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The Effect of CDC Case Definition for HIV/AIDS on Mortality among Adolescents and Adults in the United States

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Abstract - Understanding the definition and meaning of HIV/AIDS have implications not only for HIV/AIDS research, clinical practices but also the overall impact on mortality. The definitions of HIV/AIDS have changed in addition to the concepts and terminology associated with when talking about the history of HIV/AIDS. Previous study utilized World Health Organization (WHO)case definition of HIV/AIDS in predicting the relative effectiveness of HIV among individuals with tuberculosis (Kennedy, Campbell and Malinda, 2004).Their findings suggest that WHO case definitions significantly predicted HIV/AIDS among TBpositive HIV-positive participants compared to TB positive and HIV-negative participants(Kennedy, Campbell and Malinda 2004). Previous studies also indicate that WHO (1986) case definitions of HIV/AIDS, although well developed and assessed its uses were prevented by the proliferation of counseling and HIVtesting centers, particularly in the developing countries (Harries 1990; Lipson at al. 1995).

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The Effect of CDC Case Definition for HIV/AIDS on Mortality among Adolescents and Adults in the United States

Adansi Amankwaa

I. Introduction

Understanding the definition and meaning of HIV/AIDS have implications not only for HIV/AIDS research, clinical practices but also the overall impact on mortality. The definitions of HIV/AIDS have changed in addition to the concepts and terminology associated with when talking about the history of HIV/AIDS. Previous study utilized World Health Organization (WHO)case definition of HIV/AIDS in predicting the relative effectiveness of HIV among individuals with tuberculosis (Kennedy, Campbell and Malinda, 2004).Their findings suggest that WHO case definitions significantly predicted HIV/AIDS among TB-positive HIV-positive participants compared to TB positive and HIV-negative participants(Kennedy, Campbell and Malinda 2004). Previous studies also indicate that WHO (1986) case definitions of HIV/AIDS, although well developed and assessed its uses were prevented by the proliferation of counseling and HIV-testing centers, particularly in the developing countries (Harries 1990; Lipson at al. 1995).

In contrast, other research shows the need to update case definitions of existing diagnosis criteria of the oral manifestations of HIV published in 1992 and 1993 (Shiboski et al., 2009). It was argued that the proposed case definitions were designed for large scale but not HIV/AIDS oral diseases that can be used by other researchers. It is important to note that changes in case definitions were largely due to clinical evidence. With no cure for the disease current case definitions are still been updated. Consequently, different case definitions and their conceptualizations may differentially affect the accuracy of diagnosis and mortality. To examine this possibility, further investigation is necessary in order to fully understand how CDC case definitions affect mortality. Specifically, I examined not only the effects of case definitions on mortality since time of diagnosis of HIV infection but also controlled for characteristics of patients. This article, therefore, extends current knowledge about AIDS related mortality by examining the relative risk of mortality of AIDS patients since their infection using CDC surveillance data.

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II. Background

Over the years CDC compiled clinical signs and symptoms for diagnosing HIV/AIDS since it was first identified in 1981. At first, the disease was associated with "opportunistic infections" – a term used to describe AIDS symptomatology. The disease was initially observed only in persons with drug-suppressed or otherwise severely compromised immune systems. However, as new understanding of the disease emerged, the initial definition was revised to reflect medical practice as well (CDC, 1986). In 1983 the Centers for Disease Control and Prevention (CDC) published its first set of guidelines for AIDS reporting (CDC MMWR, 1983). These guidelines were changed and updated in 1985, 1987 and 1993.

In 1984, the CDC renamed the first identified human T-lymphoid tropic type III virus as human immunodeficiency virus (HIV). To understand the nature of this powerful and untreatable disease, the CDC intensified its research to track the disease. The results of scientific research culminated in subsequent changes to the CDC surveillance definition for AIDS as more information about the virus and symptoms associated with it became available. This definition was also modified in 1985. In 1987, the CDC AIDS case definition was again revised to include a broader spectrum of diseases characteristically found in persons with HIV infection and the presumptive diagnosis of selected diseases (CDC MMWR 1987).Finally, in 1993 the CDC revised the definition of AIDS once again to include pulmonary tuberculosis, recurrent pneumonia and or cervical cancer (definitive and presumptive diagnoses) and severe HIV-related immune suppression.

Each of the revised case definitions for AIDS remarkably affected the distribution of AIDS cases reported. The differences incase definition for AIDS affected the number reported by gender, sexual orientation, IV-drug users, and by race (MMWR, 1989). Although HIV/AIDS-related deaths have been extensively estimated and or documented (CDC MMWR, 1999), mortality differences with respect to case definitions have not been examined. Given the differences in case definition of HIV/AIDS, it is worthwhile to examine the relative risk of mortality associated with varying definitions of AIDS.

III. Methods

a) Data

The data cover all patients in the CDC database between 1980 and 2002 [7]. Specifically, the CDC gathers data on HIV/AIDS from individual states and health departments in the country. The data also include changes in AIDS definition. However, only cases meeting the 1993 surveillance definition are included in the data set. The purpose of data collection on AIDS is primarily to monitor both trends and the scope of severity of morbidity due to HIV. In order to ensure data quality, the CDC carefully and continuously reviews data obtained from health departments of various states in order to ensure its consistency with standards of medical care for HIV-infected persons. Surveillance data include variables such as: age of patient, the CDC AIDS case definition revisions met by the patient, sexual classification of patient, race of patient, country of birth, AIDS-related deaths, mode of exposure to HIV, patient had more than one risk factor (i.e., additional risk factors), region of residence, and other behavioral risk factors.

IV. Measures and Variables

In this analysis, country of birth is represented here by a categorical variable coded as "1" foreign born and "0" U. S. born. Race is classified into five categories with white as the reference group, Black, Hispanic, and Asian Pacific Islanders and other racial groups coded as 1.Sexual classification consists of four categories with -- adult/adolescent male has sex with other men-- as the reference category. Time since diagnosis was computed from date since diagnosis was ascertained by the CDC for each AIDS-indicator disease and calendar year 2002.

The data set used in this study included cases which met CDC case surveillance definitions. Each of the categories used in this study included whether patients met any of the seven definitions provided below. Cases that meet more than one of the definitions provided were classified into the category list first. The following are seven case definitions for AIDS by CDC (see MMWR, 1992 for details):

1) Pre 1985 CDC case definition for AIDS included: *Pneumocystis carina* pneumonia, Kaposi's sarcoma, and other opportunistic infections.
2) In 1985 CDC expanded the definition to include three distinct types of lymphoma and opportunistic infections -- those caused by bacteria, fungi, protozoa, and other infectious agents.
3) In 1987 CDC again revised AIDS definition and placed emphasis on HIV infection status and 12 diseases diagnosed definitively
4) In 1987 CDC included in its definition for AIDS diseases diagnosed presumptively. Diseases classified under diagnosed presumptively include: Candidacies of esophagus, Cytomegalovirus retinitis, Mycobacteriosis Kaposi's sarcoma, lymphoid interstitial pneumonia, Pneumocystis carinapneumonia and Toxoplasmosis.
5) 1993 pulmonary TB, recurrent pneumonia, and invasive cervical cancer … definitive diagnosis but also retain 23 clinical conditions in the AIDS surveillance case definition of 1987.
6) 1993 presumptive diagnosis.
7) 1993 severe HIV related immune suppression.

Table 1 : Variable Definitions

Variable	Definition
Race	Race of respondent 1=White 2=Black 3=Hispanic 4=Asian/Pacific Islander 5=American Indian/Alaskan Native
Case definition revisions patient meets	1. Pre 1985 *Pneumocystis carina* pneumonia, Kaposi's sarcoma, and other opportunistic infections 2. 1985 expanded to include Kaposi's sarcoma , three distinct types of lymphoma and opportunistic infections -- those caused by bacteria, fungi, protozoa, and other infectious agents 3. 1987 diagnosed definitively 4. 1997 diagnosed presumptively

	5. 1993 pulmonary TB, recurrent pneumonia … definitive diagnosis 6. 1993 presumptive diagnosis 7. 1993 severe HIV related immune suppression
Age	*1. 0-19 years* *2. 20-29 years* *3. 30-39 years* *4. 40-49 years* *5. 50+ years*
Modes of Exposure	Exposure to HIV/AIDS 0=low risk (Hemophilia, heterosexual contact, blood transfusion, mother with or at risk for HIV infection etc 1= High risk (men have sex with men, injection drug use, MSM and drug use)
Additional Risk Exposure	Indicates if patient had more than one risk of exposure to HIV 0=single exposure 1=additional exposure
Sexual Classification	Sexual preference 0=had sex with both men and women, heterosexual 1= have sex with other men
Sex with Infected HIV/AIDS person	Sex with a person known to be infected with HIV/AIDS 0=No 1=Yes
Place of Birth	Country of birth 0=foreign born 1=U.S. born
Death	Vital Status of patient 0=Survive 1= died

The data for the analysis is "right" censored due to death (i.e., a case right-censored when time of death is known only to have occurred after time t). Patients whose death notification had not been received by CDC at the time of compilation of the data are coded 0 indicating the patient is alive while patients with death certificate are classified as dead. In this study the status variable is equals death or survival. For details regarding vital status classification see Morbidity and Mortality Weekly Report, 1997 and 1998.

b) Analytical Techniques

Two types of statistical analyses were used in this study. First, descriptive statistics such as percentages and Chi square test of independence were calculated. Second, because time of diagnosis is clearly a critical dimension of AIDS-related deaths, time at risk was therefore estimated from date of diagnoses to 2002. Since deaths for those in the surveillance data relates to time of diagnoses (time-to-failure), Cox Proportional Hazards are deemed appropriate for analysis. Therefore, Cox Proportional Hazards model was used to estimate those in surveillance who had not experienced the event between1980 and 2002. The probability of the endpoint (death, or any other event of interest, e.g. recurrence of disease) is called the hazard. The statistical analyses are structured in order to analyze differences in mortality and mode of exposure as depicted in Equation 1. The hazard is modeled as:

$$h(t) = h_0(t) \times \exp(b_1X_1 + b_2X_2 + b_3X_3 + \ldots. + b_kX_k) \qquad \text{Eq. 1}$$

Where $h_0(t)$ is the baseline hazard at time t, representing the hazard for a person with the value 0 for all the predictor variables. X_1 ... X_k represent the CDC AIDS case definition revision met by the patient, age at diagnosis, race, had sex with a person known to be infected with HIV or to have AIDS but whose risk factor is unknown, and country of birth. These are the predictor variables.

By dividing both sides of the above equation by $H_0(t)$ and taking logarithms, we obtain:

$$h(t) = \{ h(t) / h_0(t)\} = (\beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \ldots. + \beta_k X_k) \qquad \text{Eq. 2}$$

We call $h(t) / h_0(t)$ the hazard ratio. The coefficients $\beta_i...\beta_k$ are estimated by Cox regression, and can be interpreted in a similar manner to that of multiple logistic regression. With country of birth, a covariate (risk factor) coded 1 if present and 0 if absent, the quantity $\exp(\beta_i)$ can be interpreted as the instantaneous relative risk of death, at any time, for patients with the risk factor present compared with individuals who survived, given that both individuals are the same on all other covariates. On the other hand, for a covariate that is continuous, then the quantity $\exp(\beta_i)$ is the instantaneous relative risk of an event, at any time, for an individual with an increase of 1 in the value of the covariate compared with another individual, given that both individuals are the same on all other covariates.

The study examined three models describing the effects of case definitions of HIV/AIDS on mortality.

$$H(t) = h_0(t)\exp(\beta_1 \text{ CDHIV/AIDS}) \qquad (1)$$

$$H(t) = h_0(t)\exp(\beta_1 \text{ CDHIV/AIDS} + \beta_2 \text{Race} + \beta_3 \text{Age} + \beta_4 \text{Place of birth}) \qquad (2)$$

$$H(t) = h_0(t)\exp(\beta_1 \text{ CDHIV/AIDS} + \beta_2 \text{ Race} + \beta_3 \text{Age} + \beta_4 \text{Place of birth} + \beta_5 \text{Sex class} + \beta_6 \text{Sex with HIV}^+) \qquad (3)$$

Model 1 tests the effects of the CDC case definitions of HIV/AIDS (CDHIV/AIDS) on the instantaneous relative risk of death, at any time, for patients with the risk factor present compared with individuals who survived. The remaining two models include the CDC case definitions of HIV/AIDS, race, age, place of birth, sexual classification and had sex with infected HIV/AIDS person. All three models were modeled with time-varying covariates.

V. Results

Descriptive Findings: AIDS definitions, Race and Sexual behavior

Table 2: provides descriptive statistics for case definitions, race, sexual classification, patient had sex with infected AIDS person, and place of birth. Each of the variables percentage is shown with actual number of deaths in parenthesis. A comparison of the percentage of deaths varies with each revised definition. However, the findings suggest that the percentage of deaths decreased from a high of 54.9 for patients who meet pre-1985 CDC case definition compared to all subsequent definitions. A chi square procedure for independence was used to discover the relationship between the vital status of patients and case definitions (see Table 2). The overall chi square for independence, χ^2 (*of* 6, N=16,383)= 3063.10, p< .000, suggested that vital status of patient and case definitions of HV/AIDS were related. This implies that vital status of patient is influenced by case definition.

Table 2 : Vacate Distribution: Risk Factors, Characteristics By Survival

Variable	Vital Status of Patient		
	% Survives	% Died	χ^2 Test
AIDS Case meets			2974***
1985 definition	25.6	57.7	
1987 definition	13.4	22.7	
1993 definition	61.0	19.6	
Race			119.63***
White	37.4	45.7	
Black	41.6	36.4	
Hispanic	19.6	17.0	
Other	1.4	0.9	
Age of Patient			16.976***
0-19	1.8	1.2	
20-29	16.4	16.2	
30-39	43.5	43.6	

40-49	27.5	26.8	
50+	10.8	12.2	
Sexual Classification			182.25***
Had sex with men	34.1	43.4	
Had sex with both	11.6	11.9	
Heterosexual male	32.9	29.2	
Female both	21.4	15.6	
Sex with Infected HIV/AIDS person			269.69***
No	25.4	32.4	
Yes	16.7	8.9	
unknown	57.9	58.8	
Place of Birth			1.291
Foreign Born	13.9	13.3	
US Born	86.1	86.7	

*** p< .000

Table 2 also shows that AIDS patients who had a single risk of exposure were more likely to die than those who have additional risks of exposure. The probability that an individual AIDS patient chosen at random has sex with a person known to be infected with HIV or to have AIDS but whose modes of exposure is unknown and died from the virus is 8.9% compared to 32.4% of those who reported that they did not. Furthermore, the results displayed in Table 2 indicate that the relationship between patient's vital status and race is very strong. A chi square test of independence suggest that AIDS patients race is significantly related to vital status, χ^2 of 3, N=16,186)= 119.63, p< .000.

Covariates and their Differences across Racial categories

Table 3: shows summary statistics for age groups, case definition and multiple risk factors, and race. In this analysis, the effects of age case definition on the vital status of patients were examined while controlling for race. For instance, among AIDS patients who died of the disease, 68.9% who met case definition for 1985 were white compared to 49.2% blacks, 21.1% Hispanic and 63.4% other population groups. However, the percentage of patient's deaths associated with case definitions for 1987 and 1993 were higher for all racial groups compared to whites.

Information in Table 3 further illustrates the relationship between patients who had sex with persons known to have HIV and their vital status while controlling for race. The table shows that non-white patients who reported having sex with a person known to be infected with AIDS were more than twice as likely to die as White. For example, for those who died of AIDS-related complications,4.4% were whites, 12.6% black, 13.1% Hispanic and 10.8% were other racial minorities. The percentages are also noticeably different across racial groups for those who reported that they did not have sex with a person known to be infected with HIV. The results in Table 3 suggest that the percentage of deaths associated with those who reported that they did not have sex with a person known to be HIV positive was higher compared to those who did. Thus, regardless of patients' racial background, those who reported not having sex with a person known to be HIV positive were more likely to die than those who reported that they had sex with a person known to be HIV positive. Further evidence suggest that there is a relationship between patient status and whether or not respondents had sex with a person known to be infected with AIDS. The analysis suggests that patient's vital status is statistically related to modes of exposure when race is held constant. Overall, race is still a significant predictor of patient's vital status.

Table 3 : Age Group at Diagnosis of the First AIDS-Indicator Opportunistic Condition by Patient Status by Race/Ethnicity

Variables	Race of Respondent							
	White		Black		Hispanic		Other	
	% Survives	% Died	% Survives	% Died	% Survives	% Died	% Survives	% Died
Age Groups								
0- 19	1.0	0.5	2.3	1.9	2.6	1.8	1.0	1.2
20-29	15.4	16.3	16.2	15.7	18.5	17.4	23.1	14.6

30-39	46.0	43.5	40.6	43.1	44.5	44.7	48.1	45.1
40-49	27.4	26.5	29.4	27.7	24.4	25.5	18.3	24.4
50+	10.3	13.2	11.6	11.5	10.0	10.6	9.6	14.6
Definition								
Case meets pre 1985	28.9	68.9	24.5	49.2	21.1	45.6	32.7	63.4
Case meets 1987	12.1	17.1	12.5	25.7	17.4	31.1	13.5	20.7
Case meets 1993	59.0	14.0	62.9	25.1	61.4	23.2	53.8	15.9
Had sex with a person known to be HIV+ [b]								
No	32.7	39.2	19.3	25.5	23.4	27.6	36.5	41.9
Yes	9.2	4.4	21.1	12.6	22.1	13.1	13.5	10.8
Multiple Risk Factors [c]								
Patient has one risk factor	77.8	83.8	65.7	75.0	69.7	76.9	66.0	76.8
Patient has additional risk factors	14.7	12.7	14.1	15.8	16.8	17.6	12.6	17.1
Patient's HIV risk factor is not reported or identified	7.5	3.4	20.1	9.3	13.5	5.5	21.4	6.1

[a]Age groups: Whiteχ^2 =19.905; df=4; p = .001

CDC Defintion for AIDS – Whites χ^2 =1568.98; df=2; p= .000; Black χ^2 =925.32; df=2; p = .000; Hispanic χ^2 =448.281; df=2; p = .000; Other χ^2 =28.654; df=2; α = .000

[b]Had sex with HIV+ person: White χ^2 =80.77; df=2; p = .000; Black: χ^2 =97.419; df=2; p = .000; Hispanic: χ^2 =42.14; df=2; p = .000; Other: NS

[c]Multiple Risk Factors: White χ^2 =64.33; df=2; p = .000; Black χ^2=148.79, df=2, p =.000; Hispanic χ^2 =55.24; df=2; p = .000and Other χ^2 =8.66; df=2; p = .013

Figure 1 : Vital Ststus of Patient

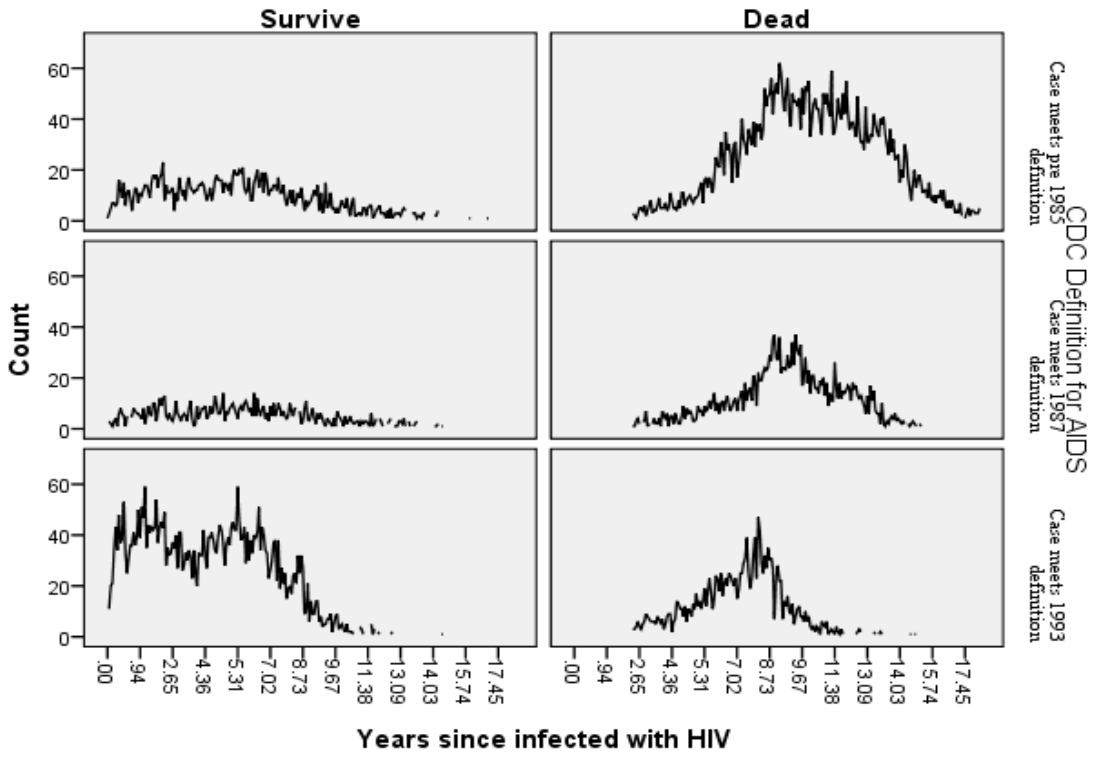


Figure 1: extends the analysis one step further by exploring patient's mortality patterns, cases definitions and years since infection. Figure 1 shows that mortality peaked between 7 and 8 years after infection for all the three summarized CDC case definitions. Of the three CDC case definitions, the number of HIV/AIDS related-deaths was higher for cases that met the pre 1985 definition compared to 1987 and 1993. Interestingly, the time it took from infection until patient's death varied with the CDC case definition.

Table 4 : Relative Risks of Hive/Aids Related Deaths in the United States

Cover its	Model 1		Model 2		Model 3		Model 4	
	Exp B	CI	Exp B	CI	Exp B	CI	Exp B	CI
Case definition revisions patient meets	1.000		1.000		1.000		1.000	
1. Pre 1985	0.730***	644-	2.160***	1.88-	2.012***	1.595-	1.925***	1.525-
2. 1985		.829		2.477		2.539		2.432
3. 1987 diagnosed definitively	0.940	.820-	1.085**	1.02-	1.251***	1.121-	1.272***	1.139-
	0.927‡	1.077	1.126	1.160	0.919	1.396	0.971	1.420
4. 1987 diagnosed presumptively		.850-		0.97-		0.709-		0.748-
		1.011		0..313		1.192		1.260
5. 1993 pulmonary TB, recurrent pneumonia … definitive diagnosis	0.874‡		0.834*		0.646**		0.673**	
	0.688*	.747-	0.947	0.687-	0.931	0.465-	0.944	0.484-
	0.978	1.023	0.906*	1.013	0.889	0.897	0.883	0.936
6. 1993 presumptive diagnosis		.487-		0.799-		0.698-		0.708-
		.972		1.123		1.241		1.260
7. 1993 severe HIV related immune suppression		.712-		0.811-		0.741-		0.735-
		1.344		1.011		1.067		1.060
Race of respondent								
1=White			1.000				1.000	
2=Black			1.179**	1.02-			1.151	0.938-
3=Hispanic			0.911	1.369			0.941	1.411
4=Asian/Pacific Islander/Other				0.813-				0.804-
			1.134***	1.021			1.184***	1.101
				1.061-				1.073-
				1.211				1.306
Age								
1. < 19 years			1.000				1.000	
2. 20-29 years			1.683***	1.484-			1.684***	1.148-
3. 30-39 years			0.898**	1.908			0.839	2.469
4. 40-49 years			0.971	0.807-			0.986	0.607-
5. 50+ years			0.964	1.000			0.968	1.160
				0.901-				0.807-
				1.046				1.204
				0.922-				0.882-
				1.008				1.063
Place of Birth								
0=foreign born			1.000				1.000	
1=U.S. born			0.943***	0.895-			0.946	0.870-
				0.993				1.029
Sexual Classification								
1. Adult/adolescent male had sex with other men					1.000		1.000	
					1.258***	1.160-	1.167***	1.072-

2. Adult/adolescent male had sex with both men and women					0.925*	1.363	0.970	1.270
3. Adult/adolescent heterosexual male					0.973	0.859-0.997	1.003	0.900-1.046
4. Female (both adult/adolescent and pediatric)						0.898-1.054		0.925-1.087
Sex with Infected HIV/AIDS person								
0=No					1.000		1.000	
1=Yes					1.264***	1.182-1.353	1.287***	1.202-1.378
-2 Log Likelihood	148979.547		149910.91		54844.159		54742.83	
Chi-square (df)	1053.109 (6) ***		1363.416 (14) ***		484.271 (10) ***		592.659.166 (18 ***	

***$p = .000$; ** $p = .001$; $.03 \geq$* $p \leq .02$; ‡$.06 \geq p \geq .06$

Multivariate Models of Case Definitions and Mortality

Table 4 presents results for the Cox proportional hazard models analyses of CDC case definitions of HIV/AIDS and relationships of covariates such as race, age, sexual classifications and place of birth. In Model 1, where case definition is the only covariate, mortality risks from time of diagnosis until death tend to decrease with each additional year compared to pre 1985 case definition. Relative risks are much lower for each revised definition for every year increase since time of infection. For example, a hazard ratio of 0.730 ($p< .0001$) suggests that there is a 27% ($p< .0001$) decrease in mortality for every additional year since infection for those who were diagnosed in 1985 compared to pre 1985. As expected, the hazard ratios for 1993 CDC case definition for presumptive diagnosis is 31.2% ($p < .03$) lower than pre 1985 for each year since infection.

In addition to Model 1, we implemented a series of models attempting to control for patients socio-demographic characteristics: race, age, place of birth, sexual classification and whether patients had sex with HIV/AIDS infected person. Model 2 for example adjusts for demographic factors (i.e., race, age and place of birth). The results show that mortality hazard ratios increased for 1985 and 1987 CDC case definitions compared to pre 1985, while hazard ratios for both 1993 remain stable. With respect to mortality, 1985 CDC case definition is associated with1.16% ($p< .0001$) increase in risk for every year increase since infection compared to the pre 1985 (reference category).

Model 3 introduces behavioral indicators (sexual classification and had sex with infected HIV/AIDS persons). Model 3 shows that the inclusion of behavioral factors did not diminish the effects of case definitions on the relative risks of mortality. Finally, Model 4 includes the full set of independent variables. Once again, the effects of CDC case definitions remain the same. Net of all the controls, with the exception of 1985 and 1987 diagnosed definitively, the hazard ratios were negative suggesting reduced mortality hazard.

The hazard function of time patients were diagnosed with AIDS until death are displayed in figures 2a and 2b. From the hazard curve, it is clear that predicted hazard function (where the hazard is mortality and time is years since infection) were indeed different for the case definitions of HIV/AIDS. In fact, the longer the time since patients were first diagnosed with AIDS the more their relative risk of mortality decreased. However, patient's relative risk of mortality varied according to case definition when holding constant other covariates.

Figure 2a

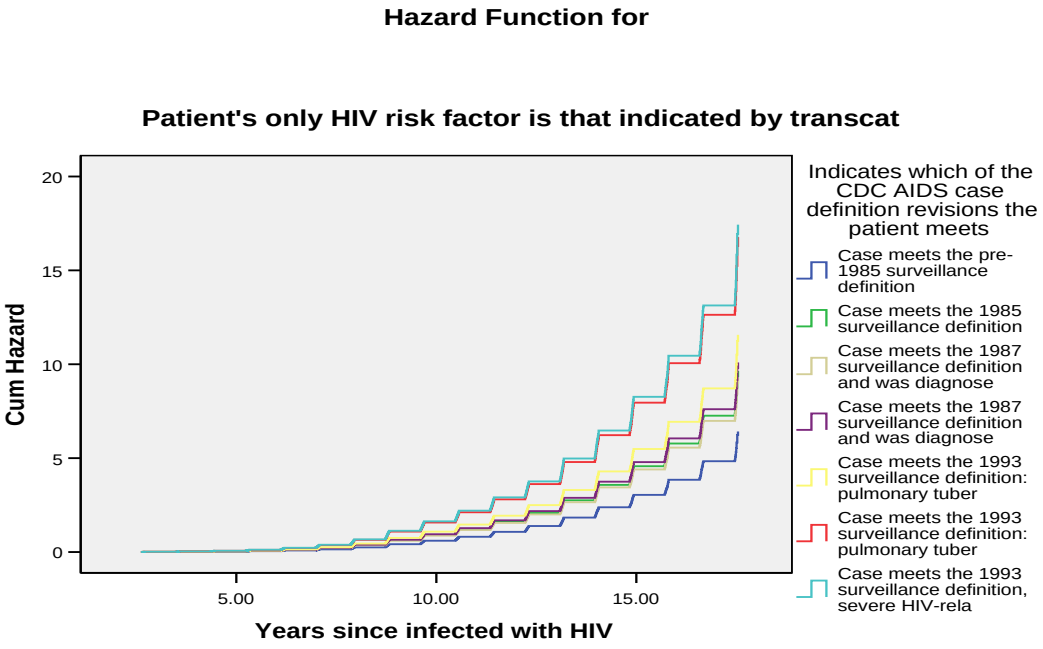
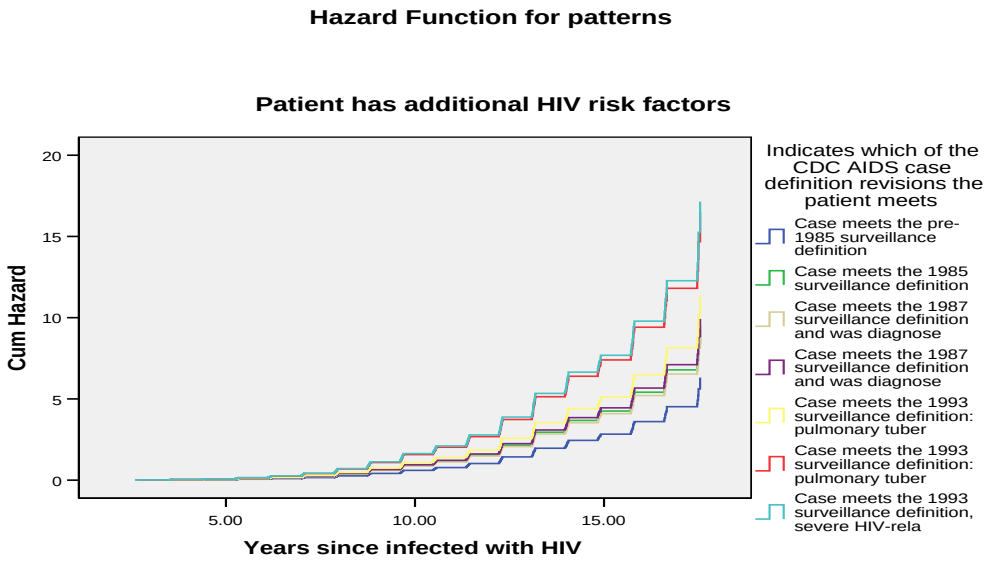


Figure 2a



VI. Discussion and Conclusions

The purpose of this study was to examine the relative risks of CDC case definition of HIV/AIDS on mortality. Our results presented in Model 1 (Table 4) indicate considerable lower hazard ratios for subsequent CDC case definitions of HIV/AIDS compared to pre 1985 for every increase in years since infection .The results suggest that CDC case definitions are associated with mortality risk in a graded manner.

To determine why CDC case definitions are associated with mortality, we controlled for socio-demographic variables. Our inclusion of socio-demographic covariates: age of patients at time of diagnosis, race, place of birth, and had sex with known HIV positive person at least illustrates the link between relative risk of mortality and CDC case definitions. Although mortality risk associated with HIV/AIDS may be declining with the introduction of anti-retroviral drugs and incessant publication of related health risks, there is

evidence from this study to suggest that mortality differences based on CDC case definitions may be attributable to socio-demographic factors. The overall model fits well as indicated by the -2 Log likelihood test of statistical significance as shown in Table 4.

Although the results suggest that the differences in AIDS definition affect risk of mortality, the finding may reflect the particular emphasis on "additional research information" about the virus and symptoms associated with it at that point in time. While case definitions provided by CDC are important, clearly understanding the impact of socio-demographic variables and changes in the definitions is an iterative process that needs further analysis. The point, however, should be clear: a more broadly defined and dynamic concept of HIV/AIDS may actually not lead to an increase in the risk of mortality but can be increased by socio-demographic variables.

Given the differential relative effects of case definition of HIV/AIDS on mortality, it is crucial that researchers and clinicians minimize ambiguity and clearly distinguished specific case definition of HIV/AIDS when performing HIV/AIDS analysis. At least for now, our findings highlight the importance of socio-demographic variables and serves as a useful guide for AIDS-related mortality studies in our struggle to better understand the role case definition plays in relative risks of mortality of infected persons.

VII. Conflict of Interest Statement

The contents of the manuscript represent the views of the authors and not those of the CDC. The authors did not receive any grant or funding from CDC to conduct this study.

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