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16. Abstract

**Introduction.** This study is a follow-up from the initial paper examining the impact of waiving annual cognitive screening for HIV-positive airmen in favor of a 5-year special issuance. The preliminary analysis indicated that this approach would miss 4.5% of cognitive screening failures, with only 1% impacting certification outcomes. Subsequent literature warned of the potential 20-50% prevalence of HIV-induced neurocognitive dysfunction. The study reevaluates these findings, considering new literature suggesting comorbidities, more common in HIV patients, as primary drivers of cognitive impairment.

**Methods.** All airmen with HIV who had at least one cognitive test during their Aerospace medical exam between January 1, 2007 and December 31, 2020 were reviewed for inclusion in the study. The study was conducted in two parts, updating cases through 2017 and including new cases through 2020.

**Results.** Results highlight that 81.8% ever received Special Issuance for HIV, with higher denial rates for those initially denied due to neurocognitive concerns. A 5-year retention rate for HIV diagnosis was 37.7%. Multivariate logistic regression affirmed associations between abnormal baseline tests, abnormal CD4/viral load, and longer HIV duration with subsequent abnormal cognitive screenings.

**Discussion.** Contrary to expectations, age and medical conditions showed no significant association. Notably, most pilots with HIV do not return for Special Issuance after initial denial, likely due to cognitive changes, as indicated by the significant association between baseline and subsequent scores. The study advocates for an initial comprehensive set of cognitive assessments to detect subtle issues early in this pilot population.

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# Assessing Potential Risk Factors of Abnormal Cognitive Function among HIV-Positive Airmen- An Updated Analysis

Ann Norris, Valerie Skaggs, Tom Chidester

## Introduction

From 2016 to 2018, the SRM team conducted a study that assessed the impact of waiving annual cognitive screening in favor of up to a 5-year length of special issuance between cognitive testing among the HIV positive airmen who display typical CD4 counts and viral suppression. During analyses, the team discovered that using this new strawman theory, certification would have missed approximately 4.5% of cases where the airmen failed their cognitive screening test. However, only two of these cases (1%) would have ultimately impacted the final certification outcome. During management discussion regarding utilization of this strawman theory in policy changes, new literature was published from the U.S. general population which cautioned that neurocognitive dysfunction caused by HIV increases over time with infection, and could be as frequent as 20% to 50% of HIV cases.

However, results from new studies conducted by UCLA researchers were presented at the 2021 AsMA conference. In this presentation, the authors conducted a 5-year study to determine individual prediction of cognitive impairment among men with HIV. They discovered that between the cognitively impaired and unimpaired, while diagnosis of AIDS is a critical risk factor, HIV infection did not convey additional risk for cognitive impairment. In fact, for the comparisons between those cognitively impaired and those who were not, the only ways they statistically differed were by age, ethnicity, education, and current alcohol use. They did not differ between HIV status or CD4 cell counts. Thus, the authors concluded it may be comorbidities, which may occur more often in people with HIV, that are in fact the primary driver of cognitive dysfunction rather than the virus itself. AAM has to balance our data with the published data from the general population, and we owe it to the pilot population and flying public to protect against cognitive impairment in HIV pilots that might result in incident or accident. Therefore, our goal of this report was to update information from the original report. Because new data were available, we have extended our analysis to include more recent cognitive assessments and add information to evaluate the association between these updated variables and cognitive abnormalities seen in pilots.

## Methods

Data were extracted from DIWS. All airmen who were assigned an HIV or AIDS pathcode and had at least one physical exam (PE) between January 1, 2007 and December 31, 2020 were reviewed for inclusion in the study. To be included in the study, an airman must have had at least one CogScreen score or other FAA-approved neuropsychological test result reported, have a diagnosis of HIV or AIDS, and apply for a pilot medical certificate during the specified time period. Of the 727 cases initially identified, it was determined that 451 met these criteria after review of the records. The majority of the 276 excluded cases was due to the airman not following up with a cognitive test. In this situation, an airman would be denied certification for failure to provide required information.

Airmen were followed longitudinally, tracking their cognitive assessments, neuropsychological evaluations, viral loads, and CD4 cell counts. We used the term cognitive assessment in the results and discussion to collectively include all neurocognitive evaluations (CogScreen-Aeromedical

Edition [AE] or other approved test battery). In most scenarios, a CogScreen-AE would be performed as a screening test, and if this screen was not passed additional testing would be performed. If the additional testing was passed, the airmen was deemed not to have a disqualifying cognitive impairment.

The study was updated in two parts. The first part of data collection was to update our previous cases through 2017 (298 of the cases) to re-review and follow forward for the complete study period. The second part was to include the remainder of the new cases through 2020.

Statistical analyses were performed using Statistical Analysis Software v9.4 (SAS). Analyses were performed on all airmen included in the study. A cognitive assessment was deemed abnormal if the CogScreen LRPV score was greater than 0.70 and/or any other approved test battery was noted as a failed test. However, if the airmen took more than one assessment and passed either test, the assessment was considered normal. Descriptive statistics were calculated and t-test and chi-square tests were performed where appropriate. Finally, multivariate logistic regression was performed to determine potential risk factors for having an abnormal cognitive test while controlling for other variables.

**Results and Discussion**

In addition to the original 298 pilots examined between 2007 and 2016, there were 153 airmen added since January 1, 2017 through 2020, totaling 451 airmen for this analysis. One hundred sixty-five (36.6%) of the 451 airmen had only one cognitive assessment and an additional 75 (16.6%) only had 2 cognitive assessments available in DIWS. Overall, 350 (77.6%) of the 451 airmen had 6 or fewer cognitive assessments in DIWS. Of the 451 airmen who applied with a cognitive test, 369 (81.8%) were ever issued with an SI for HIV.

Table 1 provides a breakdown of number and percentages of airmen remaining at each cognitive assessment, number with abnormal cognitive assessments, number of airmen with abnormal cognitive assessments who were issued even with the abnormal assessment, and total issued at each assessment. Overwhelmingly, the AAM-processes identified HIV-treated airmen with cognitive issues at the time of their first and second cogscreens. After the first two cognitive assessment, ≥90% of airmen were issued in subsequent applications.

There were 133 (29.5%) airmen who were ever denied. Unlike airmen with SSRIs that were examined in our previous report, the majority of denied airmen with HIV were never issued again (99/133=74.4%). Furthermore, of those 133 who were ever denied, 97 (73%) were denied on their initial cognitive assessment. Forty airmen were denied due to neurocognitive decline/disorder, 23 were denied due to other comorbidities that weren't HIV, and the remaining were due to other reasons, many of which was failure to provide.

Table 1: Number and Percentage of the Airmen, Abnormal Tests, and Issuance per Cog Test

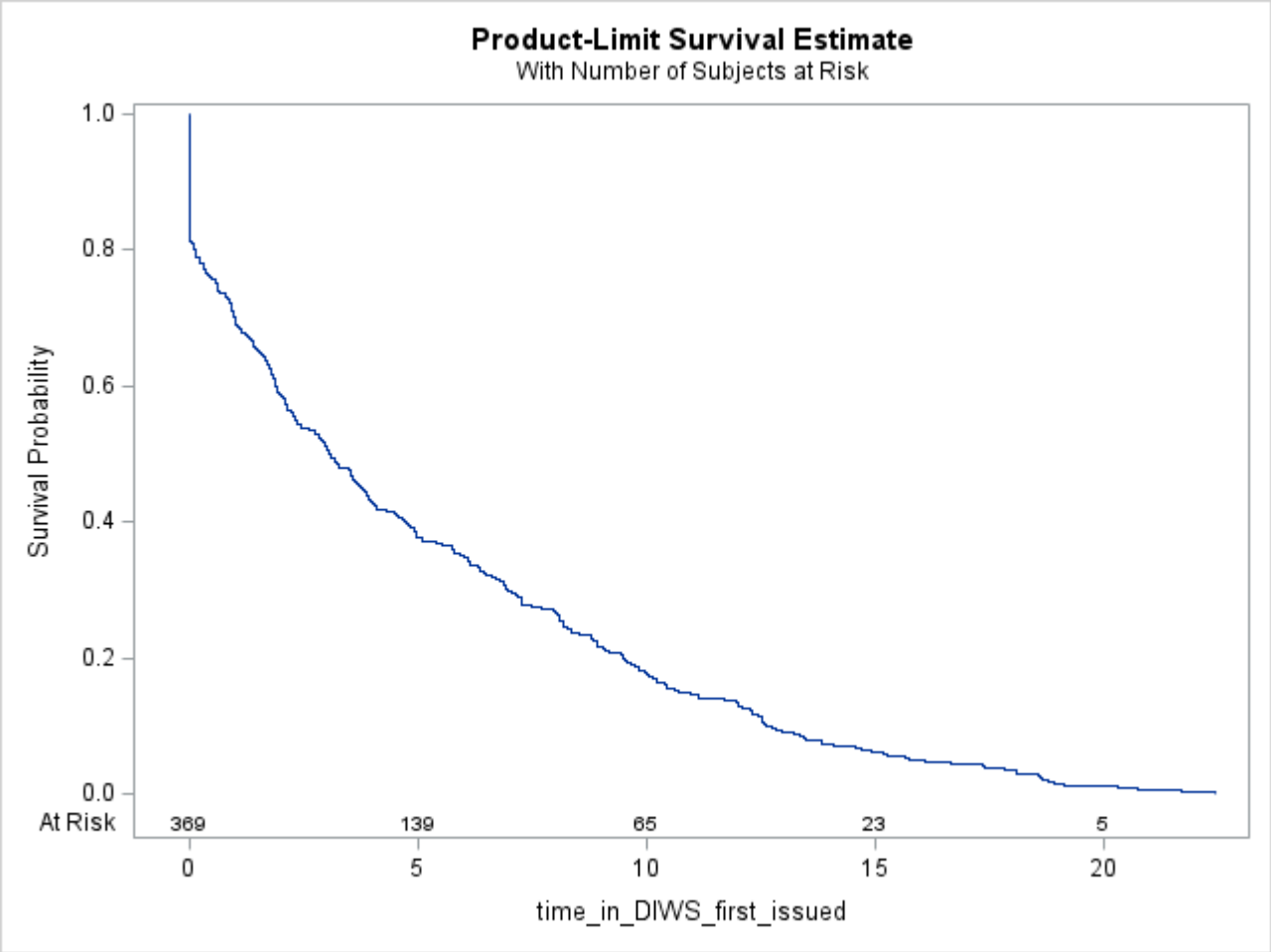
| | Number of Airmen Remaining | Number of Cogscreens with abnormal LRPV value (%) | Number of Airmen with abnormal LRPV value issued (%) | Total Number of Airmen Issued (%) |
|---|---|---|---|---|
| Cog Test 1 | 451 | 90 (20.0%) | 22 (4.9%) | 322 (71.4%) |
| Cog Test 2 | 286 | 24 (8.4%) | 12 (4.2%) | 236 (82.5%) |
| Cog Test 3 | 211 | 11 (5.2%) | 6 (2.8%) | 189 (89.6%) |
| Cog Test 4 | 161 | 8 (5.0%) | 6 (3.7%) | 153 (95.0%) |
| Cog Test 5 | 136 | 9 (6.6%) | 6 (4.4%) | 129 (94.9%) |
| Cog Test 6 | 117 | 8 (6.8%) | 8 (6.8%) | 113 (96.6%) |
| Cog Test 7 | 101 | 4 (4.0%) | 3 (3.0%) | 98 (97.0%) |
| Cog Test 8 | 81 | 5 (6.2%) | 4 (4.9%) | 79 (97.5%) |
| Cog Test 9 | 74 | 5 (6.8%) | 5 (6.8%) | 72 (97.3%) |
| Cog Test 10 | 59 | 2 (3.4%) | 2 (3.4%) | 55 (93.2%) |
| Cog Test 11 | 50 | 3 (6.0%) | 3 (6.0%) | 50 (100.0%) |
| Cog Test 12 | 40 | 2 (5.0%) | 1 (2.5%) | 38 (95.0%) |
| Cog Test 13 | 30 | 1 (3.3%) | 1 (3.3%) | 29 (96.7%) |
| Cog Test 14 | 20 | 2 (10.0%) | 2 (10.0%) | 18 (90.0%) |
| Cog Test 15 | 17 | 1 (5.9%) | 1 (5.9%) | 17 (100.0%) |
| Cog Test 16 | 13 | 0 (0.0%) | 0 (0.0%) | 13 (100.0%) |
| Cog Test 17 | 12 | 1 (8.3%) | 1 (8.3%) | 12 (100.0%) |
| Cog Test 18 | 9 | 1 (11.1%) | 1 (11.1%) | 9 (100.0%) |
| Cog Test 19 | 6 | 1 (16.7%) | 1 (16.7%) | 5 (83.3%) |
| Cog Test 20 | 4 | 0 (0.0%) | 0 (0.0%) | 4 (100.0%) |
| Cog Test 21 | 1 | 0 (0.0%) | 0 (0.0%) | 1 (100.0%) |

*Time in DIWS for Airmen with HIV*

Figure 1 displays the survival plot indicating the time airmen spent in the HIV program in DIWS (meaning the time they were first issued to their recent exam). For those 369 who were ever issued with an HIV diagnosis, the 5-year retention rate was 37.7%, 10-year was 17.6%, and 15-year was 6.2%. This 5-year retention rate was slightly less than the 5-year retention we observed in our recent SSRI population at 40%. Furthermore, this 37.7% retention rate is better than the overall rate for new applicants in 2009 (5 years was 33%), but worse than all active airmen in 2009 (5 years was 55%).

Further comparisons demonstrate 5-year retention was better than among active 2009 airmen with AFIB, MI, diabetes, or nerve disorders. Retention was worse than among active 2009 airmen with arrhythmia, vascular conditions, hypertension, valvular heart disease, brain disorders, spinal cord disorders, and no reported conditions.

Figure 1: Retention Rate of Airmen with HIV in DIWS




*Mean, Frequencies, and Association of Exploratory Variables by Abnormal Cognitive Screening*

Since our initial report of HIV airmen back in 2018, AAM-200 has reviewed policy for airmen with HIV and made changes to the initial screening process. The new protocol requires airmen to perform a complete battery of tests for the initial application, but allows single cogscreens for followup, provided the airman does not fail them. With this new protocol in place that is likely to detect more subtle cognitive deficits on the initial application, our goal for this updated analysis was to focus on descriptive statistics and potential risk factors for abnormal screening tests *AFTER* the initial cognitive assessment. There are only 6 airmen in our cohort who had their initial cognitive test after the new cognitive screening protocol was published on February 1st, 2021. These airmen are in our study because they identified as having HIV in our study timeline, but they did not receive a cognitive assessment until their most recent exams after 2020. Of these 6 airmen, three had abnormal cogscreens, but only one failed the additional battery of tests. Therefore, future analyses may be warranted for the group of airmen applying post-protocol change.

When we compared those who had an abnormal cognitive result on their *SECOND OR LATER* cognitive assessments with those who did not, the only two continuous variables that statistically differed at an alpha of 0.05 between the two groups was the HIV disease duration and the time

holding an SI for HIV in DIWS. Mean time having HIV was 14.4 years in those who had an abnormal cognitive test after initial exam, while mean time was only 10.7 years after being diagnosed with HIV for those who had normal assessments. Additionally, mean time certificated in DIWS was 8.1 years for those with abnormal cognitive tests after initial assessment, and only 4.5 years for those who had normal assessments after baseline. These variables are most likely correlated to one another, as time in DIWS with HIV will be larger for those who have been diagnosed for a longer time.

Table 2: Means, Medians, and Comparisons of Variables for Total Cohort and in Those who had an Abnormal Result on their Second or Later Cognitive Assessment vs Those who Did Not

| Variable | N | Mean Total | Median Total | Std Dev | Range | N Abn | Mean of Abnormal Cogs | N Norm | Mean of Normal Cogs | T-test p-value |
|---|---|---|---|---|---|---|---|---|---|---|
| **HIV duration** | 431 | 11.16 | 9.69 | 7.85 | 0-41.3 | 56 | 14.36 | 375 | 10.68 | **0.0010** |
| **Time in DIWS** | 369 | 4.99 | 3.06 | 5.29 | 0-22.4 | 49 | 8.08 | 320 | 4.52 | **<0.0001** |
| **Years of Education** | 344 | 15.65 | 16.00 | 2.16 | 11-25.0 | 51 | 15.37 | 293 | 15.7 | 0.3138 |
| **Baseline Age** | 451 | 41.41 | 41.39 | 10.83 | 19.2-74.8 | 58 | 43.82 | 393 | 41.06 | 0.0693 |
| **Number of Medications** | 451 | 2.61 | 2.00 | 1.96 | 0-10 | 58 | 2.93 | 393 | 2.56 | 0.1780 |
| **Number of Conditions*** | 451 | 2.11 | 2.00 | 2.05 | 0-12 | 58 | 2.72 | 393 | 2.02 | 0.0558 |

*Number of Conditions an airmen has in addition to HIV

Finally, Table 3 displays univariate significance in categorical variables between those who had an abnormal cognitive test after initial cognitive assessment and those who did not. Interestingly, the only statistically significant difference between these groups were the percentage who had an initial abnormal cognitive assessment and those who ever had a CD4 cell count of under 500 cells/ml. Even when categorizing count of medications and medical conditions (in addition to HIV), there was no univariate statistical difference.

Table 3: Frequencies of Categorical Variables and Comparisons of Variables in Those who had an Abnormal Result on their Second or Later Cognitive Assessment vs Those who Did Not

| Variables | Total Airmen N=451 (%) | Airmen Abnormal Cog N=58 (%) | Airmen Normal Cog N=393 (%) | Chi-squared p-value |
|---|---|---|---|---|
| Comorbidities of HIV* | | | | 0.6450 |
| Yes | 76 (16.9) | 11 (19.0) | 65 (16.5) | |
| No | 375 (83.1) | 47 (81.0) | 328 (83.5) | |
| Hx of Arrest or DUI | | | | 0.2925 |
| Yes | 86 (19.1) | 14 (24.1) | 72 (18.3) | |
| No | 365 (80.9) | 44 (75.9) | 321 (81.7) | |
| AIDS defining Illness ever | | | | 0.2186 |
| Yes | 36 (8.0) | 7 (12.1) | 29 (7.4) | |
| No | 415 (92.0) | 51 (87.9) | 364 (92.6) | |
| CD4 count <500 ever | | | | **0.0003** |
| Yes | 160 (35.5) | 33 (56.9) | 127 (32.3) | |
| No | 291 (64.5) | 25 (43.1) | 266 (67.7) | |
| Viral Load <400 ever | | | | 0.1929 |
| Yes | 29 (6.4) | 6 (10.3) | 23 (5.9) | |
| No | 422 (93.6) | 52 (89.7) | 370 (94.2) | |
| Age Group | | | | 0.6996 |
| Under 50 | 351 (77.8) | 44 (75.9) | 307 (78.1) | |
| 50 or Older | 100 (22.2) | 14 (24.1) | 86 (21.9) | |
| Initial Cog Assessment Outcome | | | | **0.0009** |
| Abnormal | 90 (20.0) | 21 (36.2) | 69 (17.6) | |
| Normal | 361 (80.0) | 37 (63.8) | 324 (82.4) | |
| # Meds Category | | | | 0.2007 |
| 0-1 | 171 (37.9) | 17 (29.3) | 154 (39.2) | |
| 2-3 | 170 (37.7) | 22 (37.9) | 148 (37.7) | |
| 4+ | 110 (24.4) | 19 (32.8) | 91 (23.2) | |
| # Conditions Category** | | | | 0.3666 |
| 0 | 101 (22.4) | 11 (19.0) | 90 (22.9) | |
| 1 | 117 (25.9) | 11 (19.0) | 106 (27.0) | |
| 2 | 84 (18.6) | 14 (24.1) | 70 (17.8) | |
| 3+ | 149 (33.0) | 22 (37.9) | 127 (32.3) | |
| Baseline Class | | | | 0.1317 |
| First | 153 (33.9) | 22 (37.9) | 131 (33.3) | |
| Second | 36 (8.0) | 8 (13.8) | 28 (7.1) | |
| Third | 142 (31.5) | 12 (20.7) | 130 (33.1) | |
| Not Issued | 120 (26.6) | 16 (27.6) | 104 (26.5) | |
| Gender | | | | 0.2192 |
| Female | 10 (2.2) | 0 (0.0%) | 10 (2.5) | |
| Male | 441 (97.8) | 58 (100%) | 383 (97.5) | |

*Affective disorder, substance-related disorder, or hepatitis c
**Number of Conditions an airmen has in addition to HIV

*Further Statistical Assessment*

Research published after our initial 2018 report indicated that disease severity and comorbidities, specifically neurodegenerative and cerebrovascular diseases, may be a major cause of cognitive impairment in patients with HIV. Furthermore, people with HIV without pre-existing cognitive impairment or history of HIV-associated neurocognitive disorder (HAND) demonstrate stable cognitive performance after suppressive therapy (Chan and Valcour, 2022). In addition, another study cited in this recent publication found that participants with declining cognitive functions were older, had worse baseline cognitive performance, and had a longer duration of HIV infection. While AAM's categories of medical pathcodes make it difficult to analyze specific medical conditions, in this report we added count of medications and medical conditions airmen had in addition to their HIV diagnoses as surrogates in our analysis. Therefore, we attempted to replicate findings of these recent associations in our group of airmen. To do this, we performed multivariate logistic regression to determine any variables that were significantly associated with having an abnormal cognitive assessment after baseline while controlling for other variables.

Our analysis was somewhat surprising, given that baseline age, HIV comorbidities, and counts of medications and medical conditions did not have an apparent association with odds of having a subsequent abnormal cognitive exam. Results did not change when grouping age, medication count, and condition count by categories or continuous variables. In fact, the only associations were:

- Adjusting for HIV duration since diagnoses and abnormal CD4/viral load ever, the odds of having an abnormal cognitive screening exam (anytime after initial cognitive assessment) was 2.86 (95% CI 1.52, 5.37) times greater if the pilot had an abnormal baseline cognitive test.
- Adjusting for baseline cognitive test and HIV duration, the odds of having an abnormal cognitive screening exams after baseline was 2.49 (1.37, 3.50) times greater if the pilot ever had an abnormal CD4 and/or viral load.
- Adjusting for baseline cognitive test and abnormal CD4/viral load ever, for every year increase in HIV duration, the odds of abnormal cognitive screening after initial test is 1.047 times larger (1.01-1.08).

**Conclusions**

While recent scientific literature remains mixed about whether virally-suppressed airmen with HIV experience faster cognitive decline compared with other groups, it is well documented that certain medical conditions and the aging process can accelerate cognitive decline in the general population. Thus, assuming AAM's cognitive assessments are able to detect changes in cognitive function, we expected to find associations with abnormal cognitive assessments and aging and/or increased medical conditions. However, examining all medical count and age cut-points, we did not find any associations with cognitive function and these variables in follow-up cognitive tests. We did, however, find associations between follow up cognitive assessments and initial abnormal assessment, ever having an abnormal CD4 and/or viral loads, and HIV duration. Thus, our assessment differs from the report from UCLA that found no association with abnormal CD4 counts/viral loads. Our assessment was similar to the CHARTER cohort study cited in the recent 2022 Chan and Valcour publication with our significant associations between follow-up cognitive tests and baseline assessments and HIV duration.

Unlike other populations we've examined, most pilots with HIV fail to come back to get an SI after they have been denied. While this may be for a number of reasons, one major reason pilots who fail their cognitive tests may not come back into our program is likely due to cognitive changes, as demonstrated by our significant association between baseline score and subsequent scores. With the recent 2021 change in protocol to administer the comprehensive battery of cognitive tests upon initial application of each airman with HIV, this should enhance AAM's future ability to catch more subtle cognitive issues at baseline, and thus gather more detailed information to base decisions on in future applications. In conclusion, our study supports the current new guidelines and continued active cognitive assessments in this pilot population.