Mortality Analysis in People Diagnosed with HIV/ AIDS in Puerto Rico from 2003-2011

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Abstract

HIV epidemic are still a global public health concern. In the HIV history is well documented through scientific literature, the effectivity of the antiretroviral therapies (ART). ART has dramatically improved the life expectancy of HIV. Even though, it's necessary to monitor the causes of death of people with HIV/AIDS. The objective of this study was to estimate mortality risk in people diagnosed with HIV/AIDS in Puerto Rico (PR) from 2006 through 2011. We used a population-based study from the PR AIDS Surveillance System, a total of N=2,290 deaths were reported for the study period. The Cox Proportional Hazards Regression Method was used to identify determinants of mortality. The 71% were males. The 23.5% of deaths were related to HIV/AIDS. Age and Sex adjust death rates was 4.9 deaths per 1,000 population and a fatality rate was 22.2%. The Hazard Ratio [HR] for a HIV/AIDS cause of death in intravenous drug user [IDU] was HR=1.53; 95% confidence interval [IC], 1.37, 1.70 ($p<0.001$); in AIDS stage HR=7.53; 95% IC, 2.42, 23.4 ($p<0.001$); and with CD4 cell count ≥ 500 copies HR= 0.20; 95% IC, 0.16, 0.26 (<0.001). Deaths of people with HIV/AIDS in Puerto Rico were not related to the traditional HIV/AIDS causes of death. IDU population, males, AIDS stage of the disease and with low CD4 cell count has higher risk to die to HIV/AIDS cause of death. We recommended designing specific tertiary prevention strategies for IDU population.

Keywords: HIV/AIDS, Mortality, Hazard ratio, Puerto Rico

HIV Descriptive Epidemiology

The Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) is one of the core issues of public health. UNAIDS (2014) reported that in 2013 a prevalence of 35-95% [33.2, 37.2] million people worldwide with HIV. The Office of AIDS Surveillance (2015) Department of Health reported 46.819 cases of HIV/AIDS reported from 1981 to March 31, 2015. The 73.9% (34.601) were men and 26.1% (12,218) women. The most common means of infection are sharing equipment for injecting drug use in 44% of cases (20.155); unprotected heterosexual intercourse are 29% of cases (13.364); HSH relations without protection are 19% (8,623) and MSM with a history of intravenous drug use are 6% of cases (2,839). Regarding mortality data, there have been 26.544 deaths for a fatality rate of 57% (26.544, cumulative). Puerto

Rico these data should be interpreted with the same precautions as global figures, since the problem of underreporting of cases is a reality.

These data suggest that the three groups of greatest impact in Puerto Rico AIDS cases are: injecting drug users, unprotected heterosexual contact and men who have sex with men without protection. With advances in HIV treatment through the years, HIV has become a chronic.[1,2] Like other chronic diseases co-morbidity with other diseases is also present in the natural history of HIV/AIDS. A related disease AIDS is known in the literature as conditions related to AIDS (AIDS related conditions, in English) these are: candidiasis, invasive cervical cancer, coccidioidomycosis, cryptococcosis, cryptosporidiosis, related to cytomegalovirus disease, encephalopathy (related to HIV), herpes simplex (severe infection), histoplasmosis, isosporiasis, Kaposi's sarcoma (a rare skin condition caused by a type of herpes virus), lymphomas (eg. Non- Hudking), Mycobacterium avium, pneumocystis carinii pneumonia, pneumonia (recurrent), progressive multifocal Leukoencefalopatía, Salmonella septicemia (recurrent), toxoplasmosis of the brain, tuberculosis, among others.[1] Generally, AIDS-related conditions are those of infectious origin, consistent with the commitment of the immune system by HIV.

However, there is a tendency in chronic comorbidities in people with HIV/AIDS. Recent studies in Brazil, United States, Taiwan and Puerto Rico prove it, having estimated the presence of diseases such as diabetes, liver disease, cardiovascular diseases, among others.[2-6] Which shows a change in what some have called the new generation of HIV.[2] In part, this new trend is the use of therapies that have been highly effective in the HIV population.

HIV Mortality Trends

As treatments have improved, people with HIV/AIDS live longer and therefore increases their susceptibility to chronic diseases. For the peak of the epidemic-1993, AIDS was the leading cause of death in women and men aged 25-44 years in the US and were the cause of 2% of all deaths.[7] According to adjusted death rates by age of HIV/AIDS for 1987 it was 6 deaths per 100,000 and for 1995 the rate increased to 17 deaths per 100,000. Thereafter, the mortality rates for HIV/AIDS dropped dramatically to the current date, for 1995 was estimated 17 deaths per 100,000 inhabitants compared to 2007 where 5 of every 100,000 having a 46% reduction.[8] Today about 18,000 annual deaths related to AIDS[9] were reported.

When mortality trends on HIV/AIDS around the world are the United States and Puerto Rico can point out two important issues: (1) the decline in deaths and (2) how it has changed the causes of these deaths. On the first point, many studies around the world and sustain and establish the cause of this decline the introduction of HAART.[2-6,10] For the second point, it is a relatively recent theme in the scientific literature, on how they have changed the cause of death related to AIDS. These new cases are beginning to recognize long-term aftermath of HAART.[2] Specifically, studies in the US They show as there was a significant decrease in deaths from AIDS-related diseases, but also as increased deaths from causes unrelated to AIDS from HAART.[2,11] In particular, this increase was seen in diseases such as malignant tumours unrelated to AIDS, liver disease and cardiovascular disease. In other studies, in addition to the diseases mentioned above, it has been found among new causes of death: diabetes mellitus, cancer unrelated to AIDS, liver disease and related metabolic syndrome.[3,4]

Studies have critically evaluated the new trend in mortality for HIV/AIDS, discussing the matter, that from HAART disparities by socioeconomic status and ethnic groups have increased.[12] Evidencing such as access to treatment is a problem in American society.

Justify

Mortality trends of HIV/AIDS have been extensively studied around the world, including Puerto Rico. However, knowing this trend through a data bank for the island population level is an area that has not been discussed in the past. This proposal intends to study at the population level, in addition to updating the mortality rates and the survival rate of HIV/AIDS in Puerto Rico, it intends to develop partnerships with specific causes of death other variables of interest as a means of infection, viral load, age, time to diagnosis, gender and health region. Knowing the specific causes of death for people with HIV/AIDS in Puerto Rico can have a broader impact of the epidemic on the island landscape. It also allows understanding from a public health perspective new challenges and opportunities for prevention and control of a disease that has nearly 30 years in the country.

The research intends to conduct a study on population trends in mortality of patients with HIV/AIDS in Puerto Rico by major causes of death associated with HIV/AIDS and the causes of death was not associated with HIV/AIDS in the period 2003- 2011. The lessons of the last decade of HIV/AIDS just being analysed, the changes in recent years must be significant for understanding the future of the epidemic. Learn about the situation in Puerto Rico should be a priority in the strategic plan for HIV/AIDS which trace on the island.

Research Question

The question of interest to guide the study was: What is the mortality rate and the causes of deaths for people diagnosed with HIV during the period 2003-2011 in Puerto Rico?

Methods

To reach the aim of the study, a retrospective cohort[13,14] was performed using a secondary database that comes from AIDS Surveillance System of Puerto Rico within the Department Health, to estimate mortality rates.

Sample

The subjects for this analysis to assess survival are all those individuals who had a first positive HIV test during the period 1 January 2003 to 31 December 2011. Within the AIDS Surveillance System there are 9,290 individuals with a first positive HIV test for the study period.

Follow up timeline

Eligible individuals for this study were those who got diagnosed with HIV/AIDS for the period of January 1, 2003 to December 31, 2011. For terms of mortality and survival analysis of these individuals were followed until December 31, 2011 waiting on them the result of dead or alive (Figure 1).

HIV surveillance form

The data used in this study were collected by the surveillance system AIDS, which uses a standardized by the Centers for Disease Control and Prevention (CDC, for its acronym in English) for data collection on cases instrument diagnosed with HIV /AIDS. This instrument has seven sections which are: (a) demographic data, (b) information on healthcare providers, (c) history of the patient, (d) laboratory test data, (e) clinical status, (f) treatment/referral services and (g) stage of HIV infection. In addition, this instrument

monitoring system together with the Vital Statistics Department of Health matched made to identify the cause of death of people who have been reported as cases of HIV/AIDS.

Statistical software's

The information on the variables of interest were obtained in the form of statistical program Excel, so data were incorporated into the data analysis program Statistical Package for Social Sciences (SPSS v19.0) and R program.

Missing data

To complete the missing data related to survival times use a likelihood method, namely the multiple imputation (Monte Carlo Markov models).[15] Multiple imputations are practical to complete the missing values with plausible values in a database. Regularly, this practice is often striking for cases with high percentages of missing values because it allows analysing incomplete data.[15-17]

For this study the determination of the model generate multiple imputations using 10 complaints was taken. There are several reasons for this: first, to set off 10 ensures reduce the standard error and problems with the value of p (statistical significance). Second, 10 allegations guarantee high efficiency according to the theory of Robin, that this model is 93.5%.[14,18] Although studies using data from surveillance systems for HIV at the level of the United States of America have been used up to 20 charges, even in databases with more than 70% of missing values.[17,19] It is recognized that 10 complaints help achieve adequate efficiency to subsequently perform analyses.[20]

Results

Absolute and relative frequencies were produced to describe the study variables of interest. For a description of continuous variables it was performed using different measures of central tendency and dispersion as mean, median, standard deviation and maximum and minimum values. In order to determine the percent of the causes of death and other variables of interest. To test the hypothesis Chi square (one sided test)[21] they were used. To complete the bivariate analysis, statistical differences in sociodemographic, immunological stage and mode of transmission in groups of specific causes of death related to HIV/AIDS versus unrelated through a Chi - square test and the test was evaluated Mann-Whitney. P value <0.05 was used in this test to indicate the significant difference between groups with respect to the variable of interest.

Finally, multivariate analysis 6 Cox regression models were conducted. The Cox regression models were to determine the risk of death among specific causes of death related to HIV/AIDS and specific causes of death unrelated to HIV/AIDS and interest variables controlling for potential confounding variables. The confounding variables were identified as: age, sex, educational level, CD4 cell count and mode of transmission. In this model, the dependent variable is the presence or absence of specific causes of deaths related to HIV/AIDS and the independent variable the variables of interest.

Institutional Review Board

This study protocol was approved by the Institutional Review Board of the Ponce School of Medicine under the expedite format. Finally, to ensure the confidentiality of data, you will be asked the Department of Health-AIDS Surveillance Bureau that no personal identifiers deliver health subjects.

Statistical analysis

Sociodemographic data: In this study, 71.0% (n=6,601) of subjects involved were men. 99.8% (n=9,282) were identified as Hispanic. The average age of people with HIV/AIDS for the period 2003-2011 in Puerto Rico was 53.4 years. The median age was 53 years. The median age for the group of people dead was 46. For men, the average age was 53 years and for women 51 years. The average age by way of transmission through injection drug use was 51 years, through heterosexual contact 57, through contact with man sex man of 52 years, through two exhibitions (injection drug use and man sex with men) and eventually 48 other cases with an average of 54 years (Table 1). Of those assessed in the study period, 42.1% had completed some level between first and eighth, 6.3% had a high school degree, 7.6% completed the twelfth grade, 5.9% completed technical studies associate degree or some college and 3.1% completed a bachelor's, master's or doctoral Moreover, 99.8% of the population diagnosed with HIV or AIDS in Puerto Rico for the period 2003 to 2011 were identified as Hispanic. People with HIV/AIDS for the period 2003-2011 in Puerto Rico reported being infected mostly by unprotected heterosexual 39.1% (n=3,631). Followed by contact intravenous drug use 28.9% (n=2,685); unprotected homosexual 22.5% (n=2,090); exposure by intravenous drug use and unprotected homosexual 3.1% (n=288); perinatal exposure 0.3% (n=29) and other exposures not reported or identified with 6.1% (n=567) (Table 2).

People within the study period, the distribution of the first CD4 cell count was 43.7% for the group with <200 copies; 31.1% for those between 200-499 copies and 25.3% for those with ≥ 500 copies. Finally, the distribution of CD4 cell counts to their latest results reported was: 38.1% for the group with <200 copies; 30.9% for those between 200-499 copies and 31.0% for those with ≥ 500 copies.

Hypothesis tests for the various variables of interest regarding a cause of death associated with HIV/AIDS found statistically significant differences in the variables of interest : sex, immune stage, mode of transmission, marital status, educational level and cell count CD4 ($p<0.05$). Below the Table 3 containing the summary of hypothesis tests for the various variables of interest regarding a cause of death associated with HIV/AIDS it is presented.

Mortality analysis: The crude mortality rate for HIV/AIDS for the period of 2003-2011 was 52.3 cases per 100,000 people. The mortality rate adjusted for age and sex for HIV/AIDS during the 2003-2011 periods was 12 cases per 100,000 people. This rate was adjusted data Community Survey estimated 2007 population (half of the study period). The fatality rate for HIV/AIDS for the period 2003-2011 was 22.2%. 23.5% of people diagnosed with HIV/AIDS for the period of study died for a cause associated with the disease (Table 4).

The data suggest that men have 5% higher risk of dying from causes related to HIV/AIDS compared to women was statistically significant ($p<0.001$). Divorced has 56.3% greater risk of dying cause related to HIV/AIDS compared to other marital status was statistically significant ($p<0.001$). Those diagnosed in stage AIDS had 65.3% higher risk of dying related to HIV/AIDS compared to previous stages being statistically significant ($p=0.033$).

Those who have completed a university degree 41% lower risk of dying from causes related to HIV/AIDS being statistically significant ($p<0.001$). Then the Table 5 Cox proportional hazard regressions are presented in detail for each of the categories evaluated.

Discussion

The crude mortality rate was 52.3 per 100,000 people. Adjusted mortality rate by age and gender was also calculated, it was 4.9 per 1000 people. This positions the HIV/AIDS with a high mortality rate when compared with other diseases in Puerto Rico. For example, the adjusted mortality rate for Puerto Rico in 2010 was 7.4 per 1000 people. The fatality rate was estimated at 22.2%, which also is considered high in a group of disease.

Importantly, there was a higher rate of deaths not associated with HIV/AIDS (62.4%), as expressed in the literature following antiretroviral therapy.[10] However, it is noteworthy that also is a matter for further study because new studies suggest a slight increase in causes associated with HIV/AIDS.[22] The interest on this subject is that these diseases are preventable causes related, matter that can be addressed from a public health professional model.

Moreover, within the risk groups for HIV/AIDS, people who inject drugs have a 53% higher risk of dying from causes associated with HIV/AIDS compared to other groups ($p<0.001$). Data that is consistent with the provisions of the scientific literature, as have other infectious co-morbidities such as Hepatitis C among others.[22-24] Likewise, men showed up 5% risk of dying related to HIV/AIDS than women ($p<0.001$).[22] For the group of $\geq$ 65 years is 28% higher risk of dying from causes related to HIV/AIDS compared to those <65 years ($p<0.001$).

In general, cases with more education had a protective factor of 41% lower risk of dying related to HIV/AIDS ($p<0.001$). A CD4 cell count $\geq$ 500 copies has a protective effect of up to 80% less likely to die of a cause related to HIV/AIDS compared to those with less than 200 copies ($p<0.001$) count. All these data are supported with the provisions of the scientific literature.[4,11,22,25]

Strengths

Strength of retrospective cohort studies is that less costly results through a prospective study and also you can get the time variable are obtained. This is important to see, because through medical records, death certificates and interviews carried out by technicians epidemiology; you can get the time from the time of diagnosis and to assess the effects and then the same. This able to establish causality relationship.

Another strength of this study is that when the population level allows one to see how HIV/AIDS and behaves not merely through a sample of a clinical study or as regularly presented in the literature on the subject in Puerto Rico. In addition, the universe of cases reported for the period of study is reached, which is a great strength in terms of methodology and evaluation of public health level.

Limitations

In terms of design limitations, epidemiological methodology recognizes that retrospective studies are done when there is information that could not be collected in an accurate way, since you ask subjects about health exposures. So there could be a memory bias in this process. Furthermore in this study, information on health subjects who died are under the judgment of the compilation and reporting for the attending physician completed the death certificate.

Recommendations

This study is the first population-based epidemiological study to assess death and survival in people diagnosed with HIV/AIDS in Puerto Rico. This study suggests that within this population group of injecting drug users with specific needs to be addressed at both the prevention and treatment recommendations. Since this group are at the greatest risk of dying related to HIV/AIDS compared to other risk groups. This statistically significant, implying new public health strategy specifically for this group. It also recommends expanding this effort at the state level, so established public policies to overcome the challenges to serve this population. A concrete example would be a needle exchange program state wide. Finally, continuous monitoring of the causes of deaths in people with HIV/AIDS and evaluate the factors that can be modified.

References

1. Pfizer. Control de enfermedades infecciosas- Estudio de casos. En Milestones in Public Health. Accomplishments in Public Health over the last 100 years 2006; 59-82.
2. Quinn TC. HIV epidemiology and the effects of antiviral theraphy on long-term consequences. AIDS 2008; 22: s7-s12.
3. de Aguiar-Perreira C., Jorge-Machado C., do Nascimento-Rodrigues R. Perfis de causas múltiples de morte relacionadas ao HIV/AIDS nos municipios de Sao Paulo e Santos, Brasil, 2001. Cad Saúde Pública, Rio de Janeiro 2007; 23: 645-655.
4. Pacheco AG., Tuboi SH., May SB., Moreira LFS., Ramadas L., et al. Temporal changes in causes of death among HIV-infected patients in the HAART era in Rio de Janeiro, Brazil. J Acquir Immune Defic Syndr 2009; 51: 624-630.
5. Mayor AM., Gómez MA., Ríos-Oliveras E., Hunter-Mellado RF. Mortality trends of HIV-infected patients after the introduction of highly active antiretroviral therapy: Analysis of a cohort of 3,332 HIV-infected persons. Ethn Dis 2005; 15: 57-62.
6. Yang CH., Huang YF., Hsiao CF., Yeh YL., Liou HR., et al. Trends of mortality and causes of death among HIV-infected patients in Taiwan, 1984–2005. HIV Medicine 2008; 9: 535-543. MMWR. Update: Mortality attributable to HIV infection among persons aged 25–44 years—United States, 1994. MMWR 1996; 45: 121–125.
7. CDCB. Mortality slides series. 2011.
8. CDC. HIV in the United States. 2014.
9. Lima VD., Lepik KJ., Zhang W., Muldoon KA., Hogg RS., et al. Regional and temporal changes in HIV-related mortality in British Columbia, 1987-2006. Can J Public Health 2008; 101: 415-419.
10. Palella FJ., Baker RK., Moorman AC., Chmiel JS., Wood KC., et al. Mortality in the HAART era: Changing causes of death and disease in the HIV outpatient study. Acquir Immune Defic Syndr 2006; 43: 27-34.
11. Rubin MC., Colen CG., Link BG. Mortality in the United States from a Fundamental Cause perspective. American Journal of Public Health 2009; 100: 1053-1059.
12. Gordis L. Epidemiology. 3rd edition. Elsevier Saunders 2004; Philadelphia: Pennsylvania.
13. Kelsey JL., Whittemore AS., Evans A.S., Thompson WD. Methods in observational epidemiology. 2nd edition. Chapter 10: Oxford University Press 2010; New York.

14. Rubin DB. Inference and missing data. Biometrika 1976; 63: 581-592.

15. Lee KJ., Carlin JB. Recovery of information from multiple imputation: A simulation study. Emerging Themes in Epidemiology 2012; 9: 3.

16. MMWR. Subpopulation Estimates from the HIV Incidence Surveillance System, United States, 2006. MMWR 2008; 57: 985-989.

17. Badler C., Alsina SF., Puigsubirá C., Vitelleschi MS. Imputacion múltiple en SAS para estimaciones a partir de bases de datos con información faltante. Afiche presentado en: Instituto de Investigaciones Teóricas y Aplicadas de la Escuela de Estadística. Facultad de Ciencias Económicas y Estadística. Universidad Nacional de Rosario. Argentina. Recuperado el 13de marzo de 2014.

18. Hall HI., Song R., Rhodes P., Prejean J., An Q., et al. Estimation of HIV Incidence in the United States. JAMA 2008; 300: 520–529.

19. Stuart EA., Azur M., Frangaski C., Leaf P. Multiple imputation with large data sets: A case study of the children's mental health initiative. Am J Epidemiol 2009; 169: 1133-1139.

20. Rosner B. Fundamentals of biostatistics. Thompson Belmont 2010: California.

21. The Antiretroviral Therapy Cohort Collaboration. Causes of death in HIV-1–infected patients treated with Antiretroviral Therapy, 1996–2006: Collaborative analysis of 13 HIV cohort studies. Clinical Infectious Diseases 2010; 50: 1387–1396.

22. Mayor A., Gómez M., Otero J., Vilá S., Hunter R. Pulmonary Tuberculosis mortality risk in a cohort. Cellular and molecular biology 2001; 47: 1143-1148.

23. Serfaty L., Costagliola D., Wendum, D., Picardc O., Meyohasd MC., et al. Impact of early-untreated HIV infection on chronic hepatitis C in intravenous drug users: a case-control study. AIDS 2001; 15: 2011-2016.

24. Rajagopalan N., Suchitra, JB., Shet A., Khan ZK., Martín-García, J., et al. Mortality anmong HIV-Infected patients in resourcelimited settings: A case controlled analysis of inpatients ar a community care center. Am J Infect Dis 2009; 5: 219-224.

Table 1: Median and mean age for the cases reported with HIV/AIDS diagnosis for the 2003-2011 period.

Variable	Mean	Median
Overall Subjects	53	53.4
Sex		
Male	53	53.8
Female	51	52.3
Mode of Transmission		
IDU	51	50.6
MSM	52	52.7

HET	57	57.6
IDU/MSM	48	46.4
Others	54	53.7

Table 2: Educational level, ethnicity and mode of transmission of cases reported with HIV/AIDS diagnosis for the 2003-2011 periods.

Variable	**Percentage%**	**N**
Educational Level		
Some elementary school (1-8)	42.1	3,911
Some High School	6.3	585
High School Diploma/GED	7.6	706
Some collage	5.9	548
Finished university degree	7	651
No available	31.1	2,889
Ethnicity		
Hispanic	99.8	9,271
Other	0.2	19
Mode of Transmission		
IDU	28.9	2,685
MSM	22.5	2,090
HET	39.1	3,631
IDU/MSM	3.1	288
Others	6.4	596

Table 3: Chi square test for interest variables regarding to HIV/AIDS related cause of death.

Variable	**X2**	**P**	**Df**
HIV/AIDS related cause of death	8.6	0.0033*	1

Sex	8.6	0.0033*	1
Immunologic Stage	916.2	<0.001*	1
Mode of Transmission	216	<0.001*	5
Marital Status	1018	<0.001*	8
CD4 Cell Count			
Initial Report	524.7	<0.001*	2
Recient Report	983	<0.001*	2
Educational Level	142	<0.001*	8

*Statistical Significance.

Table 4: HIV/AIDS crude and adjust mortality rates for 2003-2011period * This rate was adjusted by age and sex using data from Community Survey estimated 2007 population (half of the study period).

Mortality Indicator	**Cases**
Crude Mortality Rate	52.3 por cada 100,000 personas
Adjust Mortality Rate*	12.0 por cada 100,000 personas
Fatality Rate	22.20%

Table 5: Cox Proportional Hazards Regression for the variables of interest. Adjusted by confounding variables: sex, age, educational level, CD_4 cell count, mode of transmission and civil status. *Statistical Significance.

Variable	**Hazard Ratio (HR)**	**CI 95%**	**p**
Sex			
Female	1	--	--
Male	0.95	0.86, 1.07	0.431
Civil Status			
Others	1	--	--
Single	4.45	3.69, 5.36	<0.001*

Married	5.62	4.55, 6.94	<0.001*
Widowed	5.41	4.13, 7.08	<0.001*
Divorced	6.63	5.35, 8.23	<0.001*
Immunology Stage			
HIV	3.16	0.64,15.66	0.159
AIDS	7.53	2.42, 23.4	<0.001*
Unknown	3.43		0.033*
Mode of Transmission			
HET			
IDU	1.53	1.37, 1.70	<0.001*
MSM	1.06	0.92, 1.23	0.444
MSM/IDU	1.13	0.86, 1.49	0.395
Age Groups			
≤ 14	1	--	--
15-44	0.45	0.14, 1.47	0.184
45-64	0.76	0.23, 2.52	0.658
≥ 65	1.28	0.39, 4.24	0.688
Educational Level			
Unknown	1	--	--
1-8 vo Grades	0.84	0.70, 1.01	0.066
Some High School	0.85	0.71, 1.02	0.094
High School Diploma	0.67	0.54, 0.83	<0.001*
Some College	0.72	0.54, 0.96	<0.05*
University Degree	0.59	0.43, 0.80	<0.001*

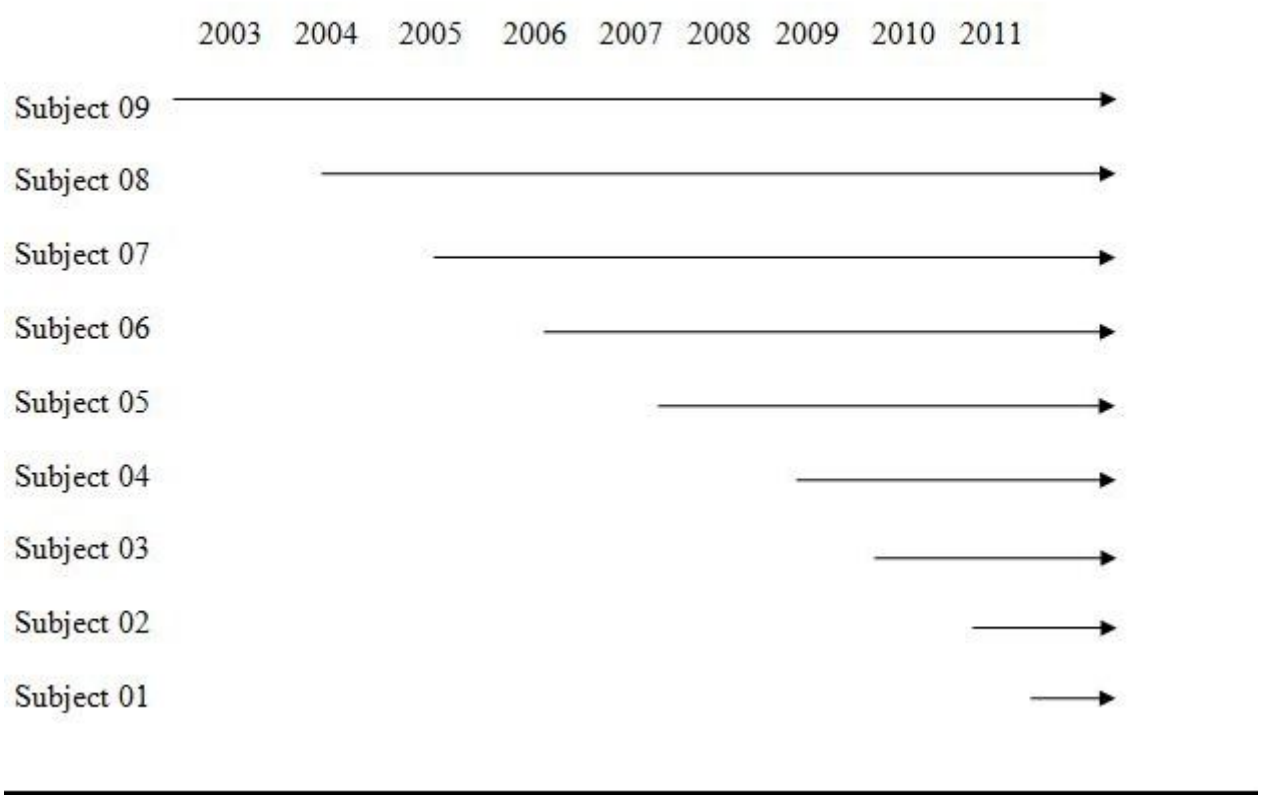

Figure 1: Follow Up Timeline. Follow up time was from January 1, 2003 to December 31, 2011.