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I. Background

- Integrase strand-transfer inhibitors (INIs) have an exceptional profile in efficacy, safety, tolerability and ease of dosing, that has made them favored choices in treatment regimens for both treatment-naïve and treatment-experienced individuals with HIV.
- As INI use has become more widespread, it warrants assessment of the drug class performance outside of clinical trials. Studies thus far have demonstrated a generally low but rising prevalence of INI-resistance.
- This study investigated trends in INI use within Washington D.C., an area with 1.9% HIV prevalence, over a six year period, to determine INI treatment effectiveness in the clinical setting, with a focus on durability and emerging drug resistance.

II. Methods

- We conducted a retrospective analysis using data from participants enrolled in the DC Cohort, an ongoing, multi-center, longitudinal observational cohort study of HIV-infected persons receiving care at thirteen academic and community-based treatment sites in DC.
- We used descriptive statistics to determine prevalence of INI use over time, incidence of INI resistance, mean time to viral suppression and durability of viral suppression (two consecutive viral loads <200 c/mL).
- The study population was also sub-divided into three groups as follows to better understand trends in INI use associated with varying antiretroviral histories:
 - Group A - Non-suppressed treatment-experienced persons starting their first INI regimen (n=716)
 - Group B - Suppressed treatment-experienced persons starting their first INI regimen (n=1466)
 - Group C - Treatment-naïve persons starting an INI regimen (n=487)
- Drug resistance was defined using the International Antiviral Society-USA classification system.
- All analyses were conducted using SAS (v9.4.2).

V. Acknowledgements

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III. Results

Table 1. Baseline characteristics and co-morbidities at time of enrollment and time of starting an INI

Characteristics	Total Cohort (at time of enrollment) n=6827	Participants starting an INI n=3638
Male, no. (%)	4998 (73.2%)	—
Female	1829 (26.8%)	—
White, no. (%)	748 (11.0%)	—
Black	5302 (77.7%)	—
Hispanic	351 (5.1%)	—
Asian	195 (2.9%)	—
Other	77 (1.1%)	—
Unknown	154 (2.3%)	—
Age, median (IQR), years	47.3 (37.1, 54.7)	49.3 (39.0, 56.9)
CD4 cell count, cells/mm ³ , median (IQR)	526 (343, 734)	530 (322, 738.5)
Viral load, copies/mL, median (IQR)	1* (1, 150)	1* (1, 1480)
Substance abuse diagnosis (by ICD code)	428 (6.3%)	427 (11.7%)
Mental health diagnosis	197 (2.9%)	173 (4.8%)
Hepatitis C antibody positive	950 (13.9%)	511 (14.1%)
Diabetes	118 (1.7%)	103 (2.8%)
Dyslipidemia	717 (10.5%)	553 (15.2%)
Overweight or obese	594 (8.7%)	594 (16.3%)

* Value of 1 denotes undetectable viral load

Figure 2. Annual frequency of individuals with loss of viral suppression

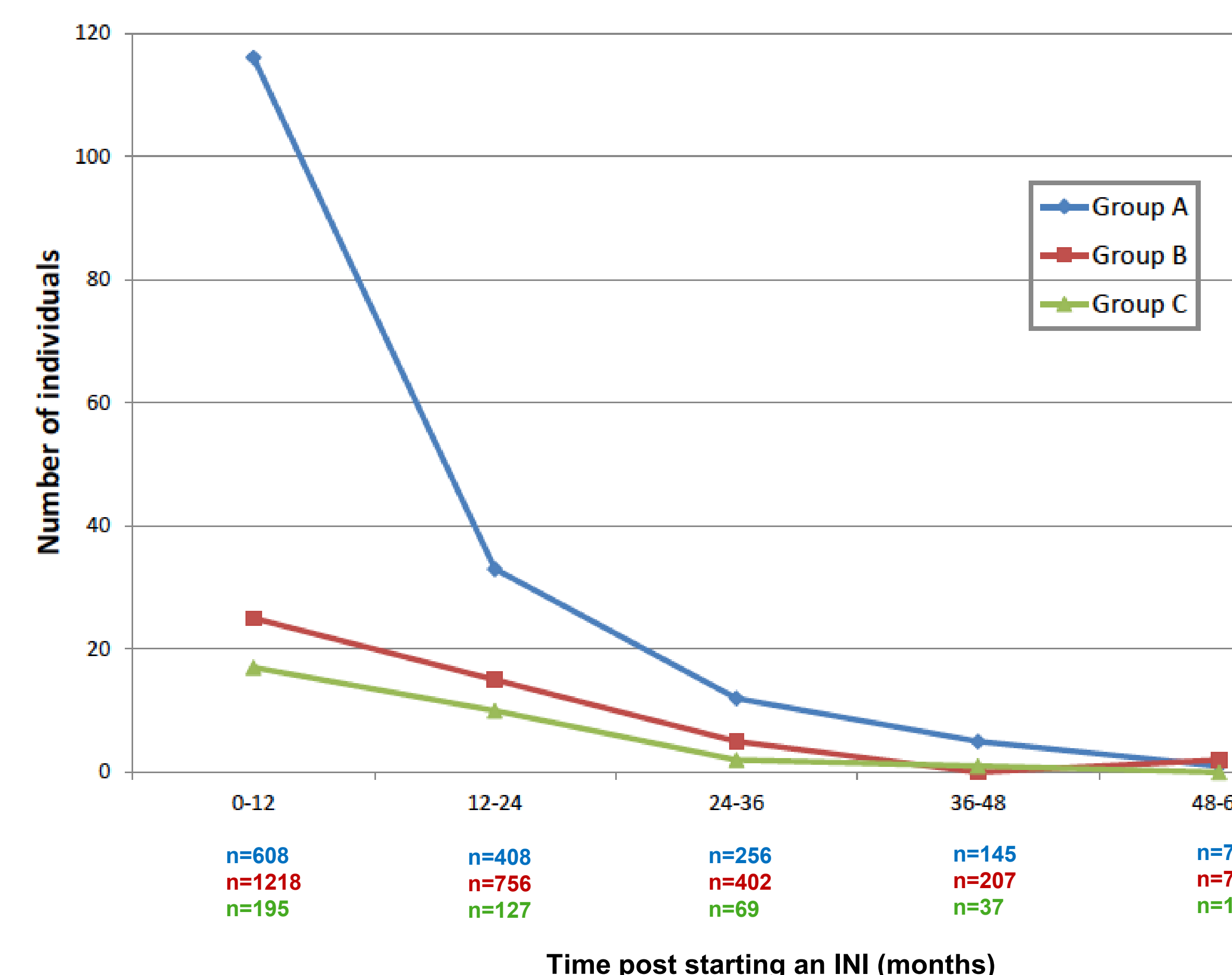
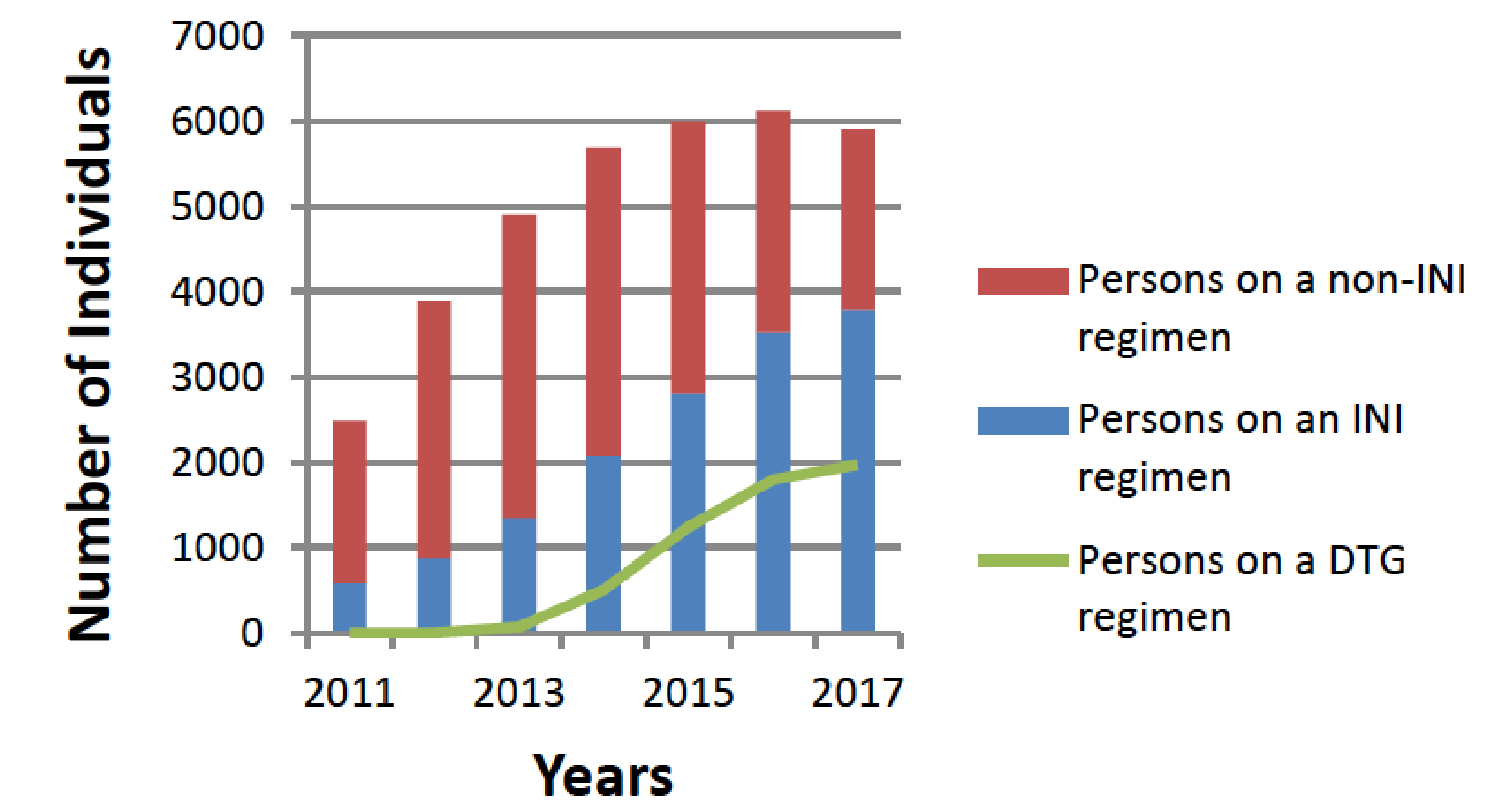


Figure 1. Prevalence of INI use over time



- Among 6827 participants, 73% were male, 78% Black, and median age was 47 years (IQR:37.1-54.7) [Table 1].
- INI-based therapy increased from 23% (582/2490) in 2011 to 64% (3783/5898) in 2017, when 52% of total participants on INIs used dolutegravir [Figure 1].
- From 2011 to 2017 INI resistance was identified in only 1% (38/3783) of participants. Major mutations included Q148H/R (n=11), N155H (n=5), F121Y (n=4), Y143H/R (n=3), and G140S (n=3). Nine individuals had baseline INI resistance mutations.
- The mean time to suppression was 163 days among non-suppressed treatment-experienced persons starting their first INI regimen (Group A) and 127 days for treatment-naïve persons starting an INI regimen (Group C), [p=0.003]. Viral suppression at 6 months was similar between these groups, 70% among non-suppressed treatment-experienced individuals switching to INI regimen (Group A) vs 76% among treatment naïve individuals initiating INI-based therapy (Group C), [p=0.116].
- Rebound viremia after suppression was most frequent in the first year post INI initiation at 7.8% (158/2021), and most frequent in particular for non-suppressed treatment-experienced persons (Group A) at 19.1% (116/608), [Figure 2].

IV. Conclusions

- The majority of participants in the DC Cohort are now on INI-based therapy.
- INI resistance remains rare.
- Long term viral suppression is evident among treatment naïve individuals starting INI-therapy, but remains a challenge for those with evidence of viremia on prior treatment regimens. Adherence likely plays a significant role, and increased attention to treatment outcomes and support measures should be in place during the first year of INI-based therapy as the risk for viremia appears to be greatest during this time period.
- INI use will likely continue to accelerate, and as it does, it is critical to continue to study outcomes associated with their use in clinical practice, to inform best practices for HIV management.