



Table VI. Logistics regression report

Response variable: Correct prediction			
Parameter estimation section			
Variable	Regression coefficient	Standard error	Probability level
Intercept	3.323	0.510	0.000
Days (in hospital)	0.005	0.010	0.602
Blunt (1 = blunt)	0.054	0.400	0.893
Age	-0.019	0.011	0.076
Hospital (1 = JH)	-0.463	0.333	0.164
Helicopter (1 = helicopter)	-1.300	0.400	0.001

JH = Johannesburg Hospital.

highly significant variable, only the patient's age is possibly significant ($P = 0.076$). Not surprisingly, the older the patient the less likely the TRISS methodology is to predict the probability of survival or death correctly.

CONCLUSION

Helicopters clearly deserve a place in the emergency care of trauma victims. However, this is only one link in the chain that will ultimately lead to either death or survival. For it to be successful, it must link reliable, efficient emergency medical services (road-based) and effective trauma centres that are staffed appropriately with a committed team of health care professionals. If used appropriately there appears to be little doubt that these expensive machines can play an important role in preventing certain unnecessary deaths while reducing costs for both individuals and health care facilities.^{8,9}

References

- Boyd CR, Tolson MA, Copes SW. Evaluating trauma care: The TRISS method. *J Trauma* 1987; 27: 370-378.
- Baker SP, O'Neil B, Haddon W, et al. The injury severity score: A method for describing patients with multiple injuries and evaluating emergency care. *J Trauma* 1974; 14: 187-196.
- Champion HR, Copes WS, Sacco WJ, et al. A new characterization of injury severity. *J Trauma* 1990; 30: 539-546.
- Eisenberg SM, Copass KM, Hallstrom PA, et al. Treatment of out-of-hospital cardiac arrests with rapid defibrillation by emergency medical technicians. *N Engl J Med* 1980; 302: 1379-1383.
- Jacobs LM, Gabram SG, Sztajnkrzyer MD, et al. Helicopter air medical transport: ten-year outcomes for trauma patients in a New England program. *Corn Med* 1999; 63: 677-682.
- Pories SE, Camelli RL, Pilcher DB, et al. Practical evaluation of trauma deaths. *J Trauma* 1989; 29: 1607-1610.
- Champion HR, Copes WS, Sacco WJ, et al. The Major Trauma Outcome Study: Establishing national norms for trauma care. *J Trauma* 1990; 30: 1356-1365.
- Champion HR. Helicopters in emergency trauma care (Editorial). *JAMA* 1983; 249: 3074-3075.
- Moylan JA. Impact of helicopters on trauma care and clinical results. *Ann Surg* 1988; 208: 673-677.

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SPECIAL ARTICLE

EXPLORING THE COSTS OF A LIMITED PUBLIC SECTOR ANTIRETROVIRAL TREATMENT PROGRAMME IN SOUTH AFRICA

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Background. The role of antiretroviral treatment for adults in the public sector in South Africa is debated with little consideration of programme choices that could impact on the cost-effectiveness of the intervention. This study seeks to explore the impact of these programme choices at an individual level, as well as explore the total cost of a rationed national public sector antiretroviral treatment programme.

Methods. Eight scenarios were modelled of limited national treatment programmes over the next 5 years, reflecting different programme design choices. The individual cost-effectiveness of these scenarios were compared. The total costs of the most cost-effective scenario were calculated, and the potential for savings in other areas of health care utilisation was explored.

Results. The direct programme costs per life-year saved varied between scenarios from R5 923 to R11 829. All the costs of the most cost-effective scenario could potentially be offset depending on assumptions of health care access and utilisation. The total programme costs for the most cost-effective scenario in 2007 with 107 000 people on treatment are around R409 million.

Conclusion. Specific policy choices could almost double the number of people who could benefit from an investment in a limited national antiretroviral treatment programme. Such a programme is affordable within current resource constraints. The consideration of antiretroviral treatment calls for a unique public health approach to the rationing of health services in the public sector.

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**Table I. Description of modelled scenarios and sensitivity analysis scenarios**

The cost per life-year gained is presented at 5 years for the following eight intervention options:

- (A) Baseline (generic medication, baseline testing and visit costs)
- (B) Optional (higher proportion of doctor visits, and additional viral load testing)
- (C) Patent medicine pricing scenario
- (D) Second-line treatment offered to 50% of those with virological failure on first-line treatment at generic medicine prices
- (E) Second-line treatment offered to 75% with virological failure on first-line treatment at generic medicine prices
- (F) Patent medicine pricing and optional testing and consultation schedule (B & C combined)
- (G) Patent medicine pricing, optional testing and consultation schedule, and 50% of those failing first line offered second-line treatment (B, C & D combined)
- (H) Second-line treatment offered to 50% of those with virological failure on first-line treatment at generic medicine prices, with optional testing and consultation parameters (B & D combined)

In addition, sensitivity analyses are produced for the following seven changes in assumptions:

- S1. (A) with no discount over time for medicines
- S2. (A) with a 15% per annum discount over time for medicines for 3 years, followed by 7.5% annually
- S3. (A) with no additional costs for each consultation compared to current services
- S4. (A) with 2.5 times the current consultation costs for each consultation
- S5. (A) with increased mean survival on first-line treatment to 3.6 years (from 2.68)
- S6. (D) with increased mean survival on first line to 3.6 years and 7.41 years for consecutive regimens
- S7. (A) with no provision for visits to the new services for people who are not on ARVs, and
- S8. (D) with no discount over time for medicines

Whereas the role for antiretroviral therapy (ART) for HIV has been an issue for scientific and public debate in South Africa, a number of middle-income and poor countries have already initiated treatment programmes in spite of resource constraints (Brazil, Chile, Thailand, Nigeria, Senegal, Cote D'Ivoire). The recent publication by the World Health Organisation¹ of guidelines for the scaling up of antiretroviral treatment programmes is indicative of both a convergence of clinical thinking and the increasing pressure on health care systems to provide antiretroviral interventions.

In addition to the survival and quality of life benefits for individual patients,^{2,3} many authors have pointed to the synergies between antiretroviral treatment programmes and preventive strategies.^{4,7} Others have compellingly described the role extended HIV survival could have in reducing the burden on society and preserving our human and social infrastructure.^{4,8}

The following model costs a rationed national antiretroviral treatment programme for adult South Africans that could conceivably begin in 2002. From the perspective of the public health system, we explore the relative cost-effectiveness of a number of ART-related policy options and the overall resource implications of a limited national antiretroviral treatment programme.

METHODS

Service model

The approach to costing ART provision is based on an

emerging service model in which:

- Specific HIV/AIDS services are required to develop the relationships between patients and clinicians, to ensure continuity of care, and to provide a mechanism through which patients can be evaluated for potential enrollment onto an ART programme.
- Consequent on meeting predetermined eligibility criteria, which are a combination of clinical and (possibly) social assessment,⁹ patients are considered eligible for ART around the time that they become AIDS symptomatic.
- After commencing treatment, patients are managed through the HIV/AIDS service, but still attend regular services for other routine and acute care.

Numbers on treatment

A spreadsheet model with eight scenarios (Table I) was used to anticipate the numbers of people on antiretroviral treatment over the next 10 years. In the model, the number of new patients receiving treatment was gradually increased over 5 years. The cumulative number of people surviving on treatment in the model by the middle of 2007 varied between scenarios from 106 911 to 117 621, depending on survival assumptions and whether or not second-line treatment was offered to a proportion of those failing the first-line regimen (Fig. 1).

Those on treatment were stratified into a number of subgroups, reflecting those on a first-line regimen, those on a second-line regimen, and those failing treatment. The first 6 months of a new regimen were distinguished from the remaining time on the regimen. The model was run for a

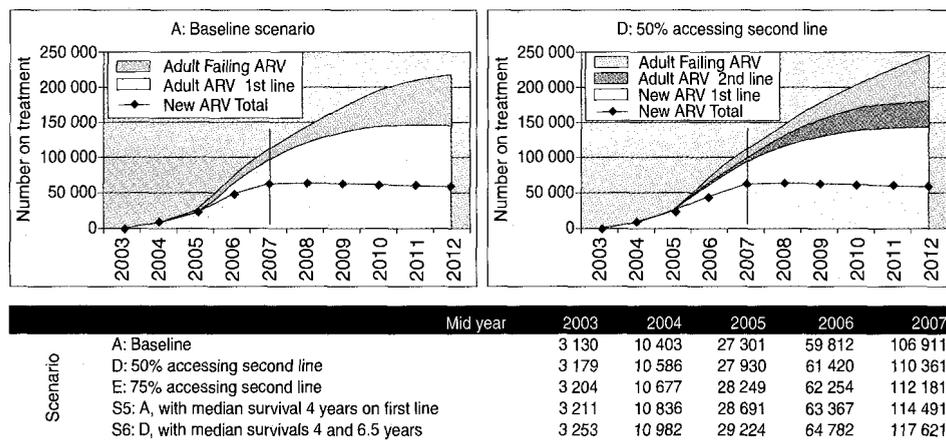


Fig. 1. Numbers on treatment by category of treatment in modelled scenarios.

further 5 years with constant assumptions in order to explore the medium-term impact of deferring costs. By 2007 the numbers of people accessing treatment in the model could represent 10% of those becoming AIDS-symptomatic that year (compared with estimates of adult deaths in the subsequent 2 years¹⁰). The combined impact on new infections of extended survival, reduced viral load and altered behaviour for those on treatment was assumed to be neutral compared with a no-treatment scenario. Additional or averted new infections are likely to have little impact on the total direct treatment costs in the timeframe of this analysis.

Direct programme costs

Medicines

The biggest cost-driver of ART is undoubtedly the medicine costs. In this model, the limited number of medicines selected is sufficient for a single regimen or for two independent regimens, while still sufficiently restricted to limit costs in both the generic and patent pricing scenarios. It is assumed that all rationally selected starting regimens have equivalent treatment outcomes.¹¹

The estimated proportion of patients likely to switch from any single medicine due to intolerance is based on the experience to date in Khayelitsha¹² validated by HIV clinicians. In cases of single-medicine changes, the first 6 months of treatment are apportioned to the starting medicine, while the remaining time on the regimen is apportioned to the medicine to which the patient changes. In effect virological failure and intolerance are modelled separately, with the crude assumption that 6 months is the average time at which a medicine is changed for reasons of intolerance. It was necessary to include intolerance-driven individual medicine switches within first- and second-line regimens as they impact significantly on overall medicine costs in the baseline scenario (where generic pricing is utilised). Where a combination tablet could

substitute for individual medicines, the price of the combination tablet was included.

Future price changes are another important variable in anticipating medicine costs. The model presented assumes an annual price reduction in real terms of 10% per year for the first 3 years and 5% annually thereafter. Sensitivity analysis explores the impact of no reduction in price and a 15% initial reduction (for the first 3 years) followed by 7.5% per annum.

Laboratory monitoring

Based on the WHO

recommendations,¹ the model incorporates two testing scenarios. The first provides for all tests (including a twice-yearly CD4 count and a CD4 count before enrolment) except for viral load testing. The second is an optional scenario in which viral load tests and CD4 counts are conducted three times a year.¹³

Visit costs for the antiretroviral treatment programme

Allowing that consultation costs (including additional staff training) may be higher than for standard primary care consultations, a factor of 1.5 is applied to the average cost of a primary care consultation in the Western Cape metropole (where there are doctor- and nurse-driven services). This factor is varied between 1 and 2.5 in the sensitivity analysis.

The visit schedule applied is that used in the current Medicin Sans Frontieres treatment protocol⁹ to estimate the additional visits required as a result of ART. Again two scenarios are built; one in which a proportion of the visits are at a lower cost structure as the visit is principally to ensure adherence and dispense medicines, and another where the majority of the visits are with a doctor.

Provision is also made for visits to HIV/AIDS services by a proportion of HIV-infected people in WHO clinical stage 3. This proportion is set equal to the proportion of patients accessing treatment when becoming AIDS-symptomatic. The model assumes an average of 3 visits per year for those not on antiretrovirals but attending the HIV/AIDS services as a prelude to possible enrolment in an ART programme. These visits are costed at the existing clinic consultation costs, and form a substantial component of the workload.

Anticipating the individual benefits of treatment

The survival benefits of ART are not yet fully described. Published data at 3 years since the initiation of therapy, however, suggest a remarkable reduction in the anticipated



mortality.²³ UNAIDS currently recommend that a survival benefit of 5 - 7 years be used for HIV modelling in rich countries.¹⁴ Early indications suggest that a rationed programme in South Africa is likely to have comparable benefits to rich countries, taking into account baseline immunological characteristics at the onset of treatment.^{15,16} The model below uses a median survival from initiating treatment of 4.5 years if two regimens are offered (weibull distribution, mean of 6.06 years of which the benefit is 4.46 years). The model assumes that treatment is failing for a period at the end of treatment of equivalent duration to WHO stage 4. It is further assumed that, of the survival benefit, 60% is derived from the first regimen, and the remainder from an alternative regimen. For the scenarios in which second-line treatment is included, it is assumed that not everyone in whom a first regimen fails will be offered a second regimen, either because they have exhausted their affordable treatment options through intolerance-driven individual medicine changes, or because they do not meet

additional eligibility criteria for second-line treatment.

The life-years gained derive directly from the survival benefit assumptions, and are calculated as life-years gained per year on treatment while treatment is not failing (Fig. 2).

Benefits on broader health care utilisation

Although antiretroviral treatment does not prevent the eventual morbidity and associated health care utilisation that occurs in the terminal stages of HIV infection, this utilisation is deferred by the duration of the survival benefit. Within the realistic timeframes of any planning exercise of this nature, this deferral could result in a real benefit to the health care system. The key contributors to the cost saving are the principal cost drivers of hospital inpatient days, ambulatory consultations and tuberculosis treatment. No discounting was applied to deferred costs.

The estimates used (Table II) are similar to those used in other HIV costing studies.^{17,18}

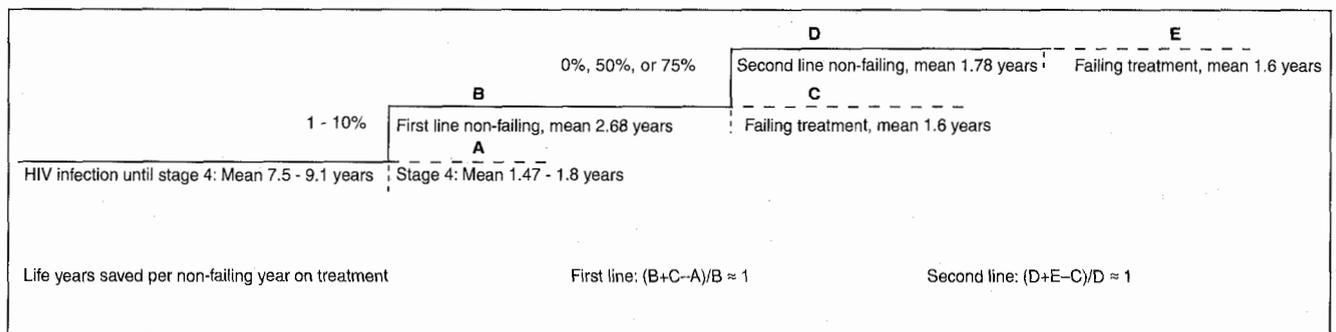


Fig. 2. Survival and effectiveness assumptions.

Table II. Cost and utilisation assumptions

	Units	Utilisation				Cost		
		Stage 4	ARV FL	ARV SL	Failing	Units	Min.	Max.
Non-ARV HIV-related clinical costs								
Hospitalisation (1)	Inpatient days	18.8	2.8	3.8	18.8	Inpatient day	R530	R530
Clinic consultations (2)	Extra consults	11	2	2	11	Visit cost	R73	R73
Tuberculosis (3)	Annual risk	36%	4%	4%	36%	Treatment cost	R1 560	R1 560
ARV-related costs								
ARV medicine costs (4)	ARV utilisation		100%	100%	50%	Annual cost	R4 612	R15 288
ARV laboratory costs (5)	Extra tests		Yes	Yes	No	Annual cost	R457	R2 206
ARV visit costs (6)	Visits		12	12	3	Annual cost	R821	R986

(1 & 2) Utilisation assumptions the same as used in the study by Abt and associates,¹⁷ with a reduction in length of stay from 10 days to 8 days for stage 4 based on more recent inpatient studies. Clinic visits are calculated at the current price per consultation in primary health care services in Cape Town, and reflect excess visits as a result of HIV. Utilisation while on ARVs is premised on an 80% reduction in hospitalisation and clinic visits compared with stage 4.
 (3) Taken from cohort data in Cape Town,²³ with additional assumption of relative risk of tuberculosis between stages 4 and 3 of 2, and relative prevalence between stages 3 and 4 of 2. Cost per completed treatment from Western Cape Department of Health, reflecting only a proportion (60%) of the DOTs-related costs so as not to double-count the tuberculosis-related PHC, medicine and hospitalisation costs.
 (4) Starting regimen in generic scenarios is Triomune (D4T, 3TC, NVP, \$295/year), with 57% still on Triomune by 6 months due to intolerance-driven individual medicine switches. Second-line regimen for generic scenarios is AZT, DDI and INV/RTV. The same regimen is the cheapest patented regimen as well (used here as individual drugs) unless DDI and D4T are combined. Medicine costs calculated for on average half of the time after treatment has started failing. It is hoped that LPV/RTV could replace INV/RTV with little impact on costs if preferential pricing is obtained.
 (5) Range of tests depending on individual medicines include FBC, diff., creatinine, ALT, cholesterol, glucose and amylase. Twice-yearly CD4 counts (R83 per test) are included additionally in pragmatic scenarios. Thrice-yearly viral loads (R550 per test) and CD4 counts are included only in the 'optional' scenarios.
 (6) 80% of visits in the 'optional' scenarios, and 60% in the remaining scenarios, are with a doctor. The non-doctor visits are with a nurse and/or counsellor, and are principally to support adherence and dispense medicines. Doctor visits are calculated at the current price per consultation in primary health care services in Cape Town, with an additional cost of 50% varied to an additional 150% in sensitivity analysis. Non-doctor visits are costed at 75% of the reference costs.



RESULTS

Direct treatment costs

The direct costs of treatment for the baseline (A and D) scenarios were stratified by regimen and by the first 6 months on each regimen (Fig. 3). The first 6 months of treatment are disproportionately expensive compared with the subsequent annual costs, especially with respect to laboratory and consultation costs. The differential between first-line and second-line medicine prices when accessing generic medicines is clearly evident. The costs per treatment year (after the first 6 months) vary between scenarios and regimens from R5 890 (A: first-line) to R15 288 (G: second-line). Medicine costs dominate expenditure across all scenarios and regimens.

Cost per life-year gained

The use of generic versus patented medicines is the single most important factor impacting on the costs per life-year gained at 5 years (Table III). The cost per life-year gained is 48 - 53% greater when patented medicine prices are utilised. Additional

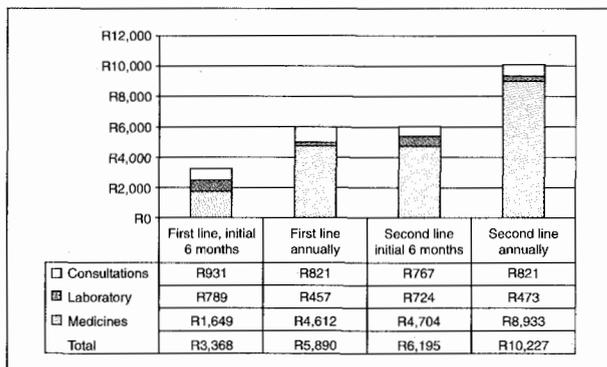
testing and switching most of the consultations to doctors increased costs by a further 45%. Combining patented medicines with optional laboratory monitoring and consultation schedules yielded a 99% increase in the cost per life-year saved (F).

In those scenarios where second-line treatment is included at generic prices (D and E), the marginal cost per life-year saved when adding this treatment is 36 - 39% higher than the baseline cost (A: first-line only).

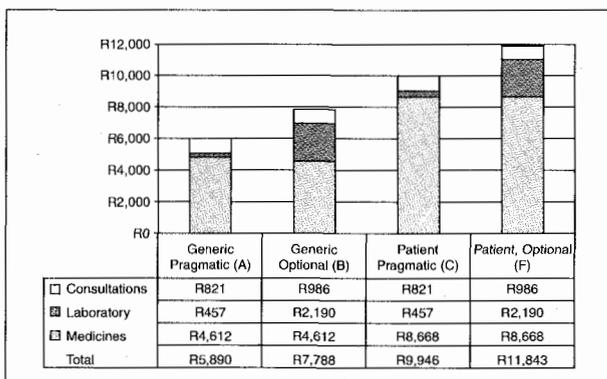
Sensitivity analysis reinforced the pivotal role of assumed changes in future medicine pricing (S1 and S2: 23% increase in the baseline cost per life-year saved over 5 years if no price reductions). It also demonstrated the relatively small impact of changing assumptions on the services required before enrolment (S7), the cost-structure for consultations (S3 and S4), or the duration of the survival benefit on treatment (S5 and S6).

Total costs and potential resource savings as a result of deferred treatment

In the most cost-effective scenario, the total direct costs of a programme of this size are estimated to be R409 million in the year 2006 - 2007. Taking into account the deferred hospitalisation and consultation costs for those on ART, there is a considerable impact on resource utilisation. When quantified financially over 5 years, this covers the cost of antiretroviral treatment (135% of direct programme costs averted). At 10 years some of the deferred costs have re-entered the system, reflected by a reduction in cumulative savings as a percentage of the direct intervention costs over this period (90% of intervention costs).



Changing costs for baseline (A) scenario based on regimen and duration on regimen, 2002 prices



Differential costs between scenarios, for the first-line regimen following the initial 6 months of treatment, 2002 prices

Fig. 3. Direct costs at an individual level for antiretroviral interventions.

DISCUSSION

This exercise illustrates how policy choices impact on the benefits of a rationed ART programme and how those benefits are distributed. It is immediately apparent that accessing cheaper medicines could significantly extend the impact of such an intervention. We used generic pricing in our baseline scenario based on the sincere belief that it is a realistic policy option which has been successfully applied in a number of countries (generics of zidovudine and lamivudine have recently been registered by the Medicines Control Council, although they are still inaccessible due to patent restrictions). It is sometimes argued that medicine costs are over-emphasised. This analysis supports a strong emphasis on medicine costs.

While the cost of monitoring patients on ART has fallen over the past year, some investigations (viral load testing in this analysis) remain prohibitively expensive for the benefit they add, and should not necessarily be an automatic component of a public sector programme until their costs are reduced.

The marginal cost per life-year saved when adding second-line treatment to the baseline scenario was considerably higher



Table III. Cost-effectiveness and sensitivity analyses

	Cost/life-year	% change from baseline	Marginal cost/life-year	% change from first line
A: Baseline	R5 923			
B: Optional	R8 595	45		
C: Patent pricing	R9 089	53		
D: 50% second-line access	R6 082	3	R8 215	39 (1)
E: 75% second-line access	R6 136	4	R8 042	36 (2)
F: B & C combined	R11 761	99		
G: B, C & D combined	R11 829	100	R12 736	8 (3)
H: B & D combined	R8 775	48	R11 202	23 (4)
Sensitivity analysis				
S1: A with no medicine discount	R7 266	23		
S2: A with medicine discounts 50% higher	R5 388	-9		
S3: A with no additional cost for consultations	R5 571	-6		
S4: A with visit cost factor 2.5	R6 627	12		
S5: A with first-line survival 4 years	R5 675	-4		
S6: D with combined survival of 6.5 years	R5 797	-2	R8 184	44 (5)
S7: A with no non-ARV visit costs	R5 398	-9		
S8: D with no medicine discounts	R7 528	27	R11 048	52 (6)

(1 & 2) compared to A, (3) compared to E, (4) compared to B, (5) compared to S5, (6) compared to S1.

(39%) than the cost without this option. This increase is partially masked by the reductions in medicine prices over time, as those accessing second-line treatment are doing so a few years into the programme. One sensitivity analysis (S8) demonstrates that the marginal increase could be as high as 52% without the effect of the medicine price reductions. Although clinicians balk at limiting ART to a single tier of therapy, the option of spreading a smaller benefit to a greater number of patients needs serious consideration, bearing in mind the additional health system implications of enrolling additional new patients. We are not necessarily advocating that only one tier of therapy be considered. A gradual implementation of ART would have relatively few people on second-line treatment by 5 years, with the total programme costs not being considerably more expensive than the baseline programme cost presented. It is also likely that the differential cost between first- and second-line treatment will reduce over time as a greater number of antiretrovirals are produced by generic manufacturers. If the price differential remains large and financial resource constraints are considered the limiting factor to more widespread treatment, and if maximal diffusion of treatment is a policy goal, then an examination of the marginal costs of second-line treatment will remain important.

Even without offsets, the total costs of a programme of this size are a small fraction of anticipated health sector expenditure on HIV/AIDS. Although many may find the size of this programme unpalatably small, a programme that is approaching 100 000 people on treatment within 5 years would be a significant achievement.

This study has a number of limitations. Importantly, in the absence of an existing policy to provide antiretrovirals as treatment for adults in the public sector, it was necessary to piece together assumptions from many different sources. Some assumptions should be treated with great caution, in particular those anticipating health service utilisation in the absence of antiretroviral treatment.

Although estimates of health care utilisation that derive from cohort studies may not apply to the whole population due to unequal access, it is likely that those who do access the ART programme would have been able to access clinical services had they not received the intervention. Given the huge excess demand for services, it is unlikely that averted utilisation will result in financial savings in any but the least-affected provinces, resulting instead in better quality of care for those who would otherwise be unable to access services. The re-entry into the system of deferred utilisation only partially erodes these gains even at 10 years, and should not deter health planners from comprehensively responding to the immediate crisis.

It has been demonstrated that with the correct policy choices, the cost of providing an ART intervention could be considerably cheaper per year of treatment than has been quoted by many of the studies that have deemed ART to be unaffordable.^{17,19,20} It has been further demonstrated that the averted costs could result in savings that make the intervention cost-saving, or at least significantly more cost-effective than an examination of the direct costs yields. This is only from the perspective of the health sector without consideration of



possible synergistic prevention gains. Even with the averted costs factored in, when the modelled intervention is scaled up to cover much greater percentages of those in need, it demands extraordinary expenditures. How can a cost-saving intervention be unaffordable?

The public health system is implicitly rationing services through reduced access to care, and the extent of this is likely to increase. A modelled ART programme that assumes more extensive access than is implicitly provided for non-ART services at present, will appear unaffordable even if it is cost-saving at an individual level.

CONCLUSIONS

There are very clear policy choices, political and clinical, which for the same expenditure could double the number of people benefitting from a rationed ART programme. A programme that utilises generic medicines, is pragmatic with respect to laboratory monitoring and consultations, and maximises the diffusion of benefits, is the most cost-effective, and is considerably cheaper than many previous estimates suggest.

Whereas we should strive to provide treatment to as many of those in need as possible through the future mobilisation of additional resources and campaigning for price reductions in medicines and laboratory tests, a rationed treatment programme is currently affordable within existing resource constraints, and would have enormous benefits. We should not make our provision of this intervention consequent on raising additional resources, and the decision to proceed could in fact aid our attempts to mobilise external financial resources. The public good resulting from the broader impact on prevention and morale, which is arguably one of the major benefits of introducing a rationed programme now, could be substantially realised with relatively small numbers on treatment.

The present and anticipated HIV burden on the public health care system is such that rationing is inevitable, with the prospect of planning for a new intervention such as ART requiring us to be explicit about our inability to meet demand. This paper serves to highlight the need for a revised public health discourse around rationing to deal with the unique challenges faced in providing antiretroviral interventions where they are most needed.

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References

1. World Health Organisation. *Scaling Up Antiretroviral Therapy in Resource Limited Settings: Guidelines for a Public Health Approach*. Geneva: WHO, 2002.
2. Egger M, May M, Chene G, et al. Prognosis of HIV-1-infected patients starting highly active

- antiretroviral therapy: a collaborative analysis of prospective studies. *Lancet* 2002; **360**: 119-129.
3. Hogg RS, Yip B, Chan KJ, et al. Rates of disease progression by baseline CD4 cell count and viral load after initiating triple-drug therapy. *JAMA* 2001; **286**: 2568-2577.
4. Berkman A. Confronting global AIDS: prevention and treatment. *Am J Public Health* 2001; **91**: 1348-1349.
5. Farmer P, Leandre F, Mukherjee JS, et al. Community-based approaches to HIV treatment in resource-poor settings. *Lancet* 2001; **358**: 404-409.
6. Moatti JP, N'Doye I, Hammer SM, Hale P, Kazatchkine MD. Antiretroviral treatment for HIV-infected adults and children in developing countries: some evidence in favour of expanded diffusion. *State of the Art: AIDS and Economics* 2002; July, 96-116.
7. Kenyon C, Heywood M, Conway S. Mainstreaming HIV/AIDS: Progress and challenges. In: Ntuli A, ed. *South African Health Review* 2001: 161-183.
8. Bradshaw D, Johnson L, Schneider H, Bourne D, Dorrington R. *Orphans of the HIV/AIDS Epidemic: The Time to Act is Now*. Tygerberg: Medical Research Council, 2002.
9. Medicin Sans Frontieres. *Affordable Antiretrovirals in South Africa: Protocol*. Cape Town: MSF, 2001.
10. ASSA2000lite Aids and Demographic Model of the Actuarial Society of South Africa, <http://www.assa.org.za> (Downloaded on 13 Sept 2001).
11. Bartlett JA, DeMasi R, Quinn J, Moxham C, Rousseau F. Overview of the effectiveness of triple combination therapy in antiretroviral-naive HIV-1 infected adults. *AIDS* 2001; **15**: 1369-1377.
12. Reuter H, Kasper T, Poole C, Skefile V, Goemaere E. Frequency, type, severity, and duration of adverse drug events on highly-active antiretroviral therapy (HAART) in a resource-poor setting. 14th International AIDS Conference, 2002.
13. Southern African HIV Clinicians Society. Clinical Guidelines: Antiretroviral Therapy in Adults. June 2002 version. *Southern African Journal of HIV Medicine* 2002; July, 22-29.
14. 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.
15. Medicin Sans Frontieres. *Providing Antiretroviral Therapy at Primary Care Clinics in Resource Poor Settings*. Cape Town: MSF, 2002.
16. Orrell C, Bekker LG, Wood R. Adherence to antiretroviral therapy — achievable in the South African context? *S Afr Med J* 2001; **91**: 483-484.
17. Abt Associates. HIV facts, figures and the future. In: Ntuli A, ed. *South African Health Review*, Durban: Health Systems Trust, 2000.
18. Karstaedt AS, Lee TCM, Kinghorn AW, Schneider H. Care of HIV-infected adults at Baragwanath Hospital, Soweto: Part II. Management and costs of inpatients. *S Afr Med J* 1996; **86**: 1490-1493.
19. Zwi K, Soderlund N, Schneider H. Cheaper antiretrovirals to treat AIDS in South Africa. They are at their most cost effective in preventing mother to child transmission. *BMJ* 2000; **320**: 1551-1552.
20. Wood E, Braitsstein P, Montaner JS, et al. Extent to which low-level use of antiretroviral treatment could curb the AIDS epidemic in sub-Saharan Africa. *Lancet* 2000; **355**: 2095-2100.
21. Badri M, Wilson D, Wood R. Effect of highly active antiretroviral therapy on incidence of tuberculosis in South Africa: a cohort study. *Lancet* 2002; **359**: 2059-2064.

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