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Using a Happiness Index to Measure the Benefits for a Cost Benefit Analysis of Antiretrovirals for Older Adults with HIV in New York City

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- Depression

Abstract

Background: Anti-retroviral (ARV) medications have greatly increased the life expectancies of those who are HIV positive. As life expectancy increases, so does the age of those on the medications. This has come at the cost of billions of dollars. It is important to carry a Cost-Benefit Analysis (CBA) to evaluate ARVs for older adults living with HIV who are often depressed to see whether the medications have been worthwhile in the past and are likely to be so in the future.

Methods: A new methodology based on a happiness index was created to value benefits of older adults with and without depression in New York City. The benefits are given as the product of the number of QALYs (Quality Adjusted Life Years) times the price of a QALY. The QALY price is determined by estimating the trade-off between health satisfaction and income in a regression equation with overall life satisfaction as the dependent variable. Cost and the number of life years gained from the medications are taken from the literature.

Results: Net-benefits and benefit-cost ratios were presented separately for those depressed and non-depressed and by era of medication. For the depressed group, the ARVs generated large positive net-benefits in all eras with Benefit-Cost ratios in the range 1.4 to 1.9. For the non-depressed groups, the net-benefits were positive only in the two periods prior to 2000.

Conclusion: In the past ARVs have been found to be socially worthwhile. But pharmaceutical companies face challenges in order for ARVs to continue being worthwhile. There are diminishing returns associated with the benefits of ARVs and costs have increased greatly. Benefits are obtained in the future and have to be discounted. Costs are immediate and have to be incurred throughout a person's lifetime. Cost containment should be a priority.

ABBREVIATIONS

HIV: Human Immunodeficiency Virus; AIDS: Acquired Immune Deficiency Syndrome; ARV: Anti-Retroviral Medication; CBA: Cost-Benefit Analysis; CEA: Cost-Effectiveness Analysis; QALY: Quality Adjusted Life Year; VSL: Value of a Statistical Life; WTP: Willingness to Pay; ROAH: Research of Older Adults with HIV; ACRIA: AIDS Community Research Initiative of America.

OVERVIEW

There are over 1.1 million persons in the United States living with HIV/AIDS [1]. The primary reason why these people are living and not dying is due to the use of anti-retroviral medications (ARVs). Extending people's lives is a powerful goal, but ARVs may not be the best intervention. There are harmful, often unknown, side effects of the drugs and the medications are very expensive. The desirability of financing ARVs should be established and only a cost-benefit analysis, CBA, can be used to achieve this objective. Surprisingly, very few CBAs of ARVs exist and certainly there are no CBAs that focus on older adults with HIV. The issue of the older adult with HIV is significant since it is the success of ARV treatment that allows people with HIV/AIDS to age. The "graying" of the HIV population needs to be recognized and economic evaluations carried out with this group in mind [2].

A CBA differs from a cost-effectiveness analysis, CEA, because it relies on a monetary valuation for outputs (to form the benefits) as well as monetarizing the inputs. A CEA accepts monetary valuations only on the input side (to form the costs). Instead of working with benefits, a CEA uses a physical output measure, typically a Quality Adjust Life year QALY, and seeks to find interventions that produce a QALY at lowest cost. Unfortunately, an intervention that is cost-effective need not be socially worthwhile, and programs that are not cost-effective could still be justified. That is, an intervention A may be more cost-effective than some alternative B, but this does not necessarily mean that A is socially worthwhile; and conversely, intervention C might be less cost-effective than some other intervention D, yet both C and D might be both socially worthwhile in that they both yield benefits greater than costs [3]. Only a CBA can determine what is socially worthwhile as this requires that benefits be greater than costs [4].

A major reason why very few CBAs of health care interventions exist is due to a perceived weakness that the methodology attempts to value a human life. However the QALY approach used in CEA also tries to value a human life, even though it is quantified in utility and not monetary terms. The missing element from CEA is the "pricing" of the QALYs which enables them to become benefits. Once a price has been established, and benefits estimated, a CBA can be undertaken and priorities for HIV/AIDS can be determined [5]. The main contribution of this paper is the presentation of a novel way of estimating a price of a QALY in the context in which the QALYs were initially derived. To illustrate the method, an application to ARVs of older adults in NYC is presented. With the benefits constructed, and separate estimates of the costs provided, we then carry out a CBA of ARVs for older adults living with HIV/AIDS that fully incorporates all the side effects of the medications.

The rest of the paper is structured as follows. We start with the literature review and outline the methods and identify the main ingredients for the CBA. Then the ingredients are assembled and we present the main result. After the sensitivity analysis, we close with the summary and conclusions.

LITERATURE BACKGROUND

A number of methods already exist for putting a price on a QALY and each of these has their advantages and disadvantages. The human capital approach, which valued benefits in terms of the present value of lifetime earnings, obtained a value of $25,961 per QALY [6]. Income is easy to estimate, but income can rise even though there is a national disaster. The value of a statistical life (VSL) approach produced a value of $87,489 per QALY [7]. Unlike the human capital approach, the VSL method uses individual preferences, in this case, related to the risk of losing one's life. However, the VSL method assumes that years of life have the same value irrespective of when they occur [8]. More generally, the fewer remaining years one has, as with the elderly, the higher will be the value of a QALY. A QALY was valued at half as much with the life expectancy adjustment (since, up till now, there are a greater number of younger than older persons in the population). Using the Willingness to Pay (WTP) approach, a price per QALY equal to $10,352 was derived [9]. WTP is considered best practice outside the health care field, but it is questioned by many undertaking health care evaluations. Lastly, using the revealed preferences of public decision-makers (related to African country grants made by the Global Fund for AIDS, TB and Malaria), estimates very close to the WTP values were obtained (the price of a Disability Adjusted Life Year, an inverse QALY, was $10,900 for the three disease burdens) [3]. Revealed preferences are more reliable than stated preferences that were used for the WTP estimates. But, using individual valuations is fundamental for CBA based on applied welfare economics. So preferences of public decision-makers should only be used if individual preferences are absent for any reason or are considered unreliable (e.g., the persons are addicts).

In none of the methods just reviewed for placing a price on a QALY is utility directly measured by data. For example, a person was assumed to say yes or no to a particular WTP figure according to whether the choice presented would increase the person's utility [9]. In this way, the discrete choice would be revealing a proxy measure for utility. In the new method that is presented in this paper, utility is going to be measured directly by using a happiness index. The price of a QALY will then be derived by the trade-off of a QALY against income which is being used as the monetary numeraire. In existing work, the method was based on the trade-off on out-of –pocket expenses rather than income for the monetary numeraire [9]. As we shall see, the QALY price that we derive of $59,758 will be within the range found by those using other methodologies.

A long literature exists that establishes that a *unique* price for a QALY may not be feasible, see for example [10], [11] and [12]. That conclusion is not unexpected given that the benefits of any health care intervention cannot be assumed constant irrespective of what is contributing to the QALY and whether those affected are young or old, rich or poor, male or female, etc. Thus the QALY price reported here is specific to the preferences of older adults living in New York City who are taking ARV mediations. The data source used was based on a research survey of 914 persons called the Research of Older Adults with HIV (ROAH) carried out by the AIDS Community Research Initiative of America (ACRIA). However, the method used to determine the QALY price is a general one that can be used for the evaluation of many types of health care interventions. This paper is a companion study which focused on estimating the utility of a life-year derived from ARVs [13].

METHODS

The cost-benefit framework that we will be using can be set out as follows. Define the net-benefits N as the difference between benefits B and costs C:

$$N = B - C \quad (1)$$

As both benefits and costs are measured in monetary terms ($US dollars in our case), N will also be expressed in monetary units. The most general outcome unit used in the health evaluation literature, which combines mortality and morbidity, is a Quality-Adjusted Life Year QALY. We will construct our benefit measure by taking this physical outcome measure and converting it into monetary terms by applying a price per QALY, i.e., $P_{QALY.}$ So we will be working with:

$$B = [P_{QALY}][QALY] \quad (2)$$

Since QALYs can be decomposed into the product of the number of life years LY and the quality, or utility, of each life year U_{LY}, the full specification of the benefits becomes:

$$B = [P_{QALY}][LY][U_{LY}] \quad (3)$$

Which means that the net-benefits expression given by (1) can be replaced by:

$$N = [P_{QALY}][LY][U_{LY}] - C \quad (4)$$

From the cost-benefit criterion that appears in (4) we can see that there are four components that make-up the net-benefits, namely, $P_{QALY,}$ LY, U_{LY} and C. In the rest of this section we explain how the four ingredients were estimated for the evaluation of HIV medications for the ROAH population. In the next section we assemble the four components to obtain the CBA outcome.

The Price of a QALY

We use a new direct utility methodology to determine P_{QALY}. The ROAH questionnaire asked people to rate their overall life satisfaction on a scale of 1 to 10, where 1 is completely dissatisfied and 10 is completely satisfied. This metric is very similar to the Cantril "ladder of life" scale that is used extensively by the happiness literature in Economics [14]. Often 1 is the worst possible level of satisfaction and 10 is the best possible [15]. Our overall satisfaction rating was a function of the many ingredients that go into the life experiences of an individual. One such ingredient was people's income, measured in monetary units, and another was their health quality of life as captured by units of their utility of a life year U_{LY}, which goes into forming a QALY. By quantifying by how much both income and the health quality of life impact overall life satisfaction one can see the relative importance of the two ingredients and thus see the trade-off of health quality units in terms of income units. Thus in this way the choice of a particular outcome for the life satisfaction rating scale "reveals" the preferences of an individual for health quality and income and thereby determines the price of a QALY. The details of the methodology will now be presented.

Overall life satisfaction S for individuals can be thought to be a function of the utility of a unit of a life year Q (i.e., the utility of one LY with $U_{LY} = 1$), the income that they have Y, and a list (vector) of other determinants Z:

$$S = S(Q, Y, Z) \quad (5)$$

For estimation, we take a linear approximation of (5) and use:

$$S = \alpha_Q Q + \alpha_Y Y + \alpha_K K \quad (6)$$

Note that in this formulation the alphas are fixed coefficients and we have suppressed the constant term and the random error. The role of the K variables in equation (6) is to act as controls to ensure that other factors are held constant and do not impact the coefficients α_Q and α_Y. The alphas show the effect on the dependent variable of a unit change in the independent variables. Hence we have:

$$\alpha_Q = \Delta S/\Delta Q; \text{ and } \alpha_Y = \Delta S/\Delta Y \quad (7)$$

Since pricing a QALY means that we are taking changes in units of health quality and converting them into monetary terms, we are seeking $\Delta Y/\Delta Q$. Using the definitions in equation (7) we obtain:

$$\Delta Y/\Delta Q = (\Delta S/\Delta Q)/(\Delta S/\Delta Y) = \alpha_Q/\alpha_Y \quad (8)$$

Thus the price of a QALY is given as the ratio of the first two coefficients that are estimated in equation (6).

Our estimation of the price of a QALY is based on equation (6). This is a single equation and so we will be using a single equation method, OLS, for estimation. We are carrying out a descriptive exercise, i.e., estimating the utility function which is always represented in economic theory by a single equation and not a system. We are therefore not estimating a causal model. This is important to understand as in the happiness literature causation is often an issue [15]. For example, income may make someone happier, but it also may be the case that happier people tend to obtain higher income. We will be using data on Q and Y from a cross-section. Q and Y will not actually be moving in our data set. For our estimate of the price of a QALY we undertaking a thought experiment whereby *if* Q and Y were to change by one unit each, what would be the trade-off between them.

The *happiness* literature also uses life-satisfaction as the dependent variable to obtain a trade-off between income and some other variable that it wants to evaluate in monetary terms. Using this approach in order to compensate a person for becoming a widow, $100,000 per year is required [16]. To compensate for unemployment requires $60,000 per annum and for being black $30,000. Note that in this literature instead of our Q in equation (6) they include the variable to be valued directly in the regression equation. So to value widowhood, for example, widowhood is included in the regression with income. The problem with this formulation is that, although a valuation is obtained, one does not know how widowhood is affecting overall satisfaction. In our method based on equation (6), ARVs are not directly included in the regression. What is included is the result of the ARVs on health quality of life H and, from the impact of ARVs on this variable, the final effect on S is determined. We pick up the transmission mechanism of ARVs on overall life satisfaction in terms of how the side-effects of the medications affect the health quality of life. As we shall see, based on the findings in the companion study in [13], a positive side effect of the ARVs was found in terms of reducing the symptoms of depression. Valuations of ARVS will therefore be higher for those who initially were depressed before they took the medications.

The exact specifications for all the variables in equation (6) and a data summary for them are given in table 1. Two variables, income Y and Quality of Life Q, had to be included as the ratio of their estimated coefficients determines the price of a QALY.

However, there was some discretion as to what to include for the controls, the Z variables. Seven controls were used and listed in table 1: depression, isolation, loneliness, religion, US citizenship, provider location and the use of complementary medications. The selection of the Z variables was largely determined by tests of statistical significance that were applied to variables that were found to be important in previous studies that used the ROAH data (in particular, [13,19-21]).

The only key variable for which the data needs further explanation is for income. Instead of using a continuous

Table 1: Definitions of the Variables and Data Description [Final sample: n = 914].

Variables	Definition	Mean	Min	Max
Dependent Variable				
S: Life satisfaction	Question: All things considered, how satisfied are you with your life? Scale from 0 (completely dissatisfied) to 10 (completely satisfied).	7.25	1	10
Price of a QALY Variables				
Q: Quality of Life	Subset of the scales from the modified MOS Short-Form.* Higher scores have higher quality of life.	0.6564	.1522	1.0000
Y: Income	Question: How well are you able to manage on your income each month? Four categories (2006$).** 1. I do not have enough. 2. I just manage to get by. 3. I have enough money with extra. 4. Money is not a problem for me.	11,280 15,966 38,631 97,178	11,280 15,966 38,631 97,178	11,280 15,966 38,631 97,178
Z_1: *Depression*	CES-D scale.† Higher scores indicate more depressive symptoms and more severe symptoms.	20.00	0	52
Z_2: *Religion*	Question: Do you regularly attend or participate in religious services. 1. Yes. 0. No.	0.468	0	1
Z_3: *Isolation*	Was the person "friend-centered".‡ 1. Yes. 0. No.	0.346	0	1
Z_4: *Complementary Treatments*	Question: Are you using alternative, complementary, holistic, or New Age treatments such as massage, herbs, etc.? 1. Yes 2. No.	0.288	0	1
Control Variables (Continued)				
Z_5: *Loneliness*	UCLA Loneliness scale version3.§ Higher scores indicate more loneliness.	43.884	21	73
Z_6: *Treatment Provider*	Question: Where do you go for treatment for HIV? 1. Private doctor. 0. Public clinic or hospital, VA hospital, day program/ treatment facility (ASO), Ryan White funded clinic, other.	0.219	0	1
Z_7: US Born	Question: Were you born in the US? 1. Yes 2. No.	0.832	0	1

* The quality of life instrument was the average of scores from five scales taken from the ten scales given in the modified Medical Outcomes Study (MOS) [17]. The five scales were related to physical function, cognitive function, social function, pain and energy/fatigue – each scale on a range of 0 to 100. Our measure is the average of the five scores.

** The four income categories were converted into numerical ranges by using a 1990 survey which used 11 income ranges to apply to the four categories listed. The amounts were the weighted averages of the ten ranges for the four categories when the highest income category (over $100,000) was capped at $500,000. The four category averages for 1990 were expressed in 2006 values by using the Bureau of Labor Statistics cost of living conversion rate which was 1.542 between these two years.

† Depression symptoms were measured by the Center for Epidemiological Studies Depression Scale (CES-D). The total score for 20 questions were weighted by frequency of occurrence during the past week on a scale of 1 to 3 (with 0 equal to no days, 1 equal to one to two days, 2 equal to three to four days, and 3 equal to five to seven days) to form a possible range 0 to 60. People with scores below 16 were not depressed, between 16 and 22 were moderately depressed, and scores 23 and above indicate people with severe levels of depression.

‡ Isolation was measured by three categories, 1 is isolated, 2 is friend-centered and 3 is integrated. Our measure is dichotomous and based on category 2, where "friend-centered" means that the person has contact with friends, but not with children, family or religious groups).

§ The UCLA scale version 3 has 20 questions each with four responses (1 is never, 2 is rarely, 3 is sometimes and 4 is always) for negative feelings (9 of the items were positive feelings and these were reverse coded) [18]. Our measure is the total score for the 20 questions and ranges from 20 to 80.

specification for income in the ROAH questions, which often is left unanswered, four categories were used related to income adequacy, ranging from "I do not have enough" to "money is not a problem for me." There is a literature that has compared the continuous income specification with a four-category version and there was found to be a strong correspondence between the two using data for 12 countries [22]. So it was not the case that the four categories are inherently too relativistic.

However, units on this ordinal scale are not useful for a quantitative analysis. It was therefore converted into a ratio scale by using a separate data set that had eleven income ranges showing the percentage that were in each of the four categories. We took the weighted average of the income ranges for the four categories to be the ratio scale, monetary equivalents. Thus the unit for our income independent variable was now dollars which is not an ambiguous unit.

Because the data set that had the eleven income categories was for an earlier year, we had to convert the values to constant 2006 values so that our income variable was in the same year as all the other variables in the ROAH data set. This meant that *Y* was contemporaneous with *S* and *H* and so the trade-off between the two was contemporaneous. The only other complication was that the upper income range was open-ended at "$100,000 or more". We tried a number of values for this upper bound. The main results conservatively use $200,000 as these are people with HIV/AIDS and therefore are not likely to be very rich. In the sensitively analysis we show what difference it makes to the results to have $1 million as the upper bound.

Table 2 presents the main results that were used to derive the estimates of the price of a QALY. Life satisfaction is the dependent variable in all of the equations. In equation (1) we just include as independent variables the two variables whose coefficients are necessary to derive the price of a QALY. Since when undertaking our evaluation of ARV medications we will be disaggregating our sample of individuals into those who are depressed and those who are not depressed, it is important to control for depression and this is why depression is added into equation (2). In equation (3), we add six other controls in addition to depression. The seven controls are listed in table 1. As the only role that the controls play in our estimation is to impact the coefficients of *Y* and *Q*, we do not report their coefficients in table 2. But note that all of the controls that appeared in equations (2) and (3) were statistically significant at least the 5% level. The income and quality of life variables were also always significant at least the 5% level. Equation (3), which had all seven controls, had the highest adjusted R^2 and so we will regard the coefficients coming from this equation as the "best estimates". As equation (3) explained almost 33% of the variation in life satisfaction, and there are potentially a myriad of factors that could determine someone's life satisfaction, the summary statistic can be judged to be reasonably high.

Rows 1 and 2 of table 2 record the estimates of the coefficients for *Y* and *Q*. The ratio of the two coefficients appear as row 3. Row (3) reports the income price *per unit* of the quality of life. Since there are 100 units in our *Q* scale, row 4 multiplies the values in row 3 by 100 to form the price of 100% of the utility corresponding to a life year. We see that the more control variables we include in an equation the lower is the price. The best estimate of the price of the utility of a life year is $58,758.

The Utility of a Life Year

We will obtain our estimates of U_{LY} from an earlier study of the ROAH population [13]. This study identified two groups of patients affected by the ARV medications, those depressed and those not depressed, and estimated three categories of utility effect of ARVs. First there was the adverse side effect of the medications in terms of their toxicity, contributing to lipodystrophy, etc. These adverse side effects were called the direct effect of the ARV medication. The estimate of the direct effect is shown in row 1 of table 3. We see that for every extra life year that the ARVs give to someone taking the medications, the loss of utility from the side effects is 0.2390. Second there is a negative effect of ARVs called the reverse effect that worked through the fact that the less depressed a person was, the more likely that s/he would take the ARVs, and so more adverse side effects of category 1 would be experienced. Row 3 of table 3 shows that the adverse reverse effect was small at 0.0273. Lastly, for those who were depressed, ARVs gave a positive, indirect effect in that the medications actually reduced feelings of depression. Row 2 of table 3 shows that this indirect effect was +0.2772 and this completely offset the two adverse effects, producing a total utility effect of the ARVs of +0.0108. Source: [13] table 4

The implications of these results for U_{LY} for the two groups of patient were the following. For those who were not depressed, the ARVs generated just the adverse direct effect, for a loss of utility of 0.2390. As we see from table 1, the typical person in the ROAH study had a starting utility score of 0.6564. So from this base someone taking ARVs would end up with each year having a utility value of 0.4174, i.e., 0.6564 – 0.2390. For those who were depressed, the strong positive, indirect effect would also have to be included and so the total effect of + 0.0108 would apply. For the depressed group then, the utility value of a life year would be 0.6672, i.e., 0.6564 + 0.0108.

Number of Life Years

We calculated the number of life years gained as the result of ARV treatment based on a study which provides era-specific estimates of the survival benefits of these medications (i.e., (1) 1996 to 1997, (2) 1998-1999, (3) 2000-2002, and (4) 2003 and later) [23]. The differences in survival estimates by era are largely a function of the improved effectiveness of ARV treatments over time in controlling the HIV virus and its effects on the immune system. Because information on when ARV treatment was started among ROAH participants was not available, we approximated the era when they began treatment based on how long they had been diagnosed with HIV, which ranged from zero to twenty-six years. The study we used did not provide separate estimates of the gain in life years by gender, and so our calculations using these data do not differentiate by gender.

However, as noted earlier, depression is a factor in the relationship between ARV and the utility of life years, and this

Table 2: OLS Estimates of the Price of a QALY as a Ratio of the Partial Derivatives (*t* values in parentheses).

Independent Variables	Equation (1)	(2)	(3)
Health Quality of Life (*Q*)	0.0323316 (8.19)	0.0124679 (2.90)	0.0063661 (2.05)
Income (*Y*)	0.0000166 (3.89)	0.0000133 (3.26)	0.000014 (3.59)
Price per 1 percent of a QALY	$ 1,948	$ 937	$ 598
Price per 100 percent of a QALY	$194,769	$93,744	$59,758
Adjusted R^2	0.1108	0.2031	0.3282

Table 3: Direct, Indirect, Reverse, and Total Effects of ARVs on the Utility of a Life Year.

Type of Effect	Effect on Utility of a Life Year
Direct Effect	– 0.2390
Indirect Effect	+ 0.2771
Reverse Effect	– 0.0273
Total Effect	+ 0.0108

Source: [13] (Table 4)

was not significantly affected by gender [13]. Depression is highly prevalent among those living with HIV, affecting approximately 48% of those with the virus with diagnoses of major depression ranging from 5% to 10% [21]. One study provided estimates of the impact of depressive symptoms in the reduction of life expectancy for young-old (i.e., age 70) men and women, finding that depressive symptoms reduced active life expectancy by 6.5 years for men and 4.2 years for women (see Table 2) [24]. We considered the estimates in this study to be good proxies for this population in as much as the psychosocial and health profile of the ROAH sample is similar to the young-old [25]. Therefore, we calculated the gain in life years for three groups; those who were not depressed, depressed men, and depressed women by era of ARV treatment for net gain in life years. Data reported below are based on the 757 participants who were on ARVs and provided information on self-reported time of HIV diagnosis reported, and completed the Center for Epidemiological Studies Depression Scale (CES-D) [26]. Participants were considered depressed if their CES-D scores were 23 or greater [21]. The resulting data provide a weighted average of gain in life years for the ROAH sample based on time era when ARV treatment was started, if the person was non-depressed/depressed, and by gender within the depressed group.

Table 4 illustrates the net gain in life years for the ROAH sample for non-depressed individuals and depressed men and women separately. On average, there were 6.5 life years gained as a result of ARV treatment among ROAH respondents. For the non-depressed group, defined as having CES-D scores of less than 23, the average gain in life years as a result of ARV treatment was 8.7 years. For the depressed group (i.e., CES-D scores of 23 or higher), the average gain in life years resulting after accounting for the negative effects of depression on life expectancy was 2.9 years.

Costs of ARVs

The advent of highly effective ARV medications began in 1995 at which time the primary cost of treatment was hospitalization costs. Today for the typical person living with HIV in the US the largest care costs are ARV medications. The yearly costs of ARVs is a variable number since the cost paid is dependent upon who pays (private insurance, out of pocket, the Veterans Administration, Medicaid, ADAP). ARV costs are negotiated by each state for its Medicaid dependent population. Depending on the state, 60% - 85% of its HIV population are Medicaid dependent. ARV cost measurement can also vary as a function of the immune system status of each person with HIV. The average annual per-person expenditures for care is greatest for those with CD4 cell counts 50 cell/µl or less and lowest for those with CD4 cell counts more than 500 cells/µl. The majority of costs today are attributable to ARV medication, except for those with CD4 cell counts 50 cells/µl or less, where inpatient costs were highest [27]. Where possible those costs for people with CD4 cell counts below 50 were not used.

There are few reports of annual ARV costs in the literature for 1995 to 2000. One primary source used in this study used a large random sample of medical care providers and patients (approximately 4000) as the data source [28]. The data is based on providers and patients from 90 urban and 22 rural areas. Data was collected from 1996 through 1999 at 6 month intervals. A monthly ARV cost is reported at each 6 month interval. An average was calculated for each era and converted to an annual cost for this study, see Table 5. For the era of 1996-1997, the average yearly cost was calculated to be $7,833 and for the 1998-1999 interval it was $9,000 [28]. For the 2000-2002 period, we used a study which used patient records to derive ARV annual costs based on sample sizes of between 13,000 and 15,000 for each year which yielded an average year ARV cost of $11,066 [29]. For the last era (2003-2006) data was derived from the following published reports: for 2003 data was taken from [30]; for 2004 and 2005 the yearly ARV cost was taken from [31] and for 2006 data was used from [27]. An average of the four year era data yielded an annual ARV cost of $12, 994.

Table 4: Gain in Life Years for ARV Treatment for Non-Depressed and Depressed Groups.

Era of ARV Treatment	N	%	Depressed Men* n = 201 (27%)	Depressed Women* n = 81 (11%)	Total Depressed n = 282 (37%)	Non Depressed n = 469 (62%)
1997 or Before	594	77.7	7.8 - 6.5 = 1.3	7.8 – 4.2 = 3.6	2.0	7.8
1998 to 1999	73	9.6	11.1 – 6.5 = 4.6	11.1 – 4.2 = 6.9	5.3	11.1
2000 to 2002	70	9.2	11.6 – 6.5 = 5.1	11.6 – 4.2 = 7.4	5.8	11.6
2003 or Later	27	3.5	13.3 – 6.5 = 6.8	13.3 – 4.2 = 9.1	7.5	13.3
All Eras	791	100	2.2	4.5	2.9	8.7

* Gain in life years calculated from [23]. Loss in life years due to depression is (men 6.5 years; women = 4.2 years) derived from [24].

Table 5: Estimated Costs of ARVs.

Era of ARV Treatment	Annual Cost per Each Life Year Gained*	Gain in Life Years**	Total Years ARV Costs Incurred	Undiscounted Lifetime ARV Cost
1997or Earlier	$ 7,833	8	19	$148,827
1998 to 1999	$ 9,000	11	22	$198,000
2000 to 2002	$11,066	12	23	$254,518
2003 to 2006	$12,994	13	24	$311,856

*Average of values taken from the literature (see text).
** Based on the life years for the non-depressed individuals in table 4.

Table 6: Net-Benefits of ARVs on Depressed and Non-depressed Groups by Era.

Type of Effect	Non-Depressed	Depressed
1997 or Earlier		
Undiscounted Benefits (B)	$199,544	$318,980
Undiscounted Costs (C)	$148,827	$148,827
Undiscounted Net-Benefits (N)	$50,717	$170,153
Undiscounted Benefit-Cost Ratio	1.34	2.14
Discounted Benefits (B)	$130,285	$208,266
Discounted Costs (C)	$115,564	$115,564
Discounted Net-Benefits (N)	$14,721	$92,702
Discounted Benefit-Cost Ratio	1.13	1.80
1998 to 1999		
Undiscounted Benefits (B)	$274,373	$438,598
Undiscounted Costs (C)	$198,000	$198,000
Undiscounted Net-Benefits (N)	$76,373	$240,598
Undiscounted Benefit-Cost Ratio	1.39	2.22
Discounted Benefits (B)	$171,728	$274,515
Discounted Costs (C)	$147,735	$147,735
Discounted Net-Benefits (N)	$23,933	$126,780
Discounted Benefit-Cost Ratio	1.16	1.86
2000 to 2002		
Undiscounted Benefits (B)	$299,316	$478,470
Undiscounted Costs (C)	$254,518	$254,518
Undiscounted Net-Benefits (N)	$44,798	$223,952
Undiscounted Benefit-Cost Ratio	1.18	1.88
Discounted Benefits (B)	$184,746	$295,324
Discounted Costs (C)	$187,424	$187,424
Discounted Net-Benefits (N)	– $ 2,678	$107,900
Discounted Benefit-Cost Ratio	0.99	1.57
2003 to 2006		
Undiscounted Benefits (B)	$324,259	$518,343
Undiscounted Costs (C)	$311,856	$311,856
Undiscounted Net-Benefits (N)	$ 12,403	$206,487
Undiscounted Benefit-Cost Ratio	1.04	1.66
Discounted Benefits (B)	$197,384	$315,527
Discounted Costs (C)	$220,078	$220,078
Discounted Net-Benefits (N)	– $ 22,694	$ 95,449
Discounted Benefit-Cost Ratio	0.90	1.43

Table 6 shows that the net-benefits of ARVs for the depressed group were positive and large for all four eras. The Benefit-Cost ratio was never below 1.4. Outcomes were most favorable in the 1998 to 1999 era. Compared to 1997 or earlier, there were 3 more years of life expectancy from the drugs and hence 3 extra years of benefits. For subsequent eras, the additional LY were only 1 per era. As table 4 reveals the cost increase in absolute terms was lower in the 1998 to 1999 period than the subsequent eras. This together with the larger benefits made the net-benefits highest between 1998 and 1999. For the non-depressed group, all four eras had positive net-benefits only if no discounting took place. With discounting, net-benefits varied by era. In the first two eras, that is, prior to 2000, the net-benefits were positive. In the two most recent eras the rise in costs were large enough to dominate the benefits of the small number of additional life-years to bring the Benefit-Cost ratios below 1.

RESULTS

The four components that are in equation (4), and have been estimated in tables 2-5, are presented in table 6 and assembled to form the benefits, costs and net-benefits. To facilitate an easy comparison of the outcomes, the benefit-cost ratios are also given. The results are given by era. Because no time dummies were significant in the regressions given in table 2, the product $P_{QALY}\ U_{LY}$ in equation (3) was invariant to the era specified. Throughout table 6, the benefit per year, $P_{QALY}\ U_{LY}$, was $24,943 ($59,758 times 0.4174) for the non-depressed group and equal to $39,873 per year (59,758 times 0.6672) for the depressed group. Thus, the only reason why benefits varied by era in equation (3) was because the added life years *LY* differed by the time period considered. To show the impact of discounting, the results are recorded with and without discounting.

As is standard in the health care evaluation field, we use 3% as the discount rate [4]. The impact of discounting in our case is to lower the net-benefits and the Cost-Benefit ratios. To help understand what is involved, we will go through the calculation of the net-benefits for the non-depressed group for the 1997 or earlier era. For this era, the ARVs generated 8 extra years of life. Without the ARVs, life years would have been 11. This means that the time horizon for this era is 19 years. The cost per year is $7,833. Note that these costs have to be incurred from year 1. So without discounting, total lifetime costs are 19 times annual costs, i.e., $148,827. With discounting, the present value of the costs is $115,564. Benefits only appear in year 12 and then proceed to year 19. The benefits per year are $24,943. For 8 years, the undiscounted total lifetime benefits are $199,544. However with discounting the benefits are much reduced because they begin in year 12. Relative to year 1, the present value of a dollar in year 12 after 11 years of discounting is only 0.72 even with a discount rate as low as 3%. Hence the present value of $24,943 is reduced to $18,019. For all years 12 to 19, the present value of the benefits is $130,285. As a consequence the undiscounted net-benefits of $50,717 are reduced by more than two-thirds with discounting as they fall to $14,721. The Benefit-Cost ratio is reduced from 1.34 to 1.13.

SENSITIVITY ANALYSIS

Our main results by disaggregating by era already allows for many alternative estimates, especially for life years, costs and discounting. Here we indicate how the results would be altered if we deviate from our constant benefits per year assumption. Recall that in table 5, the price of a QALY was fixed at $59,758 throughout as estimated in table 2. Here we examine the implications of three alternative P_{QALY} figures.

The first alternative price of a QALY figure arises from the way the data for the income variable *Y* was constructed. The income data in ROAH related to four categories, such as whether people did not have enough or that money was not a problem (see table 1). These four categories were converted into specific income amounts by taking the means of eleven income ranges that were found to be applicable for the ROAH sample in prior research. The problem was that the upper interval was open ended and stated that income was "$100,000 or more". Because HIV/AIDS persons often do not work and are not considered to be a rich

population [20], the upper bound for income was conservatively set at $500,000 and the means for the four categories of *Y* in table 1 were based on this upper bound. If instead the upper bound is set at $1 million, the income figures would be much higher. Re-estimating equation 3 in table 2 with the higher values for *Y* produced a price per QALY of $48,821 which was roughly 20% lower than the $59,758 figure. With benefits lower, all outcomes are reduced. For the non-depressed group, the discounted Benefit-Cost ratios are now below 1 for the 1997 and earlier era as well as for the two post 2000 periods. In the one era, 1998 to 1999, when net-benefits were positive, the Benefit-Cost Ratio was barely above 1. However, for the depressed group the net-benefits are still positive in all eras and the Benefit-Cost ratio is 1.17 even during the latest era when net-benefits are least.

The second alternative price of a QALY comes about because of the particular form in which income entered regression equation (2) in table 2. Although it would seem that the way *Y* is specified is usually an empirical matter, some claim that to relate life satisfaction to income in dollars is "incorrect analysis". They state, "A strong argument can be made for the logarithm of income as the preferred scale." [32] For this reason we tested to see how the results would change if *ln Y* were used instead of *Y*. With the (natural) logarithmic specification for *Y* in equation (6), our trade-off method given in equation (8) has to be modified to become:

$$\Delta Y / \Delta Q = (\Delta S / \Delta Q) / (\Delta S / \Delta \ln Y) = (\alpha_Q / \alpha_Y)\, Y \qquad (9)$$

We evaluated *Y* in equation (9) at the sample mean ($22,281). For the logarithmic *Y* version of regression equation (3) in table 2 we obtained a price of a QALY of $38,649 which is around a third below our benchmark price of $59,758.

With such a drastic reduction in benefits, the net-benefits are much reduced. So not surprising for the non-depressed group, where all but one of the Benefit-Cost ratios with discounting were below 1 with the 20% reduction in benefits, lowering the benefits even further meant that we would now find that in no era were the ARVs worthwhile. Nonetheless, for the depressed group, only for the most recent era (the 2003 to 2006 period) were the discounted net-benefits negative, with the Benefit-Cost ratios by era being 1.17, 1.20, 1.02 and 0.93, respectively.

The final alternative price of a QALY is due to the adoption of a different estimation method than OLS. Although as we explained earlier, our method for estimating the price of a QALY relies on working with a utility function that simply describes the preferences and does not attempt to explain preferences, and so is not a causal exercise, simply for the sake of completeness, it would be useful to see what difference it would make if estimation were viewed in a causal way. In a causal study income could be determined by happiness. There is also the possibility that health satisfaction, which is a part of overall satisfaction, may itself be determined by overall satisfaction. The problem would be therefore that what we had as right-hand side variables in our OLS regressions (income and health quality of life) might in fact be endogenous variables. This would lead to biased estimates. To test for this we used a set of instruments for both *Y* and *Q*. Obvious candidates as instrument were the set of controls, the *Z* variables specified in table1. We added also whether the person claimed that they needed help in the past to assist them with HIV, and the time in months since the HIV diagnosis, which was an important instrument in the earlier study using the ROAH data [13]. Time since diagnosis is a predetermined variable it cannot be endogenous. In addition, we used instruments that were found to be almost universally significant in happiness equations round the world, i.e., age, age-squared, gender and race (being black) [15]. The Two-Stage Least Squares estimates of the trade-off between *Q* and *Y* produced a price of a QALY of $60,749, almost exactly the same as our OLS estimate of $59,758. So the outcomes would not be much different with the alternative estimation technique than those in the main results shown in table 6.

SUMMARY AND CONCLUSIONS

The main contribution of this paper is methodological. It provides a new and general way to measure the benefits of a health care intervention by way of estimating the marginal rate of substitution between arguments in the utility function and to use this to obtain a price of a QALY for elderly people living with HIV. Apart from actually estimating net-benefits, rather than simply assuming that they are positive which is what policy-makers world-wide currently do, the other important contribution of the paper can be found in the way that we combined the health care evaluation literature's concern with health satisfaction – our short-hand for health related quality of life - with the happiness literature's use of overall life satisfaction. There is a debate in the QALY literature whether the utility part should be purely health related or should include also non-health determinants of utility. One side argues that all non-health characteristics of an individual other than age and sex should be ignored [33]; while the other side argues that a "capability QALY" should be used, which would be different from the standard QALY which can be called a "health QALY" because it includes non-health factors such as the ability to work, comfort and dignity [34] [35]. However, instead of choosing between non-health and health utility measures, this study used *both* in combination to form our estimate of benefits. That is, to estimate the utility part of a QALY (which was denoted by U_{LY}) we used health-utility data (based on rating scales) and we used a happiness index (life satisfaction on a scale of 1 to 10) to measure *U* from which we estimated P_{QALY}.

To illustrate the method, we estimated the benefits for a CBA of ARVs. The end result was a series of Cost-Benefit outcomes of ARVs that differed by the level of depression and the era that the medications were taken. In our main results we found that, in all eras, the net-benefits were positive for the depressed group who had the higher benefits, with the Benefit-Cost ratio never dipping below 1.4. The only case where the sensitivity analysis produced negative net-benefits was when benefits were reduced by as much as 30% and this adverse outcome was only for the most recent era. For the non-depressed group even the main results depended on the era. In the two eras prior to 2000, net-benefits were positive and they became negative thereafter. Note that when the net-benefits were positive, the Benefit-Cost ratio was only 1.1, i.e., i.e., just above 1. So in the sensitivity analysis, where benefits were reduced by 20% and more, all net-benefits were negative for all eras for this group.

There were two main determinants driving the cost-benefit results of HIV medications for the elderly. The first was the low

base utility of a life year for this population and how this was reduced by the strong adverse side effects of the ARVs, which bought the utility of a life year down to as low as 0.4174. Clearly a large number of life years would be required to produce sufficient QALYs for the medications to be worthwhile.

The second important determinant was the annual costs of the ARVs and the additional life years stemming from them. This relationship between costs and life years very much varied by era. For the 1997 or earlier period, ARVs cost $7,833 per annum and they generated 8 additional life years. In the 1998 to 1999 period costs rose to $9000, but there were 3 extras years of life expectancy produced. This meant that there were 3 extra years of benefits. There were now 11 years of benefits instead of 8 years in the previous era. In subsequent years costs continued to rise, but there was only 1 extra life-year added. So there were very little extra benefits to try to overcome the cost increases. In the process net-benefits fell.

The role of discounting was crucial. Annual costs are incurred from year 1 over all the life years that a person is expected to live. Benefits on the other hand accrue from the additional life years coming from the ARVs and this is only after the normal life expectancy without ARVs has expired. It is important then that the future life-years are sizeable to overcome the life-time costs that are incurred immediately and continue to occur over all years. The fact that costs are immediate and required for all life-years, while added life-years only produce benefits in the future, explains why discounting plays such an important role in the evaluation of ARVs, even when the discount used is as low as 3%.

The chief drawback of our study was the fact that the data we used did not specify the particular medication used. So we do not know whether first-line drugs, second-line drugs or generics generated these results. All we know are the results for an average ARV. However, by breaking down the Cost-Benefit results by era, we have four different time period averages. So we have some idea about what medications were available for particular eras. The other weakness of the study is that it evaluated the effects of the medications only on the person taking the ARVs. Any benefits in terms of reducing HIV transmission to others have not been incorporated. Given the well-known effect of ARVS to reduce the viral load, and thereby lower secondary transmissions, one should expect that the net-benefits of the medications would be higher than those reported here. In this respect, our CBA calculations are conservative estimates of the total results.

The main policy significance of this retrospective cost-benefit study of ARVs for the elderly is the challenge it makes to pharmaceutical companies for the future. To continue to be socially beneficial, new lines of ARVs have to be manufactured in such a way that they reduce the considerable adverse side effects of the medications and generate larger number of expected life-years. There seems to be diminishing returns to producing more benefits. In addition, the challenge is to produce new lines of drugs in such a way that the costs increases are minimized. Since costs are incurred immediately, while the benefits occur in the ever more distant future, cost containment may be the main ingredient to ensure that HIV medications with positive net-benefits persist into the future.

DISCLOSURE

There are no financial interests, or conflicts of interest, for any of the authors connected with this study.

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