



# A Public Health Approach to Viremic Individuals With PrEP-resistant Virus

Susan E. Buskin,<sup>1,2</sup> Richard J. Lechtenberg,<sup>1</sup> Matthew R. Golden,<sup>1,2</sup> Mark Fleming,<sup>1</sup> and Julia C Dombrowski<sup>1,2</sup>

<sup>1</sup>Public Health-Seattle & King County, WA, <sup>2</sup>University of Washington, Seattle, WA

Susan E. Buskin, PhD, MPH  
401 5th Ave, Suite 1250  
Seattle, WA, 98115  
Susan.buskin@kingcounty.gov



## BACKGROUND

- A Canadian report described a 2015 transmission of HIV resistant to tenofovir (TDF) & emtricitabine (FTC) (the components of PrEP) in a person adherent to PrEP.
- In 2016, a similar transmission likely occurred in King Co. WA.
- Preventing transmission of HIV strains potentially rendering PrEP ineffective is a public health priority.

## METHODS

People Living With HIV (PLWH) and 2017 residents of King Co. are described using National HIV Surveillance System (NHSS) data:

- Most recent viral load (VL) data from NHSS -- within 24 mos. of 12/2017 -- identified viremia, defined as plasma viral load of  $\geq 1,000$  copies per mL. Substantial viremia was VL  $\geq 10,000$ .
- Partial *pol* (~1K of PR & RT) sequences were collected since 2003.
- PrEP-resistant strains had mutations conferring intermediate to high (higher) level resistance to TDF and FTC, as categorized by the Stanford database algorithm.

Investigations: At four time-points, Data to Care (D2C) staff investigated people with viremia (or no VL) and PrEP-resistant virus (Table). Investigations include provider & patient conversations to:

- Promote engagement in HIV care and reduction of viremia.
- Discuss potential for HIV transmission to partners on PrEP.
- If other interventions promoting care engagement are not successful, staff refer to a low-barrier walk-in clinic, MAX.

Primary TDF/FTC Resistance was sought within one year of new HIV diagnoses (primary resistance) from 2008 to 2017. Genetic similarity clustering was based on a 1.5% TN93 distance threshold.

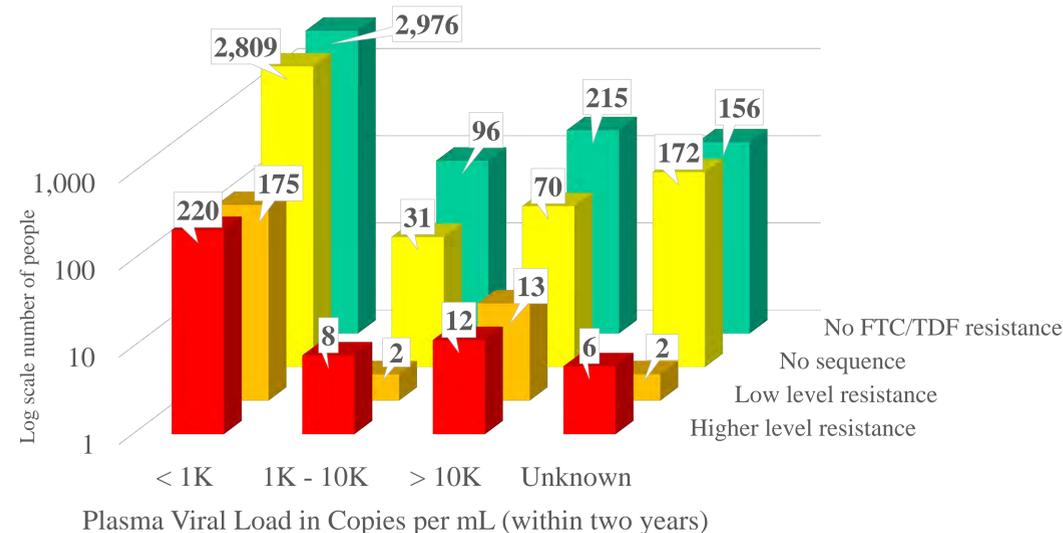
Time-points	Viremia ( $\geq 1K$ )	Substantial Viremia ( $\geq 10K$ )	No Viral Load in 2+ Years	TDF/FTC resistance at SAME time	TDF/FTC resistance at ANY time	N
2016		X		X		21
2017 (1)	X				X	21
2017 (2)	X		X		X	25
2018		X	X		X	11

## RESULTS

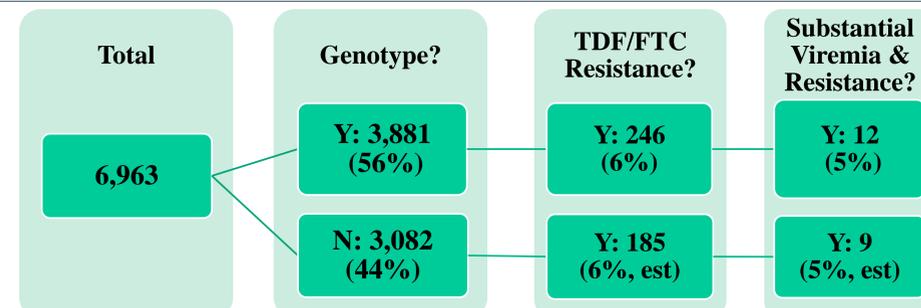
People living With HIV (PLWH)

- 3,881 (56%) of 6,963 PLWH, had one or more genotypic sequence.
- Higher level TDF/FTC resistance was found for 246 (6%); 310 had substantial viremia, and 12 had both (Fig 1).
- Assuming the same proportion of TDF/FTC resistance and substantial viremia among those with missing data, another 9 persons could have substantial viremia and TDF/FTC resistance (Fig 2); corresponding to 3 out of 1,000 PLWH.
- Relative to those without TDF/FTC resistance, TDF/FTC resistance was associated with earlier HIV diagnosis (median year 1994 vs. 2005),  $\geq 50$  years of age, male sex, & being a man who had sex with men (all  $p < 0.01$ ).

**Fig 1. TDF/FTC Resistance and Viremia; King County, WA, 2017**



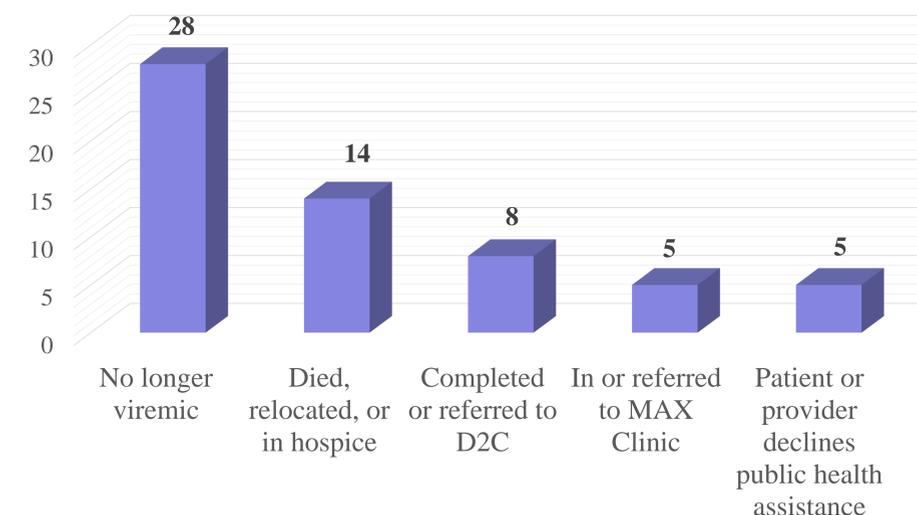
**Fig 2. Actual and Estimated TDF/FTC Resistance with Substantial Viremia**



Investigations

- From the four time-points, we investigated 60 individuals, up to four times each. The most recent outcomes are in Fig 3, below.

**Fig 3. Outcomes from 60 Investigations of PLWH in King County, WA with TDF/FTC Resistance and Viremia**



Primary TDF/FTC Resistance

- Between 2008 and 2017, three of 1,817 (0.17%) people newly diagnosed with HIV had TDF/FTC resistance in a reported sequence.
- All three were virally suppressed at their most recent VL.
- Assuming similar prevalence for people with no genotypic sequence reported (N= 506) we estimate a total of four individuals with primary TDF/FTC resistance in the decade (< 1/year).
- There has been no increasing trend in resistance since the 2012 licensure of Truvada™ (comprised of TDF & FTC) for PrEP.
- Two of three primary TDF/FDC resistant cases were in separate genetic similarity clusters consisting of 19 and 72 PLWH. (For comparison, 42% of newly diagnosed cases were in clusters.)
- Other cluster members did not have the characteristic mutations of TDF/FTC resistance present in the three with transmitted resistance: M184V & K65R.

## LIMITATIONS

- Of PLWH, 44% were missing genotypes and 5% did not have a recent VL.
- Our criteria for investigation evolved over the course of the project.
- The likelihood of transmission of a "PrEP-resistant" virus from a viremic individual identified with TDF/FTC resistance, especially with archived resistance, is unknown.

## CONCLUSIONS

- Very few PLWH in King County have both substantial viremia and resistance to TDF & FTC.
- Transmitted TDF/FTC resistance is also rare and not (yet) increasing.
- Public health surveillance databases can identify individuals with drug resistance and viral loads enabling transmission of HIV resistant to TDF/FTC (PrEP).
- Experienced field staff have investigated and continue to investigate and intervene in the setting TDF/FTC resistance with substantial viremia.

## ACKNOWLEDGEMENTS

Many thanks are due to local health care providers, patients, project participants, and colleagues at Public Health – Seattle & King County. Additional thanks to the Centers for Disease Control and Prevention for cooperative agreement funding; colleagues at the Washington State Department of Health; and Drs. J. Herbeck and R. Kerani for clustering analyses and other assistance (NIH R01 R01AI127232).