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Costs, effects and cost-effectiveness of breast cancer control in Ghana

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Abstract

OBJECTIVE Breast cancer control in Ghana is characterised by low awareness, late-stage treatment and poor survival. In settings with severely constrained health resources, there is a need to spend money wisely. To achieve this and to guide policy makers in their selection of interventions, this study systematically compares costs and effects of breast cancer control interventions in Ghana.

METHODS We used a mathematical model to estimate costs and health effects of breast cancer interventions in Ghana from the healthcare perspective. Analyses were based on the WHO-CHOICE method, with health effects expressed in disability-adjusted life years (DALYs), costs in 2009 US dollars (US$) and cost-effectiveness ratios (CERs) in US$ per DALY averted. Analyses were based on local demographic, epidemiological and economic data, to the extent these data were available.

RESULTS Biennial screening by clinical breast examination (CBE) of women aged 40–69 years, in combination with treatment of all stages, seems the most cost-effective intervention (costing $1299 per DALY averted). The intervention is also economically attractive according to international standards on cost-effectiveness. Mass media awareness raising (MAR) is the second best option (costing $1364 per DALY averted). Mammography screening of women of aged 40–69 years (costing $12 908 per DALY averted) cannot be considered cost-effective.

CONCLUSIONS Both CBE screening and MAR seem economically attractive interventions. Given the uncertainty about the effectiveness of these interventions, only their phased introduction, carefully monitored and evaluated, is warranted. Moreover, their implementation is only meaningful if the capacity of basic cancer diagnostic, referral and treatment and possibly palliative services is simultaneously improved.

keywords breast cancer, developing countries, cost-effectiveness, Ghana policy, non-communicable diseases

Introduction

Breast cancer is a major public health problem in Ghana. It is the most common type of cancer among Ghanaian women in terms of mortality and prevalence and >20 000 disability adjusted life years (DALYs) are lost every year as a result of breast cancer (WHO 2008). Ghana is facing a relatively high mortality to incidence ratio, and it is expected that the incidence will increase in Ghana in the years to come (IARC 2008, Parkin *et al.* 2008) (Table 1).

Currently, Ghana lacks a comprehensive breast cancer control policy. Breast cancer treatment guidelines are absent and treatment involving radiotherapy is only available in Ghana's two largest cities, creating important geographical barriers to access. Financial barriers also exist: although breast cancer diagnosis and treatment are covered by Ghana's National Health Insurance (NHIS), only 34% of the Ghanaian population had active NHIS membership in 2010 (National Health Insurance Authority). Studies on breast cancer in Ghana typically report poor stage distribution, survival and awareness. They

Table 1 Age distribution of breast cancer incidence and mortality in Ghana

Age groups	Female population*	Incidence (/100 000)	Number of incident cases (%)	Mortality (/100 000)	Number of deaths (%)	Mortality/ incidence ratio
0–14	4 605 974	0.1	5 (0.2%)	0.0	0 (0.0%)	n/a
15–29	3 145 512	1.0	31 (1.1%)	0.4	13 (0.7%)	0.40
30–44	2 013 112	31.7	638 (22.5%)	11.3	227 (12.3%)	0.36
45–59	1 231 140	80.1	986 (34.8%)	53.2	655 (35.3%)	0.66
60–69	482 535	104.5	504 (17.8%)	84.4	407 (22.0%)	0.81
70–79	247 858	169.3	420 (14.8%)	143.7	356 (19.2%)	0.85
80+	90 061	273.5	246 (8.7%)	218.3	197 (10.6%)	0.80

Source: WHO Global Burden of Disease data 2004 update.
*Based on population Ghana in 2009.

furthermore indicate that knowledge, beliefs and social stigma of Ghanaians are important determinants of the late-stage presentation of breast cancer (Wiredu & Armah 2006; Ohene-Yeboah 2008; Clegg-Lamptey *et al.* 2009a,b). These poor conditions point out the need to improve breast cancer control policy in Ghana, and address the needs of Ghana's relatively young female population.

Given its limited health-care resources, Ghana needs to spend money wisely and only fund interventions that provide value for money. Cost-effectiveness analysis (CEA) is a tool that systematically compares costs and effects of health interventions and that can guide policy makers in these decisions. However, the evidence base on cost-effectiveness of cancer control in Ghana – or any other low-income country – is scarce (Brown *et al.* 2006; Groot *et al.* 2006). International literature on the costs and health effects of breast cancer control focuses mainly on high-income countries and is difficult to extrapolate to low-income countries because of differences in context. Screening programmes in African countries, could, for example use different tools and target different age groups than programmes in Western settings.

This study was aimed to answer the research question 'From the health-care perspective, what are the costs, health effects and cost-effectiveness of breast cancer control interventions in Ghana, and what is the optimal mix of interventions to maximise population health?' We used an established model by Groot *et al.* (2006) on the cost-effectiveness of breast cancer control in six world subregions and adapted it to reflect the demographic, epidemiological and economic context of Ghana to the extent possible.

Methods

General approach

We used WHO-CHOICE standardised methods in CEA – described in detail elsewhere – as the basis of our analysis (Edejer *et al.* 2003; Groot *et al.* 2006). This approach compares all possible interventions to a situation where no interventions are available. This counterfactual acts as a reference to compare the cost and effects of existing and new interventions. The standardised method enables us to make comparisons of the costs and health effects across a wide range of competing interventions such as HIV/AIDS, malaria and mental disorders (Evans *et al.* 2005).

Country adaptation

WHO-CHOICE has made a number of tools and methods available to adapt its regional results to the country level (WHO 2011a). A study team, established in 2009, served as an expert panel to assess the mathematical model for its relevance in Ghana, define a meaningful set of interventions, identify data sources for the collection of country data, analyse results and interpret findings. The study team included representatives from the Ministry of Health (MoH), Ghana Health Services (GHS), breast cancer specialists, public health specialists and health economists.

Mathematical model

The model structure is presented in Figure 1 (Groot *et al.* 2006). This state transition population model simulates the development of the Ghanaian population and accounts for births, background mortality and breast cancer epidemiology of Ghana (Lauer *et al.* 2003). The model includes a healthy state, a deceased state and stage I to IV breast cancer states following the American Joint Committee on Cancer (AJCC) (Greene *et al.* 2006). The effectiveness of interventions is based on their effect on health state valuations (HSVs) and case fatality (treatment interventions), or stage distribution (awareness raising and screening interventions). Each intervention, individually and in combination, is then implemented for 10 years. Next, the model population is followed over its lifetime to

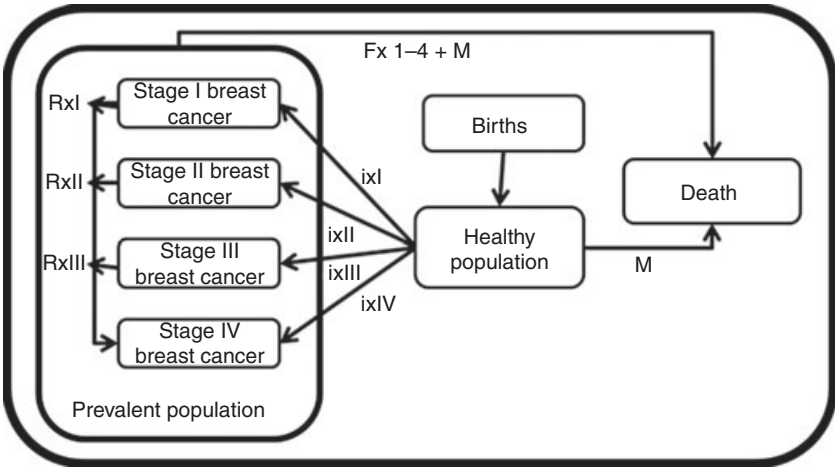

Figure 1 Graphical representation of the model showing the relationships between the different health states through the incidence rates of breast cancer (Ix1–Ix4), the different stage-specific case-fatality rates (corrected for progression) (Fx1–4) and the background mortality (M). Stage-specific relapse rates to stage IV were used to correct health state valuations only (Rx1–Rx3).

include all health effects that occur after these 10 years. As the interventions are affecting both mortality (case fatality) and morbidity, intervention effectiveness is expressed in DALYs. The difference in the total number of healthy years lived by the population between each scenario and the null-scenario gives the population health gains in DALYs averted.

We improved the initial model of Groot *et al.* (2006) by correcting HSVs for relapse, assuming that patients could only have relapse to stage IV at a constant rate. We also corrected stage-specific case fatality estimates, derived from the original study, for the addition of chemotherapy in stages I–II and mastectomy in stage IV according to the most recent Breast Health Global Initiative (BHGI) guidelines (Bland *et al.* 1998; Khan *et al.* 2002; Anderson *et al.* 2006; Adjuvant! Online).

Interventions

The expert panel identified a set of 11 interventions relevant to breast cancer control in the Ghanaian context, all related to awareness raising, screening, treatment and palliative care (Table 2). Some of these interventions do not yet exist in Ghana (e.g. mammography screening), but the expert panel judged them to be of potential benefit. The specific definition of interventions was based on consultations with the expert panel, WHO experts, BHGI guidelines and the scientific literature (Bland *et al.* 1998; Anderson *et al.* 2006; Devi *et al.* 2007; Kumar 2007; WHO 2011b). The 11 interventions were combined to construct a total of 17 intervention scenarios. This includes the current Ghanaian situation in which patients of stages I–IV are treated at a 10% coverage level (as estimated by the expert panel). All other interventions are evaluated at a geographic coverage level of 80% (i.e. reaching 80% of those people who need services) according to the expert panel and standard CHOICE method.

Data sources for health effects

Key components in the mathematical model are demography, breast cancer epidemiology, stage distribution, case-fatality and HSVs. Data used to fill in these components are discussed in turn.

Demographic data were based on formal 2009 data from the government of Ghana (Ghana Statistical Service 2010). We used Global Burden of Disease (GBD) estimates from 2004 for Ghana (personal communication), in the absence of more recent or detailed information. Information on the present stage distribution of breast cancer in Ghana was derived from records of the Korle Bu Teaching Hospital in Accra. The impact of the various screening interventions on this stage distribution (stage shift) was estimated on the basis of a simple model following Duffy & Gabe (2005) by using proportional detection rates and stage shifts from Groot *et al.* (2006). We calculated stage shifts in Ghana, and accounted for locally relevant attendance rates (60% for screening programs), sensitivity of tests, sojourn time [reducing sojourn times for clinical breast examination (CBE) by one-third] and incidence and prevalence in different age groups (Miller *et al.* 1997; Bobo *et al.* 2000; Duffy & Gabe 2005; Fracheboud *et al.* 2009). The effectiveness of the mass media awareness raising (MAR) intervention was based on the study by Devi *et al.* (2007),

Table 2 Definition and classification of individual interventions for breast cancer control in Ghana

Treatment of individual stages	Down-staging interventions*	Palliative care†
Stage I treatment: lumpectomy with axillary dissection and radiotherapy.‡ Eligible patients receive tamoxifen§ or chemotherapy.¶ (Anderson *et al.* 2006; Groot *et al.* 2006; Adjuvant! Online)	Basic Awareness Raising (BAR): community nurses training programme + opportunistic outreach activities by community nurses to raise breast cancer awareness and educate on breast self-examination techniques (BSE) + enhanced media activities. (Devi *et al.* 2007)	Basic Palliative Care (BPC): palliative care volunteers training programme + home-based visits by volunteers every fortnight + pain treatment through morphine, laxatives and palliative radiotherapy (8 Gy in 1 fraction) for eligible patients. (Anderson *et al.* 2006; Devi *et al.* 2007; Kumar 2007)
Stage II treatment: lumpectomy with axillary dissection and radiotherapy.‡ Eligible patients receive tamoxifen§ or chemotherapy.¶ (Anderson *et al.* 2006; Groot *et al.* 2006; Adjuvant! Online)	Mass-media awareness raising (MAR): BAR + mass media campaign (Devi *et al.* 2007)	Extended Palliative Care (EPC): BPC apart from community nurses instead of palliative care volunteers, pain treatment strengthened with antidepressants, anti-emetics and zelodronic acid. (Hortobagyi 2002; Anderson *et al.* 2006; Walsh & Rybicki 2006; Devi *et al.* 2007; Kumar 2007)
Stage III treatment: modified mastectomy followed by adjuvant chemotherapy¶ and radiotherapy.‡ Eligible patients receive tamoxifen.§ (Anderson *et al.* 2006; Groot *et al.* 2006)	Biennial clinical breast examination (CBE) screening in asymptomatically women aged 40–69 years: community nurses training programme + active outreach screening by community nurses + limited media activities (Zotov & Shyyan 2003; Devi *et al.* 2007)	
Stage IV treatment: adjuvant chemotherapy¶ and radiotherapy (10 Gy) + end of life hospitalisation. Eligible patients receive total mastectomy and/or tamoxifen.§ (Khan *et al.* 2002; Anderson *et al.* 2006)	Biennial mammography screening in asymptomatic women aged 50–69 years + limited media activities (Groot *et al.* 2006)	
	Biennial mammography screening in asymptomatic women aged 40–69 years + limited media activities (Groot *et al.* 2006)	

*Down-staging interventions cause a shift in stage distribution and are only modelled in combination with treatment of all stages (I–IV).
†Palliative care interventions are only applied to stage IV patients, and substitutes stage IV treatment.
‡Radiotherapy includes a standard dose of 50 Gy given in 25 fractions of 2 Gy on an outpatient basis.
§Endocrine therapy consists of 20 mg tamoxifen per day for 5 years.
¶The (neo)adjuvant chemotherapy combination regimen consists of four 21-day cycles of doxorubicin (60 mg/m^2) and cyclophosphamide (830 mg/m^2) supplemented with 4 mg dexamethasone (AC regimen). Given on an outpatient basis.

whereas we assumed that the basic awareness raising intervention (BAR) caused a 10% down-staging of late-stage breast cancer cases. In the absence of reliable Ghanaian data, data on case-fatalities of breast cancer were based on Groot *et al.* (2006) and relapse rates on the literature (Bland *et al.* 1998; Khan *et al.* 2002; Groot *et al.* 2006; Adjuvant! Online). HSVs were based on the GBD study, and corrected for relapse to stage IV (Groot *et al.* 2006; WHO 2008; Adjuvant! Online). We assumed that the palliative care interventions affect HSVs only (Khan *et al.* 2002; Connor *et al.* 2007; Kumar 2007; Devi *et al.* 2008) – its effect was determined by the expert panel. The assumed impact of each intervention is listed in Table 3.

Data sources for costs

Following standardised WHO-CHOICE methodology on CEA, we distinguished between patient-level and program-level costs (WHO 2011a). We used an ingredients approach to costing analysis, in which quantities and prices are separately reported.

Unit costs of patient services were as much as possible based on the principles of micro-costing, including detailed resource utilisation patterns and prices. Estimates of these were based on Ghanaian treatment practices and/or expert opinion and local inventories of prices (personal communication). In some instances, no detailed estimates

Table 3 Case-fatality rates, disability weights and stage distributions used for individual interventions

	Case fatality rates*				Disability weights†				Stage distribution‡			
Intervention	Stage I	Stage II	Stage III	Stage IV	Stage I	Stage II	Stage III	Stage IV	% in stage I	% in stage II	% in stage III	% in stage IV
Untreated	0.020	0.063	0.15	0.30	0.068	0.071	0.073	0.090	2.3%	20.5%	50.0%	27.3%
Stage I treatment	0.006				0.068				2.3%			
Stage II treatment		0.039				0.070				20.5%		
Stage III treatment			0.093				0.072				50.0%	
Stage IV treatment				0.227				0.0730				27.3%
Basic palliative care (BPC)				0.227				0.0720				27.3%
Extended palliative care (EPC)				0.227				0.0715				27.3%
Current country-specific situation	0.006	0.039	0.093	0.227	0.068	0.070	0.072	0.073	2.3%	20.5%	50.0%	27.3%
Basic awareness raising (BAR)	0.006	0.039	0.093	0.227	0.068	0.070	0.072	0.073	10.2%	20.1%	44.8%	24.8%
Mass media awareness raising (MAR)	0.006	0.039	0.093	0.227	0.068	0.070	0.072	0.073	21.1%	41.5%	24.1%	13.3%
Biennial clinical breast examination screening (40–69)	0.006	0.039	0.093	0.227	0.068	0.070	0.072	0.073	39.5%	30.2%	19.2%	11.1%
Biennial mammography screening (50–69)	0.006	0.039	0.093	0.227	0.068	0.070	0.072	0.073	42.0%	32.1%	16.4%	9.4%
Biennial mammography screening (40–69)	0.006	0.039	0.093	0.227	0.068	0.070	0.072	0.073	47.8%	36.5%	10.0%	5.7%

Current country-specific situation: Current situation in Ghana with treatment coverage of 10%.

*Original estimates (Groot *et al.*) were corrected for the addition mastectomy in stage IV and chemotherapy in stages I and II. (Bland *et al.* 1998, Khan *et al.* 2002; Anderson *et al.* 2006; Groot *et al.* 2006; Adjuvant! Online).

†Original estimates (Groot *et al.*) were corrected for relapse to stage IV. Relapse rates were derived from Adjuvant Online. (Anderson *et al.* 2006, Groot *et al.* 2006; Adjuvant! Online).

‡Present stage distribution is based on Korle Bu hospital registry. Effects of MAR derived from Devi *et al.* (Devi *et al.* 2007). Effects of screening interventions were based on stage shifts from baseline (Groot *et al.* 2006) to the stage distribution in the USA (Bland *et al.* 1998). Stage shifts were adapted by calculating relative differences in detection rates between the USA and Ghana (Duffy & Gabe 2005). Calculations included age-specific incidence, prevalence (WHO 2008), sojourn time (Duffy & Gabe 2005), sensitivity (Bobo *et al.* 2000) and attendance rates (75% in the USA *vs.* 60% in Ghana).

were possible and costs were based on NHIS fees charged for services from public hospitals. As a last resort, where no local resource utilisation patterns were known or fees were available, on for example lumpectomy, we used the WHO-CHOICE database on standard medical procedures (WHO Department of Essential Health Technologies 2005). From this database, we obtained the standard procedure for lumpectomy, including a series of standardised quantities on supplies and equipment needs, clinician time and protocols of care. These quantities were then multiplied by Ghanaian unit prices (salaries, drugs and equipment). Prices of traded (international) goods were based on the WHO-CHOICE database, and were marked up for transportation and distribution. To estimate the total patient costs of interventions, we multiplied the costs of patient services with the number of patients requiring these services (Table 4). The total number of patients requiring treatment is an output of the mathematical model, whereas the proportion of patients who make use of stage-specific services (e.g. diagnostics, surgery and systemic therapy) was estimated by the expert panel.

Program-level costs capture management, administrative, media and law-enforcement costs, and costs for training of health-care personnel. These costs were based on interviews with programme managers from GHS. Media and operating costs (i.e. prices for broadcasting, flyers, and posters) were based on local inventories of prices.

For all interventions, we also included costs of diagnostic tests for women presenting without breast cancer (i.e. the tested negatives of all stages) and assumed the ratio of tested negatives *vs.* tested positives to be 16.4:1 (Flobbe *et al.* 2001). Single treatment scenarios also include the costs of diagnosing all other stages, and regarding screening interventions, we included costs for evaluating false positives (Elmore *et al.* 1998; Mushlin *et al.* 1998; Flobbe *et al.* 2001; Zotov & Shyyan 2003; Fletcher & Elmore 2005).

All costs were estimated in 2009 local currency (Ghana Cedis) and converted to US dollars (US$) using the 2009 exchange rate (1 GHC = 0.701 US$). Both health effects (DALYs) and costs (US$) were discounted at an annual rate of 3%.

Cost-effectiveness analysis

Average cost-effectiveness ratios (ACERs) are calculated for each intervention by dividing its total number of DALYs averted by its total costs. Using a standard approach, we identified the set of interventions a region should purchase to maximise health gains for different budget levels. The order in which interventions would be purchased is called an expansion path and is based on the incremental costs and health effects of each intervention compared to the last intervention purchased. Only interventions that are both more effective and less costly than other (combinations of) interventions are considered on this expansion path – and these are labelled 'dominant' interventions. The incremental cost-effectiveness ratios (ICERs) for those interventions are calculated by dividing the incremental costs by the incremental health effects. WHO-CHOICE defines interventions that have a cost-effectiveness ratio (CER) of less than one time the gross domestic product (GDP) *per capita* as very cost-effective, and those with a ratio that falls between one time and three times the GDP per capita as cost-effective (WHO Commission on Macroeconomics and Health 2011). In Ghana, this means that interventions that cost <$649 per DALY averted can be considered very cost-effective, and interventions that cost between $649 and $1947 can be considered as cost-effective.

Sensitivity analysis

We performed a deterministic sensitivity analysis to assess the impact of key parameters on cost-effectiveness results. The baseline case-fatality rates and HSVs were varied by ±25%, the effect of down-staging interventions was reduced by 25% and for CBE screening, we also used effectiveness estimates from other studies (Engel *et al.* 2000; Oestreicher *et al.* 2002; Zotov & Shyyan 2003; Mittra *et al.* 2010). Furthermore, we used different sources for Ghana's current stage distribution and varied costs for outpatient visits and hospitalisation (±25%). In addition, we lowered attendance rates of screening interventions (−10%), the sensitivity of CBE and mammography tests (−25%) and the capacity utilisation of machinery (−25%).

Results

As Table 5 shows, the annual number of DALYs saved by the individual stage I–IV breast cancer treatments varies between 365 (treatment of stage I) and 1860 (treatment of stage III). Combined, these interventions can avert almost 3800 DALYs. The addition of a palliative care programme only adds very few DALYs.

Interventions to raise awareness, combined with treatment of all stages, avert between 5600 and 9500 DALYs. Biennial CBE screening averts around 12 500 DALYs, whereas biennial mammography screening can save between 13 185 and 14 580 DALYs (depending on the targeted age group), all in combination with treatment of all stages.

With increasing intervention effectiveness, costs increase as well. The individual treatment interventions cost

Table 4 Average utilisation of diagnosis and treatment services and unit costs per patient

Procedure	Ingredients	Stage I	Stage II	Stage III	Stage IV	Relapse	PC	Unit cost per patient (US$)
Initial diagnosis and evaluation during treatment	No. of health centre visits	1	1	1	1	0		3.51*
	No. of hospital visits	3	3	3	3	3		5.26*
	Bilateral Mammography	1	1	2	0	–		54.88*
	Complete blood count	7	7	7	7	6		14.21*
	FNA or core needle biopsy	1	1	1	1	–		38.78*
	Liver function tests	8	8	8	8	7		6.20†
	Ultrasonography	1	1	1	1			20.69*
	Renal function tests	8	8	8	8	7		7.01*
	Bone scan	0	0	1	1	–		109.94*
	Chest X-ray	1	1	1	1	–		23.93*
	ECG	1	1	1	1	–		13.46*
Non-breast cancer evaluation	No. of health centre visits	2	2	2	2			3.51*
	Bilateral Mammography	1	1	1	1			54.88*
	Ultrasonography	0.28	0.28	0.28	0.28			20.69*
	FNA or core needle biopsy	0.02	0.02	0.02	0.02			38.78*
Treatment	No. of hospitalisation days	2	2	6	6	6	6	10.52*
	No. of end of life hospitalisation days				7	7	4.7	10.52*
	No. of OPD visits radiotherapy	30	30	30	30	30	1	5.26*
	No. of OPD visits chemotherapy	6	6	6	6	5.3	–	5.26*
	% receiving surgical intervention	Lumpectomy 40%	Lumpectomy 30%	Lumpectomy 10%	Lumpectomy –	Lumpectomy –	Lumpectomy –	156.38†
		Mastectomy 60%	Mastectomy 70%	Mastectomy 90%	Mastectomy 5%	Mastectomy 5%	Mastectomy 5%	604.45†
	% receiving anesthesia	100%	100%	100%	5%	5%	5%	136.77†
	% receiving radiotherapy	40%	30%	100%	10%	60%	–	37.48 per 2Gy†
	% receiving endocrine treatment	100%	100%	100%	40%	40%	–	0.28/day*
	% receiving chemotherapy	0%	20%	60%	60%	80%	–	405.71* per 4 cycles
	% receiving boost radiotherapy						41%	37.48†
	% receiving home based visits						75%	3.51/visit*
	% receiving morphine						84%	1.47/day*
	% receiving laxative						50%	4.91/day*
	% receiving Ondansetron						36%	3.51/day*
	% receiving Amitriptyline						41%	0.02/day*
	% receiving Zelodronic Acid						30%	108.71/day*

PC: palliative care (substitutes stage IV treatment); Chemotherapy: four cycles of doxorubicin and cyclophosphamide, supplemented with dexamethasone (AC regimen). Endocrine treatment: daily dose of 20 mg. Tamoxifen for 5 years. Radiotherapy: 50 Gy given in 25 fractions of 2 Gy. Boost radiotherapy: 1 fraction of 10 Gy. Morphine: 40 ml/54 days. Laxatives: 35 mg/54 days. Ondansetron: 8 mg/day. Amitriptyline: 75 mg/day. Bisphosphonates: 5 mg zelodronic acid/day.

*Unit costs derived from different sources. Local unit prices derived from public (university) hospital, combined with information from WHO-CHOICE (South African) database (WHO Department of Essential Health Technologies 2005).

†Unit costs completely derived from WHO-CHOICE (South African) database in 2000 US$. First corrected for International Monetary Fund (world) inflation 2000–2009 (1.423), then the 2009 GHC/US$ exchange rate was used (0.701)

Note: Programme costs and costs for follow-up and screening procedures are not presented in this table.

Table 5 Costs (US$), effects and cost-effectiveness of breast cancer control in Ghana

Intervention scenarios*	Patients per year	Annual treatment costs†	Annual program costs†	Annual training costs†	Annual total costs†	DALYs averted a year‡	ACER	ICER
1 Current country-specific situation (10% coverage)	445	1 449 828	135 222	52 786	1 637 836	437	3745	NA
2 Stage I treatment	81	4 794 800	353 406	25 843	5 174 049	365	14 173	NA
3 Stage II treatment	727	5 984 201	353 406	25 843	6 363 450	1270	5012	NA
4 Stage III treatment	1778	9 936 648	353 406	25 843	10 315 897	1860	5547	NA
5 Stage IV treatment	970	5 893 621	353 406	25 843	6 272 870	373	16 824	NA
6 Basic palliative care (BPC)	970	4 979 912	1 011 392	45 225	6 036 528	374	16 133	NA
7 Extended palliative care (EPC)	970	7 202 892	1 024 824	45 225	8 272 941	375	22 032	NA
8 Treatment of stage I to IV	3556	11 684 609	446 962	51 685	12 183 257	3785	3219	NA
9 Basic awareness raising (BAR) + treatment of stage I to IV	3556	11 532 296	1 324 972	64 607	12 921 875	5624	2298	NA
10 Mass media awareness raising (MAR) + treatment of stage I to IV	3556	11 010 702	1 844 944	64 607	12 920 252	9473	1364	NA
11 Biennial clinical breast examination (CBE) screening (40–69) + treatment of stage I to IV	3556	14 795 753	1 435 919	79 374	16 311 046	12 560	1299	1299
12 Biennial mammography screening (50–69) + treatment of stage I to IV	3556	26 682 513	1 691 896	141 533	28 515 941	13 185	2163	NA
13 Biennial mammography screening (40–69) + treatment of stage I to IV	3556	40 499 576	1 751 124	141 533	42 392 234	14 580	2907	12 908
14 MAR + BPC + treatment of stage I to III	3556	10 538 750	2 582 414	83 989	13 205 153	9521	1387	NA
15 Biennial CBE screening (40–69) + BPC + treatment of stage I to III	3556	14 389 915	2 124 102	98 756	16 612 773	12 561	1323	NA
16 Biennial mammography screening (40–69) + BPC + treatment of stage I to III	3556	27 114 060	2 721 859	194 608	30 030 527	13 187	2277	NA
17 Biennial mammography screening (50–69) + EPC + treatment of stage I to III	3556	40 290 127	2 455 957	194 608	42 940 693	14 581	2945	553 616

ACER, Average cost-effectiveness ratio compared to the do-nothing-scenario (US$ per DALY averted); ICER, Incremental cost effectiveness ratio, ratio of additional cost per additional life year saved when next intervention is added to a mix (additional US$ per additional DALY saved); NA, not applicable because intervention is less cost-effective than others.
*Intervention scenarios are implemented at 80% coverage levels, except for scenario 1.
†In 2009 US$ (1 GHC = 0.701 US$).
‡DALYs, disability-adjusted life years (age weighted, discounted).

between $5.1 million (stage I) and $10.3 million (stage III) annually, and are among the least costly interventions. Basic and extensive palliative care cost $6.0 million and $8.3 million respectively. With an annual cost of over $42.4 million, biennial mammography screening of women between ages 40 and 69 years, combined with treatment of all stages, is the costliest intervention. The CERs of the individual treatment interventions range between $5012 (stage II treatment) and $16 824 (stage IV treatment) per DALY averted. Extended palliative care costs almost $22 000 per DALY averted.

Interventions to raise awareness and screening interventions, combined with treatment of all stages, are more cost-effective than the treatment interventions. The most cost-effective intervention for breast cancer control in Ghana is biennial CBE screening in women aged 40–69 years combined with treatment of all stages, which costs $1299 per DALY averted. MAR ($1364 per DALY averted) is slightly less cost-effective than CBE screening. Mammography screening interventions, in combination with treatment of all stages, cost between $2163 and $2907 per DALY averted.

Figure 2 shows the expansion path of breast cancer control, i.e. the order in which interventions should be implemented at different levels of resource availability. This path shows that biennial CBE screening of women aged 40–69 years is the optimal choice (incremental cost per DALY of $1299) at a cost of around $16 million, followed by mammography screening of women aged 40–69 years (with an incremental CER of $12 908 per DALY saved) at a cost of $42 million, both in combination with treatment of all stages. The addition of basic palliative

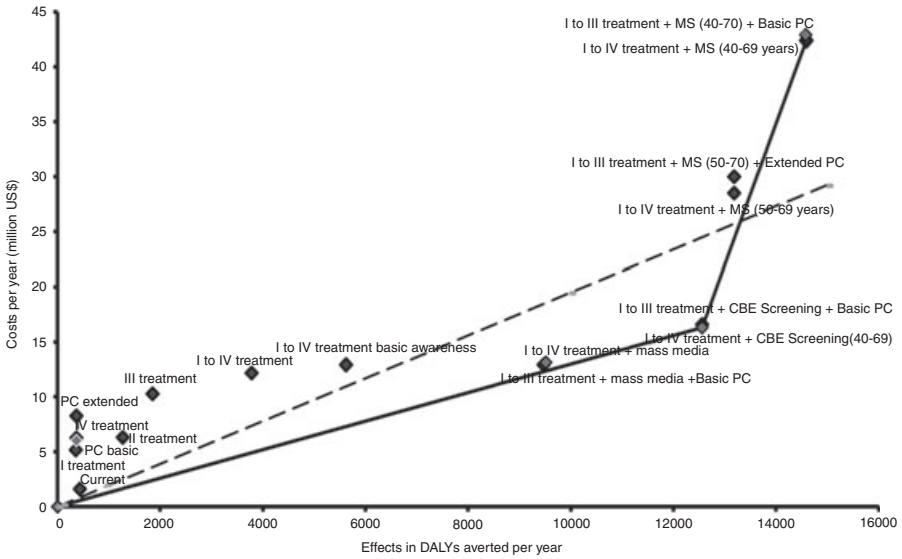

Figure 2 Cost-effectiveness of breast cancer interventions and expansion path according to Incremental cost-effectiveness ratio (ICER). Dotted line represents the cost-effectiveness threshold of 3*GDP/capita/DALY averted (1947 US$/DALY). In 2009 the Ghanaian GDP per capita was US$649. DALY, disability-adjusted life years; GDP, gross domestic product.

care to mammography screening and treatment of all stages would incur an incremental cost of $553 616 per DALY saved. The dotted line corresponds to three times the Ghanaian GDP per capita per DALY averted, and represents the suggested cost-effectiveness threshold as explained above. Both CBE screening and MAR plus treatment of all stages, combined with or without a basic palliative care programme, are beneath this threshold. Note that MAR, because it is slightly less cost-effective than CBE, is not on the expansion path and would – strictly interpreted – not be a candidate for implementation. Yet, as these small differences are likely not policy relevant, we consider MAR as a candidate for implementation.

Sensitivity analysis

Sensitivity analysis showed that our model is sensitive to alternative assumptions on case-fatality rates and stage distribution, and to a smaller extent on sensitivity of tests, capacity utilisation and attendance rates (Table 6). If higher case-fatality rates were assumed, representing poorer survival, the CER of awareness raising and screening interventions would increase 14–46%. Lower case-fatality rates would result in a 12–44% decrease of these CERs. As our assumptions on current Ghanaian stage distribution are based on hospital records, we also considered alternative sources, and these affected the CER of treatment stage I mostly (CER range −47% to +16%) and also the CER of awareness raising and screening interventions (CER ranges −26% to +22%).

Discussion

Our analysis indicates that screening by CBE, in combination with treatment of all stages, seems the most cost-effective intervention for breast cancer control in Ghana. The intervention can detect cancer in an early stage and therefore allows early treatment with relatively high effects at low costs. The intervention costs around $1300 per DALY averted, and seems cost-effective according to international thresholds on cost-effectiveness. MAR can also be considered cost-effective according to the same threshold, but mammography screening cannot.

Our study confirms the findings by Groot *et al.* (2006) that screening interventions are cost-effective and that early stage treatment is more cost-effective than late-stage treatment. One difference is the relatively few number of patients with stage I breast cancer in Ghana, which renders treatment of stage I relatively less cost-effective (considering the relatively large fixed cost for testing all women presenting with breast cancer symptoms but do not have cancer). Our results are also in line with findings by comparable CEA studies on cancer control. When expressed in International Dollars (I$), CBE screening in Ghana would cost about I$2750 per DALY averted and is in the same range of cost-effectiveness as cervical (ranging from I$307 to I$100 075 per DALY) and colorectal cancer

Table 6 Results of sensitivity analysis on average cost-effectiveness ratio (ACER)

Intervention scenarios	ACER	Alternative stage distribution A*	Alternative stage distribution B†	Case fatality rates + 25%	Disability weights + 25%	Costs outpatient visits + 25%	Capacity utilisation equipment −25%‡	Sensitivity of CBE and mammography −25%	Attendance rates screening programme 50%	Alternative effectiveness assumptions§
1 Current country-specific situation (10% coverage)	3745	4694	3297	6522	4325	3825	3885	–	–	–
2 Stage I treatment	14 173	6714	4208	16 427	16 000	14 466	15 056	–	–	–
3 Stage II treatment	5012	10 175	7467	10 181	5797	5138	5282	–	–	–
4 Stage III treatment	5547	8675	5523	11 078	6280	5745	5793	–	–	–
5 Stage IV treatment	16 824	7527	24 130	61 173	19 774	17 303	17 707	–	–	–
6 Basic palliative care (BPC)	16 133	6028	24 258	58 388	16 032	16 536	16 992	–	–	–
7 Extended palliative care (EPC)	22 032	11 359	30 321	79 159	21 895	22 461	22 948	–	–	–
8 Treatment of stage I to IV	3219	3256	2937	6197	3681	3297	3348	–	–	–
9 Basic awareness raising (BAR) + treatment of stage I to IV	2298	1701	2805	3344	2542	2352	2387	–	–	2656
10 Mass media awareness raising (MAR) + treatment of stage I to IV	1364	1077	1577	1681	1468	1390	1415	–	–	1503
11 Biennial CBE screening (40–69 years) + treatment of stage I to IV	1299	1047	1478	1499	1385	1351	1352	1451	1409	1274–1462
12 Biennial mammography screening (50–69 years) + treatment of stage I to IV	2163	1751	2454	2488	2303	2197	2304	2360	2328	–
13 Biennial mammography screening (40–69 years) + treatment of stage I to IV	2907	2373	3279	3303	3088	2950	3118	3081	3048	–
14 MAR + BPC + treatment of stage I to III	1387	1093	1605	1716	1451	1412	1437	NA	NA	–
15 CBE screening (40–69) + BPC + treatment of stage I to III	1323	1066	1505	1528	1380	1374	1376	1467	1427	1323–1478
16 Mammography screening (40–69) + BPC + treatment of stage I to III	2277	2804	2584	2620	2375	2311	2419	2496	2460	–
17 Mammography screening (50–69) + EPC + treatment of stage I to III	2945	2404	3322	3346	3068	2987	3155	3115	3083	–

CBE, clinical breast examination.
*Alternative stage distribution A, reflecting present Ghanaian situation, derived from breast clinic Kumasi (4% stage I, 7% stage II, 18% stage III, 70% stage IV).
†Alternative stage distribution B, reflecting present Ghanaian situation, according to Groot *et al.* (9.4% stage I, 14.2% stage II, 58.0% stage III, 18.4% stage IV). (Groot *et al.* 2006).
‡Mechanical equipment (e.g. mammography machines, CT and X-ray).
§Alternative assumptions on effectiveness of awareness interventions (−25%), sensitivity of CBE (Oestreicher *et al.* 2002) and stage shifts of CBE screening. (Oestreicher *et al.* 2002; Zotov & Shyyan 2003; Mittra *et al.* 2010).

(ranging from I$336 to I$15 548 per DALY) control options in the African subregion (Ginsberg *et al.* 2012).

This study leads to a number of observations on breast cancer control policy in Ghana. First, our study suggests that biennial CBE screening in women aged 40–69 years, combined with treatment of all stages, is economically attractive. This corresponds with findings from India, Egypt and Ukraine (Zotov & Shyyan 2003; Miller 2008; Okonkwo *et al.* 2008; Mittra *et al.* 2010). However, it should be taken into account that the implementation of CBE screening is highly dependent on the availability of human resources, facilities and devices for proper diagnosis and treatment. There is also a considerable uncertainty on the effectiveness of CBE screening interventions, particularly regarding sociocultural barriers: although most CBE screening studies show positive results on stage distribution, these interventions can easily fail when important aspects of education and information are neglected (Pisani *et al.* 2006; Miller 2008; Clegg-Lamptey *et al.* 2009b; Anderson *et al.* 2011). Furthermore, implementation of this intervention would costs around $16 million per year, and raises concerns on affordability. With a total health expenditure of around $40 per capita (7.8% of total GDP) (WHO 2010), the CBE screening would currently cost about $0.70 extra per capita (1.75% increase) and seems only sustainable when combined with other programmes (e.g. cervical cancer) and with long-term budgetary commitments. At this moment, a nationwide CBE screening programme therefore seems a suitable option only in the long run. Pilot studies, in which the implementation of CBE screening is explored in for example the context of current primary health-care structure, may be a first step. This could be followed by a phased introduction, in which the programme is carefully monitored and evaluated.

Second, MAR is almost as cost-effective as CBE screening but requires a smaller budget (around $13 million) and could be an alternative strategy. However, there is only very limited evidence on intervention effectiveness, and our estimates must be interpreted with great caution (Thomas *et al.* 2002; Devi *et al.* 2007; Shulman *et al.* 2010). As for CBE screening, the implementation of MAR is highly dependent on the availability of human resources and treatment services and can only commence in the long run upon careful evaluation.

Third, although treatment interventions are, themselves, not cost-effective, they are relatively affordable and deserve higher priority if only a small budget would be available. The annual costs for treating all stages are far lower ($12.18 million) than those of screening options, and scaling-up treatment of all stages to a 80% coverage level would already generate an almost 10-fold gain in DALYs annually. Moreover, treatment is an integral component of the continuum of care and essential to be scaled up if any intervention for early detection is implemented. A gradual increase in coverage of basic treatment services, along with improvements of referral systems, should then be simultaneously established (Anderson *et al.* 2011; Harford *et al.* 2011).

Fourth, the need for pain treatment of stage IV patient is evident (WHO 2011b). If management of stage IV patients entails basic palliative care, health effects slightly increase and costs slightly decrease (because of a reduction of hospitalisation days). Hence, this form of palliative care is economically attractive and seems most meaningful. Extended palliative care costs much more, averts relatively few extra DALYs and is therefore not recommended from an economic perspective.

Fifth, whereas biennial mammography screening is proven cost-effective in high-income countries, our analysis suggests it is not cost-effective in Ghana. Mammography screening would also require huge investments in equipment and human resources, demanding a considerable proportion of Ghana's health budget. Nevertheless, investments in mammographic services are still required for diagnostic purposes in Ghana, and mammography screening could become a relevant option if more resources would become available in the future.

Our study has a number of limitations. First, the national cancer registry in Ghana is not fully functional and local data on breast cancer stage distribution were derived from Korle Bu Teaching Hospital, Accra, and Komfo Anokye Teaching Hospital, Kumasi. As this is based on presenting patients rather than on all patients, this may not reflect reality and may have biased our estimates. Second, information on the epidemiology and case-fatality of breast cancer was not locally derived, but based on the GBD and observations in other countries. If for example poorer case-fatality rates would apply to Ghana, we expect CER estimates to worsen (Table 6). Third, in the absence of reliable data and following the requests from Ghanaian stakeholders, we did not include travel costs or productivity losses of patients seeking or undergoing care, and only evaluated biennial screening options. Including these costs would have probably led to increased cost generally, particularly for women with advanced stage breast cancer (Radice & Redaelli 2003; Broekx *et al.* 2011). Fourth, data on costs and treatment regimes were derived from small-scale, locally available sources or expert opinion, and may not be representative of the whole country. Fifth, evidence on the effectiveness of awareness raising, CBE and mammography screening in Ghana is absent. To arrive at Ghanaian estimates, we used a model approach that showed face validity, confirmed by the expert panel in our study. Despite these limitations,

results of our model show similarities with results from other models (Brown *et al.* 2006; Okonkwo *et al.* 2008). Moreover, although our sensitivity analysis showed that CER ranges of several interventions are overlapping, our overall study conclusions remain the same. The above limitations fit within the overall aim of WHO-CHOICE analysis to provide broad indications of cost-effectiveness on a range of interventions to inform general policy discussions rather than to deliver precise estimates on a specific intervention. Nevertheless, these limitations indicate the need to improve the evidence base of decision making in breast cancer control in Ghana.

In summary, our analysis suggests that breast cancer control in Ghana, to be efficient, should be oriented towards earlier detection. However, the provision of basic cancer diagnostic, referral, treatment and possibly palliative facilities is fundamental for breast cancer control along the continuum of care and should be established simultaneously with any intervention for early detection. A phased introduction of CBE screening or perhaps MAR, coupled with a careful monitoring and evaluation, could be a feasible option for Ghana and should be further explored.

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