremental terms, as they assume a base of physician counselling and reflect only the additional costs and benefits derived from adding pharmacotherapy to counselling. The cost per LYS in the Seychelles for counselling only was $64 for men and $97 for women.

According to the Seychelles base case assumptions, the cost per LYS ranged from $1311 to $6032 for men, and from $2052 to $9777 for women (table 3). For each treatment, the cost effectiveness ratio is lowest for men and women aged 35–49. All treatments become progressively less cost effective as patient age decreases or increases from the middle aged groups, resulting in a U shaped curve of cost effectiveness. While treatment efficacy is assumed to be equal across all age groups, for younger smokers, discounting and a relatively higher proportion that would have quit successfully without treatment sometime in the future diminish the cost effectiveness of treatment. Older smokers have relatively fewer life-years left to be saved, which diminishes the benefits but not the costs of the intervention, thereby lowering overall cost effectiveness at older ages.

The most cost effective treatment is bupropion, due to relatively high efficacy and low cost as compared to the other treatments, followed by the patch, gum, inhaler, and spray, in descending order. All treatments are more cost effective for men than for women. As men smoke in greater quantities than women, they tend to gain more units of benefit—life-years saved—from cessation at the same cost, thereby yielding lower (that is, more favourable) cost effectiveness ratios than women.[32]

Multi-way sensitivity analysis, based on a 45 year old male smoker, a range of provider salaries, treatment prices, and discount rates, demonstrated important influences on cost effectiveness (table 4). The strongest influences on cost effectiveness were treatment price and discount rate. For example, assuming Seychelles GP wages and a 3% discount rate, the cost per LYS for nicotine gum was over six times higher at 100% US treatment prices than at 12.5% treatment prices ($3712 versus $599, respectively). Based on these same assumptions, the cost per LYS for bupropion was 8.6 times higher at 100% versus 12.5% US prices ($1952 versus $227, respectively). Assuming Seychelles GP wages and 50% treatment prices, the cost per LYS for the patch was 11.4 times higher applying a 10% discount rate versus a 0% discount rate ($5219 versus $458, respectively).

The relative influence of health care provider cost was weak. For example, assuming 50% treatment prices and a 3% discount rate, the cost per LYS for gum was only 1.16 times higher at the highest salary than at the lowest ($2088 *v* $1798, respectively). Treatment efficacy also has a potentially important influence on cost effectiveness, particularly for the nicotine spray and inhaler, whose confidence intervals for efficacy are relatively wide. For example, if the odds ratio of quitting for the spray were 3.38 versus 1.63, the cost per LYS would be approximately 70% lower (data not shown).

DISCUSSION

Overall, pharmacotherapy—particularly bupropion, nicotine patch, and nicotine gum—is a cost effective intervention for reducing avoidable death and disease caused by tobacco use. Pharmacotherapy is highly cost effective as compared to other medical interventions that are often sponsored or subsidised by governments. Previous reviews have shown that the costs per quality adjusted life-year (QALY) saved for standard medications for hypercholesterolemia and hypertension ranged from $25,000 to $100,000,[33] while the cost per QALY saved for nicotine patch plus counselling was approximately 5–10 times lower, ranging from $4390 to $10 943.[11] Many chronic conditions like hypercholesterolaemia and hypertension often require lifelong treatment and hence lifelong financial investments, while the expenditure per patient associated with pharmacotherapy for smoking cessation typically lasts just three months, though in some cases up to six months.[8] It is important to note that while smoking cessation pharmacotherapy may outperform other common secondary prevention interventions in terms of cost effectiveness, practically speaking smoking cessation programmes would likely be implemented *in addition* to established interventions, which may imply increased overall spending.

Decision makers will consider implementation of pharmacotherapy within the context of highly constrained resources, though in the Seychelles and many other developing country settings, comparative cost effectiveness evidence is not yet available. Pharmacotherapy prices (that is, affordability) will likely be one of the most important deciding factors.

Table 3 Incremental cost per year of life saved (US$) for the Seychelles, by age

	Gum		Patch		Spray		Inhaler		Bupropion	
Age (years)	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
20–34	4385	7894	2341	4214	5430	9777	5069	9125	1564	2817
35–49	3675	5753	1962	3071	4551	7124	4248	6650	1311	2052
50–64	4870	6097	2600	3255	6032	7551	5630	7048	1738	2175

Table 4 Cost per life of year saved (US$) for smoking cessation therapies (for 45 year old men) by discount rate, price of drug* and salary of health service provider†

		Gum				Patch				Spray				Bupropion			
Discount	Salary	100%	50%	25%	12.5%	100%	50%	25%	12.5%	100%	50%	25%	12.5%	100%	50%	25%	12.5%
0%	4000	1680	907	521	327	916	514	313	212	2031	1049	558	313	606	333	197	129
	2000	1612	840	453	260	861	458	257	156	1997	1015	525	279	575	303	167	98
	1000	1579	806	420	227	833	430	229	128	1980	998	508	262	560	288	151	83
	500	1562	790	403	210	819	416	215	115	1972	990	499	254	553	280	144	76
	250	1554	781	395	202	812	409	208	108	1967	986	495	250	549	276	140	72
3%	4000	3867	2088	1198	754	2110	1183	720	488	4675	2415	1285	720	1394	767	453	297
	2000	**3712**	1933	1044	**599**	**1982**	1055	592	**360**	**4597**	2338	1208	**643**	**1324**	697	384	**227**
	1000	3635	1856	967	522	1917	991	527	296	4559	2299	1169	604	1290	662	349	192
	500	3597	1818	928	483	1886	959	495	264	4539	2279	1149	584	1272	645	331	174
	250	3577	1798	909	464	1870	943	479	248	4530	2270	1140	575	1263	636	322	166
5%	4000	6408	3460	1986	1249	3496	1960	1193	809	7747	4002	2130	1194	2311	1271	751	491
	2000	6152	3204	1730	993	3284	1748	980	596	7619	3874	2001	1065	2195	1155	636	376
	1000	6024	3076	1602	865	3178	1642	874	490	7554	3809	1937	1001	2137	1097	578	318
	500	5960	3012	1538	801	3125	1589	821	437	7522	3777	1905	968	2108	1069	549	289
	250	5928	2980	1506	769	3098	1562	794	411	7506	3761	1889	952	2094	1054	534	274
10%	4000	19132	10331	5929	3729	10439	5854	3561	2415	23132	11950	6359	3564	6899	3795	2243	1467
	2000	18368	9566	5165	2965	9805	5219	2927	1780	22748	11566	5975	3180	6553	3450	1898	1122
	1000	17986	9184	4783	2582	9487	4902	2609	1463	22555	11374	5783	2987	6380	3277	1725	949
	500	17795	8994	4592	2392	9329	4744	2451	1305	22459	11278	5687	2892	6294	3190	1638	862
	250	17699	8898	4496	2296	9250	4665	2372	1226	22411	11230	5639	2843	6251	3147	1595	819

*Percentage of price in the USA.
†Monthly wage for health professionals (US$).

Currently, pharmacotherapy prices vary substantially worldwide, in some cases seemingly irrespective of local income levels. For example, prices in 1998 of nicotine gum in South Africa and Thailand ($0.12 and $0.14 per unit, respectively) were essentially equal to prices in the UK and Finland ($0.13 and $0.14 per unit, respectively) (World Bank, unpublished data, 1998). Furthermore, prices for the nicotine patch in Brazil, Chile, Puerto Rico, and Uruguay were all higher than in the USA, and at least three times higher than prices in Turkey and South Africa.

Pharmaceutical prices can fall significantly when drugs are produced in developing countries. For example, 2003 prices of generic bupropion and nicotine gum manufactured in India can be as low as 12.5% of the US price (table 2) (Ceejay Healthcare Private Limited, personal communication, April 2003). Local production, however, may not be achievable in the short or medium term in many developing countries, depending on licensing, capital investment, technology requirements, and more generally, infrastructure capacity.

If developing countries being hit hard by the tobacco epidemic are to benefit from these effective and cost effective smoking cessation therapies, pharmacotherapy will need to become widely available at low cost from either local manufacturers or at significantly reduced prices from current leading manufacturers. Adding the most effective treatments to the World Health Organization's list of essential drugs would be an important early step toward improving the accessibility of pharmacotherapy for smoking cessation in the developing world.

The weak effect of the provider's salary in our study may imply that the *most competent* health care provider versus the *least costly* should oversee treatment provision and follow up counselling, though one provider may well meet both those criteria. For example, a pharmacotherapy programme in the Seychelles would likely be initiated with physician consultants providing treatment. Cost effectiveness would improve as GPs took over treatment management, but could be ideal if specialised nurses (under consultant supervision) managed treatment counselling and follow ups because of their training in behavioural therapy. Pharmacotherapy programmes limited to the non-prescription treatments—for example, gum and patch—could further extend provider roles to trained community health workers.

Applying a range of discount rates from 0–10% provides information about real investment opportunity costs (that is, trade-offs) that governments face upon implementing pharmacotherapy, which are determined by their levels of available resources and investment returns. A higher rate of discounting may better represent the situation of countries that have extremely constrained resources for public health spending. For example, the opportunity cost of implementing a pharmacotherapy programme in Rwanda, where life expectancy at birth is about 40 years and annual per capita health expenditure is $10, may be much higher than it is in the Seychelles, where life expectancy at birth is about 70 years and annual per capita health expenditure is $350.[34 35] (For comparison, annual per capita health expenditure is approximately $4000 in some high income western countries.) The lowest income countries may have just enough resources to provide only the most basic vaccinations, and countries with high mortality rates may choose to prioritise interventions that avoid morbidity and mortality earlier in the lifespan.

Different discount rates may also reflect, in a very broad way, smokers' personal preferences regarding the trade-offs between smoking and health. These preferences may be influenced by smokers' understanding of the risks associated with smoking, perceived life expectancy, present quality of life, and the present value they assign to their future life-years—particularly as it relates to their socioeconomic status—that could potentially be lost because of smoking. It has been suggested that smokers who place a low value on these factors will be less motivated to quit.[36] This may reflect the perceived or actual situation of many smokers in developing countries, where many live in severe poverty and often face several, more acute threats to their wellbeing. This would imply that many smokers in developing countries would discount the benefits of cessation more heavily, particularly in low income, high mortality countries. This raises issues of equity and the need for special interventions targeting the poor. More research, including formal cessation monitoring, is needed to better understand smoking cessation behaviours in developing countries, as well as motivations to start and stop smoking.

This analysis has certain methodological limitations. Because of a lack of available data for the Seychelles and other developing countries, some assumptions in the analysis—fore example, efficacy of treatment—are based on data in western countries. Also, our analysis did not account for the health benefits to others of a smoker quitting. Non-smokers who are exposed regularly to environmental tobacco smoke have a 20–30% increased risk of lung cancer and a 23% increased risk of heart disease.[37 38] However, if indirect health benefits are taken into account, then indirect costs (for example, additional costs associated with diseases developed during life-years saved by the intervention) should arguably also be counted, and there is currently no clear consensus regarding this methodological issue for cost effectiveness studies.

What this paper adds

Increasing cessation among smokers alive today could avert millions of tobacco caused deaths that will otherwise occur over the next 50 years, a majority of which will be in developing countries. Several pharmacological smoking cessation therapies approximately double smokers' odds of quitting. These pharmacotherapies have been shown to be cost effective in developed country settings.

Pharmacological smoking cessation therapies appear to be highly cost effective in the Seychelles, a middle income country, as compared to other government sponsored health interventions. These pharmacotherapies could also be cost effective in lower income developing countries if they are made available for purchase at significantly reduced prices.

Conclusion

We found that pharmacotherapies for smoking cessation offered in the Seychelles and other developing country settings as adjuncts to brief physician counselling would be highly cost effective as compared to treating smokers with physician counselling alone and as compared to other common health interventions. One of the primary concerns among decision makers—perhaps even irrespective of cost effectiveness—will be the present affordability of these treatments. A key to widespread implementation of pharmacotherapy for smoking cessation in the developing world would be significantly reduced drug prices.

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