0.032 instead of 0.022 maintaining significance (last line of Table 5). Therefore, we confirm our statement that in our series analyzing 87 CSF, the patients taking a treatment regimen with a higher CPE rank had a better suppression of HIV-1 in CSF.

In the absence of formal pharmacokinetic (PK) data on drug elimination in CSF, the extrapolation of the trough levels ($C_{min}$) were based on mean terminal $t_{1/2}$ in plasma which represented the only surrogate available under the assumption of an instantaneous equilibrium between plasma and CSF. The plasma elimination $t_{1/2}$ considered were all established in population pharmacokinetic models developed on the basis of a systematic review of published literature.[3] The reported values are thus to be considered as an order of magnitude, rather than as precise values, and we advocate for further evaluation of the PK behavior of antiretroviral therapy in CSF.

We agree that the increased low-level viral loads may potentially be attributed to viral blips in CSF and not necessarily to virological failure because no detectable viral loads could be confirmed in a second lumbar puncture. We finally fully support the statement of Calcango et al that incomplete control of viral replication in CSF warrants further evaluation in longitudinal studies.

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# Lifetime Costs and Quality-Adjusted Life Years Saved From HIV Prevention in the Test and Treat Era

***To the Editors***:

Lifetime HIV treatment costs and quality-adjusted life years (QALYs) are typically used in economic evaluations of HIV prevention interventions. In some cases, costs, QALYs, and changes in QALYs from alternative HIV prevention interventions or strategies are estimated through complex disease progression models or dynamic epidemic models.[1–5] In other cases, estimates of the lifetime treatment costs saved and the QALYs gained when an infection is averted are needed as input variables in a cost-utility analysis of a prevention intervention.

A simplified form of the latter analysis, where the comparison is with no intervention, is defined as follows: $(C - AT)/AQ$, where C is the total program cost of an intervention, A is the number of HIV infections averted by the intervention, T is the HIV treatment cost saved per infection averted, and Q is the number of QALYs gained per infection averted.[6,7] Policy interest focuses on situations where the cost per QALY gained equals 0, the threshold between an intervention that is cost saving (a negative cost per QALY gained, where program costs are less than the treatment costs saved by infections averted) and one that requires the use of additional resources to achieve the gain in QALYs (a positive cost per QALY gained).[8] For the latter, $100,000 represents a reasonable current estimate of the amount society is willing to pay to gain a QALY, although this estimate may be conservative.[9–11]

Holtgrave and Pinkerton[6] provided an overview of the methodology for estimating treatment costs saved and QALYs gained from preventing an infection. This methodology involved estimating the costs of treating an HIV-infected person over his/her lifetime, which would then be saved if that infection was prevented. Using utility weights drawn from the literature, Holtgrave and Pinkerton also estimated the lifetime QALYs for this infected person compared with those of an uninfected person. The difference between these 2 values is the number of QALYs lost to infection or the number that would be gained if that infection was prevented.

Holtgrave and Pinkerton developed low-, intermediate-, and high HIV treatment cost scenarios that reflected differences in life expectancy and quality of life after antiretroviral therapy (ART) initiation in the United States (Table 1). The low-cost scenario described disease progression from time of infection, assumed to occur at age 26, for someone with a low level of and delayed access to HIV treatment in 1996–1997 (zidovudine monotherapy and no viral load monitoring). The intermediate-cost scenario (the base case) reflected recommended treatment regimens in those years (viral load monitoring followed by 2 and 3 drug therapy), whereas the high-cost scenario assumed immediate viral load monitoring and 3 drug therapy from the time of infection. Holtgrave and Pinkerton assumed life expectancies for an HIV-infected person of 12, 16, and 21 years from time of

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The findings and conclusions in this study are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.
The authors have no conflicts of interest to disclose.
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**TABLE 1.** Summary of Lifetime Costs and Quality of Life Measures for HIV-Infected Persons

| Variable | Holtgrave and Pinkerton (1997)[6] | Hutchinson et al (2010)[13] | Holtgrave et al (2012)[15] | Farnham et al (2013)[16] |
|---|---|---|---|---|
| **Life expectancy after infection (years—undiscounted)** | | | | |
| Low | 12 | | | |
| Intermediate | 16 | 32 | 28 | |
| High | 21 | | | |
| By CD4 count (cells/μL)* | | | | |
| ≤200 | | | | 30.73 |
| 201–350 | | | | 36.57 |
| 351–500 | | | | 37.94 |
| >500 | | | | 38.08 |
| **Life years saved per infection averted (undiscounted)** | | | | |
| Low | 31.9† | | | |
| Intermediate | 27.9 | 12.6 | 9 | |
| High | 22.9 | | | |
| By CD4 count (cells/μL)* | | | | |
| ≤200 | | | | 14.32 (6.07)‡ |
| 201–350 | | | | 8.44 (3.56) |
| 351–500 | | | | 7.08 (3.04) |
| >500 | | | | 6.97 (2.97) |
| **Discounted (3%) QALYs saved per infection averted** | | | | |
| Low | 13.18 | | | |
| Intermediate | 11.23 | 6.43 | 5.33 | |
| High | 9.34 | | | |
| By CD4 count (cells/μL)* | | | | |
| ≤200 | | | | 7.95 |
| 201–350 | | | | 5.15 |
| 351–500 | | | | 4.52 |
| >500 | | | | 4.45 |
| Weighted average§ | | | | 5.83 |
| **Discounted (3%) treatment costs saved per infection averted (2011 dollars)** | | | | |
| Low | $153,000‖ | | | |
| Intermediate | $342,000 | $391,000¶ | N/A | |
| High | $521,000 | | | |
| By CD4 count (cells/μL)* | | | | |
| ≤200 | | | | $253,000 |
| 201–350 | | | | $327,000 |
| 351–500 | | | | $372,000 |
| >500 | | | | $402,000 |
| Weighted average§ | | | | $330,000 |

*CD4 count at diagnosis, entry into care, and initiation of ART. Those diagnosed and entering care above a CD4 count of 500 cells per microliter were assumed to initiate ART when their CD4 count reached that level.

†Calculated from Holtgrave and Pinkerton[6] with an assumed age at infection of 26 years, the number of years with infection as stated in the analysis, and a life expectancy without infection of 69.9 years.

‡Discounted life years saved reported in parentheses.

§Derived from proportions of the United States HIV-infected population diagnosed in the various CD4 count categories[17] where the proportions were adjusted to exclude cases with unknown stage of disease at diagnosis. The reported proportion of persons diagnosed with a CD4 count from 200 to 499 cells per microliter was divided equally between the categories of 201–350 and 351–500 cells per microliter.

‖Updated to 2011 dollars.

¶Derived from Schackman et al[12] updated to 2011 dollars.

infection in their 3 scenarios. Using a 3% discount rate, these researchers estimated values of discounted treatment costs saved and QALYs gained from preventing an infection in their 3 scenarios of $153,000/13.18 QALYs, $342,000/11.23 QALYs, and $521,000/9.34 QALYS (costs updated to 2011 dollars). The higher cost treatment scenarios resulted in a higher quality of life for HIV-infected persons and, therefore, fewer QALYs lost from infection or gained from preventing an infection.

In 2006, Schackman et al,[12] using the Cost-Effectiveness of Preventing AIDS Complications model and utilization data from HIV Research Network sites, estimated discounted lifetime HIV treatment costs from the time of infection of $303,100 (2004 dollars, updated to $391,000 in 2011 dollars). Hutchinson et al[13] used this estimate for treatment costs saved in their analysis of screening for acute HIV infection. Assuming infection at age 35 and drawing again on the Schackman et al[12] study, Hutchinson et al[13] assumed an additional life expectancy of 32 years for infected persons compared with 44.6 years for the uninfected. Using utility weights from Tengs and Lin,[14] these researchers estimated that 6.43 discounted QALYs were saved per infection averted. Holtgrave et al,[15] using a similar methodology with infection at an age of 35 years, a life expectancy of 28 years with infection, and 37 years without infection and utility weights from Sanders et al[1], estimated that 5.33 QALYs were saved per infection averted.

Farnham et al[16] used the Prevention and Transmission of HIV/AIDS (PATH) model, a Monte Carlo health state transition simulation of HIV-infected persons, to estimate mean lifetime treatment costs, mean life expectancy after infection, and mean life years and discounted QALYs lost per infection for 10,000 simulated HIV-infected persons under 4 CD4 count scenarios characterized by CD4 count (cells/μL) at diagnosis and entry into care: I, ≤200; II, 201–350; III, 351–500; and IV, 501–900. These researchers assumed that the HIV diagnoses were uniformly distributed across the CD4 count range in each category and that all persons entered care at the time of

diagnosis, initiated treatment with ART at a CD4 count of 500 cells per microliter or at diagnosis if at a lower CD4 count, and remained in care continuously. Estimated additional life expectancy for a person infected at age 35 years ranged from 30.73 to 38.08 years across the 4 diagnosis/entry categories. Applying the results from the study, these researchers estimated that life years saved per infection averted varied from 14.32 to 6.97 (6.07 to 2.97 discounted) and discounted QALYS gained per infection averted ranged from 7.95 to 4.45. Lifetime treatment costs saved per infection averted ranged from $253,000 to $402,000 across the 4 scenarios (Table 1).

To reflect the current state of HIV diagnosis and treatment in the United States, we developed weighted averages of discounted treatment costs saved and QALYS gained per infection averted across the 4 diagnosis/entry categories in the PATH model analysis. We used a surveillance estimate[17] of the distribution of CD4 counts at diagnosis for the US HIV-infected population based on data from 14 jurisdictions (12 states and 2 cities) that reported complete CD4 and viral load laboratory results. Adjusting the reported proportions to exclude cases where the stage at diagnosis was unknown and dividing the reported proportion of persons diagnosed with a CD4 count from 200 to 499 cells per microliter equally between the categories of 201–350 and 351–500 cells per microliter, we estimated the proportions of persons diagnosed from low to high CD4 count categories as follows: 35.1%, 19.1%, 19.1%, and 26.7%. The calculated weighted averages were $330,000 for discounted treatment costs and 5.83 discounted QALYs saved per infection averted.

The results in Table 1 indicate that the QALYs lost from HIV infection or the QALYs saved per infection averted have decreased substantially since the beginning of the ART era and are expected to decrease further under test and treat policies.[18,19] The PATH model results indicated that only 4.45 QALYs per person were lost if persons with HIV were diagnosed at CD4 counts greater than 500 cells per microliter and treatment with ART was initiated at a count of 500 cells per microliter. Based on the actual distribution of CD4 counts at diagnosis, the average number of QALYs lost per HIV-infected person in the United States is approximately 5.83, given that substantial numbers of persons are still diagnosed late in their disease stage. The QALYs lost from infection in the PATH model are also likely to be underestimates for the United States, given the assumption of optimal care made in that analysis. Data for the United States suggest that approximately 82% of infected persons are diagnosed, 66% are linked to care, 37% are retained in care, 33% have been prescribed ART, and 25% have suppressed viral load.[20–22]

Lifetime treatment costs for optimal care begun early in the course of infection have increased due to the longer life expectancy of HIV-infected persons from treatment with ART regimens. However, the widespread use of ART has decreased the rate of AIDS-defining opportunistic infections, whereas other chronic diseases and non-HIV conditions are increasingly important causes of morbidity and mortality among HIV-infected persons.[23–25] The presence of these comorbidities is changing the definition of lifetime HIV treatment costs and will affect what is included in future estimates. Likewise, the QALY estimates in Table 1 are largely based on utility values derived from clinical disease categories.[14] Recent research suggests that health states defined by clinical events may be less applicable with newer HIV treatments and the longer life expectancy of HIV-infected persons.[26]

The updated estimates in Table 1 show that the lifetime costs of early and optimal treatment have increased, whereas the lifetime QALYs from HIV infection have decreased. However, the updated average treatment costs and QALYs are similar to earlier estimates, given the ongoing problem of late diagnosis. The goal in the United States is to diagnose all HIV-infected persons earlier in the course of their disease, link them to care, and achieve viral load suppression, so that the QALYs lost from infection are reduced even further.[27] Economic evaluations of HIV prevention interventions should reflect these improvements in diagnosing and treating persons with HIV infection.

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