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Is diabetes and hypertension screening worthwhile in resource-limited settings? An economic evaluation based on a pilot of a Package of Essential Non-communicable disease interventions in Bhutan

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In response to a lack of cost-effective data on screening and early treatment of diabetes and hypertension in resource-limited settings, a model-based economic evaluation was performed on the World Health Organization (WHO)'s Package of Essential Non-communicable (PEN) disease interventions for primary health care in Bhutan. Both local and international data were applied in the model in order to derive lifetime costs and outcomes resulting from the early treatment of diabetes and hypertension. The results indicate that the current screening option (where people who are overweight, obese or aged 40 years or older who visit primary care facilities are screened for diabetes and hypertension) represents good value for money compared to 'no screening'. The study findings also indicate that expanding opportunistic screening (70% coverage of the target population) to universal screening (where 100% of the target population are screened), is likely to be even more cost-effective. From the sensitivity analysis, the value of the screening options remains the same when disease prevalence varies. Therefore, applying this model to other healthcare settings is warranted, since disease prevalence is one of the major factors in affecting the cost-effectiveness results of screening programs.

Keywords Bhutan, cost-effectiveness analysis, diabetes mellitus, hypertension, non-communicable diseases, Package of Essential Non-communicable disease interventions (PEN)

KEY MESSAGES

- An assessment of the entire intervention pathway of screening for hypertension and diabetes in patients who are overweight, obese or over 40 years visiting primary health services in Bhutan found that the current screening recommendations outlined in the WHO's PEN offered value for money.
- While opportunistic screening resulted in 70% coverage, it is likely that universal screening may even yield better value for money. Universal screening should be considered as a priority option in Bhutan and other resource-limited settings, if financially and technically feasible.

Introduction

In recent years, there has been increasing global recognition of the significant negative health and economic consequences of non-communicable diseases (NCDs) such as cardiovascular disease (CVD), diabetes, cancer and respiratory tract disease. According to one recent analysis of the global burden of disease, the last 10 years has seen an unprecedented rise in the levels of NCD-related morbidity and mortality (Lozano *et al.* 2012; Murray *et al.* 2012), with the majority of NCD-related deaths now occurring in low- and middle-income countries (LMIC) (World Health Organization 2008). Because NCDs disproportionately affect working age adults, this rise in NCD-related morbidity and mortality has particularly significant economic implications for LMICs.

Significant evidence has emerged on the benefits of early intervention and proper management for certain NCDs, such as CVD and diabetes (Chobanian *et al.* 2003; Furie *et al.* 2011; Qaseem *et al.* 2012). However, most of this evidence relies on data from randomized controlled trials (RCTs), and thus has limited generalizability (The World Bank 2011) for application in everyday clinical practice, particularly in low-resource settings. Very little research has yet been conducted into the cost-effectiveness of comprehensive programs for managing NCDs in LMICs. The World Health Organization (WHO) responded to the need for increased prevention and control of NCDs in LMICs by initiating the Package of Essential Non-communicable (PEN) disease interventions for primary health care in low-resource settings. The WHO PEN uses an integrated approach to assess and manage cardiovascular risk using hypertension and diabetes as entry points (World Health Organization 2010; Mendis and Chestnov 2013). In addition, PEN aims to strengthen primary health-care systems' ability to respond to the rise in NCDs by offering a set of cost-effective interventions for prevention and control that are feasible for implementation in resource-limited settings (World Health Organization 2010).

Bhutan is one of the LMICs where rising NCD rates have become a particularly challenging health problem. The NCDs account for 60% of the total burden of disease in terms of Disability-Adjusted Life Years (DALYs) lost (The World Bank 2011). Although there are few quality health statistics for NCDs, a study conducted by the Ministry of Health in the capital city, Thimpu, identified alarming data that 93% of the respondents were exposed to at least one of the common NCD risk factors, including unhealthy diet, physical inactivity, and consumption of alcohol and/or tobacco, more than 50% of the respondents were exposed to at least two of the risk factors, and more than 38% were exposed to at least three risk factors (Non-Communicable Diseases Division 2013). As a result, in 2009, the Ministry of Health of the Royal Government of Bhutan introduced several of the PEN interventions in two selected districts—Paro and Bumthang (Wangchuk *et al.* 2013). The interventions focused on diabetes and hypertension because implementation of screenings and treatments/lifestyle modifications for these diseases were deemed feasible within the primary health-care context of Bhutan.

Due to resource restrictions in LMIC health systems, there is often a gap between the planning and implementation of interventions. Given this, the PEN framework for implementation recommends that all programs begin with an evaluation of the likely impact and efficiency of the intervention program, emphasizing the importance of evidence-based implementation and program monitoring and evaluation (World Health Organization 2010). Given that most LMIC governments work within a context of multiple, often competing, health priorities, economic intervention evaluations can also help policymakers make evidence-based decisions about appropriate resource allocation. However, to date, very few evaluations of this kind been conducted on NCD prevention and control programs, particularly in resource-limited settings (Mulligan *et al.* 2006).

This article hopes to go some way to address this lack by assessing the cost-effectiveness of the PEN project implemented in Bhutan and analysing the costs and health consequences of the program in both the short and long term. A number of recommendations are made for the use of economic modelling to inform policy. The results of this study should be of use not only to the Bhutanese government but also to decision-makers in other resource-limited settings who are involved with the prevention and control of NCDs.

Methods

Overview of PEN interventions and policy options

Bhutan's PEN protocol informed the public about the criteria for blood glucose and blood pressure screenings. This includes patients who are aged 40 years or older, or overweight or obese [body mass index (BMI) 23+], or had a high waist circumference (WC) (WC >80 cm in females and >90 cm in males). Therefore, in order for the population to visit a health facility, they must perceive that their physical status matches the eligibility criteria. This recommendation is in line with recent findings that obesity is the best predictor of undiagnosed diabetes (odds ratio 3.2) (Junrungsee *et al.* 2011). Those diagnosed with diabetes and/or hypertension were treated according to Bhutan's PEN protocol, which focuses on lifestyle modification and medicine (Non-Communicable Diseases

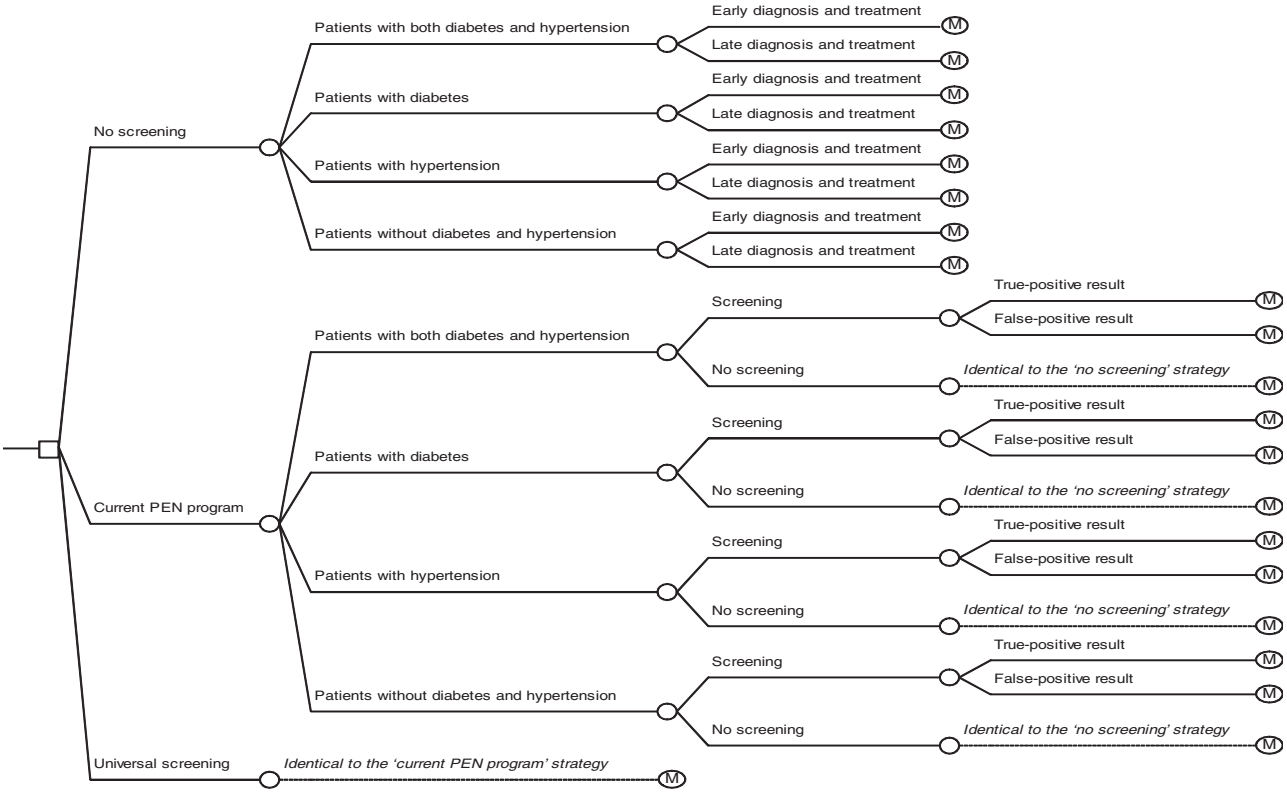

Figure 1 Decision tree model showing the three strategies for prevention and control of diabetes and hypertension.

Division 2013). Evidence from this pilot study found that screening coverage reached the program target at approximately 70% of the eligible population in the two districts studied. Another policy option is to scale up the screening program to cover the remaining 30% of the eligible population who did not perceive the risk or were not willing to visit a health facility for diabetes and hypertension screening. This strategy includes inviting the whole population aged 40 years or older or those who are younger but with perceived health risks by initiating more proactive public communication and invitations. The counterfactual scenario was set as no screening program, with most patients consequently receiving treatment at a later stage in the progression of either diabetes and/or hypertension.

Analysis and model

A model-based economic evaluation was performed to capture all of the costs and consequences of the entire pathway resulting from diabetic and hypertension screenings (from screening to death). The model consisted of a decision tree and a Markov model and was constructed using Microsoft Office Excel 2007 (Microsoft Corp., Redmond, WA). The lifetime costs and DALY averted were calculated for three possible strategies: 'no screening', 'current PEN program', and 'universal screening'. The decision tree diagram illustrating these three strategies can be found in Figure 1. In the two screening scenarios ('current PEN program' and 'universal screening'), all eligible patients underwent blood glucose and blood pressure testing. Patients who tested positive for diabetes and hypertension were then treated. In the 'no screening' option, the effect of medical treatments for diabetes and hypertension differs among the early- and late-stage of diagnosis.

For each strategy, three separate Markov models—one for diabetes, one for hypertension and one for diabetes with hypertension—were employed simultaneously to forecast the costs, complications and health outcomes associated with the diseases. The diabetes model contained the following seven health states: diabetes without complications, coronary artery disease, stroke, nephropathy, retinopathy, neuropathy and death (Figure 2a–f). The hypertension model contained the following health states: uncontrolled hypertension, controlled hypertension, stroke and death (Figure 3).

A cost-effectiveness analysis was conducted from the societal perspective. The lifetime time horizon for the adult cohort was 40 years or older, and the cycle length was set to 1 year. The main outcome measures were lifetime costs, DALY averted and the incremental cost-effectiveness ratio (ICER) per DALY averted. DALYs were calculated using WHO standard methods (World Health Organization 2003) without age weighting. In addition, the Monte Carlo simulation was performed to estimate costs and outcomes over a patient's lifetime. In accordance with the WHO's guideline (World Health Organization 2003), future costs and DALYs were discounted at a rate of 3%.

Model parameters

The model input parameters are presented in Table 1.

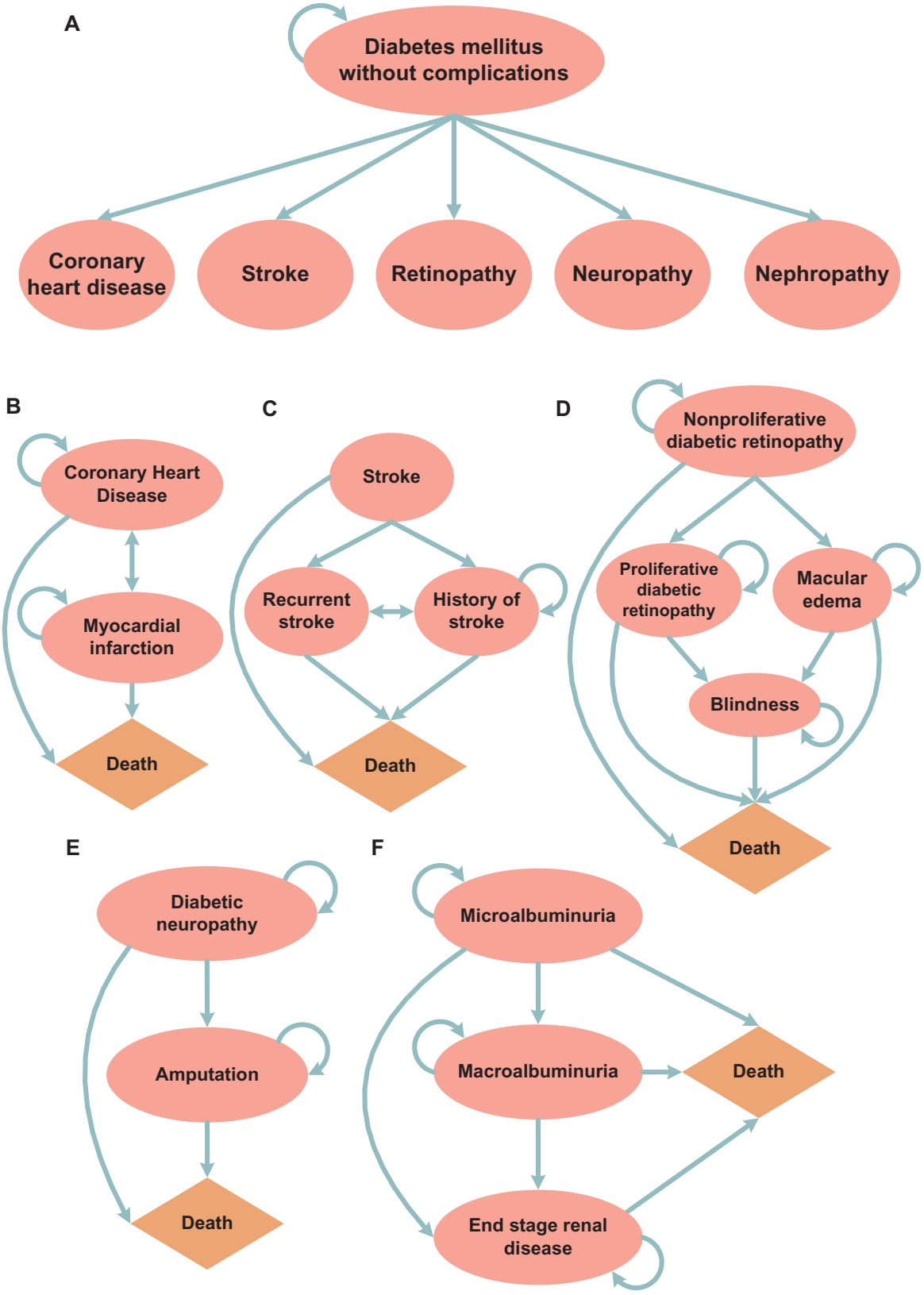

Figure 2 Markov model representing the possible events for (a) patients with diabetes without complications, (b) coronary artery disease, (c) stroke, (d) retinopathy, (e) neuropathy, (f) nephropathy and death.

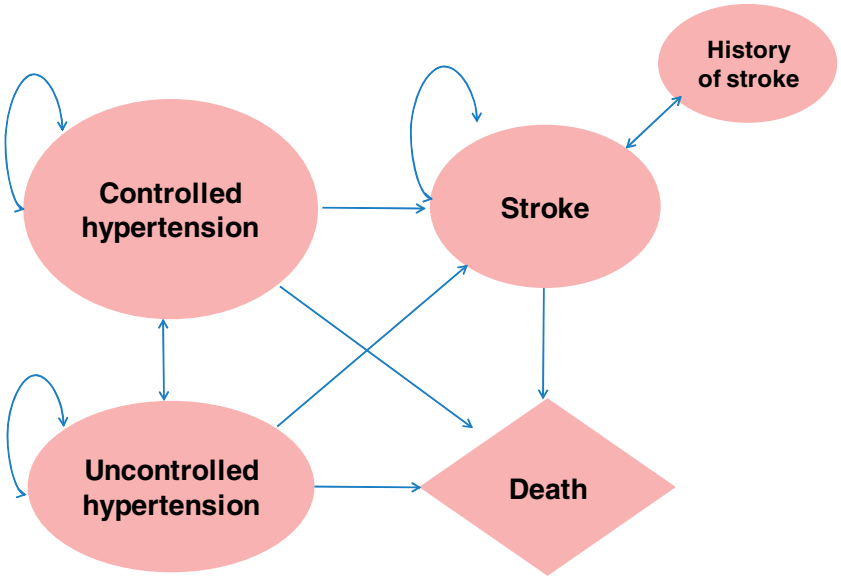

Figure 3 Markov model representing the events that could occur for patients with hypertension and its complications.

Table 1 Model input parameters

Parameters	Distribution	Mean	Standard error	Reference
Epidemiological parameter				
Proportion of hypertension in diabetes mellitus patients	Beta	54.1%	0.00122	Giri *et al.* (2013)
Prevalence of DM in Bhutan population aged 25–74	Beta	8.2%	0.00561	Giri *et al.* (2013)
Prevalence of hypertension	Beta	26%	0.0092	Giri *et al.* (2013)
Transitional probabilities				
Probability of death due to diabetes	Beta	0.0044	0.000001	Pratipanawatr *et al.* (2010)
Coronary artery disease				
Probability of patients developing coronary artery disease	Beta	0.0091	0.00001	Leelawattana *et al.* (2006)
Probability of patients developing myocardial infarction	Beta	0.0305	0.0004	World Health Organization (2010)
Probability of death due to myocardial infarction	Beta	0.1622	0.02	Srimahachota *et al.* (2012)
Probability of death due to coronary artery disease	Beta	0.0695	0.0003	Pratipanawatr *et al.* (2010)
Risk ratio of developing coronary artery disease	Normal	0.85	0.09	World Health Organization (2013)
Risk ratio of developing myocardial infarction	Normal	0.90	0.06	World Health Organization (2013)
Risk ratio of death due to coronary artery disease	Normal	1.11	0.13	World Health Organization (2013)
Stroke				
Probability of patients developing stroke	Beta	0.0055	0.0001	Leelawattana *et al.* (2006)
Probability of diabetic patients developing stroke	Beta	0.0095	0.0001	World Health Organization (2010)
Probability of death due to stroke	Beta	0.0013	0.0000004	Pratipanawatr *et al.* (2010)
Probability of death due to recurrent stroke	Beta	0.0024	0.0000004	Pratipanawatr *et al.* (2010)
Risk ratio of developing stroke	Normal	0.96	0.08	World Health Organization (2013)
Risk ratio of developing previous stroke	Normal	0.96	0.08	World Health Organization (2013)

(continued)

Table 1 Continued

Parameters	Distribution	Mean	Standard error	Reference
Risk ratio of death due to stroke	Normal	1.11	0.13	World Health Organization (2013)
Retinopathy				
Probability of patients developing diabetic retinopathy	Beta	0.0388	0.00003	Leelawattana *et al.* (2006)
Probability of progression from non-proliferative diabetic retinopathy to proliferative diabetic retinopathy	Beta	0.08	0.0102	Vijan *et al.* (2000)
Probability of progression from non-proliferative diabetic retinopathy to macular oedema	Beta	0.03	0.0102	Vijan *et al.* (2000)
Probability of progression from diabetic retinopathy to blindness	Beta	0.09	0.0102	Vijan *et al.* (2000)
Probability of progression from macular oedema to blindness	Beta	0.05	0.0102	Vijan *et al.* (2000)
Mortality multipliers for non-proliferative diabetic retinopathy	Normal	1.49	0.08	Vijan *et al.* (2000)
Mortality multipliers for proliferative diabetic retinopathy	Normal	1.76	0.03	Vijan *et al.* (2000)
Mortality multipliers for macular oedema	Normal	1.76	0.03	Vijan *et al.* (2000)
Mortality multipliers for blindness	Normal	2.34	0.03	Vijan *et al.* (2000)
Risk ratio of patients developing diabetic retinopathy	Normal	0.85	0.09	Coca *et al.* (2012)
Risk ratio of blindness	Normal	1.0	0.02	Coca *et al.* (2012)
Neuropathy				
Probability of patients developing amputation	Beta	0.0013	0.000001	Leelawattana *et al.* (2006)
Probability of patients developing foot ulcer	Beta	0.0069	0.00001	Leelawattana *et al.* (2006)
Probability of patients developing peripheral artery disease	Beta	0.0041	0.000004	Leelawattana *et al.* (2006)
Probability of progression from neuropathy to amputation	Beta	0.0015	0.000002	Krittiyawong *et al.* (2006)
Probability of death due to neuropathy	Beta	0	0	Pratipanawatr *et al.* (2010)
Probability of death due to amputation	Beta	0.1001	0.0045	Junrungsee *et al.* (2011)
Risk ratio of developing neuropathy	Normal	0.99	0.02	World Health Organization (2013)
Risk ratio of developing amputation	Normal	0.84	0.22	World Health Organization (2013)
Risk ratio of death due to amputation	Normal	0.84	0.22	World Health Organization (2013)
Nephropathy				
Probability of patients developing diabetic nephropathy	Beta	0.0835	0.00004	Leelawattana *et al.* (2006)
Probability of progression from microalbuminuria to macroalbuminuria	Beta	0.028	0.0018	Adler *et al.* (2003)
Probability of progression from macroalbuminuria to end stage renal disease	Beta	0.023	0.0038	Adler *et al.* (2003)
Probability of progression from microalbuminuria to end stage renal disease	Beta	0.003	0.0008	Adler *et al.* (2003)
Probability of death due to microalbuminuria	Beta	0.030	0.002	Adler *et al.* (2003)
Probability of death due to macroalbuminuria	Beta	0.046	0.0054	Adler *et al.* (2003)
Probability of death due to end stage renal disease	Beta	0.192	0.0265	Adler *et al.* (2003)
Risk ratio of developing microalbuminuria	Normal	0.86	0.06	Coca *et al.* (2012)
Risk ratio of developing macroalbuminuria	Normal	0.74	0.07	Coca *et al.* (2012)

(continued)

Table 1 Continued

Parameters	Distribution	Mean	Standard error	Reference
Risk ratio of developing end stage renal disease	Normal	0.69	0.21	Coca *et al.* (2012)
Risk ratio of death due to renal disease	Normal	0.99	0.30	Coca *et al.* (2012)
Hypertension				
Probability of progression from uncontrolled hypertension to controlled hypertension	Normal	0.7258	0.0006	a
Probability of progression from controlled hypertension to uncontrolled hypertension	Beta	0.05		Assumption
Probability of patients with controlled hypertension developing stroke	Beta	0.0070	0.0001	a
Probability of patients with uncontrolled hypertension developing stroke	Beta	0.0146	0.0004	a
Probability of death due to controlled hypertension	Beta	0.0285	0.00002	Blood Pressure Lowering Treatment Trialists' Collaboration (2000)
Probability of death due to uncontrolled hypertension	Beta	0.0239	0.00001	Blood Pressure Lowering Treatment Trialists' Collaboration (2000)
Probability of death due to stroke	Normal	2.72	0.02	Lovibond *et al.* (2011)
Intervention effectiveness				
Sensitivity of screening for diabetes (capillary blood glucose)	Beta	84%		Rolka *et al.* (2001)
Specificity of screening for diabetes (capillary blood glucose)	Beta	88%		Rolka *et al.* (2001)
Sensitivity of screening for hypertension (ambulatory blood pressure monitoring)	Beta	100%		Lovibond *et al.* (2011)
Specificity of screening for hypertension (ambulatory blood pressure monitoring)	Beta	100%		Lovibond *et al.* (2011)
Risk reduction of intensive glycaemic and hypertension control	Normal	0.46	0.046	CDC Diabetes Cost-effectiveness Group. (2002)
Relative risk of intensive hypertension control	Normal	0.70	0.1	Blood Pressure Lowering Treatment Trialists' Collaboration (2000)
Costs (BNT per year)				
Screening				
Diabetes (capillary blood glucose)	Gamma	1966		
Hypertension (ambulatory blood pressure monitoring)	Gamma	1721		
PEN program (per patient)	Gamma	28		a
Costs of treating diabetes and follow up				
Direct medical cost				
No complication	Gamma	24 100	13 427	
Coronary artery disease	Gamma	1 904 000	311 542	
Stroke	Gamma	337 500	73 299	
Nephropathy	Gamma	261 314	35 942	
Retinopathy	Gamma	25 107	14 309	
Neuropathy	Gamma	83 807	16 477	
Direct non-medical cost				a
No complication	Gamma	531	173	
Coronary artery disease	Gamma	2214	536	
Stroke	Gamma	2214	536	
Nephropathy	Gamma	2214	536	
Retinopathy	Gamma	531	173	
Neuropathy	Gamma	531	173	

(continued)

Table 1 Continued

Parameters	Distribution	Mean	Standard error	Reference
Costs of treating hypertension and follow up				
Direct medical cost				
No complication	Gamma	25 371	13 500	
Stroke	Gamma	337 500	73 299	
Direct non-medical cost				a
No complication	Gamma	531	173	
Stroke	Gamma	2214	536	
Disability weight				
Diabetes	Beta	0.015	0.002	World Health Organization (2004)
Coronary artery disease	Beta	0.246	0.025	
Stroke	Beta	0.920	0.092	
Previous stroke	Beta	0.266	0.017	
Nephropathy	Beta	0.091	0.006	
Neuropathy	Beta	0.072	0.003	
Blindness	Beta	0.552	0.021	
Myocardial infarction	Beta	0.439	0.018	
End stage renal disease	Beta	0.098	0.005	
Amputation	Beta	0.102	0.017	

[a]Analysis of primary data collected by the authors.

Epidemiological data

Prevalence was calculated using data provided by Giri *et al.* (2013). The prevalence of diabetes, hypertension and diabetes and hypertension was 2.08, 26 and 6.12%, respectively.

Health state transitional probabilities

Transitional probabilities between health states were obtained from published studies, as shown in Table 1. This contains the probabilities of disease occurrence, the probabilities of developing complications and the probabilities of death. In the model analysis, data on relative risk reduction of complication or death events from patients with diabetes and hypertension who were receiving medication was also taken into consideration. For example, patients taking angiotensin-converting enzyme (ACE) inhibitors had a stroke risk 30% lower compared with those taking a placebo [four trials, 12 124 patients: relative risk (RR) 0.7, 95% confidence interval (CI) 0.57 to 0.85] (Blood Pressure Lowering Treatment Trialists' Collaboration 2000).

Intervention effectiveness

The sensitivity and specificity of the screening for diabetes and hypertension were derived from the international literature. In the model, sensitivity was set to 84% and specificity to 88% for the capillary blood glucose tests (Rolka *et al.* 2001); sensitivity and specificity were both set to 100% for the sphygmomanometer due to its extremely high levels of accuracy and it is considered to be a gold standard diagnosis (Lovibond *et al.* 2011).

Because no local information was available, baseline probabilities of developing complications due to diabetes were derived from the Thai Diabetic Registry, which contains historical data of more than 5000 Thai diabetic patients (Krittiyawong *et al.* 2006). Local data from approximately 1000 hypertensive patients in Paro and Bumthang, some whom underwent screening and subsequent treatment, and some of whom did not, was used to estimate outcomes in terms of controlled vs uncontrolled hypertensions. According to the PEN protocol, the controlled hypertension defines as having a blood pressure of less than 140/90 mmHg, and otherwise for the uncontrolled hypertension ($\geq$140/90 mmHg). Baseline probabilities for patients with uncontrolled hypertension suffering a stroke and death were derived from a model developed by Lovibond *et al.* (2011).

The effectiveness of early- and late treatment for diabetes was from two large systematic reviews and meta-analyses—Boussageon *et al.*'s. on microvascular complications (World Health Organization 2013) and Coca *et al.*'s (2012) on macrovascular complications. It was found that intensive treatment reduces the risk of complications significantly more for microvascular complications than it does for macrovascular complications. The model assumed the results from the intensive treatment would be equivalent to the early treatment of diabetes. A systematic review and meta-analysis comparing the risks associated with uncontrolled (which was assumed to be the same as a placebo scenario) and controlled hypertension conducted by the Blood Pressure Lowering Treatment Trialists' Collaboration found that controlled hypertension reduced stroke incidence by 30% (95% CI, 0.57–0.85) (Blood Pressure Lowering Treatment Trialists' Collaboration 2000). For those with co-morbidities, diabetes with hypertension, we assumed similar outcomes to those for diabetes treatment, because the majority of diabetes patients in trials also had hypertension.

Cost and disability weights

Costing data was garnered using a standard questionnaire which was used to survey 16 key informants including

Table 2 Lifetime costs and health outcomes of each strategy using a societal perspective

Options	Costs (BTN)	Incremental LYs	Incremental DALYs averted	ICER (BTN per DALY averted)
No screening	210 023	–	–	–
Current PEN program	205 735	0.018	0.038	−112 906
Universal screening	203 897	0.008	0.016	−112 906

BTN, Bhutanese Ngultrum (value as of 2013); DALYs, disability adjusted life years; ICER, incremental cost-effectiveness ratio; LYs, life years.

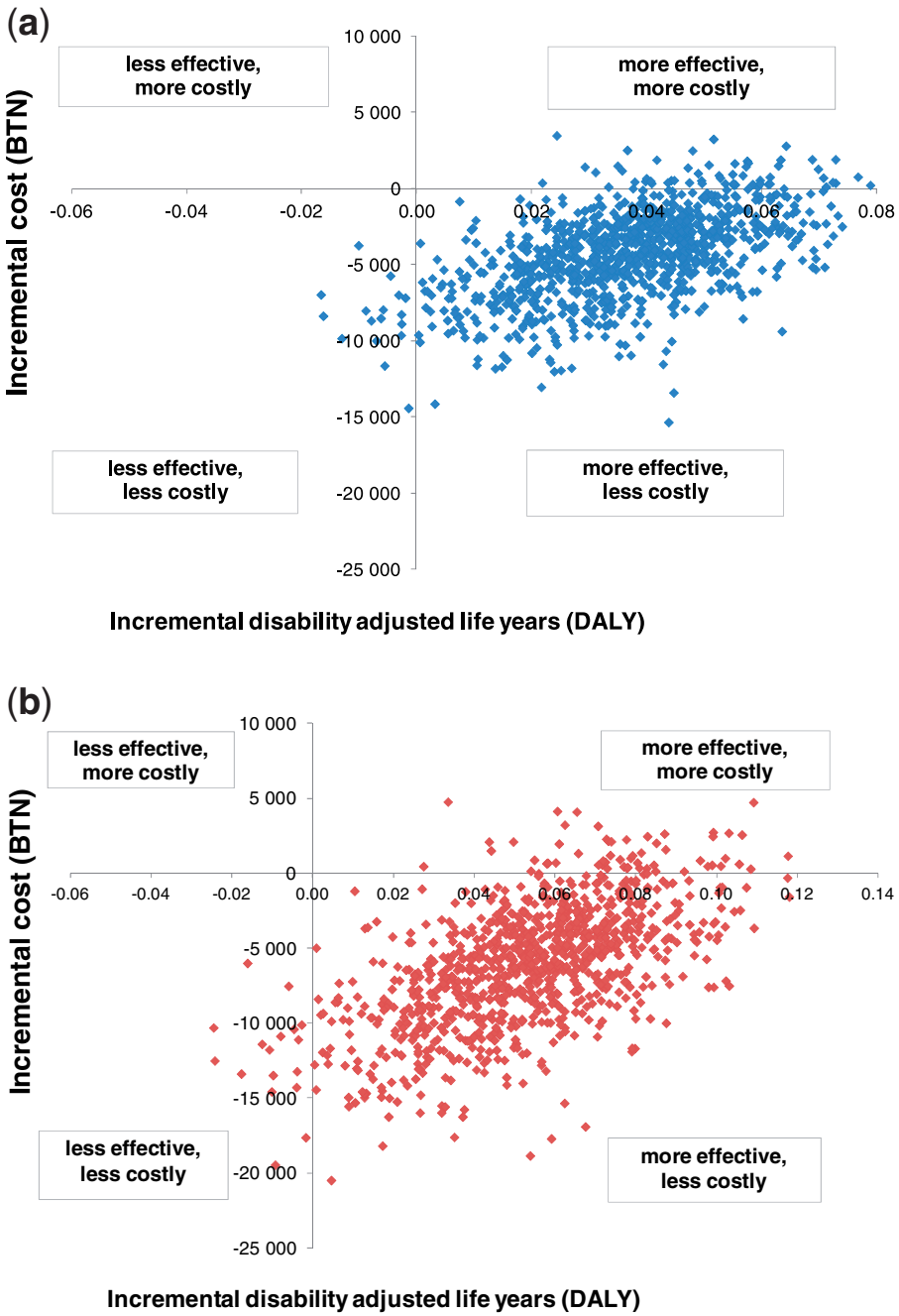

Figure 4 (a) Cost-effectiveness plane demonstrating the incremental costs and incremental disability-adjusted life years (DALYs) of 'current PEN program' compared with 'no screening. (b) Cost-effectiveness plane demonstrating the incremental costs and incremental disability-adjusted life years (DALYs) of 'universal screening' compared with 'no screening'.

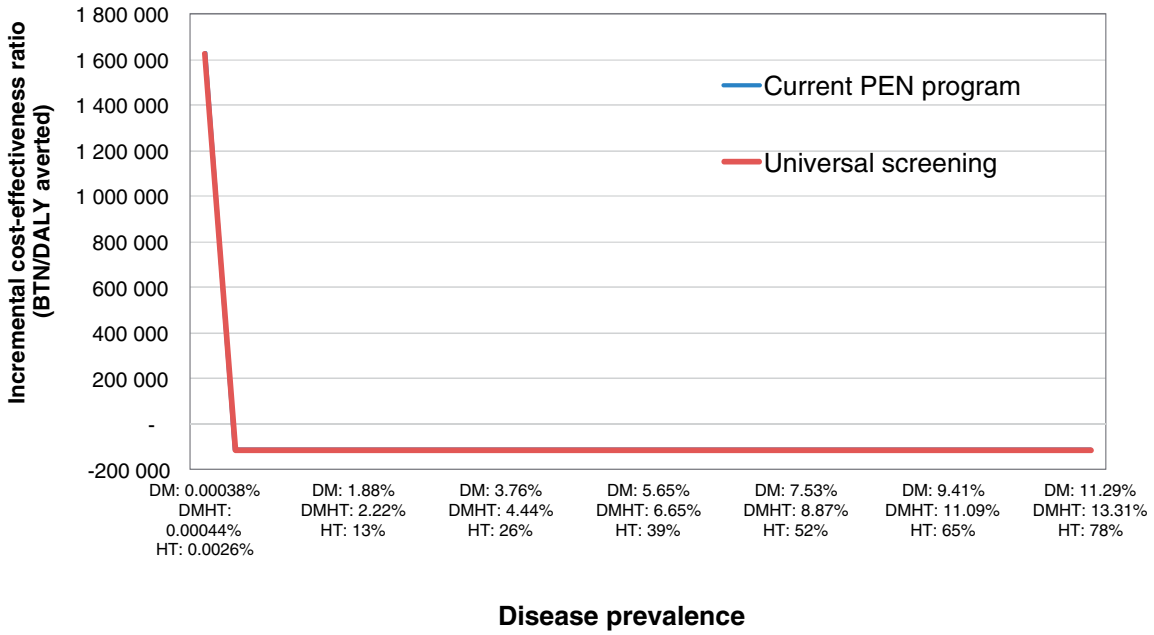

Figure 5 One-way sensitivity analysis on the prevalence of diabetes, co-morbidity of diabetes and hypertension, and hypertension, resulting in different incremental cost-effectiveness ratios of 'current PEN program' and 'universal screening' compared with 'no screening'. DM, diabetes; DMHT, diabetes with hypertension; HT, hypertension.

clinicians, pharmacists and public health experts in Bhutan. A societal perspective was adopted; as a result, both direct medical costs and direct non-medical costs are included in the model. Direct medical costs refer to the screening costs, the annual cost of treating the diseases and its complications, while direct non-medical costs refer to travel and food costs, personal facilities and opportunity costs incurred by patients. All costs were derived from 2013 values and presented in Bhutanese Ngultrum (BTN), as summarized in Table 2. For international comparison, costs can be converted into international dollars using the purchasing power parity (PPP) conversion rate. A PPP 2013 dollar is worth 22.144 BTN (The International Monetary Fund 2013).

The number of DALYs was based on the Years of Life Lost (YLL) due to premature mortality and the Years Lost due to Disability (YLD) of patients with diabetes, hypertension and resulting complications. YLDs are calculated using a disability weight for each health condition. The weight reflects the severity of the disease ranging from 0 (perfect health) to 1 (death). The disability weights of diabetes, hypertension and resulting complications were identified by the Global Burden of Disease Project (World Health Organization 2004). A standard life table with a life expectancy of 82.5 years was applied. Detailed information on the disability weights exploited in the model is presented in Table 2.

Uncertainty analyses

A probabilistic sensitivity analysis (PSA) was undertaken to explore the impact of parameter uncertainty. A cost-effectiveness analysis was also undertaken using a range of input parameters, depending on their distribution. In each simulation, one value from each variable was sampled to estimate the costs and DALYs. The model was run through 1000 simulations. The results were presented as a cost-effectiveness acceptability curve, and compared to the willingness-to-pay of 159 168-477 504 BTN/DALY averted (The International Monetary Fund 2013). In addition, a one-way sensitivity analysis was conducted where the lower and upper limits (95% confidence interval) of certain input parameters were analysed to examine the effect of that parameter on the cost-effectiveness so that the main influential parameters could be identified.

Results

Table 2 displays the probabilistic results of life-time costs, life-years gained, DALY averted and ICERs of all scenarios. Both the current PEN program and universal screening had lower life-time costs and higher health gains than no screening, and both screening scenarios had negative ICERs, showing they were cost-saving interventions. Figure 4 illustrates the cost-effectiveness planes generated from 1000 model simulations. Each dot shows how the possible costs and health gains compare between the current PEN program and no screening (Figure 4a), and universal screening and no screening (Figure 4b). Results confirm that the current PEN program and universal screening are certainly cost-effective and, most likely, cost-saving options in Bhutan.

Figure 4 depicts the cost-effectiveness acceptability curves for all options and demonstrates that both the current PEN program and universal screening are superior to no screening, at any willingness-to-pay threshold. Figure 5 shows the cost-effectiveness data from selected levels of diabetic and hypertension prevalence (threshold analysis). The current PEN program is shown to be a cost-saving intervention, as long as the prevalence of diabetes and hypertension is higher than 0.3 per 1000 people in the population. This is significantly lower

than the current prevalence of diabetes and hypertension in Bhutan, which is 342 per 1000 people in the population (2 per 1000 for diabetes, 6.12 per 1000 for diabetes and hypertension, and 26 per 1000 populations for hypertension alone).

Discussion

The WHO PEN is an innovative and action-oriented way for LMICs to reduce the burden of NCDs. By focusing on primary care interventions in low-resource settings, the program can help LMICs to ensure efficient resource use, sustainable health financing, and equitable access to basic essential health services. This is the first economic evaluation of PEN and the first economic evaluation of a joint diabetes and hypertension screening program in a resource-limited setting. The findings clearly illustrate that the current policy in Bhutan, i.e. opportunistic screening for diabetes and hypertension using the PEN approach, represents good value for money. The findings also suggest that expansion of this to a universal screening program may be even more cost-efficient. The results support the WHO's standpoint, which indicates that the WHO PEN is very cost-effective and feasible to implement in all countries (World Health Organization 2013). The findings are in line with those from previous studies that assessed the cost-effectiveness of diabetic screening (although all of these have been conducted in resource-rich settings) (Mendis and Chestnov 2013).

Furthermore, our results are consistent with those from the previous clinical studies that show the substantial benefit of the effective management of diabetes compared to hypertension. Indeed, the results of this study may somewhat overestimate the clinical benefit of screenings because similar health outcomes were assumed for both ambulatory screening visits and community screenings initiated on the basis of age. In addition, due to data limitation, this study did not assess the—potentially larger—impact of lifestyle modification in preventing diabetes and hypertension among those with negative screenings. As a result, we believe that the results of the analysis are likely to be conservative and the scaling-up of diabetic and hypertension screenings to a national-wide program should be a priority in Bhutan. Moreover, this study further recommends universal screening instead of opportunistic screening at primary care facilities because of the relatively high prevalence of diabetes in the Bhutanese population. If financially and technically feasible, universal screening though community-based programs should be introduced.

As with any study, particularly in a new and relatively unexplored area, our analysis contains certain limitations. First, the results apply only to one particular setting—Bhutan. Nevertheless, the inclusion of a sensitivity analysis allows different disease prevalence to be inputted into the model, enabling the study results to be used in other settings with similar health and economic infrastructures. Second, this study examines one-off, rather than sequential, screening options. Although PEN does not state how often diabetes screening should be performed, the American Diabetes Association recommends repeated screenings at least every 3 years for those who have received a negative screening result. The value for money of repeated screenings in Bhutan and other resource-limited settings is, as yet, unclear. Third, without availability of local data, the long-term treatment effectiveness was derived from the international literature rather than assessment of pilot districts—a limitation that may affect the results of this study. However, an evaluation of the short-term outcomes in the pilot districts did indicate a significant reduction of CVD risk and increased healthy lifestyle of the target population (Wangchuk *et al.* 2013), suggesting that this limitation is unlikely to be a factor that will affect the results. Fourth, costs were obtained from local experts rather than from costing data collected from local health providers. Although, some costs were validated with previous study data and found to be consistent, indicating that this limitation is also unlikely to result in a different study conclusion. Furthermore, we assumed a large standard error (equal to the mean) for each cost parameter and extensively assessed the impact of this in the PSA. A prospective costing study should be conducted in the future to complement our findings. Fifth, we assume that the unit cost per person screened, which includes community engagement, training staff, and providing services, of the target 30% that are not covered by the program is equivalent to the unit cost of the current policy. This is a linear assumption, which may not be true because the 30% of the population may be a marginal group that requires higher unit cost. However, due to a lack of data about the cost of access to the 30% and because we found that the PEN program is very cost-effective, scaling up the program to coverage at the highest level should be worthwhile. This is also to send the message to decision makers that although the previous target of 70% of the population has been reached, the country should aim for a coverage that is as high as possible. Lastly, this study did not include data on primary NCD prevention interventions either at a population level (such as laws or taxation aimed at reducing consumption of tobacco, alcohol or high-fat food) or at an individual level (such as increased physical activity or following a lower fat diet). Because these kinds of interventions are likely to be even more cost-effective than screenings and treatments of diabetes and hypertension, Bhutan and other countries that use this study as a resource should consider integrating these kinds of interventions alongside PEN screening and treatment options.

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