



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

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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), ≥ 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

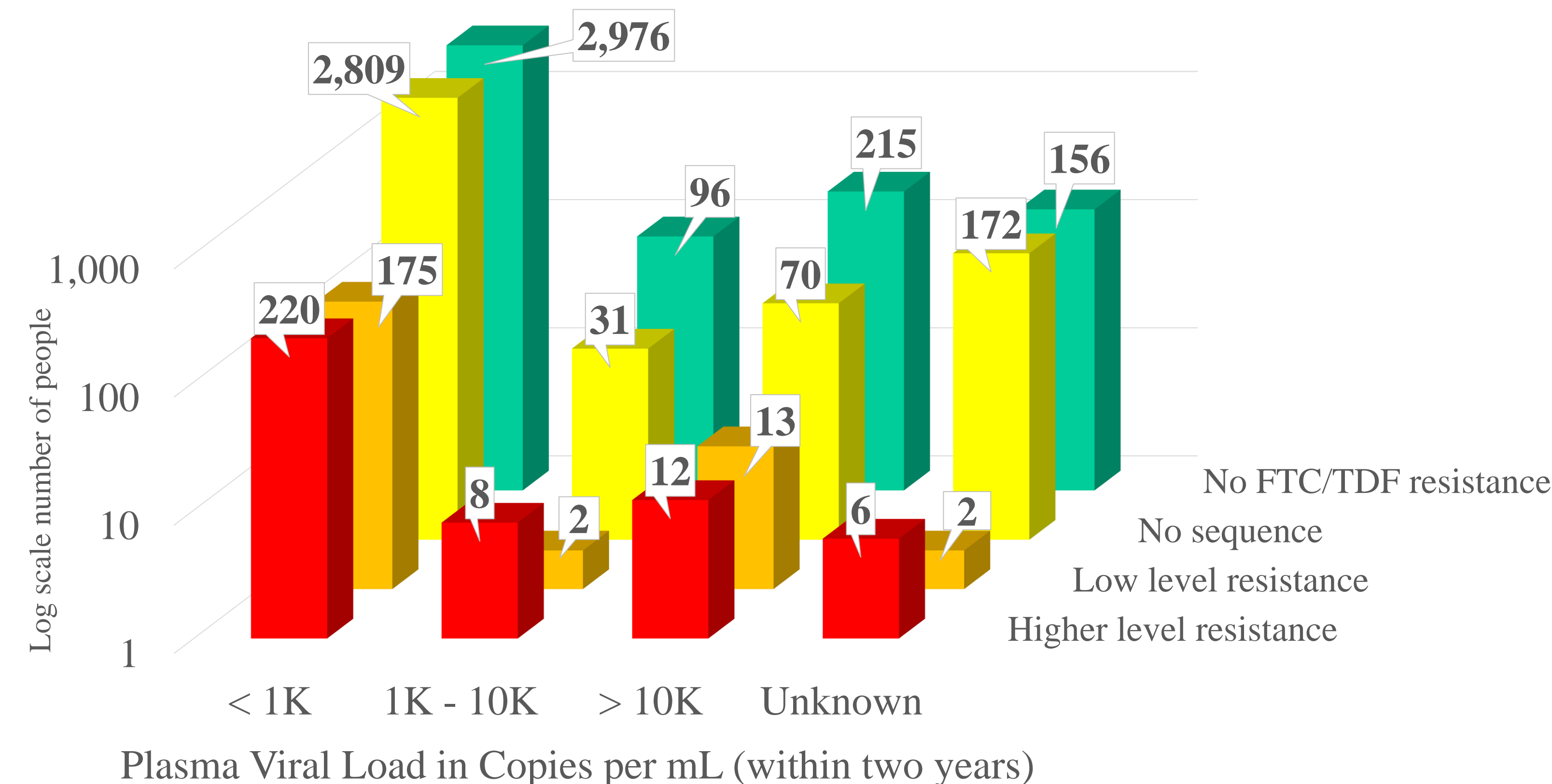
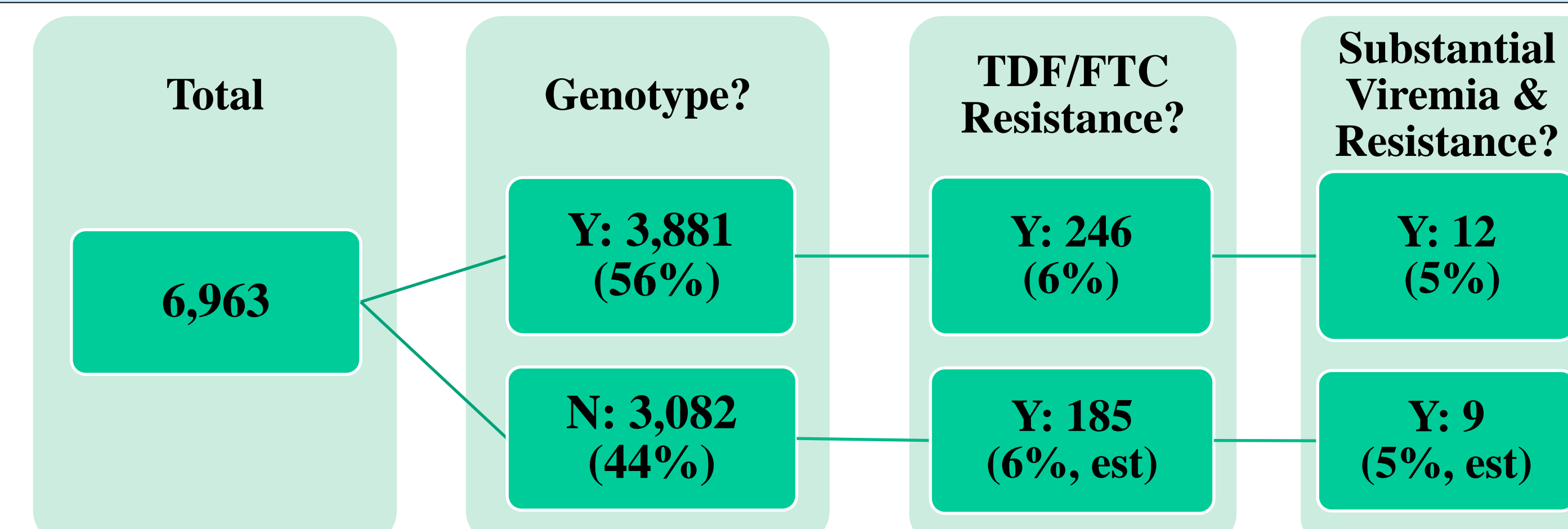


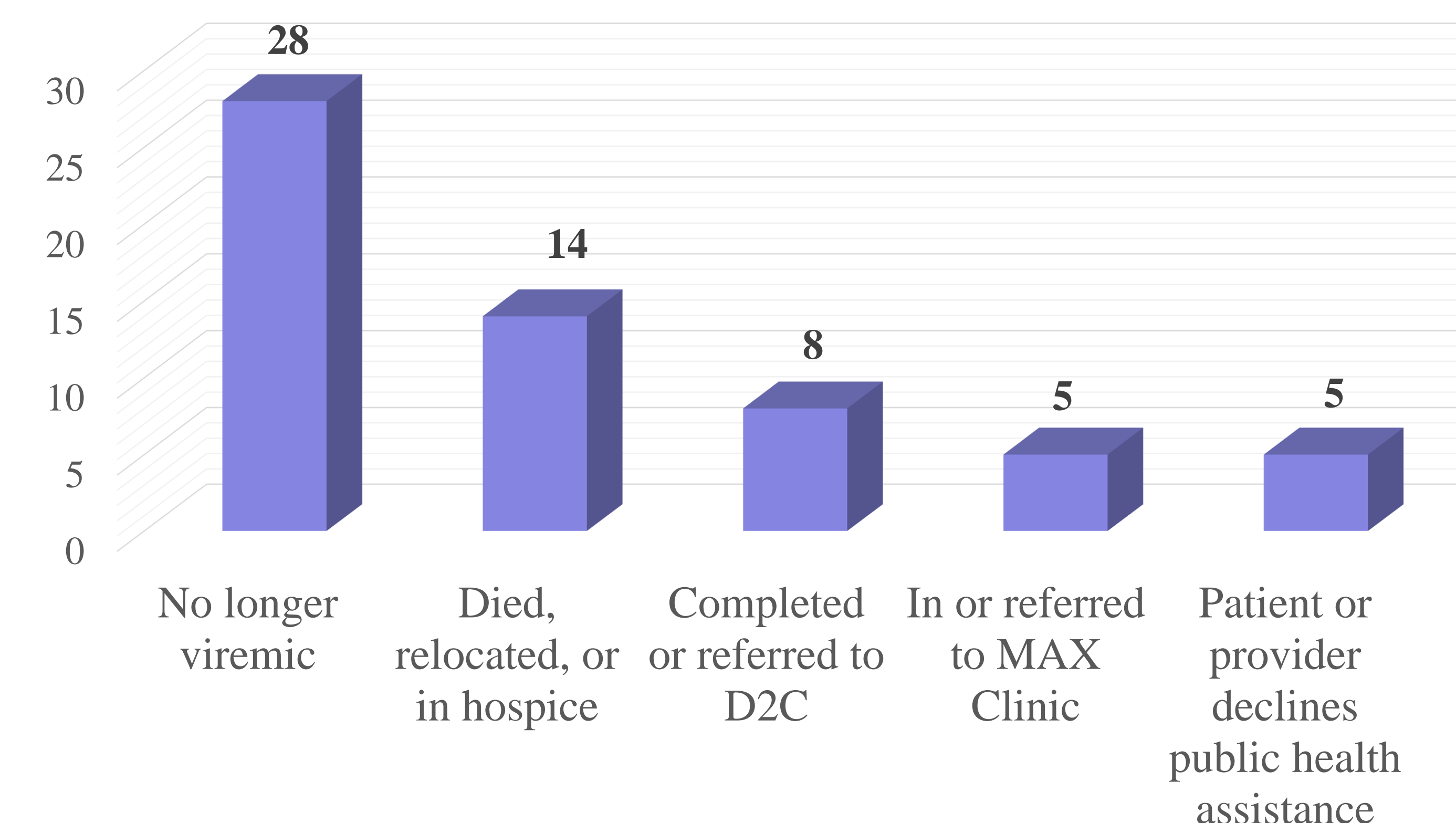
Fig 2. Actual and Estimated TDF/FTC Resistance with Substantial Viremia



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.

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