

Cost-Effectiveness of HIV Screening of Blood Donations in Accra (Ghana)

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ABSTRACT

Objectives: Areas with high HIV-incidence rates compared to the developed world may benefit from additional testing in blood banks and may show more favorable cost-effectiveness ratios. We evaluated the cost-effectiveness of adding p24 antigen, mini pool nucleic acid amplification testing (MP-NAT), or individual donation NAT (ID-NAT) to the HIV-antibody screening at the Korle Bu Teaching Hospital (Accra, Ghana), where currently only HIV-antibody screening is undertaken.

Methods: The residual risk of HIV transmission was derived from blood donations to the blood bank of the Korle Bu Teaching Hospital in 2004. Remaining life expectancies of patients receiving blood transfusion were estimated using the World Health Organization life expectancies. Cost-effectiveness ratios for adding the tests to HIV-antibody screening only were determined using a decision tree model and a Markov model for HIV.

Results: The prevalence of HIV was estimated at 1.51% in 18,714 donations during 2004. The incremental cost per disability-adjusted life-year (DALY) averted was US\$1237 for p24 antigen, US\$3142 for MP-NAT and US\$7695 compared to the next least expensive strategy. HIV-antibody screening itself was cost-saving compared to no screening at all, gaining US\$73.85 and averting 0.86 DALY per transfused patient. Up to a willingness-to-pay of US\$2736 per DALY averted, HIV-antibody screening without additional testing was the most cost-effective strategy. Over a willingness-to-pay of US\$11,828 per DALY averted, ID-NAT was significantly more cost-effective than the other strategies.

Conclusions: Adding p24 antigen, MP-NAT, or ID-NAT to the current antibody screening cannot be regarded as a cost-effective health-care intervention for Ghana.

Keywords: blood transfusion, cost-effectiveness, developing countries, NAT, screening.

Introduction

As with many other countries in the same sub-Saharan West-African region, Ghana currently faces a significant percentage of the population living with HIV/AIDS, recently estimated at 3.1% [1]. The epidemic in Ghana is mainly driven by heterosexual contact, responsible for approximately 80% of HIV transmissions. Additionally, mother-to-child transmission accounts for an additional 15% [2]. Contribution of blood transfusion as a mode to transmit HIV infection is currently not reported officially. Nevertheless, HIV transmission has recently been estimated in the litera-

ture at one per 2578 donations given, despite routine HIV-antibody screening for donations in Ghana [3]. This compares unfavorably to the developed world, where the risk of HIV transmission after serological screening is estimated below one per million donations, which has also been mainly achieved through HIV-antibody screening [3,4].

Yet, in the developed world screening techniques in addition to HIV-antibody testing invariably show low returns at high costs resulting in unfavorable cost-effectiveness ratios. Reasons for this include the low baseline and remaining undetected HIV incidence in blood donors, the likelihood that donors with high risk of HIV infection are actively deferred, donors being adequately followed, and donation being based on a voluntary nonremunerated system [4,5]. In many developing countries, including Ghana, blood banking mainly relies on donors replacing the units transfused

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to a family member, relative, or friend and active deferral is generally not pursued. Such replacement donors are prone to having a higher HIV prevalence [6]. Moreover, follow-up of replacement donors and registration of infective status is practically impossible because of poor donor registration that severely restricting traceability.

The population of blood transfusion recipients in sub-Saharan Africa is on average younger than blood transfusion recipients in the developed world, as young patients with malaria and iron deficiency-related pediatric anemia represent a large share in the patient population. Blood-transfusion HIV transmission may result in further productivity losses in sub-Saharan Africa, on top of substantial productivity losses for other reasons related to HIV/AIDS status.

In the presence of routine antibody screening, HIV transmission through blood transfusion can occur if antibody testing is performed during the window period of antibody testing. This period reflects the time between development of infectious viremia in the HIV-infected person (in this case the donor) and antibody screening reactivity. Nucleic acid amplification testing (NAT) and p24-antigen screening techniques are able to reduce the window period because these are direct tests on the virus and therefore have reactivity on the viral particles rather than the antibodies that present later [7]. As the virus may become undetectable in later stages of infection, direct tests are always performed alongside antibody screening. Weighting the costs of adding testing techniques to the health gain and monetary benefits of reduced HIV infections—i.e., reduced costs for Highly Active AntiRetroviral Therapy (HAART) and reduction of productivity loss—is crucial. This may be particularly important for resource-poor countries.

We designed this study to evaluate the cost-effectiveness of adding p24-antigen screening, mini pool NAT (MP-NAT), or individual donation NAT (ID-NAT) to the HIV-antibody screening currently in place in Ghana. The HIV-antibody test in Ghana is performed post donation, on the donated units. Additionally, we analyzed the cost-effectiveness of the current routine antibody screening, compared to a hypothetical strategy of no HIV-screening of blood donations in Ghana.

Data, Methods, and Model

General Model Outline

Cost-effectiveness of p24-antigen testing, MP-NAT, ID-NAT, HIV-antibody screening, and no screening for HIV (“do nothing” option) was evaluated from the societal perspective. In particular, both direct medical and indirect production loss costs were included. We estimated incremental cost-effectiveness ratios (ICERs)

by relating the additional costs of a screening strategy to the additional health gains of that same strategy, as compared to the next least expensive screening strategy. Screening strategies that cost more and yield less health gains than another screening strategy (i.e., were dominated) were excluded. Additionally, the relative cost-effectiveness ratio (CER) was estimated relating the additional costs and health gains of a screening strategy as compared to HIV-antibody screening. Because decision-makers in blood banking in Africa are interested in the relative value of a new test in addition to HIV-antibody screening, we report the relative risk reduction compared to HIV-antibody screening and the associated CER. Estimated ICERs and CERs were compared to the per capita Gross National Income (GNI) of Ghana. According to the World Health Organization (WHO) guidelines, strategies with an (I)CER below the per capita GNI are regarded as cost-effective, whereas strategies with an (I)CER more than three times the per capita GNI are considered not cost-effective [8–10]. Health gains were expressed in disability-adjusted life-years (DALYs) averted. DALYs averted as the outcomes captures both differences in premature death as well as morbidity achieved by averting transfusion-transmitted HIV for each specific screening strategy compared to another. DALYs were chosen to reflect burden of disease rather than quality-adjusted life-years to be in line with other analyses assessing cost-effectiveness of HIV prevention in sub-Saharan Africa, that all report ratios per DALY averted [11,12]. DALYs associated with each screening strategy were determined by multiplying the residual risk of HIV transmission (because of the window period) for the specific screening strategy with the DALYs related to transfusion-acquired HIV. DALYs were discounted at 3% and weighted for age in the base case; an evaluation without age-weighting was also performed [13]. Costs per screening strategy were estimated by adding costs of screening, health-care costs of transfusion-acquired HIV, and production losses. Future costs were also discounted at 3%.

The robustness of the model was investigated by varying key parameters in sensitivity analysis. Scenario analyses were used to explore future changes in epidemiologic parameters, such as HIV prevalence in blood donors and availability of HAART for infected patients. In a threshold analysis test costs were determined where screening strategies yielded a CER relative to HIV-antibody screening that was equal to the GNI per capita and three times the GNI per capita [9,10,14]. Uncertainty was evaluated by second-order Monte Carlo simulation (10,000 runs) using probability distributions derived from data gathered on screening methods, blood donors, and blood transfusion recipients. Where applicable, uncertainty intervals (UIs) are presented as 2.5% and 97.5% percentiles.

Acceptability curves were constructed to evaluate the probability of accepting a screening strategy for different levels of willingness-to-pay (WTP) for a DALY averted, using the net monetary benefit framework [15]. The net monetary benefit (NMB) at a given WTP for a DALY averted is defined as the difference between the respective WTP multiplied by the DALYs averted for a given strategy and the costs of that strategy:

$$\text{NMB} = \lambda \times \text{DALYs} - C$$

with λ reflecting the WTP and C costs. Analyses to derive NMBs were also based on second-order Monte Carlo simulation. The proportion of the 10,000 runs that a specific screening strategy has the highest NMB represents the estimated probability of that strategy being cost-effective. Subsequently, the probability to be cost-effective is plotted against the WTP, resulting in an acceptability curve [16]. We assumed that a decision-maker would accept the more expensive screening strategy if it has been shown to be significantly (at 5% level) more cost-effective than a less expensive strategy.

Residual Risk of HIV Transmission

The residual risk of HIV-infected transfusion despite screening was determined with an adapted version of the window-phase model [17]. Pivotal in the window-phase model is incidence of HIV in blood donors after follow. Because blood donors in Ghana are not followed, the incidence of HIV among blood donors cannot be determined. We therefore used HIV prevalence as next best approach for estimating the residual risk of HIV transmission. The risk of HIV transmission after screening was defined as a fraction with the window period for the specific screening strategy in the numerator and the mean duration of asymptomatic HIV infection (WHO stages 1 and 2) multiplied with the prevalence of HIV among blood donors in the denominator. Therefore, we implicitly assumed that only donors without clinical signs of HIV infection would be able to donate without prior deferral by blood bank employees. Within the total period from HIV infection to the development of AIDS (WHO stages 1–3; estimated at 7.89 years), the duration of HIV stages without apparent clinical signs was estimated at 5.04 years [18,19].

HIV prevalence was retrospectively determined at 1.51% from HIV-antibody screening (Vironostika Uni-Form II plus O, Boxtel, The Netherlands) of 18,714 donations to the National Blood Transfusion Service (Korle Bu Teaching Hospital, Accra, Ghana) in 2004. Initial positivity to HIV-antibody screening was found in 579 donations, and repeat reactivity was found for 282 donations. Replacement donations were 66% of the total number of donations.

Patient Population, HIV, AIDS, and DALYs

The health effects of transfusion-transmitted HIV infection were modeled using prospective data on 193 transfused patients at the Korle Bu Teaching Hospital (Accra, Ghana) during February 2003 (patient study). Mainly relatively young patients received blood transfusion. In particular, 42% of the patients receiving a blood transfusion (35 female and 46 male) were younger than 12 years and 19% (16 female and 21 male) were younger than 2 years. The average age of the blood transfusion recipient was 23.4 years, and 124 of the included patients were female. Malaria and/or related complications were the predominant indications for blood transfusion in patients under 12 years (69%). Blood transfusions in older patients were mainly used for gynecologic and obstetric conditions (37%), such as abortion (15%). To control for seasonal variations in the blood transfusion recipient population, the proportions of patients under 12 years old and above 12 years in the patient study were adjusted using the proportions of these age groups identified from the blood bank issue records from 2002 to 2004 (6734 patients below 12 years and 13,605 above 12 years). These adjusted percentages are listed in Table 1 and were conceived as probabilities in the model.

Because whole blood was the predominant blood product transfused, one donation was assumed to yield one unit for transfusion. Patients received on average 1.66 units of blood per transfusion. Patients less than 2 years old received on average 0.51 units, while patients of 2 years up to 12 years and patients of 12 years or older received 1.0 and 2.3 units, respectively. In the model, any HIV-infected unit transfused—either fully or partly—was assumed to result in HIV transmission to the recipient. Additionally, it was assumed that for each HIV-infected blood transfusion recipient there would be 0.84 secondary transmissions through heterosexual contact, which is in line with estimates of the so-called basic reproduction rate (reflecting the multiplication of the number of heterosexual partners, transmission probability per partner, and duration of the HIV stages) [20–22]. Secondary transmissions through other routes were not included [23].

As part of the estimation of DALYs, years of life lost per patient due to HIV infection were determined as the difference between the patients' remaining life expectancy without HIV infection and the life expectancy with HIV infection. Age- and sex-specific remaining life expectancies were taken from WHO and applied to patients receiving blood transfusions [24]. The health effects of HIV transmission were not included for patients who died in hospital because of the underlying disease. Long-term excess mortality for blood transfusion recipients was not included in the

Table 1 Model variables, probability distributions, and sources

Model variable	Parameters and probability distribution	Source
<i>Test characteristics</i>		
Window HIV-Ab (standard)	Normal; mean: 20.3 days; SE: 1.6	[4,5]
Window p24 antigen & HIV-Ab	Normal; mean: 15 days; SE: 1.3	[4,5]
Window MP-NAT & HIV-Ab	Normal; mean: 9 days; SE: 0.6	[4,5]
Window ID-NAT & HIV-Ab	Normal; mean: 5.6 days; SE: 0.4	[4,5]
Costs of HIV-Ab (standard)	US\$5	[4,5]
Additional costs of p24 antigen	US\$2	[4,5]
Additional costs of MP-NAT	US\$7.5	[4,5]
Additional costs of ID-NAT	US\$15	[4,5]
<i>Patients and disease</i>		
Age of patients: <2 years	Normal; mean: 0.89; SE: 0.087; 37 patients	Patient study & NBTS
Age of patients: 2–12 years	Percentage of units transfused: 8.9% Normal; mean: 4.27; SE: 0.34; 44 patients	Patient study & NBTS
Age of patients: ≥12 years	Percentage of units transfused: 12.6% Normal; mean: 38.5; SE: 1.63; 111 patients	Patient study & NBTS
Number of transfusions per donation	1.66	Patient study & NBTS
In hospital mortality, patients <2 years	10.8%	Patient study
In hospital mortality, patients 2–12 years	4.5%	Patient study
In hospital mortality, patients ≥12 years	7.3%	Patient study
Duration of HIV stages (patients <2 years)	Normal; mean: 2.41 years; SE: 0.143	Markov model
Duration of HIV stages (patients ≥2 years)	Normal; mean: 7.89 years; SE: 0.280	Markov model
Disability weight HIV stages (<12 years)	0.123	[13]
Disability weight HIV stages (≥12 years)	0.136	[13]
Duration of AIDS stage (all patients)	Normal; mean: 0.51 years; SE: 0.035	Markov model
Disability weight AIDS stage (all patients)	0.505	[13]
Coverage antiretroviral therapy	5% (s.a.: 1.25–100%)	[1]
HIV stage 3 extension by HAART	Uniform; 11–13 years extension (s.a.: 8–10 and 23–25 years extension)	[29,30]
R0	0.84	[21–23]
Annual costs of basic care for HIV/AIDS	US\$32.54	[18]
Annual costs of antiretroviral therapy	US\$1087.67 (s.a.: US\$380–2200)	[18]
<i>Productivity losses</i>		
Unemployment	20%	[32,39]
Age adjustment for earnings	0–5 years = 0 6–15 years = 0.15 16–50 years = 1 51–65 years = 0.85 ≥66 years = 0.25	[32]
Average annual earnings	US\$127	[32]

Test costs are expressed per donation. All costs in 2004 US\$.

Ab, antibody; HAART, Highly Active AntiRetroviral Therapy; ID-NAT, individual donation nucleic acid amplification testing; MP-NAT, mini pool nucleic acid amplification testing; NBTS, National Blood Transfusion Service (Korle Bu Teaching Hospital, Accra, Ghana); R0, basic reproduction rate; s.a., sensitivity analysis; SE, standard error.

model as this is only described for the developed world, where patients transfused are older and suffer from other underlying diseases that often severely affect life expectancy [5,25,26].

Years lived with disability were calculated by multiplying the time in HIV stages or AIDS with the appropriate disability weights [13]. Using Markov modeling, the duration of HIV stages 1 to 3 was estimated at 7.89 years, and the duration of the AIDS stage was estimated at 0.5 years [19]. Extension of HIV stage 3 due to longevity by HAART was included with a baseline assumption of 5% availability of antiviral drugs, reflecting the current scarce availability in Ghana [1,27,28]. HAART was estimated to yield an additional 12 life-years in the baseline, with 9 and 24 years of life extensions explored in the sensitivity analysis [29–31].

Finally, DALYs associated with HIV infection—and potentially averted through improved testing

strategies—were calculated by summing years of life lost and years lived with disability.

Screening Costs, Health-Care Costs, and Productivity Losses

All costs were expressed in 2004 price levels. Screening costs were estimated by multiplying the cost of screening per donation with the number of units transfused per patient. Screening costs were obtained from literature and subjected to sensitivity analysis [3,5]. Costs of HAART were calculated using official Ghanaian drug prices and a costing study for health-care costs associated with the provision of HAART [18]. All infected patients received basic care for sequelae of HIV infection [17]. Productivity losses were estimated by cumulating annual earnings weighted for age and corrected for unemployment, for the expected survival from the moment of HIV infection, see Table 1 [32].

Table 2 HIV infections averted and relative cost-effectiveness ratios of the base case (per 10,000 donations)

Strategy	HIV infections averted UI [95%]	DALYs averted UI [95%]	Net costs (US\$) UI [95%]	Cost-effectiveness (US\$/DALY) UI [95%]
Base case				
Ab vs. no screening	241 [240.6 to 241.5]	5159 [4876 to 5448]	-444,901 [-469,567 to -420,972]	-86 [-79.84 to -93.29]
p24 vs. Ab screening	0.70 [0.17 to 1.23]	15.0 [3.74 to 26.34]	18,560 [17,484 to 19,635]	1237 [652 to 4568]
MP-NAT vs. Ab screening	1.50 [1.05 to 1.94]	32.0 [22.55 to 41.75]	71,931 [70,997 to 72,832]	2248 [1701 to 3228]
ID-NAT vs. Ab screening	1.95 [1.51 to 2.37]	41.6 [32.33 to 51.27]	146,007 [145,086 to 146,879]	3508 [2830 to 4543]

All costs in 2004 US\$.

Ab, antibody; DALY, disability-adjusted life-year; ID-NAT, individual donation nucleic acid amplification testing; MP-NAT, mini pool nucleic acid amplification testing; UI, uncertainty interval.

Results

Base-Case Analysis

The residual risk of HIV transmission was estimated at 2.76 per 10,000 donated units for HIV-antibody screening. Implementing p24 antigen (additional cost per donation: US\$2), MP-NAT (additional cost per donation: US\$7.5), or ID-NAT (additional cost per donation: US\$20) in addition to HIV-antibody screening would lower HIV-transmission risks to 2.04, 1.22, and 0.76 per 10,000 units donated, respectively. When added to HIV-antibody screening, ID-NAT averted most HIV transmissions and DALYs, followed by MP-NAT and p24-antigen screening (see Table 2). HIV-antibody testing compared to no screening showed the highest reduction in transmission of HIV and averted the most DALYs. The incremental net costs of performing p24-antigen screening, MP-NAT, or ID-NAT alongside HIV-antibody testing were highest for ID-NAT followed by MP-NAT and p24-antigen screening (see Fig. 1). HIV-antibody screening results in an estimated cost-savings of US\$444,901 and 5159 DALYs averted per 10,000 donations compared to no screening, i.e., antibody screening dominates no screening. This translates to US\$73.85 cost-savings

and 0.86 DALYs averted per transfused patient. The ICER of p24-antigen testing, MP-NAT, and ID-NAT in addition to HIV-antibody screening was least favorable for ID-NAT, followed by MP-NAT and p24-antigen screening, respectively (see Fig. 1). The same rank order was found for the relative CER for p24-antigen testing, MP-NAT, and ID-NAT compared to HIV-antibody screening (see Table 2).

The reduced production losses and health-care savings from expanded testing are estimated to be US\$1440 (95% UI: 390–2544), US\$3069 (95% UI: 2191–4015), and US\$3993 (95% UI: 3119–4918) per 10,000 donations for p24 antigen, MP-NAT, and ID-NAT relative to HIV-antibody screening, respectively. Compared to no screening, HIV-antibody screening is estimated to save US\$494,901 per 10,000 donations (95% UI: 471,412–519,992) in reduced production losses and health-care costs. Per transfused patient this amounts to US\$82.15.

If accepting only the screening strategy that demonstrates significantly greater cost-effectiveness (at the 5% level), the acceptability curve indicates that up to a WTP of US\$2736 per averted DALY HIV-antibody screening is the preferred strategy. At a per capita GNI of US\$380 in Ghana, antibody screening

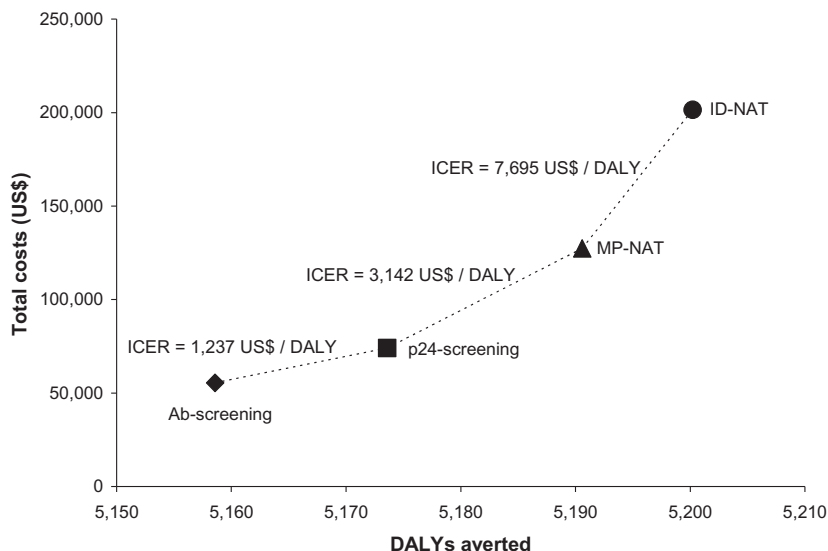
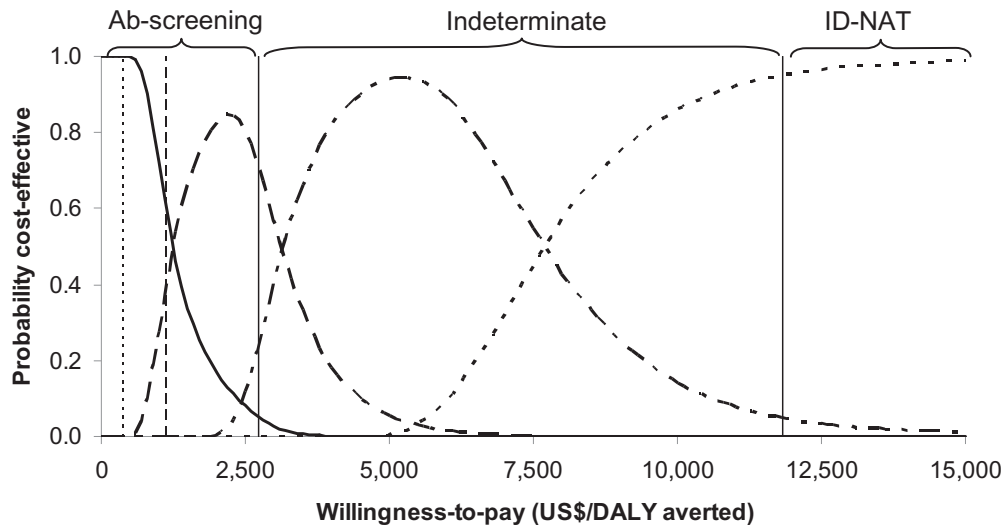


Figure 1 Total costs (cost of screening, health care, and productivity loss) of the screening strategies and averted loss of life and health (disability-adjusted life-years [DALYs]) per 10,000 donations. All costs in 2004 US\$. No screening for HIV is not displayed, because this strategy is clearly dominated: 0 DALYs were averted and total costs were US\$500,415. Relative to no screening, HIV-antibody (Ab) screening saved US\$444,901 in total costs. ICER, incremental cost-effectiveness ratio; ID-NAT, individual donation nucleic acid amplification testing; MP-NAT, mini pool nucleic acid amplification testing.

Base case



Scenarios

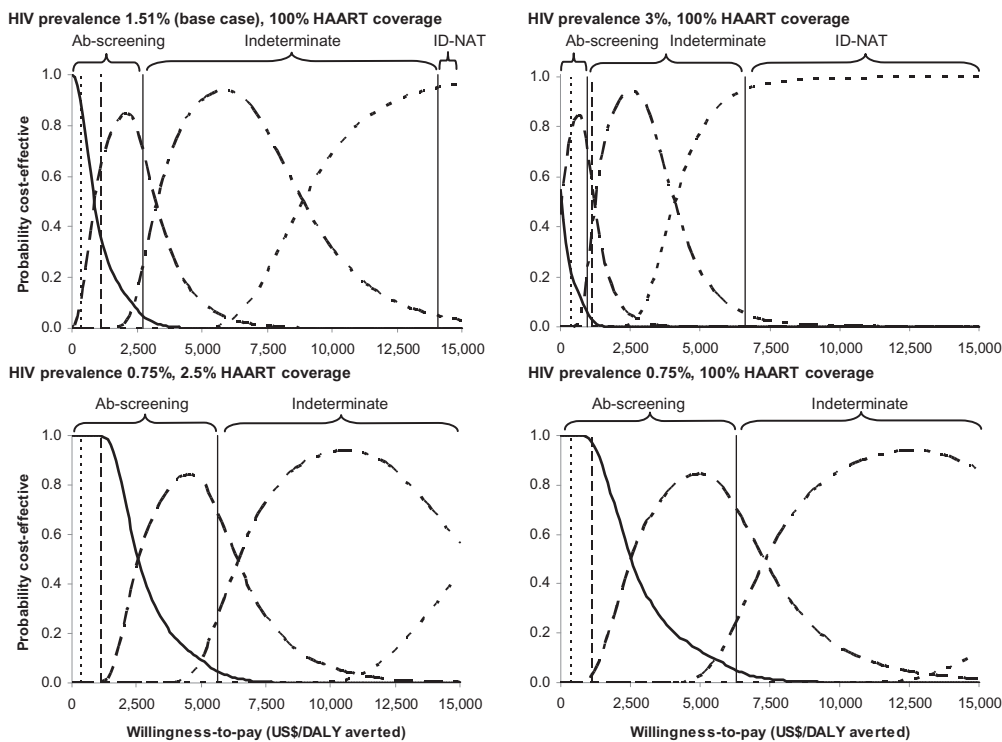


Figure 2 Acceptability curves for the base case and selected scenarios of expanded HIV-screening. More expensive screening techniques are accepted if significantly cost-effective (at 5% level) compared to the current strategy (accepted strategy above accolade). Ab-screening, HIV-antibody screening (—); p24-screening, p24-antigen screening (---); MP-NAT, mini pool nucleic acid amplification testing (- - -); ID-NAT, individual donation nucleic acid amplification testing (- . - .); HAART, Highly Active AntiRetroviral Therapy. Vertical lines: — represents the switching points where a more expensive screening strategy becomes significantly more cost-effective (at the conventional 5% level); and ----- represent the per capita Gross National Income (GNI) (US\$380) and three times the per capita GNI (US\$1140) of Ghana as indicated potential thresholds by the World Health Organization.

was the preferred strategy up to the three-times-per-capita GNI threshold of US\$1140 (see Fig. 2). ID-NAT in addition to HIV-antibody screening was considered to be the most cost-effective approach at a

WTP of US\$11,828 per averted DALY and above. Between both switching points no clear preference existed for adding p24 antigen or MP-NAT to HIV-antibody screening. The probability of accepting a no

screening strategy for HIV being cost-effective was zero (this is not shown in the acceptability curves as it coincides with x-axis).

For a decision-maker choosing the most cost-effective strategy, HIV-antibody screening alone would be the preferred strategy up to a WTP of US\$1245 per DALY averted. p24-antigen screening in addition to HIV-antibody screening represents the most cost-effective screening strategy from a WTP of US\$1246 up to 3143 per averted DALY (although not significantly so, as mentioned above). MP-NAT was the most cost-effective screening technique for a WTP between US\$3144 up to 7698 per DALY averted, and over this range ID-NAT added to HIV-antibody screening was the most cost-effective strategy.

Scenario and Conventional Sensitivity Analysis

Expected changes in the availability of HAART and the impact of changing HIV prevalence among blood donors were evaluated in a worst and best case scenario. In particular, within the “3 by 5 initiative” framework, it is envisioned that HAART will be provided to all HIV-infected patients fulfilling the require-

ments for CD4 counts and WHO stage. In 2005, 3500 out of approximately 71,000 patients eligible for treatment were provided with HAART in Ghana (5%), but with 29,000 patients (41% of patients eligible for treatment) targeted to receive HAART by the end of 2005 [1]. Compared to other African countries, the prevalence of HIV has grown modestly. Nevertheless, there is no evidence to suggest that prevalence is declining or even reaches a plateau because of the preventive measures being undertaken nationally.

The scenario with a HIV prevalence of 3% among blood donors and 100% availability of HAART to eligible infected transfusion recipients showed lower CERs compared to the base case for adding p24 antigen, MP-NAT, or ID-NAT to HIV-antibody screening (Fig. 3). Up to a WTP over US\$979 per DALY averted, HIV-antibody screening is the preferred strategy; whereas more than US\$6614 per DALY averted, ID-NAT in addition to HIV-antibody screening is significantly more cost-effective (see Fig. 2).

In a scenario exploring an HIV prevalence of 1.51% (base case) among blood donors and 100% of eligible HIV-infected patients having access to

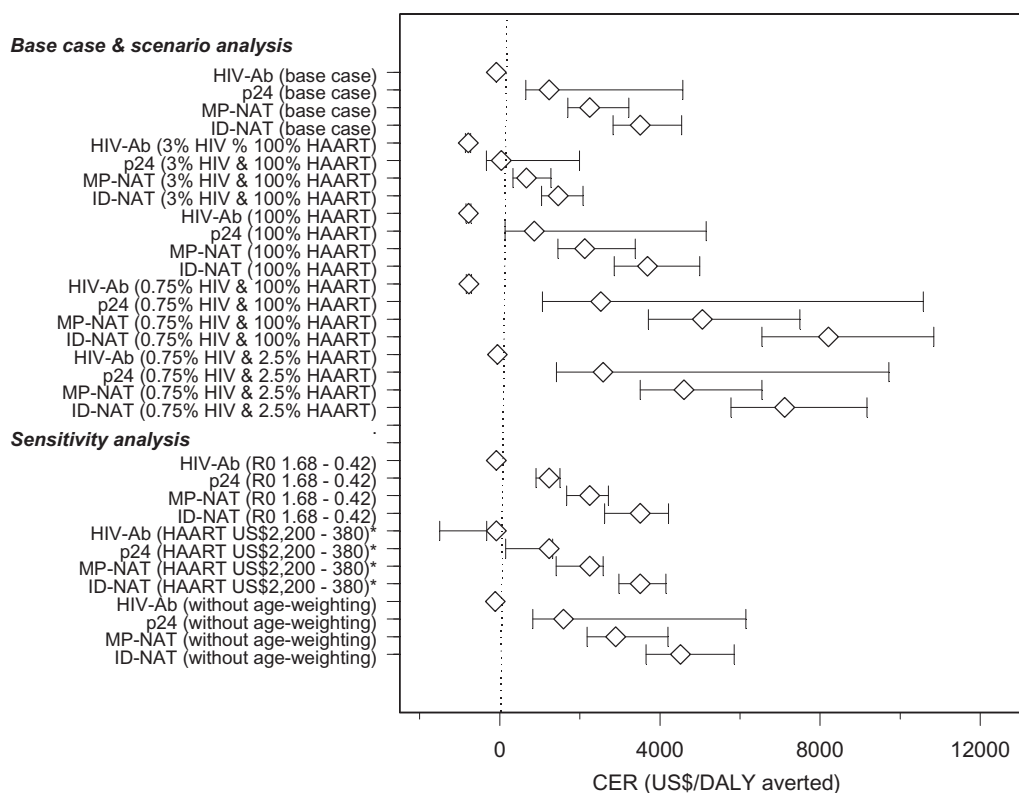


Figure 3 Cost-effectiveness ratio (CER) ranges and mean (diamond) of the base case, scenario, and sensitivity analysis. Error bars represent the 95% uncertainty interval for the base case and the scenario analysis and age-weighting in the sensitivity analysis. At sensitivity analysis error bars represent the CER for the specified range with the base-case CER (diamond). *With accessibility to HAART of 100%. All tests are evaluated in addition to HIV-antibody screening and the displayed CER is relative to HIV-antibody screening. HIV-antibody screening is compared to no screening. All costs in 2004 US\$. Ab, antibody; DALY, disability-adjusted life-year; HAART, Highly Active AntiRetroviral Therapy; ID-NAT, individual donation nucleic acid amplification testing; MP-NAT, mini pool nucleic acid amplification testing; R0, basic reproduction rate; % HIV, HIV prevalence among donors; % HAART, accessibility to HAART for infected recipients.

HAART, lower CERs were also found for expanding HIV screening of blood donors, except for ID-NAT (see Fig. 3). The rank order did not change compared to the base case. HIV-antibody screening alone was the preferred strategy up to a WTP of US\$2739 per DALY averted HIV and for a WTP over US\$14,061 per DALY averted adding ID-NAT was significantly the most cost-effective option (see Fig. 2). For a HIV prevalence in donors of only 0.75% and with only 2.5% of the patients having access to HAART, the CERs for extended testing approximately doubled compared to the base case. Also, cutoff points for cost-effectiveness were much higher at US\$5622 and US\$23,903 per DALY averted for antibody screening and ID-NAT, respectively.

The estimated relative CERs were very sensitive to changes in costs per test. Figure 4 illustrates this for plausible ranges of the total costs per screening strategy. Within the cost range explored, the CER for ID-NAT relative to HIV-antibody screening was always well more than three times the GNI per capita. The CER for MP-NAT relative to HIV-antibody screening fell less than three times the GNI per capita only in the lower part of the cost range.

Threshold analyses on test costs revealed that highest test costs would be accepted for the most effective test strategy of ID-NAT, whereas acceptable extra test costs were the lowest for the least effective strategy. ID-NAT became cost-saving at total costs per donation of US\$5.39 (including costs for antibody

screening), followed by MP-NAT and p24 total test costs at US\$5.30 and US\$5.14, respectively. At threshold of the GNI per capita level per DALY averted, the total test costs could increase up to US\$6.98, US\$6.52, and US\$5.71 for the three strategies, respectively. If the WHO guidelines and World Bank recommendations were followed and meaning that the strategies cannot be regarded as cost-effective if the relative CER increases more than three times the GNI per capita, the respective thresholds for the total screening costs were US\$10.14, US\$8.95, and US\$6.85 per donation for ID-NAT, MP-NAT, and p24-antigen screening, respectively.

In the base case, it was assumed that each person infected with HIV by blood transfusion would infect 0.84 other persons by heterosexual intercourse. Halving and doubling this estimate has a large effect on the CERs (Fig. 3). Nevertheless, the rank order remains the same compared to the base case. The CER of p24-antigen screening relative to HIV-antibody screening would fall less than three times the GNI per capita at twice the base-case value for this secondary transmission. The outcomes of the model are robust to variations in accessibility to HAART and costs and health gains of HAART: varying parameters separately has little impact (<5%) on the cost-effectiveness of expanded HIV-screening strategies. At high levels of accessibility to HAART for eligible patients (100%), the cost of HAART has an impact on the results (Fig. 3). Increasing the cost of HAART results in lower CERs for a strategy of expanding HIV-antibody screening; the rank order remains the same.

Performing DALY estimation without age-weighting lowered the health gains associated with extended screening; the DALYs averted per 10,000 donations for p24-antigen screening, MP-NAT, and ID-NAT were 11.7, 24.9, and 32.3, respectively. The corresponding CERs were US\$1592, US\$2894, and US\$4515 per DALY averted for p24 antigen, MP-NAT, and ID-NAT relative to HIV-antibody screening, respectively. Antibody screening averted 4008 DALYs and remained cost-saving compared to no screening, still dominating the no screening strategy.

Discussion

We investigated the cost-effectiveness of screening blood donations for HIV in Accra (Ghana) using a model comprising country- and patient-population-specific survival, blood-product utilization, indirect and direct cost data. The current HIV-antibody screening strategy was found to save costs and avert morbidity and mortality compared to no screening (dominant). Also, base-case ICERs of screening strategies added to HIV-antibody screening were all well more than three times the GNI per capita for Ghana (US\$1140). Therefore, adding screening techniques

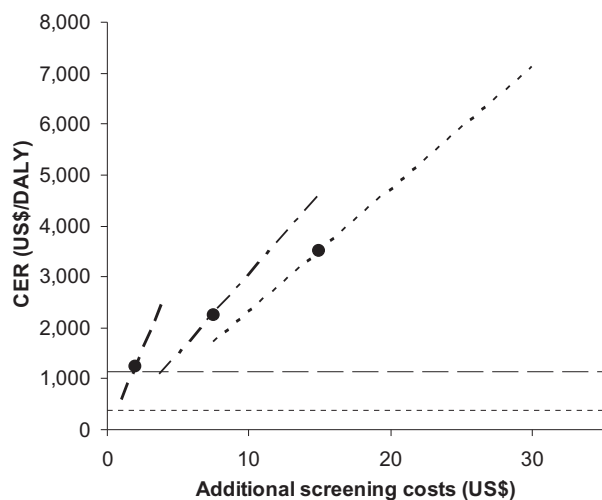


Figure 4 Sensitivity of the relative cost-effectiveness ratio (CER) to changes of additional screening costs per donation (above HIV-antibody screening costs). Only plausible ranges are plotted for the additional screening costs. p24-antigen screening (---), mini pool nucleic acid amplification testing (MP-NAT; ···), and individual donation nucleic acid amplification testing (ID-NAT; - · -) were compared to HIV-antibody screening. The base case is represented by (●); ---- and — represent the Gross National Income (GNI) (US\$380) and three times the GNI (US\$1140) of Ghana.

cannot be regarded as cost-effective based on this threshold criteria that has been suggested by both the WHO and World Bank. Moreover, no other screening strategy was shown to be significantly more cost-effective up to the threshold of three times the Ghanaian GNI per capita. In scenario analysis, antibody screening remained significantly more cost-effective even beyond three times the GNI per capita threshold. If a decision-maker accepts the strategy which has the highest probability to be cost-effective (without requiring this to be statistically significantly so), HIV-antibody screening would still remain the preferred screening strategy up to three times the GNI per capita. Adding either p24-antigen screening or MP-NAT was significantly more cost-effective than antibody screening alone at an HIV prevalence of 3% and an assumption of full access to HAART. No clear distinction could be made between p24-antigen screening and MP-NAT as separately neither were significantly more cost-effective. Addition of ID-NAT to HIV-antibody screening would only be undertaken if Ghanaian decision-makers would be willing to pay US\$11,828 per DALY averted, which is more than 10 times the GNI per capita for Ghana.

In the last decade, several measures have been undertaken to attempt to alter the course of the HIV/AIDS epidemic in Ghana and further activities are planned in the future. The implementation of programs to induce (sexual) behavioral changes, reduce mother-to-child transmission, and increase blood transfusion safety might curb the HIV-epidemic, and thereby influence the cost-effectiveness of expanded HIV screening. ICERs for HIV screening are fourfold to fivefold lower (more favorable) for doubling compared to halving base-case HIV prevalence. Also, the WTP for adding tests to HIV-antibody screening is fourfold lower for high compared to low HIV prevalence.

Clearly, varying test costs has a profound impact on the cost-effectiveness. Lowering test costs in the model would give considerable more favorable cost-effectiveness of adding tests to HIV-antibody screening. Also, through price reductions for HAART, alongside the expected progressive implementation of accessibility to HAART for eligible patients considerable better cost-effectiveness may be achieved for adding tests. Nevertheless, variations in the costs of HAART alone had hardly any impact on the CERs in the base case (with low accessibility at 5% only). Since age-weighting in the DALY calculation is controversial [33], we also presented results without age-weighting. Evaluations without age-weighting yielded higher, more unfavorable cost-effectiveness ratios. If through education and behavior change the number of secondary infections could be decreased in the future, this would lead to less favorable CERs for adding screening tests to the current antibody screening. In our analysis, only secondary infections caused

by heterosexual sexual contact were included. This means that we underestimate the attractiveness of expanded screening as, for example, contributions of unsafe injections and vertical transmissions will further add to secondary cases. Only p24-antigen screening, however, falls below three times the GNI per capita at twice the base-case value for the number of secondary transmissions per infected blood transfusion recipient.

One limitation of our evaluation is the determination of the residual risk of HIV transmission by using the HIV prevalence instead of the preferred HIV-incidence window-phase approach or the application of a de-tuned assay [17,34]. Nevertheless, our estimated residual risk may be a good approximation, as the risk of 2.76 per 10,000 donated units after HIV-antibody screening in the present study falls well within the range from a previously reported direct determination. In this study, performed in Kumasi (Ghana) with a comparable HIV prevalence, 0.6 to 3.9 infective units per 10,000 donated units were found [4]. A further limitation of this evaluation is that only window-phase HIV transmissions are considered, disregarding HIV transmission due to technical or human failure which could also potentially be reduced by additional screening tests [35]. Also, blood transfusion utilization data in this study are obtained in urban Accra at the Korle Bu Teaching Hospital, which may not represent the situation in rural areas of Ghana.

The use of cost-effectiveness ratios to prioritize funding of health-care interventions and to compare them in different settings is increasing as an approach but is not without controversy. Thresholds for regarding interventions as cost-effective in low-income countries were suggested ranging from once the GNI per capita up to three times the GNI per capita [9,10,14]. Screening blood donations on HIV-antibody was estimated to be cost-saving and to gain DALYs and should therefore always be implemented. Only if the costs of additional screening techniques were reduced considerably, would the corresponding cost-effectiveness ratios fall below the GNI per capita thresholds. ID-NAT screening could fall within the range of these thresholds if price cuts on test kits, license fees, and equipment results in reduced test costs per donation at least to US\$10.14.

Health-care interventions in sub-Saharan Africa targeted at communicable diseases are associated with cost-effectiveness ratios ranging from US\$121 per DALY averted for malaria control, US\$310 per DALY averted for prevention of mother-to-child HIV transmission up to US\$542 to 1280 per DALY averted or US\$1180 per life-year gained for providing HAART [11,12,36]. Expanding blood donation screening with HIV-antigen tests does not compare favorably to these specific interventions. Compared to cost-effectiveness ratios for expanding HIV screening in the more devel-

oped world, which easily exceed US\$1 million per DALY averted, (incremental) cost-effectiveness ratios found for introducing additional screening in Ghana represent much greater value.

Our study shows that the current policy of HIV-antibody screening of blood donations is saving costs and provides health gains in Accra (Ghana), justifying the broad implementation of this strategy. Currently, introducing either MP-NAT or ID-NAT testing alongside HIV-antibody screening cannot be regarded cost-effective in Accra (Ghana). Reduction in test costs could change this. Certainly, screening cost reductions could bring p24-antigen screening within acceptable limits. It is essential that implementing any additional screening test should also include improvement in training of personnel, simplification and automation of administration, and dispensing systems to reduce human and technical failure. Equally important, blood banks should move from solely testing donations or donors to maintaining a low-risk regular voluntary donor pool combined with an adequate follow-up of these donors [37,38]. Furthermore, consolidation of blood banking activities and steering by a national transfusion authority is necessary to build technology and human resource for implementing demanding screening techniques such as NAT testing ever in the future.

M. van Hulst and M.J. Postma had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. K.W.C. Sagoe, J.E. Vermande, I.P. van der Schaaf, E.K. Torpey, J. Ansah, and J.A. Mingle acquired the data. M. van Hulst, K.W.C. Sagoe, W.P.A. van der Tuuk Adriani, E.K. Torpey, C. Th. Smit Sibinga, and M.J. Postma drafted the manuscript. The anonymous reviewers and the editor are thanked for their valuable comments on the article which improved our manuscript considerably. We also thank K. Tolley for critically reviewing our manuscript.

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References

- 1 Ministry of Health/Ghana Health Service. 2004 HIV Sentinel Survey Report. Accra: Ministry of Health/Ghana Health Service, 2005.
- 2 Ministry of Health/Ghana Health Service. HIV/AIDS in Ghana. Accra: National AIDS/STI Control Programme/Ghana Health Service, 2005.
- 3 Candotti D, Sarkodie F, Allain JP. Residual risk of transfusion in Ghana. *Br J Haematol* 2001;113:37–9.
- 4 Marshall DA, Kleinman SH, Wong JB, et al. Cost-effectiveness of nucleic acid test screening of volunteer blood donations for hepatitis B, hepatitis C and human immunodeficiency virus in the United States. *Vox Sang* 2004;86:28–40.
- 5 Jackson BR, Busch MP, Stramer SL, Aubuchon JP. The cost-effectiveness of NAT for HIV, HCV, and HBV in whole-blood donations. *Transfusion* 2003;43:721–9.
- 6 Sarkodie F, Adarkwa M, du-Sarkodie Y, et al. Screening for viral markers in volunteer and replacement blood donors in West Africa. *Vox Sang* 2001;80:142–7.
- 7 Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ. The risk of transfusion-transmitted viral infections. The Retrovirus Epidemiology Donor Study. *N Engl J Med* 1996;334:1685–90.
- 8 Baltussen R, Stolk E, Chisholm D, Aikins M. Towards a multi-criteria approach for priority setting: an application to Ghana. *Health Econ* 2006;15:689–96.
- 9 World Bank. World Development Report 1993. New York: Oxford University Press, 1993.
- 10 World Health Organization. Investing in Health Research and Development: Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options. Geneva: WHO, 1996.
- 11 Creese A, Floyd K, Alban A, Guinness L. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. *Lancet* 2002;359:1635–43.
- 12 Hogan DR, Baltussen R, Hayashi C, et al. Cost effectiveness analysis of strategies to combat HIV/AIDS in developing countries. *BMJ* 2005;331:1431–7.
- 13 Murray CJL, Lopez AD. The Global Burden of Disease. A Comprehensive Assessment of Mortality and Disability for Diseases, Injuries and Risk Factors in 1990 and Projected to 2020. Cambridge, MA: Harvard University Press, 1996.
- 14 World Bank. GNI per capita in 2004, Atlas method and PPP. Available from: <http://www.worldbank.org/data/datatopic/GNIPC.pdf> [Accessed August 1, 2005].
- 15 Stinnett AA, Mullahy J. Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis. *Med Decis Making* 1998;18(2 Suppl.):S68–80.
- 16 Briggs AH, O'Brien BJ, Blackhouse G. Thinking outside the box: recent advances in the analysis and presentation of uncertainty in cost-effectiveness studies. *Annu Rev Public Health* 2002;23:377–401.
- 17 Kleinman S, Busch MP, Korelitz JJ, Schreiber GB. The incidence/window period model and its use to assess the risk of transfusion-transmitted human immunodeficiency virus and hepatitis C virus infection. *Transfus Med Rev* 1997;11:155–72.
- 18 Torpey EK. Estimating the Cost of HIV Related Clinical Care Services. Accra: Family Health International, 2003.
- 19 Anonymous. Improved methods and assumptions for estimation of the HIV/AIDS epidemic and its impact: recommendations of the UNAIDS Reference Group on Estimates, Modelling and Projections. *AIDS* 2002;16:W1–14.

- 20 Deuchert E, Brody S. Plausible and implausible parameters for mathematical modeling of nominal heterosexual HIV transmission. *Ann Epidemiol* 2007;17:237–44.
- 21 Gray RH, Wawer MJ, Brookmeyer R, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. *Lancet* 2001;357:1149–53.
- 22 Wawer MJ, Gray RH, Sewankambo NK, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis* 2005;191:1403–9.
- 23 Schmid GP, Buve A, Mugenyi P, et al. Transmission of HIV-1 infection in sub-Saharan Africa and effect of elimination of unsafe injections. *Lancet* 2004;363:482–8.
- 24 World Health Organization. Life Tables for 191 Countries, Ghana 2001. Available from: http://www3.who.int/whosis/life/life_tables/life_tables_process.cfm?country=gha&year=2001 [Accessed January 21, 2004].
- 25 Vamvakas EC, Taswell HF. Epidemiology of blood transfusion. *Transfusion* 1994;34:464–70.
- 26 Tynell E, Norda R, Shanwell A, Bjorkman A. Long-term survival in transfusion recipients in Sweden, 1993. *Transfusion* 2001;41:251–5.
- 27 Anonymous. Predicting the failure of 3 by 5. *Lancet* 2005;365:1597.
- 28 Felling B, Amenyah J, Sam-Abbenyi A, et al. Ghana: Preparing for the Management of Antiretroviral Drugs—Findings and Recommendations of the ARV Assessment Team. Arlington, VA: John Snow Inc./DELIVER/U.S. Agency for International Development, 2003.
- 29 Sterne JA, Hernan MA, Ledergerber B, et al. Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study. *Lancet* 2005;366:378–84.
- 30 Beck EJ, Mandalia S, Gaudreault M, et al. The cost-effectiveness of highly active antiretroviral therapy, Canada 1991–2001. *AIDS* 2004;18:2411–18.
- 31 Etard JF, Ndiaye I, Thierry-Mieg M, et al. Mortality and causes of death in adults receiving highly active antiretroviral therapy in Senegal: a 7-year cohort study. *AIDS* 2006;20:1181–9.
- 32 Ekwueme DU, Weniger BG, Chen RT. Model-based estimates of risks of disease transmission and economic costs of seven injection devices in sub-Saharan Africa. *Bull World Health Organ* 2002;80:859–70.
- 33 Goodman CA, Coleman PG, Mills AJ. Cost-effectiveness of malaria control in sub-Saharan Africa. *Lancet* 1999;354:378–85.
- 34 Wang B, Schreiber GB, Glynn SA, et al. Does prevalence of transfusion-transmissible viral infection reflect corresponding incidence in United States blood donors? *Transfusion* 2005;45:1089–96.
- 35 Moore A, Herrera G, Nyamongo J, et al. Estimated risk of HIV transmission by blood transfusion in Kenya. *Lancet* 2001;358:657–60.
- 36 Goldie SJ, Yazdanpanah Y, Losina E, et al. Cost-effectiveness of HIV treatment in resource-poor settings—the case of Cote d’Ivoire. *N Engl J Med* 2006;355:1141–53.
- 37 Owusu-Ofori S, Temple J, Sarkodie F, et al. Predonation screening of blood donors with rapid tests: implementation and efficacy of a novel approach to blood safety in resource-poor settings. *Transfusion* 2005;45:133–40.
- 38 Heyns Ad, Benjamin RJ, Swanevelder JPR, et al. Prevalence of HIV-1 in blood donations following implementation of a structured blood safety policy in South Africa. *JAMA* 2006;295:519–26.
- 39 African Development Bank and Organisation for Economic Co-operation and Development, Ghana, eds. *African Economic Outlook (2004/2005 edn)*. Paris: OECD Publishing, 2005.