Time from HIV diagnosis to viral load suppression: 2007-2012

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Abstract

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The HIV care continuum, the steps from diagnosis to engagement in care to viral load suppression, has recently received increased attention. While many analyses have focused on the proportion and characteristics of individuals reaching each step in the continuum, this analysis examines time from diagnosis to viral load suppression in newly diagnosed King County, Washington residents as a way to assess how quickly individuals are moving along the care continuum. A total of 1261 (85% of 1477) persons achieved viral suppression in a median time of 241 days between 2007 and 2012. Forty eight percent of all persons diagnosed in 2007 and sixty eight percent in 2012 were virologically suppressed within the first 12 months following HIV diagnosis. Differences in time to suppression by calendar year persisted when stratifying by CD4 count at diagnosis. Race was not significantly associated with time to viral suppression.

In 2012 U.S. national antiretroviral treatment (ART) guidelines for HIV changed. The new guidelines recommended that all persons infected with human immunodeficiency virus (HIV) receive ART, updating previous recommendations that treatment initiation be focused on persons with CD4+ T lymphocyte counts <500 cells/mm^3 [i] (Table 1). The U.S. Health Resources and Service Administration (HRSA) adopted these changes in response to improvements in ART that have simplified regimens and decreased the side-effects associated with treatment, and new evidence showing that early HIV treatment decreases HIV associated morbidity and mortality, and by decreasing viral loads, the likelihood of HIV transmission[ii iii iv v].

Table 1: ART initiation recommendation issued by "International AIDS Society-USA Panel" (2006-2012)

2006	After CD4 count <350/mm^3 and before 200/mm^3
2008	Before CD4 count <350/mm^3 with individualized initiation decisions >350/mm^3
2010	CD4 count ≤500 mm^3
2012	ART to all patients regardless of CD4 count

Due to the importance of viral loads in transmission, the goal of both clinical care and public health HIV prevention is to maximize the proportion of HIV infected persons who have suppressed viral loads. From a public health and healthcare services delivery perspective, this goal has led to a new focus on the HIV care continuum: the sequential steps from HIV diagnosis, to linkage to and retention in care, ART initiation and viral suppression. The HIV care continuum has recently received national attention with President Obama issuing an executive order launching the U.S. HIV Care Continuum Initiative[vi].

Quantifying the number of individuals who reach or fail to reach the final stage in the care continuum, viral suppression, is critical in understanding the success and failures of the HIV prevention and care system and an important measure of success in the care continuum. Researchers in New York City and San Francisco have documented significant improvements in both time to viral suppression and the proportion of individuals achieving viral suppression, but the US system as a whole is still failing to achieve suppression in the majority of people living with HIV/AIDS (PLWHA) particularly for certain demographics [ii,vii, viii]. National CDC estimates suggest that only 28-43% of all HIV-infected people in the US have a suppressed viral load[ix,x], though there is substantial geographical and demographic/HIV risk variability, and limitations in U.S. surveillance data likely lead to substantial underestimates of viral suppression at the population level[xi].

We calculated time from diagnosis to suppression as a measure of the King County care continuum's success, and to identify populations in which success is low. We identified potential HIV-related disparities by examining demographics and exposure categories associated with increased time to viral suppression. Reducing HIV-related disparities is a dominant focus of the National HIV/AIDS Strategy[xii] and we hypothesized we would see disparities in age, race/ethnicity, and transmission category[xiii]. If disparities were seen, follow-up work could examine why slower viral suppression is being seen in certain groups and how to possibly increase engagement/adherence.

With an increased national focus on the care continuum and the importance of viral suppression in health and transmission, an understanding of viral suppression trends in King County is vital to improving local treatment and prevention efforts. By emphasizing the time to, rather than proportion with viral suppression, we present a less frequently utilized way to examine the care continuum. Typically the continuum is portrayed as a cross sectional snapshot, but this approach may obscure improvements

in moving persons with newly diagnosed HIV infection along the continuum more quickly which can be more clearly defined by explicitly examining time from HIV diagnosis to viral suppression.

Materials and Methods:

This study examined the time from HIV diagnosis to viral suppression among persons diagnosed with HIV infection in King County, WA, from 2007-2012. The work was conducted at the Public Health -- Seattle & King County (PHSKC) Prevention Division HIV/AIDS Epidemiology section. The study subjects included all HIV infected individuals > 14 years of age diagnosed between 2007-2012 who resided in King County at the time of diagnosis and have been reported to PHSKC as of the time of the April 7th, 2014 analysis. Individuals must have had a viral load done subsequent to HIV diagnosis to be included in this analysis and must not be enrolled in a study, as studies do not report labs. Individuals that had less than one month of follow up were excluded. Investigations of these individuals found most had relocated, died, or their reported labs were all part of the initial battery of tests, but no subsequent laboratory results were received (CD4 count, CD4%, or plasma viral load). People who achieved viral suppression within 25 days of HIV diagnosis were also excluded. Newly diagnosed cases achieving viral suppression in 26 days or more likely did so due to ART initiation. Those who appeared to achieve viral suppression more rapidly were more likely due to errors in HIV diagnosis date and probably had true HIV diagnosis date (and ART use) earlier than that captured by HIV surveillance.

This study is a secondary data analysis of data collected through public health HIV surveillance, including HIV Incidence and Core HIV Surveillance data sources. We defined first HIV diagnosis as the earliest positive HIV diagnostic test or self-reported HIV diagnosis. In the event that these differed by more than 40 days, follow up was done to establish which was the more accurate. The date of initial viral suppression was defined as the date of first reported plasma HIV RNA test result showing an HIV viral load ≤200 copies/ml. The main analytic outcome was time to suppressed VL of ≤200 for comparability to other reports. The following variables were assessed for associations with time to viral suppression: age (15-24, 25-34, 35-44, 45-54, 55+), sex, race/ethnicity (non-Hispanic White, foreign born Black, non-Hispanic US born Black, Hispanic, and Other), HIV exposure category (men who have sex with men [MSM], injection drug user [IDU], MSM-IDU, unknown exposure, or heterosexual exposure as indicated in eHARS), CD4 lymphocyte count within the first 6 months of diagnosis, (defined in groups <350, 350-500, >500 per mm^3) and year of diagnosis (2007, 2008, 2009, 2010, 2011, and 2012). CD4 counts more than six months after diagnosis were changed to missing due to concerns these are unrepresentative of CD4 counts at diagnosis, which is the variable of interest.

We calculated estimates of time taken for 50% and 75% of the population to reach viral suppression and created Kaplan-Meier survival plots to visually present surveillance data. Individuals contributed time from their date of HIV diagnosis to the date of initial viral suppression (event) or their last reported CD4 or viral load test (censored). In the event that individuals were censored, follow-up was done to see if a reason for censorship could be determined. Log rank testing p value was used to assess differences. We used multivariate Cox proportional hazard regression to identify independent risk factors associated with time to achieve suppression and to estimate hazard ratios with 95% confidence intervals (CI). People with CD4 counts more than six month after diagnosis were removed from the multivariate model.

Results:

During the period of 2007-2012, 1623 persons were newly diagnosed with HIV infection in King County, WA. Ten of these persons were excluded due to being involved in a study. Of the 1613 persons not identified as involved in studies, 1552 (96%) had a viral load subsequent to their initial diagnoses. From this population, 32 persons (2%) with less than a month of follow-up time were removed. Another 32 persons (2%) were removed due to achieving viral suppression within 25 days. Finally 11 persons <14 years of age were removed as perinatal exposures leaving a final population included in the study of 1477 (92% of those newly diagnosed in King County) (Figure 1). A total of 99 (7%) people did not have a CD4 lymphocyte count reported to Public Health in the first 6 months following HIV diagnoses; these persons were excluded from analysis that included CD4 count as an independent variable. The population was predominantly non-Hispanic White (61%), 25-44 years of age (59%), and composed of men who have sex with men (MSM) (69%). Of those with CD4 counts done within 6 months of diagnosis, 45% had <350 cells per mm^3 (Table 2). There is no clear indication that over this time period the demographics, risk characteristics, or CD4 counts at diagnosis have significantly changed.

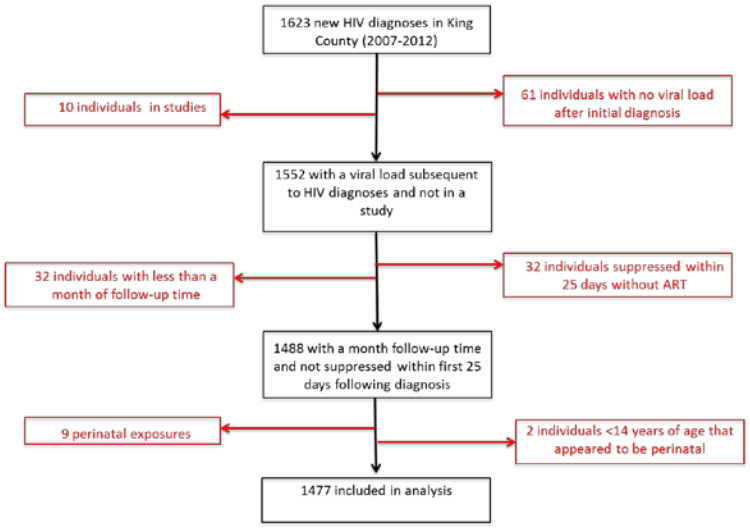


Figure 1: Persons included in the analysis

The study population included 1477 newly diagnosed persons who achieved viral suppression or were censored after for a median time of 272 days (31-2557 days). Of these persons, 217 persons were censored without achieving viral suppression. Follow-up on these patients found that 16 died (7%), 42 moved out of the state (19%), 104 were still in care with labs 2013 or later (48%), and 55 didn't have labs more recent than 2012 (25%) (Figure 2). This indicates roughly 4% of our initial population never achieved viral suppression and appeared to be out of care as of 2014 (i.e. no laboratory results reported in the 12 months prior to the end of observation).

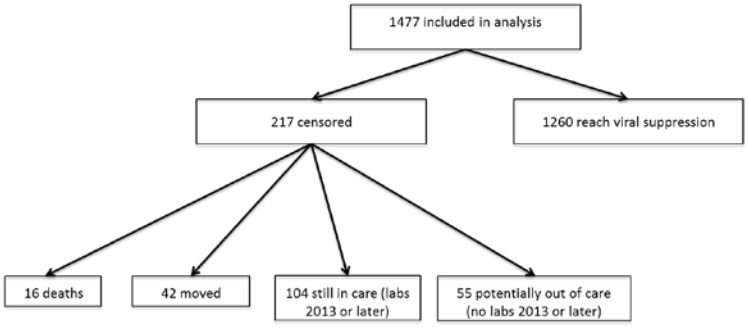


Figure 2: Reasons persons included in the analysis were censored

A total of 1261 (85%) persons achieved viral suppression in a median time of 241 days. In 2007, half of newly diagnosed persons had achieved virologic suppression 633 days following diagnosis. In contrast, by 2012, half of all newly diagnosed persons were virologically suppressed 207 days following diagnosis. In 2007, 48% of all persons diagnosed were virologically suppressed within the first 12 months following HIV

diagnosis while in 2012, 68% were suppressed 12 months following HIV diagnosis. The trend toward more rapid viral suppression following HIV diagnosis was evident in all CD4 strata, but was most pronounced among persons diagnosed with a CD4 count >500 cell/mm^3 (Figure 3). Among persons with these higher CD4 counts, the time from diagnosis to when 50% of persons were virologically suppressed decreased 68%, from 1172 days in 2007 to 376 days in 2012. On univariate analysis, more rapid viral suppression was significantly associated with unknown HIV risk or heterosexual transmission categories, female gender, CD4 lymphocyte count <350 cells per mm^3, older age, and being foreign born Black (Figure 4). When using Cox multivariate analysis, CD4 count, age, and year of diagnosis were all significantly associated with time to viral suppression (Table 3).

Conclusions:

Evaluating data collected in King County, WA between 2007 and 2013, we found that the median time from diagnosis to viral load suppression declined 67% between 2007 and 2012, and was most pronounced among persons diagnosed with higher CD4 counts. We observed no significant indication of racial disparities in time to suppression. These findings highlight the success of one U.S. urban area in acting on national HIV treatment guidelines, and have potential implications related to the clinical outcomes of persons living with HIV/AIDS, HIV transmission, and the costs of care.

Although much of the change in time to viral suppression is likely a consequence of changes in clinical practice prompted by changes in U.S. national HIV treatment guidelines, our findings suggest that guidelines changes alone do not entirely explain the dramatic increase in how quickly patients become virologically suppressed. Stratifying by CD4 count, we found that time to viral suppression declined in all CD4 count strata, including persons with CD4 counts <350 cells/mm^3, a group for which national guidelines recommended antiretroviral therapy throughout the study period. Moreover, the time to viral suppression among persons with the highest CD4 counts clearly declined prior to the 2012 change in HIV treatment guidelines recommending that all persons with HIV be treated with antiretroviral therapy. This finding demonstrates that clinical practice, at least in King County, WA, changed well in advance of national treatment guidelines.

San Francisco and New York City (NYC) have looked at time from diagnoses to viral load suppression by diagnosis year with the latter also looking at time by CD4 count at diagnosis. San Francisco found that the median time to virologic suppression decreased roughly 69% from 32 months (~960 days) in 2004 to 10 months (~300 days) in 2009[viii]. NYC found that those diagnosed in 2009 achieved viral suppression significantly faster than those in 2006 and those with the lowest CD4 count at diagnosis (0-199 cells/mm^3) were significantly faster than higher CD4 counts[ii]. Neither jurisdiction looked at CD4 count stratified by year of diagnosis or other demographic/transmission factors associated with time to suppression. The former is important to include in exploring the improvements beyond guideline changes while the later allows us to see what groups are having particular slow times to suppression. The New York analyses demonstrate a number of differences relative to this study. First of all, NYC used <400 copies per ml as definition of suppression, which is no longer the standard “suppressed” definition[xiv]. NYC also classified all invalid and missing viral loads (VL) as detectable and assumed that all patients with no VL would be viremic which may not be accurate due to high levels of migration that likely resulted in patients’ receiving care from other jurisdictions.

Our study has several limitations. First, laboratory reporting improved over the study period. This may have biased our findings such that time to viral suppression decreased in part due to our failure to ascertain suppressed viral load results in earlier

calendar years. Laboratory reporting differences were unlikely to have an impact on other variables as the characteristics of those newly diagnosed with HIV hasn't significantly changed over this time period. Missing actual HIV diagnosis dates and missing viral loads beyond those impacted by improvements in laboratory reporting could also be problematic. The impact of missing HIV diagnosis dates was reduced by using all available data including both documented HIV diagnoses and individual's self-reported first positive dates. The second element of missing viral load was more challenging to address. PLWHA receiving medical care out of the county or getting viral loads done through participation in a clinical trial, which are not reportable, means these individuals might be contributing inaccurate time to the model. Requiring individuals to have a minimum of one laboratory result reported subsequent to their initial diagnosis hopefully minimize inaccuracies due to people relocating or being in clinical trials.

For those not virally suppressing, a portion appear to have fallen out of care. While this is a small percentage, these numbers may make the time to viral suppression appear quicker than it is in actuality as this group only contribute time until their last lab. By looking at time for 50% and 75% of the population to be virally suppressed, we attempt to account for people that may have dropped out of care. Further, suppression based on a single suppressed viral load probably misclassifies a substantial portion of the people who are not stably engaged in treatment.[xv] However, progressing through the care continuum to at least initial suppression indicates some success in the process. Additionally, there is likely residual confounding by socioeconomic status (SES). Our multivariate models account for HIV risk factors and race/ethnicity, but lack more direct measure of SES such as income, insurance, and education status.

With the guideline changes in 2012 to recommend that all HIV-infected individuals be prescribed ART, it will be important to see if those with CD4 counts >500 cells/mm^3 close the gap in time to viral suppression relative to individuals with lower CD4 levels. Even with the new guidelines, it may be challenging to get comparable time to viral suppression in those with high versus low CD4 counts given that at high counts individuals may not feel ill and thus may be reluctant to initiate medication. The association of recent calendar year with time to viral suppression may be indicative of increased availability of more effective ART with fewer side effects and more convenient dosing regiments (for example one pill a day). While national numbers show racial disparities, particularly in undetectable viral loads (21% in Blacks compared to 30% in Whites[xvi]), our study found no significant difference by race in time to viral suppression when controlling for other variables. This could be due to more effective outreach, reduced stigma, less socioeconomic disparities, or a better safety net with no Ryan White waiting lists within King County. Interestingly, foreign born Blacks have much quicker time to viral suppression compared to US born Blacks, although this finding was not statistically significant after adjusting for other variables in the model.

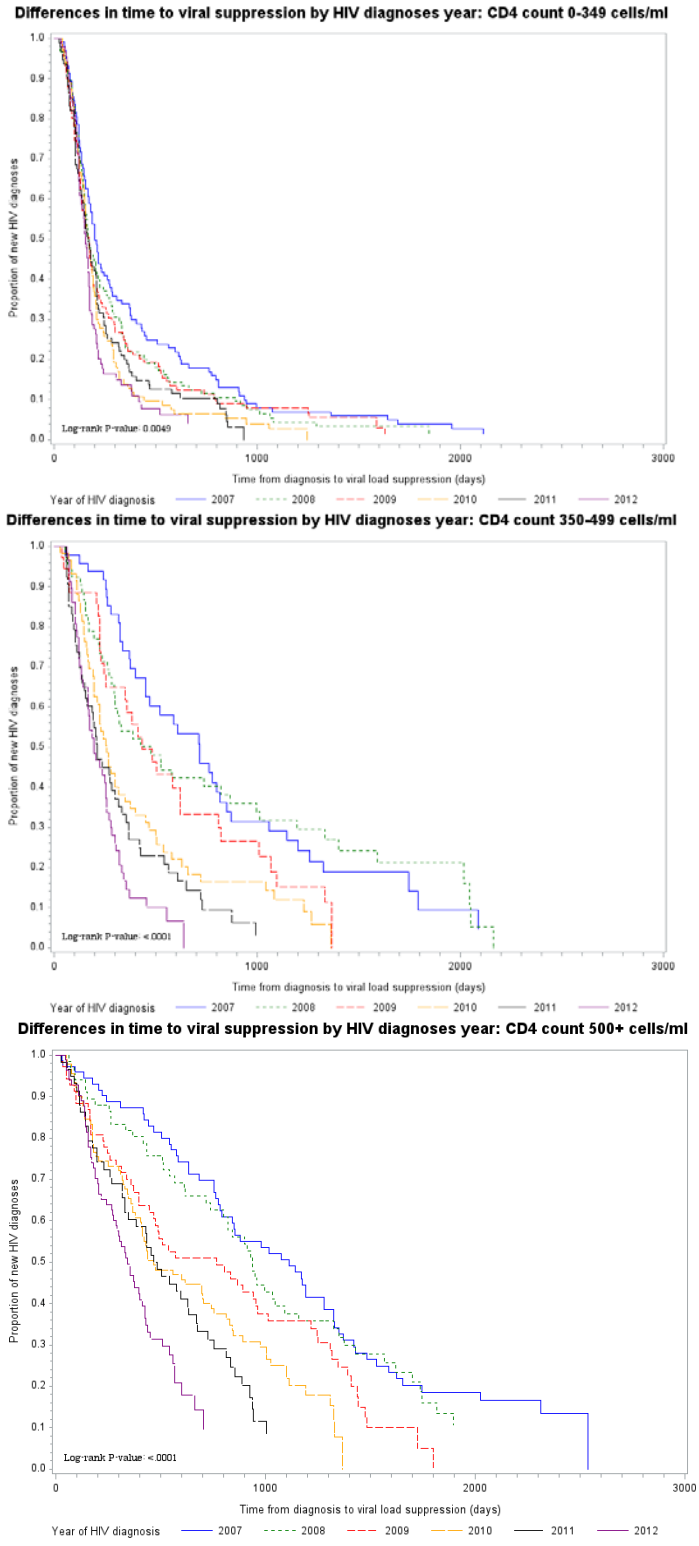
With an increased national focus on the care continuum and the importance of viral suppression in health and HIV transmission, understanding viral suppression trends in King County is vital to improving local treatment and prevention efforts. When using time to viral suppression as an outcome, King County appears largely successful in reducing or eliminating racial disparities in the care continuum. Improvement in time to viral suppression for those with high CD4 counts is still warranted. In summary, by looking at the time to viral suppression, we are able to describe not only what proportion of individuals newly diagnosed with HIV are reaching viral suppression, but how fast, which indicates how quickly individuals have improved health outcomes and decreased transmissibility.

Table 2: Demographic and transmission characteristics among those newly diagnosed with HIV in King County (2007-2012)							
	2007	**2008**	**2009**	**2010**	**2011**	**2012**	**Total**
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Risk							
MSM	172 (65.9)	167 (65.0)	165 (70.8)	196 (74.0)	156 (70.90)	158 (65.6)	1014 (68.7)
MSM/IDU	26 (10.0)	16 (6.2)	16 (6.9)	19 (7.2)	24 (10.9)	22 (9.1)	123 (8.3)
IDU	5 (1.9)	6 (2.3)	9 (3.9)	10 (3.8)	8 (3.6)	10 (4.2)	48 (3.3)
Heterosexual	28 (10.7)	30 (11.7)	21 (9.0)	22 (8.3)	11 (5.0)	15 (6.2)	127 (8.6)
Unknown	30 (11.5)	38 (14.8)	22 (9.4)	18 (6.8)	21 (9.6)	36 (14.9)	165 (11.2)
Race/ethnicity							
Foreign Born Black	19 (7.3)	24 (9.3)	12 (5.2)	7 (2.6)	18 (8.2)	17 (7.1)	97 (6.6)
US Born Black	26 (10.0)	25 (9.7)	21 (9.0)	18 (6.8)	22 (10.0)	24 (10.0)	136 (9.2)
Non-Hispanic White	152 (58.2)	143 (55.6)	146 (62.7)	176 (66.4)	131 (59.6)	151 (62.7)	899 (60.9)
Hispanic	44 (16.9)	37 (14.4)	37 (15.9)	39 (14.7)	35 (15.9)	26 (10.8)	218 (14.8)
Other	20 (7.7)	28 (10.9)	17 (7.3)	25 (9.4)	14 (6.4)	23 (9.5)	127 (8.6)
Age at diagnosis (yr)							
15-24	38 (14.6)	39 (15.2)	31 (13.3)	44 (16.6)	39 (17.7)	31 (12.9)	222 (15.0)
25-34	73 (28.0)	83 (32.3)	73 (31.3)	88 (33.2)	71 (32.3)	86 (35.7)	474 (32.1)
35-44	78 (30.0)	71 (27.6)	60 (25.8)	70 (26.4)	51 (23.2)	68 (28.2)	398 (27.0)
45-54	44 (16.9)	43 (16.7)	51 (21.9)	51 (19.3)	41 (18.6)	38 (15.8)	268 (18.1)
55+	28 (10.7)	21 (8.2)	18 (7.7)	12 (4.5)	18 (8.2)	18 (7.5)	115 (7.8)
Sex							
Female	31 (11.9)	27 (10.5)	24 (10.3)	27 (10.2)	21 (9.6)	30 (12.5)	160 (10.8)
Male	230 (88.1)	230 (89.5)	209 (89.7)	238 (89.8)	199 (90.5)	211 (87.6)	1317 (89.2)
CD4 (#/mm^3)							
<350	103 (45.8)	118 (49.4)	113 (51.6)	103 (40.7)	95 (46.1)	90 (38.1)	622 (45.1)
350-500	48 (21.3)	54 (22.6)	36 (16.4)	59 (23.3)	53 (25.7)	59 (25.0)	309 (22.4)
500+	74 (32.9)	67 (28.0)	70 (32.0)	91 (36.0)	58 (28.2)	87 (36.9)	447 (32.4)
Total	**261 (100)**	**257 (100)**	**233 (100)**	**265 (100)**	**220 (100)**	**241 (100)**	**1477**

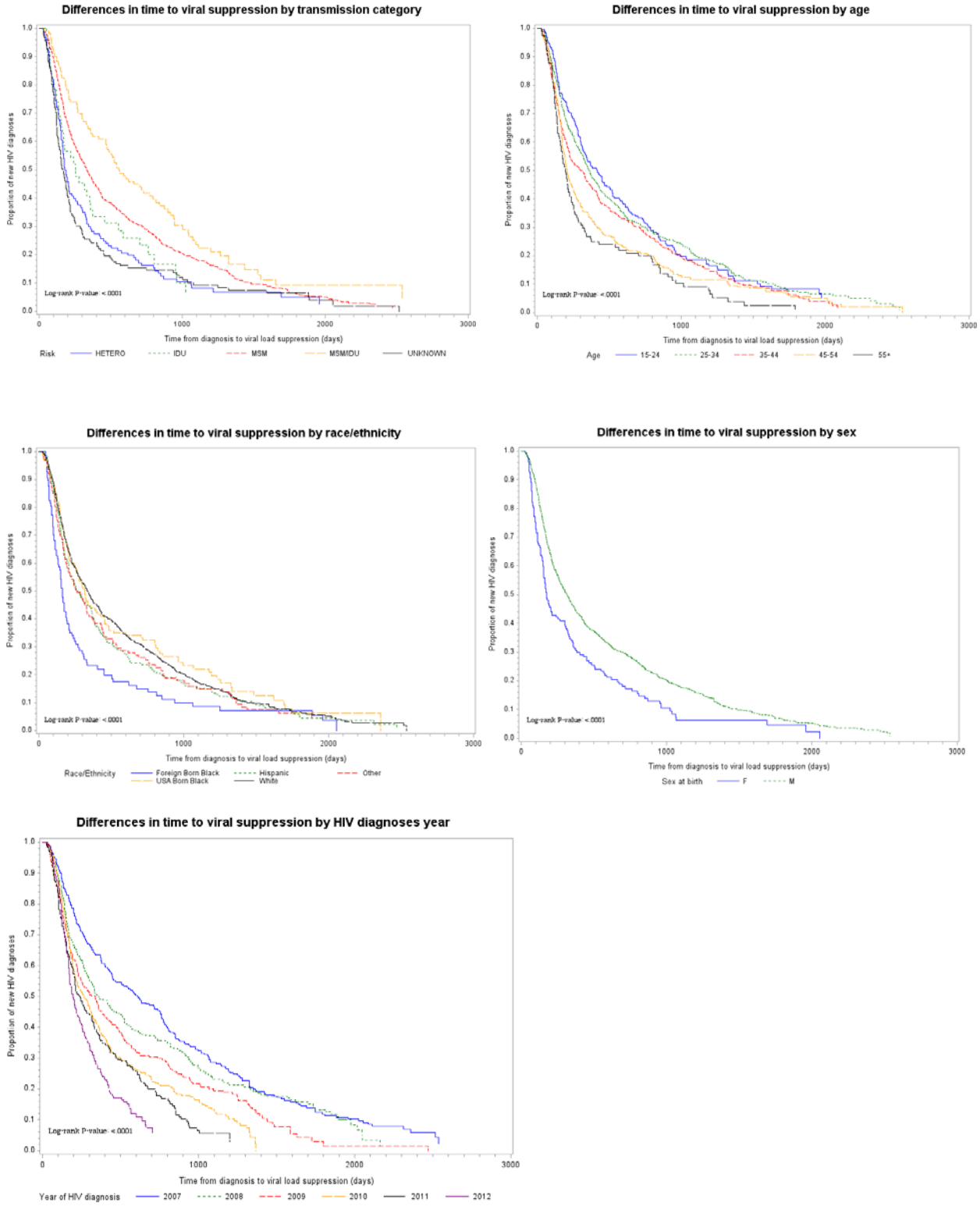
Table 3: Multilevel proportional Cox analysis of variables associated with time to viral suppression

	Time (days) for 50% of persons to be suppressed	Time (days) for 75% of persons to be suppressed	HR_{adj}	95% CI	P
Race/ethnicity					
Foreign Born Black	163	333	1.02	0.78-1.35	0.87
US Born Black	321	1326	0.90	0.72-1.12	0.35
Hispanic	287	851	1.14	0.96-1.34	0.14
Other	263	764	1.00	0.81-1.23	0.99
Non-Hispanic White	353	1034	Ref		
CD4 (#/mL)					
<350	172	343	2.72	2.36-3.13	<.0001
350-500	319	872	1.57	1.34-1.85	<.0001
500+	702	1739	Ref		
Sex					
Female	176	590	1.33	0.97-1.83	0.07
Male	331	1004	Ref		
Age at diagnosis (yr)					
15-24	449	1251	0.62	0.48-0.81	<.001
25-34	371	1113	0.64	0.51-0.81	<.001
35-44	330	1014	0.77	0.61-0.97	0.03
45-54	208	590	0.82	0.65-1.04	0.10
55+	200	567	Ref		
Risk					
Unknown	176	430	1.16	0.83-1.63	0.37
IDU	254	805	0.84	0.56-1.25	0.38
MSM	347	1004	0.95	0.68-1.33	0.77
MSM/IDU	626	---	0.69	0.47-1.03	0.07
Heterosexual	189	551	Ref		
Year of Diagnosis					
2007	633	1329	0.38	0.30-0.46	<.0001
2008	417	1326	0.44	0.36-0.54	<.0001
2009	349	1096	0.56	0.46-0.69	<.0001
2010	279	702	0.74	0.68-0.91	<.01
2011	236	620	0.79	0.64-0.98	0.03
2012	207	453	Ref		

Figure 3: Kaplan-Meier Curves depicting time to viral load suppression by diagnosis year, among those with CD4 counts <350 cells/mm^3, 350-500 cells/mm^3, and >500 cells/mm^3



Figures 4: Kaplan-Meier Curves depicting time to viral load suppression among newly diagnosed cases by age, CD4 count, year of diagnosis, race, sex, and transmission category



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