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The Effect of Prophylaxis on Pediatric HIV Costs

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Abstract

The objective of this study was to determine and compare the cost to treat HIV(+) and HIV(−) pediatric patients both before and after HIV prophylaxis became the standard of care. Retrospective chart review of a pediatric HIV/AIDS specialty clinic's medical charts was conducted for clinical and healthcare utilization data on 125 children diagnosed from 1986–2007. Mean HIV-related costs were compared using bootstrapped t-tests for children born in the pre-prophylaxis (1979–1993) and prophylaxis eras (1994–2007). Patients were also stratified into two categories based on death during the follow-up period. Lastly, national cost-savings were estimated using mean costs, national number of at-risk births and national perinatal HIV transmission rates in each era. For HIV(+) children, mean annual per patient treatment cost was \$15,067 (95% CI: \$10,169–\$19,965) in the pre-prophylaxis era (n=40) and \$14,959 (95% CI: \$9,140–\$20,779) in the prophylaxis era (n=14), difference not statistically significant (p>0.05). For HIV(−) children, mean annual per patient treatment cost was \$204 (95% CI: −\$219–\$627) for the pre-prophylaxis era (n=2) and \$427 (95% CI: \$277–\$579) for the prophylaxis era (n=69), different statistically significant (p<0.05). A projected cost-savings of \$16–23 million annually in the US was observed due to the adoption of prophylaxis treatment guidelines in pediatric HIV care. The prophylaxis era of pediatric HIV treatment has been successful in decreasing perinatal HIV transmission and mortality, as reflected by clinical trials and national cost-savings data, and emphasizes the value of the rapid adoption of evidence-based practice guidelines.

Keywords

HIV; AIDS; Pediatric; Cost; Cost-savings; Prophylaxis

Introduction

Significant therapeutic advances in HIV/AIDS treatment and prophylaxis from the 1980s to today changed the disease evolution from a rapidly fatal, acute infection to today's chronic illness. This study will determine how the cost of pediatric HIV care has changed with these therapeutic innovations.

Early in the HIV epidemic, children with perinatal HIV-infection had delayed diagnosis and many were in critical condition requiring substantial and costly healthcare resources for diagnosis and treatment. They had long hospital stays, suffering early mortality (Hegarty et al., 1988; Hellinger, 1993; Hsia, Fleishman, East & Hellinger, 1995; Kourtis, Bansil, Posner, Johnson & Jamieson, 2007; Parrott, 1991; Centers for Disease Control [CDC], 1986). Many early studies estimated treatment costs of pediatric HIV demonstrated that care was costly due to morbidity, mortality rather than from treatment options (Hegarty et al., 1988; Hellinger, 1993; Hsia et al., 1995; Parrott, 1991). They often used inpatient hospitalization records alone to estimate costs and mean pediatric HIV costs were between \$34,713 (Parrott, 1991) and \$37,928 (Hsia et al., 1995) annually.

In contrast, present care standards have significantly improved outcomes for children born to HIV-infected women resulting in greatly reduced mortality and morbidity. (Kourtis et al., 2007; Viani, Araneta, Deville & Spector, 2004; Patel et al., 2008). Furthermore, mother-to-child transmission (MTCT) rates in the U.S. are reduced to approximately 1% with the combination of refined treatments and perinatal and prophylaxis guidelines (Connor et al., 1994; Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children [Working Group], 2010; Mofenson, 2002; McGown & Shah, 2000; Wade et al., 1998; Cooper et al., 2002; Sharma & Spearman, 2008; Committee on Pediatric AIDS, 2008). Centers for Disease Control & Prevention's most recent data (CDC, 2007), have identified 159 new cases of children (<13 years old) living with HIV/AIDS (87.4% perinatally acquired) and 9,209 cumulative cases of pediatric AIDS. In recent years, due to the implementation of perinatal and prophylaxis protocols, most research has focused on clinical outcomes but little has been done to accurately assess the costs of care.

One exception is a study by Sansom et al. (2006) which looked at pediatric HIV costs in 1995 and 2001 in 6 US cities using retrospective medical records. They found a 2001 annual cost of \$12,663 per perinatally HIV-infected child. Unfortunately, Sansom et al did not include outpatient treatment costs and their study was conducted too early to include Highly Active Anti-Retroviral Therapy (HAART), both of which are a large portion of costs for HIV(+) children today.

The objective of this study is to determine and compare the cost to treat HIV(+) and HIV(-) pediatric patients both before and after prophylaxis became the standard of care and aims to improve upon previous cost estimates. This study will enhance our knowledge of pediatric HIV costs by 1) providing the most current cost estimates in the US, 2) describing the cost-savings from implementation of evidence-based prophylaxis guidelines, 3) outlining mortality effects on cost for pediatric HIV(+) patients, and 4) providing new cost estimates for HIV(-) pediatric patients at-risk for HIV infection.

Methods

Design

This was a retrospective, longitudinal, observational study utilizing patient chart review at one referral medical center to collect healthcare utilization data on babies born to HIV(+) mothers from 1986–2007.

Participants

Participants were drawn from a complete sample of babies born to an HIV-infected or high-risk mother and treated at the UCSF Pediatric HIV/AIDS Treatment Center from January 1986 to June 2007. Inclusion criteria specified birth or treatment at UCSF, complete medical records for at least one year from birth to 6/30/2007, perinatally acquired HIV, age 18 years or younger at study entry, and birth from an HIV(+) or high-risk mother (defined as mothers known as intravenous drug users or engaging in unprotected sexual activity with HIV(+) persons or intravenous drug users). Patients were excluded if they received the majority of their HIV-related care outside of the center, moving or transferred for most care or had incomplete or unavailable medical records, leaving 137 study patients. After restricting the sample to those with a minimum of 7 years of follow-up but including those who died, the final sample consisted of 125 patients.

Cost Variables and Procedures

We collected demographics, including basic disease-related information, and healthcare utilization from clinic medical records. The three main components of the total cost of HIV-related care were inpatient hospitalizations, outpatient provider visits and drug therapies. Once all utilization data were collected, national costs were applied to each care type. An annual and cumulative cost was determined for each patient. Each of our three cost categories (inpatient, outpatient and drug) were adjusted to constant 2007 dollars using the medical-care component of the consumer price index (CPI) (US Department of Labor Statistics [USDLS], 2009).

To estimate inpatient cost, the dates of each hospitalization with corresponding discharge diagnoses and length of stay were collected. Costs were applied using ICD-9 (International Classification of Diseases, Ninth Revision) codes and the 1999 KID (Kids Inpatient Database) Healthcare Cost and Utilization Project (HCUP) database. The KID is a subset of HCUP which includes a sample of pediatric discharges from over 2,500 community hospitals in the US. It provides cost and utilization information related to the clinical resources used during a typical hospital stay and is weighted to produce national estimates (CDC, 1994; Agency for Healthcare Research and Quality [AHRQ], 2009).

For outpatient cost estimates, the date, type and reason of each provider visit were collected. Costs for each visit were applied by Common Procedural Terminology (CPT) codes using the 1999 Medical Fee Schedule (MFS) (Medical Fees in the United States [MFUS], 1999). The MFS is a listing of CPT codes with corresponding Medicare fees and is regarded as a conservative cost estimate as they represent the lowest reimbursable costs. HIV-related outpatient provider visits included outpatient physician, emergency department, urgent care,

nutrition, psychiatry/psychology, dental, ophthalmology, social worker, nurse management, HIV treatment team meetings as well as miscellaneous consults and specialist referrals.

All HIV/AIDS-related drugs prescribed at each office visit (including strength, dose form, and duration) were recorded. HIV/AIDS-related drugs included treatment of HIV/AIDS treatments, complications and treatment of adverse effects of HIV/AIDS-related medications. We used the mean Average Wholesale Price (AWP) of all available brand and generic forms of drugs as listed in the Drug Topics RedBook (1999), inflated to 2007 dollars using the CPI (USDLS, 2009) minus a mean manufacturer rebate of 17%. Costs for drugs receiving FDA approval after 1999 were costed using the RedBook in which the drug first appeared. If a drug dose, interval or duration was missing it was extrapolated by pharmacists using the Physician's Desk Reference (PDR) standard dosing for the child's height, weight and age (Physicians' Desk Reference [PDR], 2007).

For patients with missing drug cost data (6.9%) in a given year, we imputed an annual drug cost if their average drug cost had a normal distribution or remained constant over their entire follow-up period, decreasing missing drug cost observations to 4.3%. All other cost variables (inpatient and outpatient costs) had less than 3% missing observations so did not require imputation.

Analysis

Patients were divided into two mutually exclusive historical time categories: those born in the pre-prophylaxis era (1/1/1979–12/31/1993) and those born in the prophylaxis era (1/1/1994–6/30/2007). Patients were also stratified by HIV status, and in an ad hoc analysis, were stratified by mortality status (those who died and those who remained alive during the 7-year follow-up period).

The arithmetic mean annual and cumulative per patient HIV-related treatment cost was calculated for each patient by HIV status and prophylaxis era. In order to determine if statistically significant differences existed between our strata, the mean costs were bootstrapped before conducting t-tests. Bootstrapping of mean costs allows for a fair comparison between groups given that cost data is inherently skewed (Wooldridge, 2002).

To estimate national cost-savings, both mean annual and cumulative per patient costs, stratified by era and HIV status, were multiplied by the HIV infection rates from each era (pre: 25.5%, post: 8%) (Connor et al., 1994). This provided individual patient costs, which were subsequently multiplied by the estimated annual number of infants at risk for infection (7,000 per year) (Davis et al., 1995), resulting in the total estimated costs for the national population of at-risk patients. The difference in costs between the two eras yielded the estimated annual national treatment related cost-savings in pediatric HIV treatment due to prophylaxis. Sensitivity analysis for cost-savings incorporated the current MTCT transmission rate, 1%, in contrast to the 8.3% rate described in 1994 by the Pediatric AIDS Clinical Trials Group (PACTG), now known as the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Group (Connor et al., 1994; McGowan & Shah, 2000; Wade et al., 1998; Cooper et al., 2002; Sharma & Spearman, 2008; Committee on Pediatric AIDS, 2008).

To obtain a robust mean annual cost per patient, the longest follow-up time was desired. Mean follow-up time for HIV(+) patients was 6.58 years therefore a rounded 7 years minimum follow-up was used to select the final sample for analysis. However, HIV(+) patients who died during the 7-year follow-up had a significant impact on overall costs, so were included in the final sample in our main analysis. HIV(−) patients, on average, generated costs only for 2 years, as is consistent with current guidelines indicating an 18 month follow-up period to definitively rule out HIV-infection (Read & Committee on Pediatric AIDS, 2007). A zero annual HIV cost was assumed for each HIV(−) patient for each year of care after HIV-related treatment had ceased resulting in an equivalent 7-year follow-up period.

Results

The study period covered 21 years of data (1986–2007). There were 54 HIV(+) (43.2%) and 71 HIV(−) (56.8%) patients in the sample. Table 1 shows patient characteristics by HIV status and prophylaxis eras. There were 40 HIV(+) (95.2%) and 2 HIV(−) (4.8%) patients born in the pre-prophylaxis era (1979–1993) versus 14 HIV(+) (16.9%) and 69 HIV(−) (83.1%) born in the prophylaxis era (1994–2007). The mean age at diagnosis for an HIV(+) patient in the pre-prophylaxis era was 3.34 years (0.00–13.01) and the mean age at diagnosis for an HIV(+) patient in the prophylaxis era was 0.79 years (0.00–5.20), reflecting earlier diagnoses in the prophylaxis era. Eleven HIV(+) patients died in the pre-prophylaxis era and 3 in the prophylaxis era.

Treatment Costs by Prophylaxis Era

Table 2 shows estimated cumulative and annual costs by HIV status and prophylaxis era. For HIV(+) patients in the pre-prophylaxis era, HIV treatment cost was \$15,242/patient (95% CI: \$10,085 – \$20,399) and for \$14,959 for HIV(+) patients in the prophylaxis era (95% CI: \$9,135 – \$20,784), difference was not statistically significant ($p=0.945$) (Table 2). For HIV(−) patients in the pre-prophylaxis era, cost was \$204/patient (95% CI: \$137 – \$270) and \$438 for HIV(−) patients in the prophylaxis era (95% CI: \$283 – \$593) the difference here was statistically significant ($p<0.05$). When comparing HIV(+) to HIV(−) patients within the same era, the mean annual costs were significantly different ($p<0.001$) for both eras.

Mortality Effects

Table 3 demonstrated that mortality had a significant effect on increasing total HIV costs.. In the sub-sample of patients alive during follow-up, the pre-prophylaxis era treatment cost decreased from \$15,242/patient/year (95% CI: \$10,085 – \$20,399) to \$8,661 (95% CI: \$6,001 – \$11,322) and in the prophylaxis era decreased from \$14,959 (95% CI: \$9,135 – \$20,784) to \$11,593 (95% CI: \$8,427 – \$14,759). In contrast, the HIV treatment cost/patient/year in the sub-sample of patients including deaths increased to \$33,667 (95% CI: \$21,278 – \$46,057) and \$27,304 (95% CI: \$3,753 – \$50,872) in the pre- and prophylaxis eras respectively. There was a statistically significant difference in ($p<0.001$) cost between the sub-samples of those who lived and those who died during follow-up in the pre-

prophylaxis era demonstrating the high cost of mortality. This was not a statistically significant difference in the prophylaxis era though trended ($p=0.149$).

Costs by Era, HIV status and Type of Utilization

The proportion of each cost type varied according to HIV status, prophylaxis era and mortality status as shown in Table 4. For HIV(+) patients in the pre-prophylaxis era (main analysis sample: both patients who died had survived the 7-year follow-up period), 12% was outpatient, 39% was inpatient and 49% was drug cost. This is in contrast to the sub-sample of patients who remained alive during follow-up, for which 14% was outpatient cost, 26% was inpatient and 60% was drug cost, demonstrating the lower inpatient utilization and high drug utilization of patients who live. These cost patterns are similar during the prophylaxis era as well. The HIV(+) patient costs (main analysis sample) in the prophylaxis era were 10% outpatient, 46% inpatient and 44% drug cost, while in the sub-sample of patients who remained alive, were 14% outpatient, 16% inpatient and 70% drug cost.

National Cost Savings

Applying the mean annual cost per patient for each strata to the number of infants at risk (7,000/year) (Davis et al., 1995) and the HIV transmission rate in each era (25.5% and 8.3%, respectively) (Connor et al., 1994), resulted in an annual cost-savings in patient treatment cost alone of over \$16 million due to the use of prophylaxis regimens. In sensitivity analysis, using the current MTCT transmission rate (1%) the cost-savings in patient treatment was found to be as high as \$23 million annually (McGowan & Shah, 2000; Wade et al., 1998; Cooper et al., 2002; Sharma & Spearman, 2008; Committee on Pediatric AIDS, 2008). Cumulative HIV treatment cost-savings over the total 7-year follow-up period for the same at-risk population of infants are over \$115 million to \$167 million using HIV transmission rates of 8.3% and 1%, respectively.

Discussion

We provide a more current estimate of HIV treatment costs for both HIV(+) and HIV(-) pediatric patients and demonstrate that they did not significantly differ across the two treatment eras. However, we did find treatments cost estimates are very sensitive to mortality and its associated high costs. National pediatric patient HIV treatment cost-savings are estimated to be \$16–23 million annually which can be attributed to the decreased MTCT of HIV and the savings from decreased mortality. These cost-savings result despite the treatment guidelines advocating for the initiation of prophylactic drug regimens, a more costly option than the previous standard of practice prior to 1994, as well as the current costly but effective drug treatments (HAART). Both the high cost associated with mortality and the greater frequency of deaths in the HIV(+) patients in the pre-prophylaxis era have been reduced, offsetting the higher costs of treatment in the prophylaxis era; keeping mean treatment costs the same across the eras.

The cost-savings identified here are both informative and valuable, especially in light of recent state and federal budget cuts to healthcare funding, as well as national interests in restructuring the US healthcare system. In our patient sample, approximately 90% of

patients have state- and nationally-funded insurance to pay for their healthcare (such as MediCal / Medicaid, California Children's Services, and similar public programs in other states). As such, it is essential that policymakers and other key decision leaders be informed of the current costs of care and the degree to which new treatments reduce long-term costs in order to create policy and align budgets appropriately.

There were many studies (Hegarty et al., 1988; Parrott, 1991; Hsia et al., 1995; Hellinger, 1993) which aimed to estimate the cost of treating pediatric HIV early in the epidemic. At that time, HIV-infected children with perinatally-acquired disease were often undiagnosed until the disease process had advanced to the degree that hospitalization was necessary. Given that early in the pandemic, HIV treatment was primarily conducted in the hospital, initial cost studies used inpatient hospitalization records alone to estimate lifetime cost. In 1988, Hegarty et al. estimated a mean lifetime cost of \$90,347 per child. This estimate is similar to what we found in the pre-prophylaxis era (\$106,694) for cumulative cost. They reported a mortality rate of 9/32 patients (28.1%) which is also comparable to our pre-prophylaxis era mortality rate of 27.5%. In 1991, Parrott et al. found that pediatric HIV/AIDS patients cost \$34,713 annually. These cost projections are higher than what we have found in the pre-prophylaxis era (\$15,242) but comparable to what we found in our sub-sample of patients who died (\$33,667). Lastly, Hsai et al. (1995) estimated mean annual charges for HIV(+) children and found total annual charges to be \$37,928 per patient, similar to Parrot et al. (1991) and our sub-sample of patients who died. However, Hsai et al. (1995) found that HIV(+) children who had not progressed to AIDS only cost \$9,382. This estimate is similar to what we report for HIV(+) children in the pre-prophylaxis era who did not die during follow-up (\$8,661), a healthier sub-sample such as Hsia's HIV(+) children who had not progressed to AIDS .

There are fewer studies which examine cost in the prophylaxis era (Sansom et al., 2006; Wilson et al., 2007). Sansom et al. (2006) utilized patients from the PSD study sponsored by the CDC. They found a mean 2001 annual cost of \$12,663 per perinatally HIV-infected child: \$2,164 (17%) for hospitalizations, \$9,505 (75%) for HIV-related prescription drugs and \$994 (8%) for laboratory tests. This is similar to our mean annual cost of \$14,959 per HIV(+) patient in the prophylaxis era. However, our breakdown of cost type is somewhat different from that found by Sansom et al. (2006) at \$6,894 (46%) inpatient cost, \$6,541 (44%) drug cost and \$1,525 (10%) outpatient cost. This difference could be due to the fact that Samson et al. (2006) only used patients alive and enrolled in the PSD in 2001. Since our cost breakdown includes patients who died, we report a much higher utilization of inpatient resources and cost. Also important to note, Sansom and colleagues did not include either outpatient treatment costs or HAART therapy in their study. Had these costs been included, Sansom's mean annual cost would likely be similar to what we report here.

Our study has several limitations. Results are from a single medical center and therefore may not be representative of national experience. In addition, our costs may be underestimated as some care may have been provided but not documented in the clinic records, and we were not able to include laboratory costs due to time and budget constraints.

Another factor to consider is how to best include patients who died in our cost estimates so as not to bias the results while including a long follow-up period (7 years). We chose to include them but if we were to reduce the follow-up period to 3 years, the mean annual cost for HIV(+) patients in the pre-prophylaxis era would remain relatively constant; however, the respective mean annual cost in the prophylaxis era would increase. More specifically, there would be 42 HIV(+) pre-prophylaxis era patients with a mean annual cost of \$14,541 and 20 HIV(+) prophylaxis era patients with a mean annual cost of \$23,656. The higher cost reflected in the prophylaxis era, with this analysis, is likely attributed to patients who were severely ill, thus having higher costs, and subsequently transferred out of UCSF care for various reasons.

Finally, an important limitation is our small sample size, particularly for the number of HIV(−) patients within the pre-prophylaxis era. For example, of our 32 patients diagnosed in the pre-prophylaxis era, only 2 were HIV(−) patients. According to the MTCT transmission rates of that era, we would have expected 8 HIV(−) patients in this strata. Given our patients are from an HIV/AIDS specialty clinic at an academic medical center, we likely had a higher proportion of HIV(+) patients than national averages. It is unlikely that our small sample size affected our results greatly; however, because the HIV(−) patients within pre-prophylaxis era had zero costs for HIV-related care for the majority of their follow-up period, having too few HIV(−) patients in the sample may artificially increase final cost-savings results.

Conclusion

This study provides a longitudinal pediatric HIV treatment cost comparison in the pre- and prophylaxis eras and estimates annual national cost-savings of \$16–23 million. These data demonstrate the substantial impact that HIV(+) patient deaths have on overall costs in both eras. While the total HIV treatment costs are not significantly different between the two eras, the reduction in the perinatal HIV transmission rate and the savings from the reduction in deaths are the two likely driving forces responsible for the considerable national cost-savings. The prophylaxis era of pediatric HIV treatment has been successful in decreasing perinatal HIV transmission and mortality as well as national pediatric HIV treatment costs, and further emphasizes the value of the rapid adoption of evidence-based practice guidelines.

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References

- Agency for Healthcare Research and Quality. HCUPnet: National Statistics on Children. 2009. Retrieved from HCUPnet website: <http://hcupnet.ahrq.gov/>

- Centers for Disease Control and Prevention. Current Trends Update: Acquired Immunodeficiency Syndrome--United States. MMWR Weekly. 1986; 35(2):17–21. Retrieved from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00000667.htm>.
- Centers for Disease Control and Prevention. Revised classification system for human immunodeficiency virus infection in children less than 13 years of age: official addenda: human immunodeficiency virus infection codes and official guidelines for coding and reporting ICD-9-CM. MMWR Recommendations & Reports. 1994; 43(RR-12):1–10. Retrieved from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00032890.htm>.
- Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2009; 2007. p. 1–63. Retrieved online: <http://cdc.gov/hiv/topics/surveillance/resources/reports/2007report/pdf/2007SurveillanceReport.pdf>
- Committee on Pediatric AIDS. HIV testing and prophylaxis to prevent mother-to-child transmission in the United States. Pediatrics. 2008; 122(5):1127–1134. [PubMed: 18977995]
- Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, VanDyke R, Bey M, Shearer W, Jacobson RL, Jimenez E, O'Neill E, Bazin B, Delfraissy JF, Culnane M, Coombs R, Elkins M, Moye J, Stratton P, Balsley J. Reduction of maternal-infant transmission of Human Immunodeficiency Virus Type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med. 1994; 331(18):1173–1180. [PubMed: 7935654]
- Cooper ER, Charurat M, Mofenson L, Hanson IC, Pitt J, Diaz C, Hayani K, Handelsman E, Smeriglio V, Hoff R, Blattner W. Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. JAIDS. 2002; 29(5):484–494. [PubMed: 11981365]
- Davis SF, Byers RH Jr, Lindegren ML, Caldwell MB, Karon JM, Gwinn M. Prevalence and incidence of vertically acquired HIV infection in the United States. JAMA. 1995; 274(12):952–955. [PubMed: 7674525]
- Drug Topics Redbook. Montvale, NJ: Physicians' Desk Reference (PDR), Inc.; 1999.
- Hegarty JD, Abrams EJ, Hutchinson VE, Nicholas SW, Suarez MS, Heagarty MC. The medical care costs of human immunodeficiency virus-infected children in Harlem. JAMA. 1988; 260(13):1901–1905. [PubMed: 3418851]
- Hellinger FJ. The lifetime cost of treating a person with HIV. JAMA. 1993; 270(4):474–478. [PubMed: 8320787]
- Hsia DC, Fleishman JA, East JA, Hellinger FJ. Pediatric human immunodeficiency virus infection: Recent evidence on the utilization and costs of health services. Arch Pediatr Adolesc Med. 1995; 149(5):489–496. [PubMed: 7735400]
- Kourtis AP, Bansil P, Posner SF, Johnson C, Jamieson DJ. Trends in hospitalizations of HIV-infected children and adolescents in the United States: analysis of data from the 1994–2003 Nationwide Inpatient Sample. Pediatrics. 2007; 120(2):e236–e243. [PubMed: 17606535]
- McGowan JP, Shah SS. Prevention of perinatal HIV transmission during pregnancy. J Antimicrob Chemother. 2000; 46(5):657–668. [PubMed: 11062184]
- Medical fees in the United States: Nationwide charges for medicine, surgery, laboratory, radiology and allied health services. Los Angeles, CA: Practice Management Information Corporation (PMIC); 1999.
- Mofenson L. U.S. Public Health Service Task Force recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. MMWR Recommendations & Reports. 2002; 51(RR-18):1–40. Retrieved from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5118a1.htm>.
- Parrott RH. Childhood human immunodeficiency virus infection: the spectrum of costs. JAIDS. 1991; 4(2):122–129.
- Patel K, Hernan MA, Williams PL, Seeger JD, McIntosh K, Van Dyke RB, Seage GR III. Long-term effectiveness of highly active antiretroviral therapy on the survival of children and adolescents with HIV infection: A 10-year follow-up study. Clin Infect Dis. 2008; 46(4):507–515.
- Physicians' Desk Reference. Montvale, NJ: Physicians' Desk Reference (PDR), Inc.; 2007.

- Read JS. Committee on Pediatric AIDS. Diagnosis of HIV-1 infection in children younger than 18 months in the United States. *Pediatrics*. 2007; 120(6):e1547–e1562. [PubMed: 18055670]
- Sansom SL, Anderson JE, Farnham PG, Dominguez K, Soorapanth S, Clark J, Sukalac T, Earp MJ, Bohannon B, Fowler MG. Updated estimates of healthcare utilization and costs among perinatally HIV-infected children. *JAIDS*. 2006; 41(4):521–526. [PubMed: 16652063]
- Sharma D, Spearman P. The impact of cesarean delivery on transmission of infectious agents to the neonate. *Clinics in Perinatology*. 2008; 35(2):407–420. [PubMed: 18456077]
- US Department of Labor Statistics. Databases, tables and calculators by subject - inflation & prices. 2009. Retrieved from Bureau of Labor Statistics website: <http://www.bls.gov/data/>
- Viani RM, Araneta MR, Deville JG, Spector SA. Decrease in hospitalization and mortality rates among children with perinatally acquired HIV type 1 infection receiving highly active antiretroviral therapy. *Clin Infect Dis*. 2004; 39(5):725–731. [PubMed: 15356789]
- Wade NA, Birkhead GS, Warren BL, Charbonneau TT, French PT, Wang L, Baum JB, Tesoriero JM, Savicki R. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med*. 1998; 339(20):1409–1414. [PubMed: 9811915]
- Wilson LS, Basu R, Christenson M, Hensic L, Paoli C, Wara D, Moskowitz JT. Pediatric HIV costs across three treatment eras from 1986 to 2007. *Pediatrics*. 2010; 126(3):e241–e249.
- Wooldridge, JM. *Econometric Analysis of Cross Section and Panel Data*. Cambridge MA: MIT Press; 2002.
- Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the use of antiretroviral agents in pediatric HIV infection. 2010. p. 1-219. Retrieved from: <http://aidsinfo.nih.gov/ContentFiles/PediatricGuidelines.pdf>

Table 1

Characteristics of Pediatric Patients at UCSF from 1986–2007 Stratified by HIV Status and Prophylaxis Era, n=125

Characteristics	HIV (+)		HIV (–)		Total
	Pre-Prophylaxis Era (n=40)	Prophylaxis Era (n=14)	Pre-Prophylaxis Era (n=2)	Prophylaxis Era (n=69)	
Gender (%)					
Male	22 (55)	1 (7.1)	0 (0)	37 (53.6)	60 (48)
Female	18 (45)	13 (92.9)	2 (100)	32 (46.4)	65 (52)
Race/Ethnicity (%)					
Asian	1 (2.5)	0 (0)	0 (0)	2 (2.9)	3 (2.4)
Black	11 (27.5)	5 (35.7)	0 (0)	18 (26.1)	34 (27.2)
Hispanic	6 (15)	4 (28.6)	0 (0)	15 (21.7)	25 (20)
White	7 (17.5)	4 (28.6)	0 (0)	13 (18.8)	24 (19.2)
Unknown/Other	15 (37.5)	1 (7.1)	2 (100)	21 (30.5)	39 (31.2)
Mean age at confirming diagnosis (range)	3.34 yrs (0.00–13.01 yrs)	0.79 rs (0.00–5.20 yrs)	n/a	n/a	2.68 yrs (0.00–13.01 yrs)
Mean age at last observation (range)	9.13 rs (6.00–19.01 yrs)	6.99 yrs (6.00–11.20 yrs)	1.14 yrs (1.11–1.17 yrs)	2.25 yr (0.07–6.90 yrs)	4.71 yrs (0.07–19.01 yrs)
Number of patients who died (%)	11 (27.5%)	3 (21.4%)	0	0	14 (11.2%)
Mean # of inpatient days during follow-up (range)	32.9 (0 – 202)	37 (0 – 241)	0	0.65 (0 – 15)	15.03 (0 – 241)
Any hospitalization during the follow-up period (%)	29 patients (72.5%)	11 patients (78.8%)	0	6 patients (8.7%)	46 patients (26.8%)

Table 2

Mean Cumulative Cost Per Patient, Mean Annual Cost Per Patient and Mean Cost Per Patient by Year After Diagnosis Stratified by HIV Status & Prophylaxis Era

	Pre-Prophylaxis Era			Prophylaxis Era		
	HIV(+) n=40 mean (95% CI)	HIV(-) n=2 mean (95% CI)	Estimated US National HIV(+) Cost Total Per Year*	HIV(+) n=14 mean (95% CI)	HIV(-) n=69 mean (95% CI)	Estimated US National HIV(+) Cost Total Per Year**
Cumulative Mean Cost Per Patient	\$106,694 ^{†‡} (\$70,598-\$142,790)	\$1,427 ^{†~} (\$962-\$1,893)	\$162,379,154	\$104,716 ^{†‡} (\$63,942-\$145,490)	\$3,064 ^{†~} (\$1,979-\$4,148)	\$6,322,287
Annual Mean Cost Per Patient	\$15,242 ^{†‡} (\$10,085-\$20,399)	\$204 ^{†~} (\$137-\$270)	\$23,860,753	\$14,959 ^{†‡} (\$9,135-\$20,784)	\$438 ^{†~} (\$283-\$593)	\$929,009
Year 0-1 After Diagnosis	\$9,852 ^{†‡} (\$4,158-\$15,547)	\$741 ^{†~} (\$315-\$1,167)	\$17,585,820	\$23,843 ^{^‡} (\$2,412-\$45,274) #	\$1,967 ^{^~} (\$1,066-\$2,869)	\$1,669,010
Year 1-2 After Diagnosis	\$13,715 ^{†‡} (\$6,965-\$20,464) #	\$686 ^{†‡} (\$647-\$725)	\$23,800,057	\$16,283 ^{^‡} (\$3,099-\$29,466)	\$655 ^{^‡} (\$391-\$920)	\$1,108,094
Year 2-3 After Diagnosis	\$24,677 ^{†‡} (\$12,418-\$36,936) #	\$0 ^{†‡}	\$42,301,010	\$30,152 ^{†‡} (\$1,354-\$58,951) ##	\$332 ^{†‡} (-\$39-\$702)	\$2,026,909
Year 3-4 After Diagnosis	\$14,376 ^{†‡} (\$8,589-\$20,163) ##	\$0 ^{†~}	\$24,590,633	\$9,979 ^{†‡} (\$6,516-\$13,441)	\$48 ^{†~} (\$12-\$84)	\$666,838
Year 4-5 After Diagnosis	\$23,637 ^{†‡} (\$9,024-\$38,250) ###	\$0 ^{†~}	\$40,274,368	\$9,952 ^{†‡} (\$7,399-\$12,504)	\$41 ^{†~} (\$17-\$66)	\$659,398
Year 5-6 After Diagnosis	\$18,575 ^{†‡} (\$5,656-\$31,494) ###	\$0 ^{†~}	\$31,148,452	\$15,430 ^{†‡} (\$8,408-\$22,452)	\$23 ^{†~} (\$3-\$42)	\$1,014,690
Year 6-7 After Diagnosis	\$14,588 ^{†‡} (\$10,365-\$18,810)	\$0 ^{†‡}	\$24,128,683	\$12,692 ^{†‡} (\$8,152-\$17,231)	\$10 ^{†‡} (-\$1-\$22)	\$823,186

Note: Inferential statistics were completed with t-tests on bootstrapped means of above costs, p-values reported below.

^{†‡} p<0.01 when comparing HIV(+) to HIV(-) patients within the same era (both eras)

[^] p<0.05 when comparing HIV(+) to HIV(-) patients within the prophylaxis era

⁺ p>0.05 when comparing HIV(+) to HIV(-) patients within the prophylaxis era

[‡] $p > 0.05$ when comparing HIV(+) patients in the pre-prophylaxis era to HIV(-) patients in the prophylaxis era & HIV(-) patients in the pre-prophylaxis era to HIV(-) patients in the prophylaxis-era

[~] $p < 0.05$ when comparing HIV(-) patients in the pre-prophylaxis era to HIV(-) patients in the prophylaxis-era

* Costs from pre-prophylaxis era HIV(+) patients weighted according to US prevalence (25.5%), at-risk births (7000/yr) and annual mortality rate (Patel et al., 2008)

** Costs from prophylaxis era HIV(+) patients weighted according to US prevalence (1%), at risk births (7000/yr) and annual mortality rate (Patel et al., 2008)

For every # in a given follow-up year, one patient has died

Table 3

Mean Cumulative Cost Per Patient, Mean Annual Cost Per Patient and Mean Cost Per Patient by Year After Diagnosis for HIV(+) Patients Stratified by Prophylaxis Era & Sub-Samples With and Without Patient Deaths During Follow-Up

	Pre-Prophylaxis Era			Prophylaxis Era
	Those Who Died During Follow-Up n=11 mean (95% CI)	Those Who Did Not Die During Follow-Up n=29 mean (95% CI)	Those Who Died During Follow-Up n=3 mean ^{†‡} (95% CI)	Those Who Did Not Die During Follow-Up n=11 mean ^{†‡} (95% CI)
Mean Cumulative Cost Per Patient [‡]	\$235,672 ^{†‡} (\$148,946–\$322,398)	\$60,630 ^{†‡} (\$42,005–\$79,256)	\$191,125 ^{*‡} (\$26,148–\$356,103)	\$81,150 ^{*‡} (\$58,989–\$103,311)
Annual Mean Cost Per Patient [‡]	\$33,667 ^{†‡} (\$21,278–\$46,057)	\$8,661 ^{†‡} (\$6,001–\$11,322)	\$27,304 ^{*‡} (\$3,735–\$50,872)	\$11,593 ^{*‡} (\$8,427–\$14,759)
Year 0–1 After Diagnosis	\$22,208 ^{*‡} (\$3,363–\$41,052)	\$5,440 ^{*‡} (\$2,629–\$8,250)	\$73,551 ^{*‡} (\$–\$17,899–\$165,000) #	\$10,286 ^{*‡} (\$5,435–\$15,136)
Year 1–2 After Diagnosis	\$26,565 ^{*‡} (\$8,054–\$45,076) #	\$8,278 ^{*‡} (\$3,723–\$12,833)	\$49,548 ^{*‡} (\$–\$41,196–\$140,292)	\$10,234 ^{*‡} (\$5,023–\$15,445)
Year 2–3 After Diagnosis	\$68,544 ^{†‡} (\$37,585–\$99,503) #	\$8,430 ^{†‡} (\$4,819–\$12,042)	\$126,814 ^{**‡} (\$–\$16,402–\$270,030) ##	\$12,578 ^{**‡} (\$5,053–\$20,102)
Year 3–4 After Diagnosis	\$37,350 [†] (\$19,569–\$55,131) ###	\$8,038 ^{†‡} (\$5,441–\$10,635)	No Observations	\$9,979 [‡] (\$6,144–\$13,813)
Year 4–5 After Diagnosis	\$74,448 [†] (\$18,667–\$130,229) ####	\$9,620 ^{†‡} (\$6,805–\$12,435)	No Observations	\$9,952 [‡] (\$7,125–\$12,778)
Year 5–6 After Diagnosis	\$112,074 [†] (\$27,117–\$197,030) ###	\$8,903 ^{†‡} (\$6,320–\$11,485)	No Observations	\$15,430 [‡] (\$7,677–\$23,182)
Year 6–7 After Diagnosis	No Observations	\$14,589 [‡] (\$10,312–\$18,864)	No Observations	\$12,692 [‡] (\$7,691–\$17,693)

Note: Inferential statistics were completed with t-tests on bootstrapped means of above costs, p-values reported below.

[†] p<0.01 when comparing patients in the same era who died during follow-up with patients who did not die during follow-up (both eras)

^{*} p>0.05 when comparing patients in the same era who died during follow-up with patients who did not die during follow-up (both eras)

^{**} p<0.05 when comparing patients in the same era who died during follow-up with patients who did not die during follow-up (both eras)

[‡] p>0.05 when comparing patients in the pre-prophylaxis and prophylaxis eras (both samples)

For every # in a given follow-up year, one patient has died

Table 4
Mean Annual Cost Per Patient by Utilization Type Stratified by HIV Status, Prophylaxis Era & Mortality Status

	Pre-Prophylaxis			Prophylaxis		
	HIV(+) Sample (includes deaths) n=40	HIV(+) Sample w/o Deaths* n=29	HIV(-) Sample n=2	HIV(+) Sample (includes deaths) n=14	HIV(+) Sample w/o Deaths* n=11	HIV(-) Sample n=69
Outpatient Mean Cost (95% CI)	\$1,823 (\$1,343–\$2,303)	\$1,229 (\$910–\$1,547)	\$204 (–\$219–\$627)	\$1,525 (\$1,116–\$1,934)	\$1,578 (\$1,176–\$1,980)	\$258 (\$205–\$310)
Inpatient Mean Cost (95% CI)	\$6,055 (\$3,181–\$2,303)	\$2,317 (\$1,159–\$3,475)	\$0	\$6,894 (–\$258–\$14,046)	\$1,924 (\$308–\$3,539)	\$121 (–\$2–\$244)
Drug Mean Cost (95% CI)	\$7,511 (\$3,594–\$9,032)	\$5,386 (\$3,167–\$7,605)	\$0	\$6,541 (\$3,695–\$9,367)	\$8,091 (\$5,158–\$11,025)	\$53 (–\$3–\$109)
Total Mean Cost (95% CI)	\$15,242 (\$10,085–\$20,399)	\$8,661 (\$6,001–\$11,322)	\$204 (\$137–\$270)	\$14,959 (\$9,135–\$20,784)	\$11,593 (\$8,427–\$14,759)	\$438 (\$283–\$593)
Pre-Prophylaxis Era						
HIV(+) Sample (includes deaths), n=40		HIV(+) Sample W/o Deaths, n=29		HIV(–) Sample, n=2

Prophylaxis Era						
HIV(+) Sample (includes deaths), n=14		HIV(+) Sample W/o Deaths, n=11		HIV(–) Sample, n=69