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Trends in Diagnoses Among Hospitalizations of HIV-Infected Children and Adolescents in the US: 2003-2012

Stacey A. Hurst, MPH, **Alexander C. Ewing, MPH**, **Sascha R. Ellington, MSPH**, and **Athena P. Kourtis, MD, PhD, MPH**

Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Abstract

Objective—Using data from 2003-2012, we updated a previous analysis of trends in hospitalizations of HIV-infected children and adolescents in the US.

Methods—We used data from the Kids´ Inpatient Database of the Healthcare Cost and Utilization Project to derive nationally representative estimates of the number of hospitalizations and the rates per 1000 hospitalizations of select discharge diagnoses and procedures in 2003, 2006, 2009, and 2012 among HIV-infected and HIV-uninfected children and adolescents ≤18 years, excluding hospitalizations for conditions related to pregnancy/delivery and neonatal diagnoses. We also examined trends in the prevalence of select discharge diagnoses and procedures using multivariable logistic regression models.

Results—During 2003-2012 the number of hospitalizations for HIV-infected children declined 58% vs 17% for uninfected, but the odds of having discharge codes for most of the diagnoses and procedures studied, including death during hospitalization, remained higher among HIV-infected compared to uninfected children. Among HIV-infected children, the prevalence of discharge diagnoses for pneumonia, pneumococcal disease, and varicella/herpes zoster infections, and odds of death during hospitalization decreased over time, while bacterial infections/sepsis and MRSA increased. Among HIV-uninfected children there was no increase in diagnoses of bacterial infection/sepsis, but otherwise trends were similar.

Conclusion—The number of hospitalizations for HIV-infected children declined from 2003 to 2012. The decreased prevalence of several discharge diagnoses and lower risk of death during hospitalization likely reflect improvements in HIV therapies and increased uptake of other preventive strategies. However, the increasing prevalence of discharge diagnoses for bacterial infections/sepsis warrants further attention and monitoring.

Address correspondence to: Stacey A. Hurst, DRH/NCCDPHP/CDC, 4770 Buford Highway NE, MS F-74, Atlanta, GA 30341-3717, shurst1@cdc.gov, 770-488-4641.

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SDC 1: Appendix: Diagnosis and Procedure Codes.doc

Introduction

Previous analysis of hospitalization trends among HIV-infected children and adolescents in the United States (US) from 1994-2003 indicated that there were dramatic decreases in the number of hospitalizations with the widespread use of highly active antiretroviral therapy (HAART) in the US.[1] Since 2003, the pediatric HIV treatment guidelines have evolved, with greater emphasis on starting combination antiretroviral therapy very early in life.[2,3] Guidelines for the prevention and treatment of opportunistic infections among HIV-infected children have also changed during this time period.[4,5] Other potential factors that may have more recently influenced the number of hospitalizations include increased use of preventive strategies, such as the pneumococcal conjugate (PCV)[6] and the influenza vaccines.[7]

The purpose of this study was to update and expand on the previous analysis using more recent data to describe trends in hospitalizations for children and adolescents aged ≤18 years with HIV infection in the US during 2003–2012. Information on recent trends in hospitalizations of HIV-infected children is important in a climate of rapidly changing health care and practices to identify potential areas for future research.

Methods

Description of the database

The Kids´ Inpatient Database (KID) is part of the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality (AHRQ) and is the largest publicly-available all-payer pediatric inpatient care database in the US.[8] It is released every three years; we used 2003, 2006, 2009, and 2012 data for this analysis. The KID is a sample of pediatric discharges (defined as discharges where a patient was ≤20 years at admission) from all community, non-rehabilitation hospitals in participating states.[8,9]

Pediatric discharges are stratified by reason for hospital stay (uncomplicated in-hospital birth, complicated in-hospital birth, and all other pediatric cases). The KID is constructed using systematic random sampling to select a percentage of discharges by reason for hospital stay.[8] The KID contains information on about 3 million hospital stays from an average of about 3800 hospitals for each year studied. The discharge records in the KID do not contain a patient identifier, and thus repeat hospitalizations cannot be identified. To obtain national estimates, hospitals are post-stratified by six characteristics (geographic region, ownership, rural/urban location, teaching status, bed size, and hospital type), and discharge weights for each record are created to account for the complex sampling design.[8]

Hospital discharge diagnoses and procedures were coded according to the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) and the Clinical Classifications Software (CCS) tool, developed by the AHRQ for clustering diagnoses and procedures into clinically meaningful categories.[10]

Study Design and Statistical Analysis

This analysis examined trends from 2003 to 2012 in the burden of hospitalizations among HIV-infected children and adolescents. For comparison, these same trends were examined in

hospitalizations of HIV-uninfected children. The term “children” is used throughout the paper and refers to both children and adolescents. Data from children who were ≤18 years were included in these analyses for consistency with the age range used in the prior analysis.[1] Hospitalizations for conditions related to pregnancy and delivery (ICD-9-CM codes are in Supplemental Digital Content 1, appendix) and hospitalizations for neonatal diagnoses (using the neomat variable in the KID that flags hospitalizations for neonates) were excluded.

Our outcomes of interest included deaths during hospitalization, hospital charges, and select discharge diagnoses and procedures. Hospital charges were adjusted to 2012 dollars using the Bureau of Labor Statistics’ Consumer Price Index. Discharge diagnoses of interest included *Pneumocystis jiroveci* pneumonia (PCP), pneumonia, pneumococcal disease, bacterial infections/sepsis, mycoses, M*ycobacterium avium* complex infections, varicella/herpes zoster infections, lymphocytic interstitial pneumonia (LIP), influenza, and methicillin-resistant *Staphylococcus aureus* (MRSA). Procedures of interest included injection of antibiotic, diagnostic spinal tap, esophagogastroduodenoscopy, percutaneous gastrostomy, transfusion of packed red blood cells, and bronchoscopy. The ICD-9-CM and CCS codes used are in Supplemental Digital Content 1 (appendix).

Our primary independent variables were HIV status (defined by CCS code 5) and year of hospitalization. For 2003 and 2012, hospitalized patients were described by sociodemographic and hospital characteristics, including gender, age group (0-4 years, 5-9 years, 10-14 years, and 15-18 years), expected primary payer (public [Medicare/Medicaid], private, and other [self-pay, no charge, and other]), hospital location (rural, urban non-teaching, or urban teaching), and hospital region (Northeast, Midwest, South, or West). Race was not examined because it is often not reported by states or there are inconsistencies and missing values.[11]

Wald χ^2 tests with a significance level of 0.05 were used to assess differences in the characteristics of hospitalized children with and without HIV infection. Student’s *t* tests were used to compare the average length of hospital stay, inflation adjusted hospital charges, and number of discharge diagnoses and procedures per hospitalization by HIV infection status.

For 2003, 2006, 2009, and 2012, we compared the rates of death and select discharge diagnoses and procedures per 1000 hospitalizations among HIV-infected and HIV-uninfected children. Multivariable logistic regression models were used to assess the odds of death during hospitalization and of having discharge codes for each diagnosis and procedure for HIV-infected versus HIV-uninfected children, adjusting for patient gender and age group (0-9 years and 10-18 years). To assess trends over time, we compared data across the four study years: 2003 (reference period), 2006, 2009, and 2012, in multivariable logistic regression models, stratified by HIV status and adjusting for patient gender and age group (0-9 years and 10-18 years). Additionally, we evaluated differences in trends by HIV status testing the significance of an interaction term for study year by HIV status. To assess trends in inflation adjusted mean hospital charges by HIV status, multivariable linear regression was performed adjusting for patient gender and age group (0-9 years and 10-18 years).

All statistical analyses were conducted with SAS callable SUDAAN, version 9.3 (Research Triangle Institute, NC).

Results

We estimated there were 1343 hospitalizations among children with an HIV diagnosis in the US in 2012 compared with 3172 in 2003, which is a 58% decrease (Table 1); in comparison, hospitalizations among HIV-uninfected children decreased by 17% during this time period. In both 2003 and 2012, HIV-infected as compared to uninfected children had longer mean hospital stays (2003: 7.0 vs 3.8 days [P <0.001]; 2012: 8.0 vs 4.0 days [P <0.001]), higher mean hospital charges (2003: $33 867 vs $18 578 [$P$<0.001]; 2012: $69 595 vs $33 061 [$P$ <0.001]), and higher mean number of discharge diagnoses (2003: 5.4 vs 3.0 [P <0.001]; 2012: 8.6 vs 4.5 [P <0.001]) and procedures (2003: 1.3 vs 0.9 [P<0.001]; 2012: 1.7 vs 1.0 [P<0.001) per hospitalization. From 2003 to 2012, the mean hospital charges for HIV-infected children increased by 105% while mean hospital charges for HIV-uninfected children increased by 78%.

Girls comprised a higher proportion of hospitalizations than boys among HIV-infected children in 2003 but not in 2012, while boys comprised a higher proportion among HIV-uninfected hospitalizations in both 2003 and 2012 (Table 1). For both 2003 and 2012, the 0-4 age group accounted for the highest percentage of hospitalizations among HIV-uninfected children, and the 15-18 year age group accounted for the highest percentage of hospitalizations among HIV-infected children, with adolescents 15-18 years accounting for 33.1% of hospitalizations among HIV-infected children in 2003 and 52.9% in 2012 (Table 1). However, the estimated number of HIV-infected children's hospitalizations decreased for all age groups from 2003 to 2012.

Overall, there was a 62% decrease in the number of hospitalizations among HIV-infected girls from 2003 to 2012 and a decrease of 52% for boys (Table 1).

In both 2003 and 2012, most HIV-infected pediatric patients had Medicaid or Medicare as their expected payer and were hospitalized mainly in urban teaching hospitals (Table 1). The South had the highest burden of all HIV pediatric hospitalizations in both 2003 and 2012. These characteristics were similar for HIV-uninfected children's hospitalizations, except that most HIV-uninfected children had private insurance as their primary expected payer in 2003.

The rate of death per 1000 hospitalizations decreased by 48% from 2003 to 2012 for HIV-infected children, but remained higher than that of HIV-uninfected hospitalized children in 2012 (9.3/1000 hospitalizations compared with 3.4/1000 hospitalizations) (Table 2). HIV-infected as compared with uninfected children had greater odds of death during hospitalization in both 2003 and 2012 (2003: adjusted odds ratio [aOR], 3.76; 95% confidence interval [CI]: 2.61-5.42 and 2012: aOR, 2.76; 95% CI: 1.38-5.52). Additionally, the odds of having discharge codes for most diagnoses and procedures of interest were higher among hospitalizations of HIV-infected compared to HIV-uninfected children in both 2003 and 2012 (Table 2). Adjusting for age and sex generally had little effect on the estimated associations presented in Table 2, with a small number of exceptions. For

example, the unadjusted OR for HIV and bacterial infections/sepsis was 1.02 (95% CI: 0.91, 1.15), while the adjusted OR was 1.41 (1.22-1.62). This association was driven by an OR of 2.10 (1.81, 2.44) for bacterial infections/sepsis among HIV-infected compared to uninfected children aged 10-18 years. This association was not significant for children aged <10 years (OR: 0.84 [0.68, 1.03]). The only conditions for which there was not a significant difference between the two groups included influenza and MRSA for 2003. The rates of hospitalizations with discharge diagnoses for bacterial infection/sepsis and pneumonia (per 1000 hospitalizations) for HIV-infected and uninfected children in 2003, 2006, 2009, and 2012 are presented in Figure 1 and for varicella/herpes zoster and MRSA in Figure 2.

Among hospitalized HIV-infected children, the odds of discharge diagnoses for pneumonia, pneumococcal disease, and varicella/herpes zoster infections decreased significantly from 2003 to 2012 (pneumonia: aOR, 0.66; 95% CI: 0.51-0.87, pneumococcal disease: aOR, 0.30; 95% CI: 0.10-0.87, varicella/herpes zoster infections: aOR, 0.44; 95% CI: 0.23-0.85; Table 3; Figs 1&2). Conversely, among hospitalized HIV-infected children, the odds of discharge diagnoses for bacterial infections/sepsis and MRSA increased from 2003 to 2012 (bacterial infections/sepsis: aOR, 1.26; 95% CI: 1.03-1.55, MRSA: aOR, 6.75; 95% CI: 2.34-19.45; Table 3). The odds of a discharge diagnosis for influenza were significantly greater in 2009 compared to 2003 among HIV-infected children (aOR, 4.06; CI: 2.32-7.11; Table 3).

Similar trends were observed among hospitalizations of HIV-uninfected children for deaths during hospitalization and discharge diagnoses for pneumonia, pneumococcal disease, varicella/herpes zoster infections and MRSA (Table 3; Figs 1&2). Conversely, the decreases observed for hospitalizations with the discharge diagnosis of pneumonia were greater for HIV-infected, compared with uninfected children (test for interaction: P=.02). There were also significant interactions between year and infection status for discharge diagnoses for bacterial infections/sepsis and influenza. Among HIV-uninfected children, the odds of discharge diagnoses for bacterial infections/sepsis remained fairly stable (P=.02), and influenza generally decreased over time with an increase in 2009 that was more modest than for HIV-infected children (P=.01). In addition, there were increases in discharge diagnoses for mycoses, Mycobacterium avium infections, and cytomegalovirus among HIV-uninfected children (Table 3).

Regarding procedures of interest, use of antibiotic injections decreased significantly for both HIV-infected and uninfected hospitalized children (Table 3). The odds of other procedures studied did not change significantly for HIV infected children.

Discussion

In this analysis of multiple years of nationally representative data on hospital admissions in the US, we found the estimated numbers of hospitalizations among HIV-infected children and adolescents ≤18 years decreased by 58% from 2003 to 2012. US-wide HIV surveillance data a decrease in the number of youth ≤19 years living with a diagnosed HIV infection in the US (from an estimated 11,997 in 2009 to 9,790 in 2012).[12,13] The decrease in the estimated numbers of hospitalizations among HIV-infected children and adolescents ≤18 years mirrors the 71% decrease from 1994 to 2003 noted in our previous analysis.[1] That

decrease was noted to have occurred since the advent of highly active antiretroviral therapy in the US around 1997. Since 2003, antiretroviral therapy regimens have improved and treatment has become more aggressive, which may contribute to this continued decline.[3,14,15]

Another factor that may be contributing to the decreasing numbers of hospitalizations could be the shift in age patterns as HIV-infected adolescents age out of this population. From 2009 to 2014, the overall estimated rates of new HIV diagnoses for adolescents 15-19 years has been decreasing (from 10.3 to 8.7 per 100,000 population).[12,13] The rates for adolescents 13-14 years and children younger than 13 have been more stable from 2009-2014 and are fairly low (0.4 and 0.3 respectively per 100,000 population in 2014).[12,13]

We found that the rates and odds of death during hospitalization for HIV-infected children decreased from 2003-2012 but were still higher than the odds for HIV-uninfected children. Two prior studies have shown that mortality rates for HIV-infected children are about 30 times higher than rates for the general US pediatric population.[16,17] Another study found declining hospitalization rates from 2003-2010 among 5–16 and 17–24 year-olds perinatally infected with HIV.[18] While use of HAART has led to decreases in mortality for HIV-infected children,[19] finding the optimal treatment strategies remains a challenge, particularly for adolescents who are likely to face adherence issues.[20,21]

The rates and adjusted odds ratios of most of the outcomes described in this analysis were higher among hospitalizations of HIV-infected children compared to HIV-uninfected children in all years studied (2003, 2006, 2009, and 2012). The trends examined show decreases in the likelihood of discharge codes for pneumonia, pneumococcal disease, and varicella/herpes zoster infections among hospitalized HIV-infected children, but increases in discharge codes for bacterial infections/sepsis and MRSA.

The increase in discharge codes for bacterial infections/sepsis is in contrast to the decrease noted in our previously published analysis comparing the pre-HAART (1994-1996) and HAART (2001-2003) eras.[1] In a recent systematic review and meta-analysis of the causes of hospital admissions among people living with HIV worldwide, AIDS-related illnesses and bacterial infections were the leading causes of hospitalization among children.[22] It should be noted that the incidence of hospitalizations with coding for sepsis has increased in the US, while hospitalizations with objective clinical markers of infection have remained stable or decreased,[23] likely reflecting changes in coding practices. Although this could explain the increases we found in discharge diagnoses for infections in HIV-infected pediatric population, particularly those aged >10 years, a corresponding increase was not observed among HIV-uninfected children.

We found that the prevalence of hospitalizations with discharge diagnoses for pneumococcal disease decreased from 2003 to 2012, coinciding with the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) in the US in 2000 and PCV13 in 2010.[24] An analysis of hospitalization trends for invasive pneumococcal disease among HIV-infected adolescents and adults noted a significant decrease in 2004-2005 compared to 1994-1995.[25]

The Centers for Disease Control (CDC) estimates that 92.3% of children age 19-35 months received ≥ 3 doses of PCV in 2012.[6]

Invasive MRSA infection incidence in children has been reported to have increased during the early part of our study period,[26] but there is evidence that it may be now decreasing,[27,28] consistent with our findings that the rate per 1000 hospitalizations decreased from 2009 to 2012 for both HIV-infected and uninfected children.

The increase in incidence of discharge diagnoses of influenza in 2009 are due to the H1N1 pandemic.[29] The decreases noted for HIV-uninfected children for 2006 and 2012 compared to 2003 may be due to increased uptake of the seasonal influenza vaccine.[7] Similar decreases were not noted for hospitalizations among HIV-infected children, possibly due to influenza vaccinations not being as effective in HIV-infected young children.[30] There was a downward trend in hospitalizations among children with discharge diagnoses of varicella/herpes zoster infections, in contrast to cytomegalovirus, another opportunistic viral pathogen for which there is no vaccine available, which has not changed. The CDC estimates that 90.2 % of children age 19-35 months had received ≥ 1 dose of varicella vaccine in 2012,[6] and it is recommended for all but the most severely immunocompromised HIV-infected children.[31]

This study has some limitations. The sampling frame for the KID changes over time as states are added (e.g. 36 in 2003 and 44 in 2012), so estimates from earlier years may be subject to more sampling bias than later years.[8] A few states prohibit the release of discharge records for patients with an HIV diagnosis. The KID includes discharge records for patients up to age 20 years at admission, but some states suppress the reporting of age for children with an HIV diagnosis. Although our analysis was limited to children ≤18 years, we included records where age was suppressed. Assuming the age distribution for these children was similar to those with a reported age, ~33 records in 2003 and ~67 in 2012 included may be for HIV-infected children >18 years old at admission. We analyzed data for all discharge diagnoses, so some conditions may not have been the reason for hospital admission. However, this provided a full picture of the morbidity burden of hospitalized HIV-infected children.

Other limitations include those common to research using administrative data: The data reflect hospital discharges rather than individual patients, so some children may be represented more than once for any given year, as well as across years. The resulting interdependence of observations could increase the likelihood that the associations measured were found significant, and is important to take into account when interpreting the results. Because of incomplete data on race, we were unable to evaluate its effect on our estimates. Codes used for some conditions may have poor sensitivity or positive predictive value.[32,33] Changes in health care and in coding practices over time may have influenced some of the trends observed. Strengths of this analysis include the large, nationally representative sample and the availability of charge and length of stay data.

Conclusion

Our results demonstrate that despite decreasing numbers of hospitalizations among HIV-infected children, the rates and adjusted odds of most of the outcomes examined are still higher among hospitalized HIV-infected children compared to HIV-uninfected children from 2003-2012. The trends in discharge diagnoses among hospitalized HIV-infected children are generally similar to the trends for HIV-uninfected children with decreases in the prevalence of discharge codes for pneumonia, pneumococcal disease, and varicella/herpes zoster infections and an increase in MRSA. The most notable exception is the trend of increasing prevalence of discharge diagnoses for bacterial infection/sepsis among hospitalized HIV-infected children which is not seen among HIV-uninfected children. Further research is warranted to address evolving trends and causes of this important issue for this population as it may impact treatment guidelines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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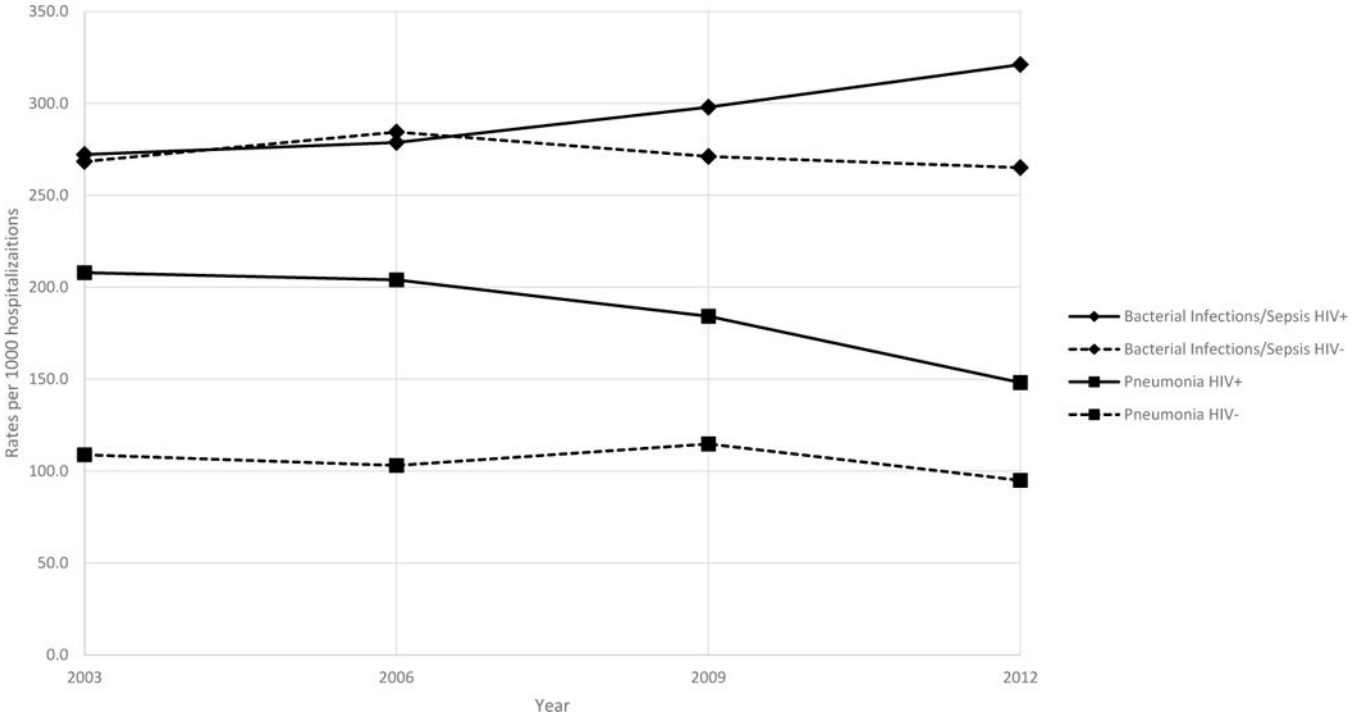

Figure 1.

Rates of discharge diagnoses for Bacterial Infection/Sepsis and Pneumonia per 1000 hospitalizations among HIV-infected and uninfected children in the US in 2003, 2006, 2009, and 2012 (KID)

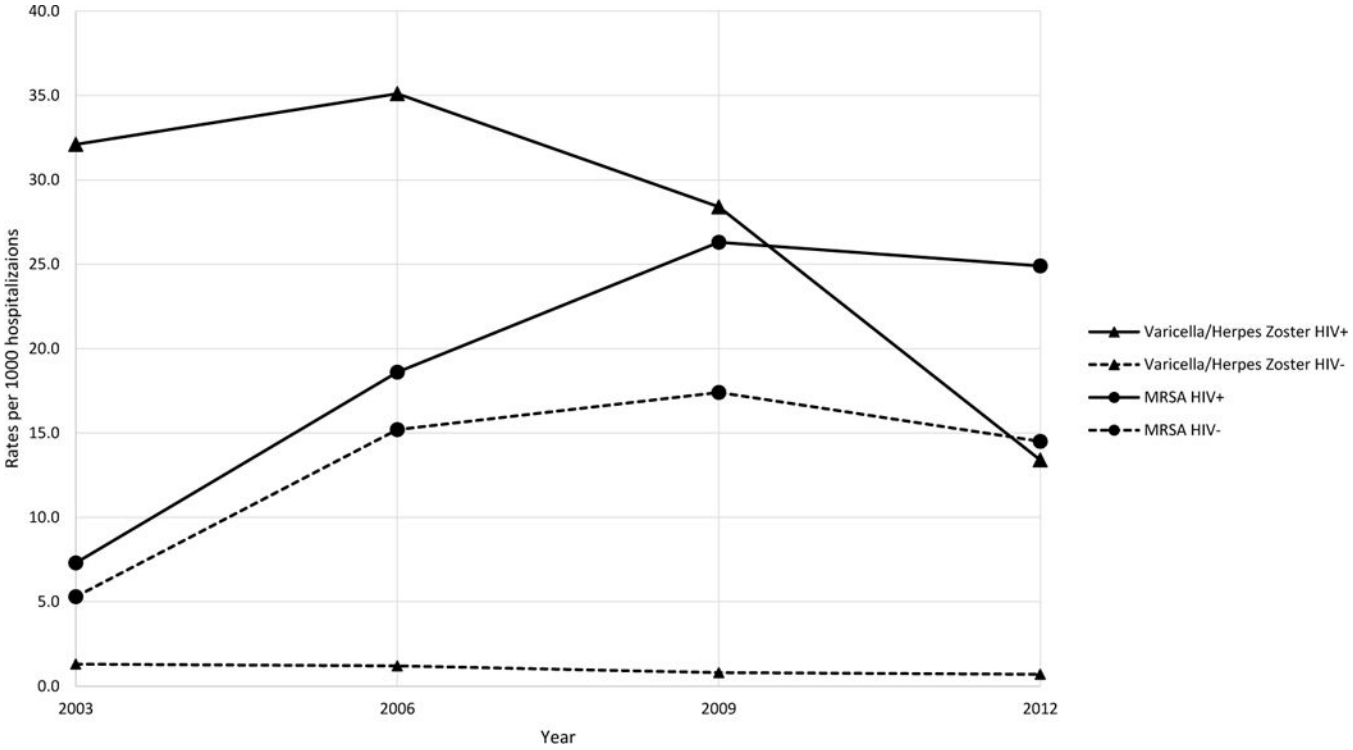

Figure 2.

Rates of discharge diagnoses for Varicella/Herpes Zoster and MRSA per 1000 hospitalizations among HIV-infected and uninfected children in the US in 2003, 2006, 2009, and 2012 (KID)

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Table 1

Demographic and hospital characteristics and select outcomes among HIV-infected and HIV-uninfected children and adolescents hospitalized in the US in 2003 and 2012 (Kids´ Inpatient Database).

Characteristics	2003			2012		
	HIV-infected N = 3172	HIV-uninfected N = 2 319 596	P	HIV-infected N = 1343	HIV-uninfected N = 1 921 984	P
Gender, n (%)						
Male	1391 (44.0)	1 241 776 (54.5)	<.001[a]	665 (49.5)	1 032 282 (53.7)	.09[a]
Female	1769 (56.0)	1 035 405 (45.5)		677 (50.5)	889 510 (46.3)	
Age, n (%)						
0-4 years	432 (14.4)	1 080 418 (47.0)	<.001[a]	249 (20.8)	810 168 (42.3)	<.001[a]
5-9 years	590 (19.6)	369 281 (16.1)		134 (11.2)	321 401 (16.8)	
10-14 years	988 (32.9)	397 753 (17.3)		180 (15.1)	354 446 (18.5)	
15-18 years	995 (33.1)	449 597 (19.6)		632 (52.9)	427 875 (22.4)	
Primary expected payer, n (%)						
Public (Medicaid or Medicare)	2396 (75.7)	975 364 (42.1)	<.001[a]	963 (71.8)	978 804 (51.0)	<.001[a]
Private, including HMO	467 (14.7)	1 143 793 (49.4)		226 (16.9)	790 544 (41.2)	
Other, (self-pay, no charge, or other)	303 (9.6)	195 465 (8.4)		152 (11.3)	148 211 (7.7)	
Location of hospital, n (%)						
Rural	84 (2.7)	299 187 (13.3)	<.001[a]	28[b] (2.1)	138 882 (7.2)	<.001[a]
Urban, non-teaching	314 (10.1)	605 188 (26.9)		155 (11.6)	358 599 (18.7)	
Urban, teaching	2703 (87.1)	1 341 601 (59.7)		1160 (86.4)	1 424 503 (74.1)	
Region of hospital, n (%)						
Northeast	1209 (38.1)	423 298 (18.2)	<.001[a]	369 (27.5)	361 287 (18.8)	<.001[a]
Midwest	328 (10.3)	534 811 (23.1)		250 (18.6)	429 459 (22.3)	
South	1373 (43.3)	864 091 (37.3)		583 (43.4)	725 120 (37.7)	
West	261 (8.2)	497 396 (21.4)		141 (10.5)	406 118 (21.1)	
Died during hospitalization, n (%)	57 (1.8)	8959 (0.4)	<.001[a]	13[b] (0.9)	6530 (0.3)	.05[a]
Median length of stay, days	3.3	1.8	<.001 [c]	3.2	1.9	<.001 [c]

Characteristics	2003			2012		
	HIV-infected N = 3172	**HIV-uninfected N = 2 319 596**	**P**	**HIV-infected N = 1343**	**HIV-uninfected N = 1 921 984**	**P**
Median charges, (in 2012 $)	15 481	8738	<.001 [c]	25 060	14 713	<.001 [c]
Median # of discharge diagnoses	4.1	1.9	<.001 [c]	6.7	2.9	<.001 [c]
Median # of procedures	0.2	0	<.001 [c]	0.3	0	<.001 [c]

[a] Wald χ^2

[b] Estimates should be used with caution: relative SE >30%

[c] Student's *t* test

Table 2

Rates[a] and adjusted odds ratios of select discharge diagnoses and procedures and in-hospital deaths among HIV-infected and HIV-uninfected children and adolescents hospitalized in the US in 2003 and 2012 (Kids´ Inpatient Database)

	2003				2012			
	HIV-infected	HIV-uninfected	aOR[b]	95%CI	HIV-infected	HIV-uninfected	aOR[b]	95%CI
	Rate	Rate			Rate	Rate		
Deaths	18.0	3.9	**3.76**	**(2.61 -5.42)**	9.3 [c]	3.4	**2.76**	**(1.38-5.52)**
Charges[d] (in 2012 $)	33867 (29488-38246)	18578 (17542-19613)		<.001	69595 (58109-81081)	33061 (30963-35159)		<.001
Discharge Diagnoses								
PCP	27.9	0.1	**383.87**	**(258.86-569.24)**	28.9	0.1	**303.81**	**(189.49-487.10)**
Pneumonia	207.9	108.8	**3.24**	**(2.75-3.81)**	148.1	94.9	**2.42**	**(1.89-3.10)**
Pneumococcal disease	15.5	2.2	**8.13**	**(5.39-12.27)**	–	1.5	**3.83**	**(1.44-10.81)**
Bacterial Infections/sepsis	272.2	268.4	**1.41**	**(1.22-1.62)**	321.1	265.0	**1.78**	**(1.48-2.14)**
Mycoses	147.0	14.9	**13.26**	**(11.05-15.91)**	134.8	17.1	**9.32**	**(7.49-11.59)**
Mycobacterium avium complex infections	24.0 [c]	0.2	**131.70**	**(71.15-243.78)**	18.8 [c]	0.4	**43.89**	**(20.66-93.24)**
Cytomegalovirus	16.4	0.8	**15.44**	**(9.87-24.16)**	23.5	1.2	**18.85**	**(10.58-33.59)**
Varicella or herpes Zoster infections[e]	32.1	1.3	**23.72**	**(17.78-31.66)**	13.4	0.7	**18.20**	**(10.00-33.12)**
Lymphocytic interstitial pneumonia	11.1	0.4	**32.66**	**(21.38-49.89)**	15.5 [c]	0.3	**54.98**	**(25.08-120.53)**
Influenza[e]	10.5	16.4	0.91	(0.58-1.41)	14.0 [c]	9.4	**1.99**	**(1.03-3.85)**
MRSA[e]	7.3 [c]	5.3	0.62	(0.25-1.59)	24.9	14.5	**1.77**	**(1.08-2.90)**
Procedures								
Injection of antibiotic	96.3	18.9	**6.28**	**(4.25-9.28)**	33.8 [c]	12.6	**3.42**	**(2.14-5.47)**
Diagnostic spinal tap	55.8	47.8	**1.52**	**(1.16-2.00)**	66.1	31.7	**2.69**	**(2.04-3.56)**
Esophagogastroduodenoscopy	19.5	6.1	**2.67**	**(1.87-3.82)**	20.5	9.6	**1.83**	**(1.12-3.01)**
Percutaneous gastrostomy	19.5	4.3	**5.79**	**(4.11-8.15)**	17.2	5.2	**4.36**	**(2.54-7.49)**
Transfusion of packed red blood cells	59.5	21.7	**2.52**	**(1.94-3.28)**	73.2	31.6	**2.33**	**(1.63-3.34)**
Bronchoscopy	36.5	7.3	**5.80**	**(4.47-7.52)**	48.6	8.5	**6.66**	**(4.64-9.55)**

aOR, adjusted odds ratio; CI, confidence interval; PCP, *Pneumocystis jiroveci* pneumonia

[a] Rates are per 1000 hospitalizations

[b] Adjusted for gender and age group (0-9 years and 10-18 years)

[c] Derived from estimates with relative SE >30%, findings should be interpreted with caution

[d] Means with 95% CI and *P* values from Student's *t* test reported

[e] Changes to ICD-9-CM codes are noted in the Appendix

– Too few to report

Table 3

Multivariable logistic and linear regression analysis for deaths, mean hospital charges, and select discharge diagnoses and procedures among HIV-infected and HIV-uninfected children and adolescents hospitalized in the US in 2003, 2006, 2009, and 2012 (Kids´ Inpatient Database)

	aOR (95% CI)[a]			
	2003 (REF)	**2006**	**2009**	**2012**
HIV-infected				
Deaths	1.0	0.95 (0.51-1.76)	0.67 (0.33-1.35)	0.60 (0.27-1.30)[c]
Charges[b] (in 2012 $)	32972 (28397-37547)	43990 (37987-49993)	50380 (42162-58597)	71400 (58924-83875)
Discharge Diagnoses				
PCP	1.0	1.09 (0.68-1.75)	0.88 (0.51-1.50)	0.91 (0.54-1.55)
Pneumonia*	1.0	0.99 (0.81-1.21)	0.89 (0.70-1.14)	**0.66 (0.51-0.87)**
Pneumococcal disease	1.0	0.77 (0.43-1.40)	0.63 (0.30-1.31)	**0.30 (0.10-0.87)**[c]
Bacterial Infections/sepsis*	1.0	1.09 (0.90-1.31)	**1.25 (1.02-1.54)**	**1.26 (1.03-1.55)**
Mycoses	1.0	0.88 (0.67-1.16)	1.02 (0.78-1.33)	0.86 (0.65-1.13)
Mycobacterium avium complex infections	1.0[c]	1.02 (0.48-2.14)	1.26 (0.58-2.74)	0.73 (0.29-1.86)[c]
Varicella or herpes Zoster infections	1.0	1.18 (0.79-1.76)	0.96 (0.60-1.53)	**0.44 (0.23-0.85)**
Cytomegalovirus	1.0	1.27 (0.68-2.35)	0.90 (0.44-1.85)	1.62 (0.81-3.23)
Lymphocytic interstitial pneumonia	1.0	1.41 (0.69-2.90)[c]	0.61 (0.25-1.52)[c]	1.14 (0.47-2.78)[c]
Influenza*	1.0	1.23 (0.63-2.39)	**4.06 (2.32-7.11)**	1.25 (0.56-2.78)[c]
MRSA	1.0[c]	**4.28 (1.51-12.07)**	**6.60 (2.35-18.50)**	**6.75 (2.34-19.45)**
Procedures				
Injection of antibiotic	1.0	0.66 (0.35-1.25)	**0.47 (0.25-0.87)**	**0.35 (0.17-0.75)**[c]
Diagnostic spinal tap*	1.0	0.99 (0.69-1.42)	0.85 (0.57-1.26)	1.20 (0.83-1.75)
Esophagogastroduodenoscopy	1.0	1.08 (0.65-1.80)	1.28 (0.72-2.29)	1.06 (0.58-1.92)
Percutaneous gastrostomy	1.0	1.22 (0.72-2.07)	1.09 (0.57-2.09)	0.90 (0.48-1.71)
Transfusion of packed red blood cells	1.0	1.16 (0.78-1.72)	1.43 (0.99-2.05)	1.28 (0.81-2.03)
Bronchoscopy	1.0	1.28 (0.86-1.89)	0.90 (0.57-1.42)	1.33 (0.86-2.05)
HIV-uninfected				
Deaths	1.0	0.96 (0.87-1.06)	0.91 (0.83-1.01)	**0.86 (0.77-0.95)**
Charges[b] (in 2012 $)	18645 (17599-19691)	22407 (21159-23654)	27172 (25658-28685)	32819 (30724-34915)
Discharge Diagnoses				
PCP	1.0	1.17 (0.85-1.60)	1.14 (0.85-1.53)	1.21 (0.91-1.61)
Pneumonia*	1.0	0.95 (0.90-1.00)	**1.08 (1.03-1.15)**	**0.89 (0.84-0.93)**
Pneumococcal disease	1.0	1.06 (0.97-1.15)	**1.33 (1.22-1.45)**	**0.70 (0.64-0.77)**
Bacterial Infections/sepsis*	1.0	**1.10 (1.06-1.14)**	1.03 (1.00-1.07)	1.01 (0.98-1.05)

	aOR (95% CI)[a]			
	2003 (REF)	**2006**	**2009**	**2012**
Mycoses	1.0	1.05 (0.99-1.12)	**1.08 (1.02-1.15)**	**1.15 (1.08-1.23)**
Mycobacterium avium complex infections	1.0	1.10 (0.83-1.46)	**1.47 (1.13-1.92)**	**1.91 (1.49-2.45)**
Varicella or herpes Zoster infections	1.0	0.95 (0.86-1.04)	**0.63 (0.57-0.70)**	**0.54 (0.49-0.59)**
Cytomegalovirus	1.0	**1.17 (1.01-1.36)**	**1.31 (1.13-1.52)**	**1.47 (1.23-1.76)**
Lymphocytic interstitial pneumonia	1.0	0.81 (0.64-1.02)	0.96 (0.76-1.21)	0.78 (0.57-1.06)
Influenza *	1.0	**0.47 (0.43-0.51)**	**1.87 (1.75-2.00)**	**0.59 (0.54-0.63)**
MRSA	1.0	**2.89 (2.59-3.23)**	**3.30 (2.97-3.67)**	**2.74 (2.47-3.04)**
Procedures				
Injection of antibiotic	1.0	0.89 (0.62-1.27)	**0.64 (0.44-0.95)**	**0.66 (0.44-0.99)**
Diagnostic spinal tap *	1.0	**0.82 (0.78-0.87)**	**0.75 (0.71-0.80)**	**0.67 (0.63-0.71)**
Esophagogastroduodenoscopy	1.0	1.13 (0.99-1.29)	**1.32 (1.16-1.50)**	**1.50 (1.33-1.70)**
Percutaneous gastrostomy	1.0	1.09 (0.97-1.23)	1.09 (0.97-1.23)	**1.22 (1.09-1.37)**
Transfusion of packed red blood cells	1.0	**1.22 (1.02-1.47)**	**1.41 (1.18-1.67)**	**1.44 (1.22-1.70)**
Bronchoscopy	1.0	1.07 (0.89-1.28)	1.07 (0.90-1.27)	1.18 (1.00-1.38)

aOR, adjusted odds ratio; CI, confidence interval; REF, referent group; PCP, *Pneumocystis jiroveci* pneumonia

[a] Adjusted for gender and age group (0-9 years and 10-18 years)

[b] Multivariable linear regression adjusted for gender and age group (0-9 years and 10-18 years)

[c] Derived from estimates with relative SE >30%, findings should be interpreted with caution

* Interaction noted