Improvements in the Clinical Status of HIV-Infected Children: a Longitudinal Assessment of the Effects of Advancements in Care

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Abstract

Title: Improvements in the Clinical Status of HIV-Infected Children; a Longitudinal Assessment of the Effects of Advances in Care

Background: The 1994 CDC HIV clinical classification (HCC) system classifies HIV-infected children into the most severe clinical category ever experienced, including: not (N), mildly (A), moderately (B) or severely (C) symptomatic. A child's HCC can only become more severe or remain unchanged over time and does not reflect most recent clinical improvements in children surviving from the pre-HAART era. The Pediatric Spectrum of HIV Disease (PSD) study monitors the HCC of children in six U.S. states.

Methods: We adapted the CDC HCC system to classify children in PSD into their most severe category based only on those conditions experienced in their most recent year of follow-up and compared it to the most severe category experienced in their lifetime. HIV-infected children born before 1996 who were followed actively through 1998 or later and had at least 12 consecutive months of follow-up between January 1, 1998 and December 31, 2001 were eligible for this analysis.

Results: 1612 children were eligible and had a median age of 11.4 years. Over 88.8 % of children had ever been reported as moderately or severely symptomatic compared to only 22.1% during their most recent year of follow-up. In addition, 78.0 % of children were not symptomatic or mildly symptomatic during their last year of follow-up, compared to 11.2% over their long term follow-up.

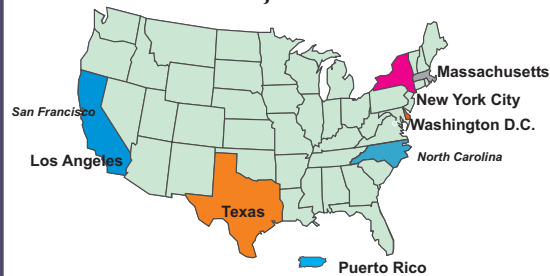| Clinical Category	No. (%) of children by most severe clinical category of HIV-related conditions experienced	
	In lifetime	In most recent year of follow-up
N = Not symptomatic	58 (3.6)	1102 (68.4)
A= Mildly symptomatic	122 (7.6)	154 (9.6)
B= Moderately symptomatic	995 (61.7)	316 (19.6)
C=Severely symptomatic	437 (27.1)	40 (2.5)

Conclusions: Dramatically fewer HIV-infected children surviving from the pre-HAART era were moderately or severely symptomatic during their most recent year of follow-up. The CDC HCC system remains useful in that it provides us with a historical marker of severity of disease. However, adapting the HCC to include a classification based on last year of follow-up allowed us to describe recent clinical improvements in the PSD cohort. As HIV-infected children age into adolescence, the PSD cohort provides an invaluable resource in monitoring whether such hard-won gains can be maintained or improved upon. These improvements underscore the importance of continued support for the comprehensive services responsible for these dramatic changes.

Background – 1
Objective of Study and CDC Pediatric HIV Classification System

CDC MMWR — *Recommendations and Reports*

September 30, 1994 / Vol. 43 / No. RR-12

1994 Revised Classification System for Human Immunodeficiency Virus Infection in Children Less Than 13 Years of Age

Official Authorized Addenda: Human Immunodeficiency Virus Infection Codes and Official Guidelines for Coding and Reporting ICD-9-CM

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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- **Objective:** Use of CDC Pediatric HIV Classification system to assess recent improvement in HIV clinical and immunologic categories in Pediatric Spectrum of HIV Disease cohort (PSD)
- CDC classification system:
  - first established in 1987
  - updated in 1994 and 1997
- 1994 definition bases severity of HIV infection on:
  - clinical symptoms
  - immunologic categories

Background - 2
CDC Pediatric Human Immunodeficiency Virus (HIV) Classification System

Immunologic categories	Clinical categories			
	N: No signs/ symptoms	A: Mild signs/ symptoms	B: Moderate signs/ symptoms	C: Severe signs/ symptoms
1: No evidence of suppression	N1	A1	B1	C1
2: Evidence of moderate suppression	N2	A2	B2	C2
3: Severe suppression	N3	A3	B3	C3

Ref.: CDC. 1994 Revised Classification system for HIV infection in chidren<13 years of age. MMWR 1994;43(No.RR12).

Background - 3
CDC Pediatric HIV Classification System

- Based on the <u>most severe</u>
  - <u>clinical category</u> experienced in lifetime and
  - <u>immunologic category</u> experienced in lifetime
- A child's HIV classification can only become more severe or remain unchanged over time
- Classification system is:
  - Useful for historical purposes
  - Not necessarily descriptive of most recent clinical status

Methods – 1
PSD Cohort

- Longitudinal pediatric cohort study of HIV-exposed & HIV-infected children
- All children must be $\leq$ 13 years of age at HIV diagnosis
- Medical record abstractions occur every 6 months
- Over 18,000 children have been enrolled since 1988
- Cohort provides a "real world" representative sample of HIV-exposed and –infected children in the United States

Methods - 2
PSD Project Sites*

Massachusetts
New York City
Washington D.C.
North Carolina
San Francisco
Los Angeles
Texas
Puerto Rico

* Note: San Francisco & North Carolina were sites up until 1997

Methods – 3
Characteristics of PSD Enrollees Eligible for Analysis

- HIV-infected
- Assigned a clinical category prior to Jan. 1, 1996 (Pre-HAART era)
- Had at least one continuous year of recent clinical data documented
- Two successive PSD follow-up forms filled out between 1/1/98 and 12/31/01

Methods – 4
Adaptation of CDC Pediatric Clinical and Immunologic Categories

- Compared most severe category <u>in last year</u> versus most severe category <u>in lifetime</u>
- Reassigned categories based <u>only</u> on the lowest CD4% and pertinent clinical diagnoses documented in the last year
- Assumed chronic conditions not mentioned in the last year of medical record abstraction were not important for current care

Results - 1
Study Sample Characteristics

- 1612 children met eligibility criteria and had a clinical classification
  - 1475 (91%) also had an immunologic classification

Characteristic	Description
Age at last follow-up	Median = 11.3 years (Range: 2.6-26.1 years)
Gender (%)	Male (51.2%) ; Female (48.8%)
Race/ethnicity (%)	Black (50.3%); Hispanic (38.6%); White (9.9%); Asian (0.4%); Other/unknown (0.8%)
Mode of Transmission (%)	Perinatal (89.9%); Other/ Unidentified Risk (4.8%); Transfusion (4.1%); Hemophiliac (1.7%)

Results - 2
Comparison of Most Severe Clinical Category in Last Year of follow-up versus Lifetime

Clinical Category	No. (%) of children by most severe clinical category of HIV-related conditions experienced in:			
	Lifetime		Last year of follow-up	
N = No signs/ symptoms	58	(3.6)	1102	(68.4)
A = Mild signs/ symptoms	122	(7.6)	154	(9.6)
B = Moderate signs/ symptoms	995	(61.7)	316	(19.6)
C = Severe signs/ symptoms	437	(27.1)	40	(2.5)
Total	1612	(100.0)	1612	(100.0)

Results - 3
Comparison of Most Severe Immunologic Category in Last Year of follow-up versus Lifetime

Immunologic Category	No. (%) of children by most severe immunologic category of HIV-related conditions experienced in:			
	Lifetime		Last year of follow-up	
1 = No evidence of suppression	39	(2.6)	592	(40.1)
2 = Evidence of moderate suppression	372	(25.2)	569	(38.5)
3 = Severe suppression	1064	(72.1)	314	(21.3)
Total	1475	(100.0)	1475	(100.0)

Results – 4
Changes in Clinical Categorization

- Proportion of children in moderately/severely symptomatic (B or C) categories decreased by 66.7%
  - from 88.8% in lifetime to 22.1% in last year of follow-up
- Proportion of children in asymptomatic category (N) increased by 64.8%
- Overall, 1,297 (80%) of 1612 children with a clinical categorization moved to a less severe clinical category in the last year of follow-up

Results – 5
Changes in Immunologic Categorization

- Proportion of children with no evidence of suppression (Category 1) increased by 37.5 % in last year compared to lifetime
- 973 (66.0%) of 1,475 children with a clinical and immunologic categorization moved to a less severe category of suppression in their last year of follow-up
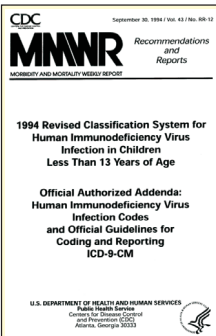
Conclusions

- Most children surviving from the pre-HAART era through 1998-2001 have experienced dramatic improvements in their clinical and immunologic categories in their last year of follow-up
- However, improvements in immunologic category lag behind improvements in clinical status
- The CDC Pediatric HIV Classification system remains useful as it provides a historical marker of disease severity
  - Adapting it to classify children based on their last year of follow-up allowed us to describe recent clinical improvements in the PSD cohort
- These improvements underscore the importance of continued support for the comprehensive services responsible for these dramatic changes.