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Using cost as a consideration for antiretroviral regimen selection: an example using average wholesale prices

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Abstract

Funding for the AIDS Drug Assistance Program (ADAP) has lagged behind the number of persons needing antiretroviral therapy, leading to waiting lists and reduction of needed treatments and services. This paper demonstrates a method of providing more treatment for the same amount of money by selecting clinically equivalent, but lower cost drug regimens. Average wholesale prices (AWPs) were used to calculate the annual costs of preferred, alternative and acceptable regimens. The cost of each regimen was divided into \$1,000,000 to determine how many patients could be treated per \$1,000,000 that an ADAP had to spend. AWPs for preferred regimens ranged from \$25,318 to 35,645 per year. For alternative regimens, the range of annual AWPs was \$22,002 to \$32,335. The range for the acceptable regimens was \$19,031 to \$31,543. The range of person treated/\$1,000,000 per year was from 28 to 52. Funding shortages will lead ADAPs to resort to waiting lists or other means of denying appropriate care unless alternative approaches to treatment are sought. Cost conscious selection of regimens where there is no harm to individual patients is one alternative approach. Medical conditions that allow exceptions to a lower cost based regimens must be developed with the assistance of clinicians.

Keywords

Cost; Antiretroviral drugs; regimen selection

Introduction

The U.S government is a major provider of antiretroviral therapy (ART) to HIV infected individuals. 226,419 persons were receiving services or medications through the AIDS Drug Assistance Program (ADAP) in March 2012 including 32,522 clients who were newly enrolled in 2011-12 (National Alliance of State and Territorial AIDS Directors, 2012a). The April 2012 appropriation for ADAP was \$900 million, an increase of \$15 million from 2011. Because of increased demand for ADAP services, the funding was supplemented by 69 million dollars. The supplement eliminated most of the waiting lists for patients who were eligible ART but lived in states where all available ADAP funds were exhausted (National Alliance of State and Territorial AIDS Directors, 2012b). Waiting lists had reached 9298 persons in September 2011. The waiting lists have been reduced to 58 persons

in December, 2012 through either the additional funds or changing eligibility requirements. (National Alliance of State and Territorial AIDS Directors, 2012c).

The funding crisis is quite likely to re-occur in future years. Increases in new clients each year will require more funding. However, it does not seem likely additional funds will be forthcoming. The U.S. Senate committee recommended an appropriation of \$963.3 million while the House of Representatives has not yet acted. The Senate committee's recommendation increased last year's original appropriation but is less than the supplemented 2012 ADAP budget. The current congressional climate seems more concerned about expenditure reduction rather than program expansion. Other funding sources are unlikely. ADAP is administered by the states and has been supplemented by state appropriations in 37 states. State funding amounted to 16% of total ADAP funding in 2011, a decline from 21% 2009. (Kaiser Family Foundation. 2012; Kaiser Family Foundation, 2009). States are unlikely to provide additional funds because they are faced with fiscal crises and have reduced their HIV expenditures by \$170,000,000 in 2009 alone (Centers for Disease Control, 2010).

When faced with shortfalls in available funds, policy makers have to deal with the simple formula:

$$\text{Total cost} = \text{Cost per patient} \times \text{number of patients.}$$

To control total cost, policies must either reduce the number of patients or reduce cost per patient. Reducing the number of persons being served has been done by two methods. Putting a cap on- the number of patients in a state's ADAP program and/or putting a cap on expenditures per person was being used in seven states in December, 2012 (National Alliance of State and Territorial AIDS Directors, 2012c). Other care depriving strategies for reducing cost include reducing income eligibility requirements, eliminating non-ART drugs from formularies and not paying for laboratory tests.

The other approach to dealing with funding shortages would be to find ways for getting the same clinical impact for less money. This could be done by comparing costs of drug regimens that are considered clinically equivalent and determining if additional persons could be treated by using lower cost regimens. This paper examines potential cost reductions that could be achieved by utilizing either a less expensive regimens.

Methods

The Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents classifies various combinations of drugs as appropriate therapies for the initial treatment of HIV infection in adults and adolescents. These are classified into three categories: 1) Preferred regimens, 2) Acceptable regimens and 3) Alternative regimens. Drug combinations are put in these categories based on the strength of the science that determines the regimen's effectiveness and the potential disadvantages associated with its use (Department of Health and Human Services, 2012a).

This paper assumes that any regimen in one of these categories is clinically equivalent to others in the category. Therefore, a lower cost regimen is a more preferable combination unless there are contraindications for its use in an individual patient. The cost of a regimen is idiosyncratic to the particular purchaser of the medications. Good negotiators or large volumes purchasers will usually pay less for medications. The authors of this paper recognize that different prices will be paid by different purchasers and are merely showing a method by which costs of regimens can be compared. In addition, the paper will show how

different regimens will be able to treat different numbers of patients. It will do this by determining how many persons could be treated per year with every regimen for each \$1,000,000 that a payer (e.g. a state ADAP) might have to spend. This will be done by dividing \$1,000,000 by the annual cost for each regimen.

The prices for each of the drugs were derived from the “average wholesale prices (AWP) that were published in the March 27, 2012 Guidelines (Department of Health and Human Services, 2012b). Coformulated combination AWP were used for Abacavir/lamivudine (Epzicom®), Tenofovir/emtricitabine (Truvada®), zidovudine/lamivudine (Combivir®), lopinavir/ritonavir (Kaletra®), rilpivirine/tenofovir/emtricitabine (Complera®) and efavirenz/tenofovir/emtricitabine (Atripla®). The daily cost for all of the drugs at their recommended doses in a regimen was then multiplied by 365 to determine the annual cost.

Results

Table 1 shows the annual AWP costs of the panel’s four preferred regimens for initial treatment of HIV infection. The combination based on efavirenz, tenofovir and emtricitabine had the lowest AWP at \$25,318 per year while combinations including either atazanavir/ritonavir or darunavir/ritonavir together with coformulated tenofovir and emtricitabine had AWP of approximately \$35,000 per year. The raltegravir based regimen had an intermediate AWP of \$31,178. An ADAP program could provide drugs for 39 persons who were on an efavirenz based regimen, 32 persons on a raltegravir based regimen and 28 persons on darunavir/ritonavir or atazanavir/ritonavir based regimens for every \$1,000,000 of expenditure.

The alternative regimens have annual average AWP that range from \$22,002 to \$32,335 per year. Persons treated per year per \$1,000,000 range from 30 to 45. The regimen containing efavirenz with coformulated abacavir and lamivudine has the lowest annual cost, while the regimen including darunavir/ritonavir and co-formulated abacavir and lamivudine has the highest AWP.

The AWP of acceptable regimens ranged from \$19,031 to 31,543. The combination including extended release nevirapine with co-formulated abacavir and lamivudine has the lowest annual cost of all evaluated regimens and is closely followed by the NNRTI-based regimen containing efavirenz and coformulated zidovudine and lamivudine. An ADAP program could provide drugs for up to 52 persons who were prescribed an acceptable NNRTI-based regimen for every \$1,000,000 in its annual budget. The regimen containing atazanavir/ritonavir/abacavir/lamivudine would treat 31 persons per year.

Discussion

AWP is not the price that an ADAP will pay for a drug because of discounting. However, AWP provides a common benchmark against which all of the combinations could be compared. Purchasers of ART can adjust the calculations to reflect their prices for ART drugs. Some of these drugs are now available in generic form. These have AWP that are 10-37% lower than brand name medications (Department of Health and Human Services, 2012c). However, these ostensibly lower prices do not reflect the market where discounts or rebates may eliminate differences.

This paper did not intend to find the lowest ART cost or to suggest that it should be the one that is prescribed by clinicians. No single regimen is the best combination for any particular patient. Side effects, concurrent conditions, resistance patterns, drug interactions and patient preferences all play a role in determining which is the best regimen a given patient. However, when there is therapeutic indifference between regimens, cost should become an

important consideration in a time of constrained resources. The potential savings can be seen by the fact that the AWP per/year difference of \$16,614 between the most expensive regimen (\$35,645/year) and the least expensive regimen (\$19,031/year). This suggests that 1.9 times as many patients could be treated using the lowest cost regimen. Once similar cost calculations are done using local prices, ADAP administrators can ask for a justification for prescribing more expensive combinations. However, this should not be done lightly as great harm could be done without proper safeguards. These safeguards should follow rules that are developed by highly experienced HIV clinicians. These rules could lay out the exceptions to using less costly regimens. These are not bureaucratic decisions but rather clinical decisions that have life threatening implications and thus should be made by clinicians.

Conclusion

It seems likely that either patients will be denied access to ART or someone will make cost based decisions to assure access. The latter would seem to be the best approach because it seems patently unfair to deny some HIV infected individual's access to ART while others consume resources that do not provide them a clinical advantage over less expensive alternatives. If deciding to use lower cost alternatives becomes the means for staying within a budget, it is hoped that the decisions will be based on science as well as costs. Expert panels who establish levels of preference for various regimens should consider costs when they evaluate regimens. Otherwise non-clinician administrators will make these decisions based only on cost without the knowledge of how their decisions may harm patients.

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Table 1

Average Wholesale Prices (AWP) of Preferred Regimens

Regimen	AWP (monthly) package	(\$ AWP / daily dose	(\$ Annual cost	Number of persons treated per \$1million
Atripla	2,080.97 (30 tabs)	69.36	25,318	39
Atazanavir 150-mg cap	1,176.23 (60 caps)	39.20	34,988	28
Ritonavir 100-mg tab	308.60 (30 tabs)	10.28		
Truvada (coformulation)	1,391.45 (30 tabs)	46.38		
Atazanavir 200-mg cap	1,176.23 (60 caps)	39.20	34,988	28
Ritonavir 100-mg tab	308.60 (30 tabs)	10.28		
Truvada (coformulation)	1,391.45 (30 tabs)	46.38		
Atazanavir 300-mg cap	1,165.12 (30 caps)	38.83	34,853	28
Ritonavir 100-mg tab	308.60 (30 tabs)	10.28		
Truvada (coformulation)	1,391.45 (30 tabs)	46.38		
Darunavir 400-mg tab	1,230.20 (60 tabs)	41.00	35,645	28
Ritonavir 100-mg tab	308.60 (30 tabs)	10.28		
Truvada (coformulation)	1,391.45 (30 tabs)	46.38		
Raltegravir 400-mg tab	1,171.30 (60 tabs)	39.04	31,178	32
Truvada	1,391.45 (30 tabs)	46.38		

Table 2

Average Wholesale Prices of Alternative Regimens

Regimen	(\$ AWP (monthly) package	(\$ AWP / daily dose	(\$ Annual cost	Number of persons treated per \$1million
<u>NNRTI-Based Regimens</u>				
Efavirenz 600-mg tab + Epzicom (coformulation)	689.52 (30 tabs) + 1,118.90 (30 tabs)	60.28	22,002	45
Complera (coformulation)	2,195.83 (30 tabs)	73.19	26,714	37
Rilpivirine + Epzicom	804.38 (30 tabs) + 1,118.90	64.10	23,396	42
<u>PI-Based Regimens</u>				
Atazanavir/ritonavir + Epzicom	1,165.12 (30 caps) + 308.60 (30 tabs) + 1,118.90	84.42	31,543	31
Darunavir/ritonavir + Epzicom	1,230.20 (60 tabs) + 308.60 (30 tabs) + 1,118.90	88.59	32,335	30
Fosamprenavir/ritonavir + Epzicom	906.34 (60 tabs) + 308.60 (30 tabs) + 1,118.90	77.79	28,393	35
Fosamprenavir/ritonavir + Truvada	906.34 (60 tabs) + 308.60 (30 tabs) + 1,391.45	86.87	31,707	31
5) Kaletra (once or twice daily)(coformulation) + Epzicom	871.36 (120 tabs) + 1,118.90	66.34	24,214	41
6) Kaletra (once or twice daily) + Truvada	871.36 (120 tabs) + 1,391.45	75.42	27,528	36
<u>INSTI-Based Regimen</u>				
1) Raltegravir + Epzicom	1,171.30 (60 tabs) + 1,118.90	76.34	27,864	35

Table 3

Average wholesale prices of Acceptable Regimens

Regimen	(\$ AWP (monthly) package	(\$ AWP / daily dose	(\$ Annual cost	Number of persons treated per \$1million
<u>NNRTI-Based Regimen</u>				
Efavirenz + Combivir	689.52 (30 tabs) + 931.61 (60 tabs)	54.03	19,720	50
Nevirapine + Truvada	723.08 (60 tabs) + 1,391.45	70.48	25,725	38
Nevirapine XR + Truvada	632.68 + 1,391.45 (30 tabs)	67.47	24,626	40
Nevirapine + Combivir	723.08 (60 tabs) + 931.61	55.15	20,129	49
Nevirapine XR + Combivir	632.68 (30 tabs) + 931.61	52.14	19,031	52
Nevirapine + Epzicom	723.08 (60 tabs) + 1,118.90	61.39	22,407	44
Nevirapine XR + Epzicom	632.68 (30 tabs) + 1,118.90	58.38	21,308	46
Rilpivirine + Combivir	804.38 (30 tabs) + 931.61	57.86	21,118	47
<u>PI-Based Regimens</u>				
Atazanavir/ritonavir + Combivir	1,165.12 (30 caps) + 308.60 (30 tabs) + 931.61	80.17	29,262	34
Atazanavir/ritonavir + Epzicom	1,165.12 (30 caps) + 308.60 (30 tabs) + 1,118.90	86.42	31,543	31
Darunavir/ritonavir + Combivir	1,230.20 (60 tabs) + 308.60 (30 tabs) + 931.61	82.34	30,054	33
Fosamprenavir/ritonavir + Combivir	906.34 (60 tabs) + 308.60 (30 tabs) + 931.61	71.55	26,115	38
Kaletra + Combivir	871.36 (120 tabs) + 931.61	60.09	21,932	45
<u>INSTI-Based Regimen</u>				
Raltegravir + Combivir	1,171.30 (60 tabs) + 931.61	70.09	25,582	39
<u>CCR5 Antagonist-Based Regimens</u>				
Maraviroc + Combivir	1,148.16 (60 tabs) + 931.61	69.32	25,301	39
Maraviroc + Truvada	1,148.16 (60 tabs) + 1,391.45	84.65	30,897	32
Maraviroc + Epzicom	1,148.16 (60 tabs) + 1,118.90	75.56	27,579	36
Regimens that may be acceptable but should be used with caution				
<u>PI-Based Regimens</u>				
Saquinavir/ritonavir + Truvada	1,088.84 (120 tabs) + 1,391.45	82.67	30,174	33
Saquinavir/ritonavir + Combivir	1,391.45 (30 tabs) + 931.61	77.43	28,261	35

Regimen	(\$ AWP (monthly) package	(\$ AWP / daily dose	(\$ Annual cost	Number of persons treated per \$1million
Saquinavir/ritonavir + Epzicom	1,391.45 (30 tabs) + 1,118.90	83.67	30,539	32