**Table S1**. List of 113 PI-associated mutations included in one or more of four expert 2020 lists: prevalence in PI-naïve and PI-experienced persons before and after 2009.

| Pos[1] | AA[1] | Lists | | <2009 | | | | | | | | | | | ≥2009 | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 2009 | 2020 | %PI | %PI-Naive | | | | | | | | | | %PI | %PI-Naive | | | | | | | | | |
| | | | | | ALL | A | B | C | 01 | 02 | D | F | G | Other | | ALL | A | B | C | 01 | 02 | D | F | G | Other |
| | | | | (22,266) | (61,067) | (4,316) | (33,132) | (8,935) | (5,265) | (3,743) | (1,497) | (726) | (2,036) | (1,438) | (10,534) | (54,813) | (3,209) | (21,435) | (10,194) | (10,189) | (3,616) | (891) | (794) | (1,425) | (3,039) |
| 10 | C | 1 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 10 | F | 4 | 4 | 8.6 | 0.2 | 0.1 | 0.3 | 0.1 | 0.1 | 0.0 | 0.3 | 0.0 | 0.1 | 0.5 | 6.7 | 0.2 | 0.2 | 0.3 | 0.1 | 0.2 | 0.1 | 0.5 | 0.0 | 0.0 | 0.0 |
| 10 | I | 4 | 3 | 31 | 8.5 | 14 | 8.9 | 2.3 | 10 | 6.0 | 6.1 | 9.1 | 11 | 26 | 16 | 8.4 | 20 | 9.2 | 2.2 | 7.7 | 7.7 | 6.6 | 10 | 19 | 15 |
| 10 | M | 1 | 1 | 0.2 | 0.3 | 0.6 | 0.0 | 0.8 | 0.3 | 0.1 | 0.2 | 0.1 | 1.5 | 1.4 | 0.3 | 0.5 | 0.8 | 0.2 | 1.2 | 0.2 | 0.5 | 0.0 | 0.3 | 2.5 | 2.0 |
| 10 | R | 3 | 1 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 10 | V | 4 | 3 | 11 | 4.8 | 8.5 | 3.4 | 1.8 | 5.9 | 11 | 8.1 | 33 | 0.5 | 7.6 | 11 | 5.9 | 12 | 4.4 | 1.7 | 5.9 | 12 | 8.6 | 50 | 1.6 | 4.8 |
| 11 | I | 4 | 4 | 3.0 | 0.6 | 0.5 | 0.3 | 0.5 | 0.5 | 3.3 | 0.5 | 0.0 | 1.1 | 1.4 | 1.4 | 0.8 | 1.1 | 0.3 | 0.5 | 0.6 | 4.6 | 0.2 | 0.6 | 1.6 | 0.3 |
| 11 | L | 1 | 1 | 0.7 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 |
| 15 | A | 1 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 15 | V | 1 | 1 | 33 | 28 | 15 | 22 | 85 | 12 | 10 | 17 | 75 | 17 | 32 | 41 | 33 | 19 | 25 | 81 | 14 | 16 | 18 | 60 | 22 | 25 |
| 16 | E | 3 | 1 | 6.2 | 9.4 | 20 | 4.2 | 7.2 | 25 | 23 | 9.0 | 26 | 4.5 | 16 | 13 | 14 | 24 | 6.2 | 9.1 | 26 | 31 | 9.8 | 30 | 6.0 | 19 |
| 20 | I | 4 | 2 | 8.4 | 9.9 | 2.7 | 0.1 | 0.1 | 2.7 | 95 | 0.7 | 0.4 | 98 | 8.9 | 6.2 | 11 | 5.4 | 0.2 | 0.1 | 1.9 | 95 | 2.4 | 3.1 | 97 | 9.8 |
| 20 | M | 4 | 3 | 3.3 | 0.5 | 0.1 | 0.4 | 0.6 | 0.1 | 0.6 | 1.3 | 1.3 | 0.9 | 1.8 | 1.7 | 0.5 | 0.1 | 0.6 | 0.6 | 0.0 | 0.5 | 2.7 | 2.3 | 0.6 | 1.1 |
| 20 | R | 4 | 3 | 17 | 8.2 | 17 | 2.8 | 19 | 16 | 1.7 | 12 | 43 | 0.0 | 18 | 18 | 13 | 20 | 3.0 | 22 | 27 | 2.3 | 13 | 31 | 0.4 | 11 |
| 20 | T | 4 | 3 | 5.3 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.2 | 0.0 | 0.0 | 0.8 | 4.1 | 0.1 | 0.0 | 0.1 | 0.1 | 0.2 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 |
| 20 | V | 3 | 2 | 1.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 1.5 | 0.2 | 0.0 | 0.6 | 0.2 | 0.5 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 1.4 | 0.0 | 0.0 | 0.9 | 0.5 |
| **23** | **I** | 2 | 2 | 1.3 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 1.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 24 | F | 2 | 1 | 0.6 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 |
| **24** | **I** | 4 | 4 | 5.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 2.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 24 | M | 0 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **30** | **N** | 4 | 4 | 6.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 2.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **32** | **I** | 4 | 4 | 5.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 2.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 |
| 32 | ins | 1 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 33 | F | 4 | 4 | 12 | 0.4 | 1.0 | 0.2 | 0.1 | 1.4 | 0.4 | 0.7 | 0.0 | 0.4 | 0.5 | 6.9 | 0.5 | 1.6 | 0.1 | 0.2 | 1.2 | 0.6 | 0.4 | 0.3 | 0.2 | 0.7 |
| 33 | I | 4 | 3 | 2.2 | 0.6 | 0.3 | 1.0 | 0.0 | 0.2 | 0.2 | 1.4 | 0.1 | 0.2 | 0.6 | 1.7 | 0.7 | 0.8 | 1.4 | 0.0 | 0.1 | 0.2 | 0.9 | 0.6 | 0.2 | 0.6 |
| 33 | V | 4 | 2 | 1.8 | 1.7 | 0.5 | 2.6 | 0.1 | 0.5 | 0.2 | 7.0 | 0.6 | 0.3 | 0.8 | 1.4 | 1.3 | 0.7 | 2.6 | 0.3 | 0.3 | 0.4 | 6.4 | 1.0 | 0.1 | 0.8 |
| 34 | Q | 1 | 1 | 2.6 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.5 | 0.0 | 0.0 | 0.7 | 0.0 | 1.3 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.7 | 0.0 | 0.0 | 0.4 | 0.3 |
| 35 | G | 3 | 1 | 1.1 | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 1.5 | 0.1 | 0.1 | 0.3 | 1.2 | 0.7 | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 1.4 | 0.2 | 0.0 | 0.4 | 0.7 |
| 35 | N | 1 | 1 | 1.6 | 0.6 | 1.0 | 0.1 | 0.2 | 1.7 | 2.6 | 0.3 | 0.7 | 2.9 | 0.3 | 1.9 | 1.0 | 3.0 | 0.1 | 0.3 | 1.1 | 3.8 | 1.9 | 0.9 | 3.1 | 1.5 |
| 36 | I | 4 | 2 | 49 | 51 | 98 | 17 | 84 | 97 | 97 | 63 | 97 | 98 | 79 | 62 | 62 | 97 | 18 | 85 | 97 | 97 | 71 | 96 | 98 | 69 |

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 36 | L | 3 | 2 | 2.6 | 1.3 | 0.4 | 1.0 | 3.6 | 0.3 | 0.9 | 2.5 | 0.7 | 0.3 | 1.8 | 2.5 | 1.4 | 0.6 | 1.2 | 3.6 | 0.2 | 0.8 | 1.3 | 0.8 | 0.5 | 1.0 |
| 36 | V | 3 | 2 | 2.1 | 1.0 | 0.4 | 0.4 | 4.7 | 0.6 | 0.2 | 0.5 | 0.1 | 0.2 | 1.2 | 1.4 | 1.1 | 0.2 | 0.4 | 3.4 | 0.4 | 0.3 | 0.6 | 0.8 | 0.1 | 2.7 |
| 38 | W | 1 | 1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 41 | T | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.1 | 0.0 | 0.1 | 0.3 | 0.1 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.1 |
| 43 | R | 1 | 1 | 2.4 | 2.7 | 1.4 | 3.0 | 1.3 | 2.4 | 5.6 | 1.6 | 3.7 | 3.1 | 5.0 | 3.0 | 3.2 | 2.7 | 3.4 | 1.3 | 2.7 | 7.8 | 4.5 | 2.3 | 4.1 | 3.9 |
| 43 | T | 3 | 3 | 5.6 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.2 | 0.1 | 0.1 | 0.1 | 1.2 | 3.0 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.4 |
| 46 | I | 4 | 4 | 21 | 0.3 | 0.3 | 0.3 | 0.2 | 0.3 | 0.2 | 0.1 | 0.0 | 0.0 | 0.2 | 13 | 0.3 | 0.3 | 0.4 | 0.1 | 0.6 | 0.2 | 0.1 | 0.4 | 0.2 | 0.0 |
| 46 | L | 4 | 4 | 9.2 | 0.3 | 0.3 | 0.4 | 0.1 | 0.3 | 0.1 | 0.2 | 0.1 | 0.4 | 0.3 | 3.4 | 0.4 | 0.2 | 0.3 | 0.1 | 0.9 | 0.1 | 0.0 | 0.4 | 0.0 | 0.6 |
| 46 | V | 1 | 1 | 0.5 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 |
| 47 | A | 4 | 4 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 47 | V | 4 | 4 | 4.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 2.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 |
| 48 | A | 2 | 2 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 48 | L | 0 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 48 | M | 2 | 2 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 48 | Q | 0 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 48 | S | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 48 | T | 1 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 48 | V | 4 | 4 | 3.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 50 | L | 4 | 4 | 1.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 2.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 50 | V | 4 | 4 | 1.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 53 | L | 4 | 4 | 5.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 3.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 |
| 53 | W | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 53 | Y | 3 | 2 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.1 | 0.0 | 0.0 | 0.0 |
| 54 | A | 4 | 4 | 1.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 54 | L | 4 | 4 | 3.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.4 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 54 | M | 4 | 4 | 2.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 54 | S | 4 | 3 | 0.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 54 | T | 4 | 4 | 0.8 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 |
| 54 | V | 4 | 4 | 23 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 12 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 58 | E | 4 | 3 | 6.3 | 0.3 | 0.1 | 0.4 | 0.4 | 0.0 | 0.0 | 1.2 | 0.1 | 0.1 | 0.2 | 4.3 | 0.4 | 0.1 | 0.6 | 0.5 | 0.0 | 0.0 | 0.7 | 0.5 | 0.3 | 0.4 |
| 60 | E | 2 | 2 | 12 | 9.0 | 5.2 | 8.9 | 17 | 2.8 | 0.6 | 16 | 11 | 2.1 | 37 | 13 | 15 | 6.2 | 18 | 19 | 2.9 | 1.0 | 15 | 27 | 2.4 | 32 |
| 62 | V | 3 | 3 | 34 | 17 | 6.3 | 27 | 4.6 | 4.7 | 1.4 | 19 | 19 | 3.2 | 20 | 25 | 17 | 7.9 | 33 | 5.1 | 5.5 | 2.2 | 21 | 23 | 6.3 | 16 |
| 63 | P | 3 | 2 | 63 | 40 | 15 | 55 | 36 | 12 | 19 | 35 | 9.1 | 20 | 14 | 49 | 37 | 17 | 54 | 37 | 17 | 22 | 39 | 9.6 | 24 | 33 |
| 64 | L | 1 | 1 | 2.9 | 3.6 | 1.2 | 4.5 | 1.9 | 0.6 | 7.3 | 3.1 | 2.6 | 3.6 | 2.4 | 3.4 | 3.6 | 2.3 | 4.7 | 2.2 | 0.6 | 9.8 | 5.2 | 2.8 | 5.1 | 2.9 |
| 64 | M | 2 | 2 | 1.7 | 2.6 | 2.0 | 1.6 | 1.6 | 0.8 | 13 | 0.8 | 2.1 | 9.6 | 3.6 | 2.2 | 3.3 | 3.4 | 1.9 | 1.9 | 0.6 | 18 | 0.9 | 1.9 | 13 | 2.1 |
| 64 | V | 2 | 3 | 18 | 11 | 0.8 | 16 | 0.5 | 0.4 | 1.7 | 66 | 0.6 | 0.4 | 13 | 13 | 7.1 | 1.2 | 14 | 0.8 | 0.6 | 1.8 | 57 | 1.5 | 0.7 | 5.5 |
| 66 | V | 0 | 1 | 1.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.4 | 0.1 | 0.0 | 0.1 | 1.4 | 0.4 | 0.1 | 0.1 | 0.0 | 0.1 | 0.0 | 0.2 | 0.0 | 0.1 | 0.4 | 0.4 |

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 69 | I | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 |
| 69 | K | 3 | 2 | 15 | 41 | 96 | 1.5 | 98 | 97 | 96 | 2.8 | 1.4 | 94 | 61 | 41 | 54 | 92 | 2.6 | 97 | 96 | 96 | 6.4 | 3.7 | 89 | 58 |
| 69 | N | 1 | 1 | 1.0 | 0.5 | 0.1 | 0.7 | 0.1 | 0.1 | 0.2 | 0.3 | 0.1 | 0.3 | 0.2 | 0.2 | 0.3 | 0.3 | 0.6 | 0.0 | 0.2 | 0.3 | 0.1 | 0.6 | 0.4 | 0.4 |
| 69 | Q | 1 | 1 | 3.3 | 2.4 | 2.1 | 2.9 | 1.1 | 0.7 | 1.0 | 5.1 | 8.4 | 1.4 | 11 | 4.2 | 2.8 | 4.4 | 4.0 | 1.3 | 0.7 | 1.1 | 16 | 7.3 | 1.1 | 6.7 |
| 69 | R | 1 | 2 | 1.5 | 0.6 | 0.7 | 0.4 | 0.3 | 1.0 | 1.2 | 0.3 | 1.0 | 4.0 | 1.2 | 1.0 | 0.9 | 1.3 | 0.4 | 0.4 | 0.9 | 2.3 | 0.3 | 0.6 | 8.4 | 0.8 |
| 69 | Y | 1 | 1 | 2.2 | 1.9 | 0.0 | 2.5 | 0.0 | 0.0 | 0.0 | 18 | 7.2 | 0.0 | 1.2 | 1.9 | 1.4 | 0.2 | 2.3 | 0.0 | 0.0 | 0.0 | 9.7 | 17.9 | 0.0 | 0.7 |
| 71 | I | 4 | 2 | 3.2 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.7 | 0.1 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 71 | L | 3 | 2 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 71 | T | 4 | 3 | 9.9 | 4.7 | 0.1 | 8.2 | 1.0 | 0.2 | 0.2 | 1.9 | 0.1 | 0.4 | 0.3 | 6.3 | 4.7 | 0.2 | 11 | 1.0 | 0.3 | 0.3 | 3.0 | 0.5 | 0.5 | 2.5 |
| 71 | V | 4 | 2 | 27 | 3.3 | 0.0 | 5.9 | 0.2 | 0.3 | 0.2 | 0.3 | 0.1 | 0.3 | 0.5 | 12 | 3.5 | 0.2 | 8.0 | 0.3 | 0.2 | 0.1 | 0.6 | 0.1 | 1.1 | 6.1 |
| **73** | **A** | 4 | 2 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **73** | **C** | 3 | 3 | 1.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 73 | D | 0 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 |
| **73** | **S** | 4 | 4 | 8.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.3 | 2.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.2 |
| **73** | **T** | 4 | 4 | 2.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 73 | V | 1 | 1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 74 | A | 1 | 1 | 1.8 | 0.6 | 0.3 | 0.5 | 2.2 | 0.2 | 0.1 | 0.0 | 1.1 | 0.3 | 0.3 | 1.4 | 0.8 | 0.4 | 0.6 | 2.5 | 0.3 | 0.2 | 0.1 | 0.5 | 0.1 | 0.2 |
| 74 | P | 3 | 4 | 1.9 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.2 | 1.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 |
| 74 | S | 2 | 1 | 7.3 | 2.3 | 1.5 | 0.4 | 11 | 0.9 | 1.3 | 0.3 | 7.9 | 0.8 | 1.4 | 7.1 | 3.0 | 2.5 | 0.3 | 12 | 1.0 | 1.2 | 0.1 | 3.0 | 0.6 | 1.5 |
| **76** | **V** | 4 | 4 | 3.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 3.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 77 | I | 3 | 2 | 27 | 21 | 12 | 33 | 7.4 | 2.0 | 2.6 | 15 | 10 | 2.7 | 26 | 26 | 19 | 12 | 37 | 7.4 | 4.0 | 3.3 | 13 | 15 | 2.5 | 21 |
| **82** | **A** | 4 | 4 | 22 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 12 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 |
| **82** | **C** | 3 | 2 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **82** | **F** | 4 | 4 | 1.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 82 | G | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **82** | **L** | 3 | 3 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **82** | **M** | 3 | 2 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 |
| **82** | **S** | 4 | 4 | 1.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **82** | **T** | 4 | 4 | 2.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **83** | **D** | 2 | 3 | 0.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 |
| **84** | **A** | 3 | 3 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 84 | C | 2 | 2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **84** | **V** | 4 | 4 | 12 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 3.8 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| **85** | **V** | 3 | 3 | 4.6 | 0.2 | 0.1 | 0.2 | 0.1 | 0.1 | 0.1 | 0.5 | 0.0 | 0.0 | 0.2 | 2.1 | 0.2 | 0.4 | 0.2 | 0.1 | 0.1 | 0.1 | 0.2 | 0.0 | 0.0 | 0.2 |
| **88** | **D** | 4 | 4 | 5.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 2.7 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 |
| 88 | G | 1 | 1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 |
| **88** | **S** | 4 | 4 | 1.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

| 88 | T | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 89 | I | 3 | 2 | 2.9 | 1.3 | 1.6 | 0.1 | 2.3 | 2.1 | 5.9 | 0.2 | 1.0 | 2.4 | 11 | 4.0 | 2.0 | 2.6 | 0.2 | 3.2 | 2.1 | 7.9 | 0.1 | 1.4 | 3.6 | 5.8 |
| 89 | M | 2 | 1 | 14 | 40 | 97 | 1.6 | 82 | 96 | 93 | 2.1 | 80 | 96 | 55 | 38 | 51 | 95 | 1.9 | 76 | 94 | 92 | 4.9 | 83 | 95 | 51 |
| 89 | R | 1 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 |
| 89 | T | 3 | 2 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 89 | V | 4 | 4 | 3.7 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 0.4 | 0.1 | 0.1 | 0.1 | 0.2 | 1.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.2 | 0.0 | 0.1 | 0.1 | 0.1 |
| **90** | **M** | 4 | 4 | 30 | 0.2 | 0.0 | 0.3 | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 0.3 | 0.2 | 9.6 | 0.2 | 0.1 | 0.4 | 0.1 | 0.0 | 0.2 | 0.0 | 0.1 | 0.4 | 0.1 |
| 93 | L | 2 | 1 | 40 | 41 | 21 | 42 | 96 | 19 | 3.5 | 3.9 | 8.8 | 4.2 | 21 | 45 | 49 | 17 | 53 | 96 | 35 | 0.7 | 11 | 14 | 2.5 | 42 |
| 93 | M | 3 | 1 | 0.7 | 0.1 | 0.3 | 0.1 | 0.0 | 0.2 | 0.3 | 0.1 | 0.6 | 0.2 | 0.6 | 0.2 | 0.1 | 0.3 | 0.1 | 0.0 | 0.3 | 0.4 | 0.0 | 0.4 | 0.0 | 0.4 |

**Abbreviation**: Pos – amino acid position; AA – amino acid; List – Number of expert lists with the mutation in 2009 and 2020; %PI – percent prevalence among PI-experienced persons; %PI-Naïve – percent prevalence among PI-naïve persons.

The parenthetical numbers in the headers represent the number of persons from whom a sequence was available.

[1]40 PI-associated surveillance drug resistance mutations at 18 positions (Bennett 2009) were indicated in bold.

**Table S2.** List of 66 NRTI-associated mutations included in one or more of four expert 2020 lists: prevalence in RTI-naïve and NRTI-experienced persons before and after 2009.

| Pos[1] | AA[1] | Lists 2009 | Lists 2020 | %NRTI (32,363) | ALL (54,910) | A (4,245) | B (30,428) | C (7,596) | 01 (4,571) | 02 (2,871) | D (1,279) | F (606) | G (1,003) | Other (2,361) | %NRTI (24,210) | ALL (45,940) | A (2,423) | B (18,847) | C (4,811) | 01 (9,495) | 02 (2,382) | D (612) | F (777) | G (495) | Other (6,048) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | **<2009 %RTI-Naive** | | | | | | | | | | **≥2009 %RTI-Naive** | | | | | | |
| 40 | F | 0 | 1 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **41** | **L** | 4 | 4 | 33 | 0.3 | 0.1 | 0.4 | 0.1 | 0.0 | 0.2 | 0.8 | 0.2 | 0.5 | 0.0 | 15 | 0.2 | 0.5 | 0.3 | 0.1 | 0.1 | 0.3 | 0.5 | 0.3 | 0.2 | 0.1 |
| 44 | A | 3 | 1 | 1.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 44 | D | 3 | 1 | 8.7 | 0.3 | 0.8 | 0.2 | 0.1 | 0.0 | 0.1 | 2.2 | 0.5 | 0.2 | 0.3 | 4.3 | 0.1 | 0.5 | 0.1 | 0.2 | 0.0 | 0.1 | 1.5 | 0.4 | 0.6 | 0.1 |
| 62 | V | 2 | 2 | 4.1 | 0.7 | 6.9 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.3 | 0.1 | 0.1 | 6.9 | 0.5 | 6.5 | 0.1 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 |
| 65 | E | 0 | 3 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.2 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.1 |
| 65 | N | 2 | 4 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| **65** | **R** | 4 | 4 | 4.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 10 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 67 | del | 2 | 2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **67** | **E** | 2 | 1 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 |
| **67** | **G** | 3 | 2 | 2.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 2.3 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 |
| 67 | H | 1 | 1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **67** | **N** | 4 | 4 | 30 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.2 | 0.1 | 0.0 | 0.0 | 0.0 | 16 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 |
| 67 | S | 1 | 1 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 67 | T | 1 | 1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 68 | del | 0 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 69 | A | 3 | 1 | 1.1 | 0.2 | 0.0 | 0.3 | 0.2 | 0.2 | 0.1 | 0.2 | 0.5 | 0.1 | 0.1 | 0.9 | 0.3 | 0.2 | 0.4 | 0.3 | 0.2 | 0.3 | 0.0 | 0.4 | 0.0 | 0.1 |
| **69** | **D** | 3 | 3 | 6.9 | 0.1 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 3.1 | 0.1 | 0.0 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| 69 | del | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 69 | G | 2 | 1 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **69** | **ins** | 4 | 4 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 69 | N | 3 | 2 | 6.5 | 0.6 | 0.3 | 0.6 | 0.3 | 2.1 | 0.4 | 0.2 | 0.3 | 0.0 | 0.1 | 5.1 | 0.8 | 0.5 | 0.7 | 0.2 | 1.7 | 0.5 | 0.7 | 0.5 | 0.8 | 0.3 |
| 69 | S | 2 | 1 | 1.1 | 0.8 | 0.9 | 0.8 | 0.4 | 0.7 | 0.4 | 0.8 | 0.7 | 0.5 | 0.7 | 1.0 | 1.2 | 1.4 | 0.6 | 0.4 | 1.3 | 0.8 | 0.2 | 0.4 | 1.8 | 0.6 |
| 70 | del | 0 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **70** | **E** | 4 | 4 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 | 2.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 70 | G | 2 | 2 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 70 | N | 1 | 1 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.1 | 0.4 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 |
| 70 | Q | 0 | 1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **70** | **R** | 4 | 4 | 21 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.2 | 0.0 | 0.0 | 12 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 70 | S | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 70 | T | 1 | 1 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 74 | I | 3 | 3 | 4.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 3.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 74 | V | 4 | 4 | 8.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 3.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 75 | A | 3 | 2 | 0.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 75 | I | 2 | 3 | 3.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 1.0 | 0.0 | 0.1 | 0.0 | 2.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.1 |
| 75 | M | 3 | 2 | 3.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 3.5 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 75 | S | 3 | 2 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 75 | T | 3 | 2 | 1.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 77 | L | 2 | 3 | 1.9 | 0.2 | 0.0 | 0.2 | 0.0 | 0.1 | 0.1 | 0.0 | 0.2 | 0.0 | 0.0 | 1.2 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 115 | F | 4 | 4 | 2.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 4.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |
| 116 | Y | 2 | 2 | 2.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 118 | I | 2 | 1 | 18 | 2.7 | 2.4 | 3.2 | 2.6 | 2.1 | 0.9 | 3.5 | 2.6 | 2.0 | 2.2 | 8.5 | 4.4 | 3.0 | 6.1 | 2.8 | 5.1 | 1.1 | 2.0 | 3.5 | 2.8 | 3.8 |
| 151 | L | 1 | 1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 151 | M | 4 | 4 | 2.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 184 | I | 4 | 4 | 2.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 3.3 | 0.1 | 0.0 | 0.1 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.2 | 0.0 |
| 184 | V | 4 | 4 | 55 | 0.2 | 0.2 | 0.3 | 0.1 | 0.2 | 0.1 | 0.2 | 0.2 | 0.2 | 0.1 | 61 | 0.1 | 0.0 | 0.2 | 0.1 | 0.1 | 0.2 | 0.2 | 0.0 | 0.2 | 0.2 |
| 210 | W | 4 | 4 | 21 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 7.7 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.1 | 0.0 | 0.2 |
| 215 | A | 2 | 3 | 0.3 | 0.1 | 0.1 | 0.2 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.2 | 0.1 | 0.3 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.2 | 0.0 | 0.2 | 0.0 |
| 215 | C | 3 | 3 | 0.9 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.1 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 215 | D | 3 | 3 | 0.8 | 0.3 | 0.0 | 0.5 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.4 | 0.2 | 0.0 | 0.4 | 0.0 | 0.0 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 |
| 215 | E | 3 | 3 | 0.2 | 0.1 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.2 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 215 | F | 4 | 4 | 12 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 8.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 215 | G | 2 | 2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 215 | H | 2 | 2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 215 | I | 3 | 3 | 2.2 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 2.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 |
| 215 | L | 2 | 3 | 0.2 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.2 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 215 | N | 2 | 3 | 1.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 215 | S | 3 | 3 | 2.5 | 0.4 | 0.1 | 0.6 | 0.1 | 0.1 | 0.1 | 0.0 | 0.5 | 0.2 | 0.3 | 1.8 | 0.3 | 0.0 | 0.6 | 0.1 | 0.2 | 0.1 | 0.5 | 0.1 | 0.2 | 0.1 |
| 215 | V | 3 | 3 | 0.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 215 | Y | 4 | 4 | 31 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 13 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 219 | E | 4 | 4 | 6.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.1 | 6.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 219 | H | 1 | 1 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 219 | N | 3 | 2 | 3.4 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.1 | 0.1 | 0.2 | 0.0 | 0.3 | 1.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.1 |
| 219 | Q | 4 | 4 | 13 | 0.1 | 0.2 | 0.1 | 0.0 | 0.1 | 0.2 | 0.2 | 0.2 | 0.1 | 0.0 | 6.9 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.3 | 0.0 | 0.0 | 0.0 |
| 219 | R | 3 | 2 | 2.7 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.3 | 1.3 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 |
| 219 | W | 1 | 1 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

**Abbreviation**: Pos – amino acid position; AA – amino acid; List – Number of expert lists with the mutation in 2009 and 2020; %NRTI – percent prevalence among NRTI-experienced persons; %RTI-Naïve – percent prevalence among RTI-naïve persons.

The parenthetical numbers in the headers represent the number of persons from whom a sequence was available

[1]34 NRTI-associated surveillance drug resistance mutations at 15 positions (Bennett 2009) were indicated in bold.

**Table S3**. List of 69 NNRTI-associated mutations included in one or more of four expert 2020 lists: prevalence in RTI-naïve and NNRTI-experienced persons before and after 2009.

| Pos[1] | AA[1] | Lists | | <2009 | | | | | | | | | | | ≥2009 | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 2009 | 2020 | %NNRTI | %RTI-Naive | | | | | | | | | | %NNRTI | %RTI-Naive | | | | | | | | | |
| | | | | (27,755) | ALL (54,910) | A (4,245) | B (30,428) | C (7,596) | 01 (4,571) | 02 (2,871) | D (1,279) | F (606) | G (1,003) | Other (2,361) | (22,219) | ALL (45,940) | A (2,423) | B (18,847) | C (4,811) | 01 (9,495) | 02 (2,382) | D (612) | F (777) | G (495) | Other (6,048) |
| 90 | I | 2 | 3 | 5.9 | 1.9 | 1.4 | 2.1 | 1.0 | 0.5 | 6.8 | 2.6 | 0.2 | 1.2 | 0.8 | 8.6 | 1.6 | 1.9 | 1.7 | 1.1 | 0.5 | 7.2 | 1.6 | 0.0 | 3.6 | 0.5 |
| 98 | G | 4 | 4 | 6.4 | 0.2 | 0.1 | 0.1 | 0.8 | 0.2 | 0.1 | 0.1 | 0.5 | 0.3 | 0.0 | 8.3 | 0.2 | 0.1 | 0.2 | 0.6 | 0.1 | 0.3 | 0.2 | 0.9 | 1.0 | 0.2 |
| **100** | **I** | 4 | 4 | 4.5 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 3.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 100 | V | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| **101** | **E** | 4 | 4 | 7.2 | 0.1 | 0.1 | 0.2 | 0.1 | 0.0 | 0.1 | 0.4 | 0.0 | 0.1 | 0.0 | 9.3 | 0.2 | 0.2 | 0.2 | 0.3 | 0.1 | 0.1 | 0.2 | 0.0 | 0.8 | 0.1 |
| 101 | H | 1 | 3 | 1.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 101 | I | 0 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 101 | N | 2 | 1 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.7 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |
| **101** | **P** | 4 | 4 | 1.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 101 | Q | 2 | 1 | 4.9 | 0.5 | 0.4 | 0.6 | 0.5 | 0.3 | 0.6 | 0.2 | 0.2 | 0.7 | 0.1 | 3.9 | 0.7 | 0.9 | 0.9 | 0.6 | 0.4 | 0.8 | 0.5 | 0.5 | 0.2 | 0.9 |
| 101 | R | 2 | 2 | 1.6 | 1.0 | 0.3 | 1.2 | 0.9 | 0.7 | 0.3 | 1.1 | 0.8 | 0.6 | 2.0 | 1.6 | 1.1 | 0.7 | 1.2 | 1.1 | 0.9 | 0.6 | 0.5 | 0.6 | 0.0 | 1.0 |
| 101 | T | 0 | 1 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 103 | H | 2 | 3 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **103** | **N** | 4 | 4 | 36 | 1.3 | 0.5 | 1.8 | 1.1 | 0.2 | 0.7 | 0.9 | 1.5 | 0.9 | 0.7 | 36 | 1.6 | 2.1 | 2.3 | 1.5 | 0.4 | 2.4 | 2.3 | 1.5 | 3.0 | 1.3 |
| 103 | R | 2 | 2 | 2.4 | 1.9 | 0.2 | 2.9 | 1.2 | 0.8 | 0.2 | 0.4 | 0.3 | 0.2 | 0.4 | 2.8 | 2.0 | 0.3 | 3.1 | 1.2 | 2.1 | 0.7 | 0.3 | 1.0 | 0.6 | 1.6 |
| **103** | **S** | 3 | 4 | 2.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 2.3 | 0.1 | 0.2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.1 |
| 103 | T | 3 | 3 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **106** | **A** | 4 | 4 | 1.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 1.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 106 | I | 4 | 4 | 3.9 | 1.9 | 1.3 | 2.2 | 0.0 | 4.8 | 0.5 | 1.6 | 4.6 | 1.1 | 2.0 | 3.5 | 3.0 | 1.7 | 4.5 | 0.2 | 2.9 | 1.4 | 2.1 | 16 | 2.2 | 1.1 |
| **106** | **M** | 4 | 4 | 2.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 9.1 | 0.1 | 0.0 | 0.0 | 0.2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |
| 106 | T | 0 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 108 | I | 3 | 3 | 8.6 | 0.5 | 0.7 | 0.5 | 0.2 | 0.2 | 0.7 | 0.3 | 0.3 | 0.1 | 0.4 | 9.4 | 0.4 | 0.3 | 0.5 | 0.2 | 0.2 | 0.9 | 0.3 | 0.3 | 0.2 | 0.1 |
| 138 | A | 0 | 4 | 3.1 | 2.5 | 3.2 | 1.9 | 6.0 | 0.4 | 2.7 | 3.0 | 3.3 | 2.2 | 1.6 | 4.9 | 2.2 | 6.2 | 1.9 | 5.4 | 0.3 | 2.7 | 2.1 | 1.7 | 1.8 | 0.6 |
| 138 | G | 0 | 4 | 0.7 | 0.2 | 0.2 | 0.2 | 0.3 | 0.4 | 0.1 | 0.5 | 2.0 | 0.1 | 0.1 | 1.1 | 0.4 | 0.2 | 0.3 | 0.3 | 0.2 | 0.3 | 0.3 | 0.5 | 0.2 | 1.6 |
| 138 | K | 2 | 4 | 0.4 | 0.1 | 0.0 | 0.1 | 0.2 | 0.0 | 0.1 | 0.3 | 0.0 | 0.0 | 0.0 | 0.7 | 0.1 | 0.0 | 0.1 | 0.1 | 0.1 | 0.1 | 0.3 | 0.1 | 0.2 | 0.2 |
| 138 | Q | 0 | 4 | 1.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.2 | 0.0 | 0.0 | 1.6 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |
| 138 | R | 0 | 4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 138 | S | 0 | 2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 179 | D | 4 | 4 | 2.2 | 1.6 | 0.2 | 2.1 | 1.1 | 2.2 | 0.0 | 0.2 | 3.8 | 0.0 | 0.7 | 3.3 | 2.4 | 0.5 | 3.1 | 1.8 | 3.3 | 0.0 | 0.5 | 0.8 | 0.0 | 1.9 |
| 179 | E | 2 | 2 | 1.2 | 0.6 | 0.0 | 0.6 | 0.1 | 0.2 | 0.8 | 0.4 | 0.0 | 4.3 | 0.5 | 1.8 | 1.5 | 0.0 | 1.4 | 0.3 | 0.7 | 1.0 | 0.2 | 0.3 | 3.4 | 15 |

| 179 | F | 4 | 3 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 179 | I | 2 | 1 | 13 | 8.9 | 54 | 4.3 | 3.1 | 16.2 | 3.9 | 7.0 | 5.3 | 0.4 | 6.6 | 16 | 10 | 51 | 5.4 | 3.7 | 20 | 5.3 | 6.9 | 17 | 0.8 | 6.1 |
| 179 | L | 0 | 4 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| 179 | M | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 |
| 179 | T | 1 | 3 | 0.5 | 0.3 | 1.6 | 0.1 | 0.0 | 1.1 | 0.1 | 1.0 | 0.2 | 0.0 | 0.4 | 0.9 | 0.8 | 1.7 | 0.2 | 0.1 | 2.9 | 0.2 | 1.5 | 0.1 | 0.0 | 0.9 |
| 181 | C | 4 | 4 | 18 | 0.2 | 0.1 | 0.1 | 0.3 | 0.2 | 0.1 | 0.2 | 0.0 | 0.2 | 0.0 | 18 | 0.2 | 0.2 | 0.1 | 0.2 | 0.1 | 0.3 | 0.7 | 0.1 | 0.4 | 0.3 |
| 181 | F | 0 | 1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 181 | G | 0 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 181 | I | 4 | 4 | 0.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 181 | S | 1 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 |
| 181 | V | 4 | 4 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 188 | C | 4 | 4 | 0.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 188 | F | 1 | 2 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 188 | H | 4 | 4 | 0.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 188 | L | 4 | 4 | 4.5 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 4.4 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.5 | 0.0 | 0.0 | 0.1 |
| 189 | I | 0 | 1 | 2.6 | 1.2 | 0.9 | 1.2 | 0.6 | 0.7 | 3.3 | 1.8 | 0.8 | 2.7 | 0.7 | 2.3 | 1.3 | 1.2 | 1.3 | 0.9 | 1.3 | 2.5 | 1.6 | 1.0 | 1.8 | 1.0 |
| 190 | A | 4 | 4 | 15 | 0.2 | 0.0 | 0.2 | 0.1 | 0.1 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 | 15 | 0.2 | 0.3 | 0.2 | 0.3 | 0.1 | 0.1 | 4.7 | 0.1 | 0.0 | 0.1 |
| 190 | C | 3 | 3 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 190 | E | 3 | 4 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.1 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 190 | Q | 3 | 3 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 190 | S | 4 | 4 | 2.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 3.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 |
| 190 | T | 3 | 3 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 190 | V | 3 | 3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 221 | Y | 1 | 4 | 6.5 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.1 | 0.2 | 0.2 | 0.0 | 0.1 | 8.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.2 | 0.0 | 0.4 | 0.1 |
| 225 | H | 4 | 4 | 4.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 7.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 227 | C | 2 | 4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 227 | I | 0 | 2 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 227 | L | 2 | 3 | 2.2 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 3.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 227 | R | 0 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 227 | V | 0 | 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 230 | I | 0 | 4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 230 | L | 3 | 4 | 1.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 2.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 230 | V | 0 | 1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 234 | I | 1 | 3 | 0.3 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 236 | L | 2 | 2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.2 | 0.0 | 0.2 | 0.2 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 238 | N | 1 | 2 | 0.6 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.1 | 0.2 | 0.1 | 0.0 | 0.4 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.8 | 0.0 |
| 238 | T | 2 | 2 | 2.7 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 3.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 |

| 318 | F | 2 | 2 | 1.2 | 0.1 | 0.1 | 0.1 | 0.1 | 0.0 | 0.2 | 0.0 | 0.8 | 0.0 | 0.0 | 1.3 | 0.2 | 0.0 | 0.1 | 0.2 | 0.1 | 0.8 | 0.0 | 0.0 | 1.9 | 0.0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 348 | I | 0 | 1 | 14 | 0.2 | 0.3 | 0.2 | 0.4 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 7.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

**Abbreviation**: Pos – amino acid position; AA – amino acid; List – Number of expert lists with the mutation in 2009 and 2020; %NNRTI – percent prevalence among NNRTI-experienced persons; %RTI-Naïve – percent prevalence among RTI-naïve persons.

The parenthetical numbers in the headers represent the number of persons from whom a sequence was available

[1]19 NNRTI-associated surveillance drug resistance mutations at 10 positions (Bennett 2009) were indicated in bold.

**Table S4.** Number of sequences according to treatment and subtype

| Subtype | #Protease sequences | | #RT sequences | |
|---|---|---|---|---|
| | PI-Naïve (n=115,880) | PI-Experienced (n=32,800) | RTI-Naïve (n=100,850) | RTI-Experienced (n=56,573) |
| All | 115,880 | 328,00 | 100,850 | 56,573 |
| A | 7,525 | 1,532 | 6,668 | 3,873 |
| B | 54,567 | 22,236 | 49,275 | 29,132 |
| C | 19,129 | 3,617 | 12,407 | 12,109 |
| CRF01_AE | 15,454 | 696 | 14,066 | 3,061 |
| CRF02_AG | 7,359 | 366 | 5,253 | 2,289 |
| D | 2,388 | 390 | 1,891 | 983 |
| F | 1,520 | 1,529 | 1,383 | 1,611 |
| G | 3461 | 401 | 1,498 | 1,548 |
| CRF06_cpx | 393 | 7 | 1,134 | 356 |
| CRF07_BC | 651 | 9 | 3,311 | 16 |
| CRF08_BC | 225 | 29 | 814 | 29 |
| CRF12_BF | 411 | 1,164 | 267 | 673 |
| CRF18_cpx | 224 | 40 | 104 | 55 |
| CRF35_AD | 430 | 30 | 241 | 16 |
| CRF45_cpx | 320 | 49 | 64 | 48 |
| CRF63_02A1 | 128 | 77 | 127 | 86 |
| Other | 1,695 | 628 | 2,347 | 688 |

**Table S5**. Recently published transmitted drug resistance (TDR) studies containing sequences from >1,000 ART-naïve persons: TDR prevalence using 2009 surveillance drug resistance mutation (SDRM) list and expanded SDRM list[*]

| Author-year | PMID | Country | Median sample year | #Pts | %TDR using 2009 SDRM list | | | | %TDR using expanded SDRM list | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Overall | PI | NRTI | NNRTI | Overall | PI | NRTI | NNRTI |
| Meixenberger14 | 24920768 | Germany | 2008 | 2,203 | 12.1 | 2.3 | 7.4 | 3.6 | 12.8 | 2.8 | 7.4 | 3.9 |
| Li15 | 26121491 | China | 2012 | 1,265 | 3.2 | 2.1 | .7 | .7 | 3.8 | 2.4 | .9 | .9 |
| Li15 | 26577039 | China | 2010 | 1,205 | 3.2 | 1.7 | 1.1 | .8 | 3.7 | 1.9 | 1.1 | 1.1 |
| Pouran Yousef16 | 27400403 | Germany | 2007 | 1,159 | 11.4 | 2.9 | 6.2 | 3.5 | 12.0 | 3.2 | 6.2 | 4.0 |
| Zhao16 | 27352965 | China | 2011 | 1,316 | 2.0 | .7 | 1.0 | .5 | 2.1 | .8 | 1.0 | .5 |
| Hattori16 | 26428230 | Japan | 2010 | 2,148 | 8.9 | 3.4 | 4.5 | 1.5 | 9.5 | 3.8 | 4.6 | 1.7 |
| Hachiya17 | | Japan | 2014 | 2,132 | 8.7 | 2.5 | 5.4 | 1.2 | 9.6 | 2.7 | 5.5 | 1.8 |
| Derache18 | 30321314 | South Africa | 2014 | 1,148 | 8.1 | .3 | .7 | 7.7 | 8.4 | .3 | .7 | 7.8 |
| Arruda18 | 29504269 | Brazil | 2015 | 1,566 | 10.7 | 2.3 | 4.1 | 5.8 | 11.4 | 2.7 | 4.2 | 6.2 |
| Rhee18 | 29846534 | U.S. | 2011 | 3,292 | 14.2 | 3.3 | 5.2 | 8.2 | 14.7 | 3.6 | 5.3 | 8.4 |
| Machnowska19 | 30650082 | Germany | 2012 | 2,052 | 10.3 | 2.9 | 6.0 | 3.5 | 11.3 | 3.3 | 6.0 | 4.0 |

*Expanded SDRM list include 2009 SDRMs, six NRTI-associated DRMs (K65N, T69deletion, K70G/N/Q/T), six NNRTI-associated DRMs (E138K/Q, V179L, H221Y, F227C/L) and three PI-associated DRMs (L10F, T74P, L89V).

**Table S6.** NRTI-associated SDRMs and candidate SDRMs: Comparisons of prevalence in RTI-naïve and NRTI-experienced persons before and after 2009 using Fisher's exact test.

| Pos | AA | SDRM | RTI-Naive | | | | | NRTI-Experienced | | | | |
|-----|-----|------|-----------|-----------|------|--------|------------|-----------|-----------|------|--------|------------|
| | | | % in <2009 (n=54,910) | % in ≥2009 (n=45,940) | OR | p | Adjusted p | % in <2009 (n=32,363) | % in ≥2009 (n=24,210) | OR | p | Adjusted p |
| 41 | L | SDRM | 0.003 | 0.002 | 0.62 | 5.9E-05 | **2.0E-03** | 0.330 | 0.148 | 0.35 | 0.0E+00 | **0.0E+00** |
| 65 | R | SDRM | 0.000 | 0.000 | 0.85 | 4.3E-01 | 1.0E+00 | 0.040 | 0.104 | 2.80 | 3.0E-198 | **8.9E-197** |
| 67 | E | SDRM | 0.000 | 0.000 | 0.75 | 3.0E-01 | 1.0E+00 | 0.006 | 0.002 | 0.37 | 1.1E-11 | **1.2E-10** |
| 67 | G | SDRM | 0.000 | 0.000 | 0.50 | 6.9E-02 | 1.0E+00 | 0.024 | 0.023 | 0.93 | 9.3E-02 | 3.7E-01 |
| 67 | N | SDRM | 0.001 | 0.000 | 0.52 | 2.7E-02 | 6.9E-01 | 0.302 | 0.157 | 0.43 | 0.0E+00 | **0.0E+00** |
| 69 | D | SDRM | 0.001 | 0.001 | 1.17 | 2.8E-01 | 1.0E+00 | 0.069 | 0.031 | 0.43 | 8.9E-95 | **2.3E-93** |
| 69 | ins | SDRM | 0.000 | 0.000 | Inf | 4.6E-01 | 1.0E+00 | 0.010 | 0.002 | 0.21 | 1.5E-33 | **2.9E-32** |
| 70 | E | SDRM | 0.000 | 0.000 | 0.64 | 2.4E-01 | 1.0E+00 | 0.006 | 0.026 | 4.04 | 3.6E-79 | **9.0E-78** |
| 70 | R | SDRM | 0.001 | 0.000 | 0.52 | 8.3E-03 | 2.5E-01 | 0.206 | 0.124 | 0.54 | 1.6E-151 | **4.6E-150** |
| 74 | I | SDRM | 0.000 | 0.000 | 1.02 | 5.5E-01 | 1.0E+00 | 0.046 | 0.037 | 0.79 | 2.6E-08 | **2.6E-07** |
| 74 | V | SDRM | 0.000 | 0.000 | 0.40 | 2.1E-01 | 1.0E+00 | 0.086 | 0.039 | 0.43 | 5.0E-115 | **1.4E-113** |
| 75 | A | SDRM | 0.000 | 0.000 | 0.60 | 3.5E-01 | 1.0E+00 | 0.008 | 0.002 | 0.32 | 4.4E-18 | **6.5E-17** |
| 75 | M | SDRM | 0.000 | 0.001 | 1.62 | 8.7E-02 | 1.0E+00 | 0.036 | 0.035 | 0.96 | 2.0E-01 | 3.7E-01 |
| 75 | S | SDRM | 0.000 | 0.000 | 0.00 | 5.4E-01 | 1.0E+00 | 0.003 | 0.001 | 0.47 | 8.3E-05 | **5.0E-04** |
| 75 | T | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.015 | 0.005 | 0.32 | 2.4E-33 | **4.1E-32** |
| 77 | L | SDRM | 0.002 | 0.001 | 0.42 | 1.3E-05 | **4.6E-04** | 0.019 | 0.012 | 0.62 | 6.8E-12 | **8.1E-11** |
| 115 | F | SDRM | 0.000 | 0.000 | 0.20 | 9.7E-02 | 1.0E+00 | 0.020 | 0.045 | 2.27 | 3.0E-62 | **7.3E-61** |
| 116 | Y | SDRM | 0.000 | 0.000 | 0.00 | 8.8E-02 | 1.0E+00 | 0.022 | 0.010 | 0.43 | 1.4E-32 | **2.3E-31** |
| 151 | M | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.029 | 0.012 | 0.43 | 4.8E-42 | **9.6E-41** |
| 184 | I | SDRM | 0.000 | 0.001 | 1.91 | 3.3E-02 | 8.2E-01 | 0.023 | 0.033 | 1.45 | 4.5E-13 | **5.8E-12** |
| 184 | V | SDRM | 0.002 | 0.001 | 0.70 | 1.0E-02 | 3.0E-01 | 0.545 | 0.606 | 1.28 | 9.2E-48 | **2.0E-46** |
| 210 | W | SDRM | 0.001 | 0.001 | 1.55 | 3.5E-02 | 8.5E-01 | 0.208 | 0.077 | 0.32 | 0.0E+00 | **0.0E+00** |
| 215 | C | SDRM | 0.001 | 0.001 | 0.92 | 3.9E-01 | 1.0E+00 | 0.009 | 0.004 | 0.42 | 8.3E-15 | **1.2E-13** |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 215 | D | SDRM | 0.003 | 0.002 | 0.64 | 6.4E-04 | **2.1E-02** | 0.008 | 0.004 | 0.55 | 4.7E-08 | **3.7E-07** |
| 215 | E | SDRM | 0.001 | 0.002 | 1.25 | 1.1E-01 | 1.0E+00 | 0.002 | 0.001 | 0.75 | 1.2E-01 | 3.7E-01 |
| 215 | F | SDRM | 0.000 | 0.000 | 0.60 | 5.7E-01 | 1.0E+00 | 0.118 | 0.083 | 0.68 | 3.9E-42 | **8.2E-41** |
| 215 | I | SDRM | 0.000 | 0.000 | 1.05 | 5.1E-01 | 1.0E+00 | 0.022 | 0.020 | 0.94 | 1.4E-01 | 3.7E-01 |
| 215 | S | SDRM | 0.004 | 0.003 | 0.82 | 4.5E-02 | 1.0E+00 | 0.025 | 0.018 | 0.73 | 3.2E-08 | **2.9E-07** |
| 215 | V | SDRM | 0.000 | 0.000 | 0.80 | 5.8E-01 | 1.0E+00 | 0.009 | 0.005 | 0.57 | 6.8E-08 | **4.8E-07** |
| 215 | Y | SDRM | 0.000 | 0.000 | 0.09 | 2.6E-03 | 7.9E-02 | 0.305 | 0.134 | 0.35 | 0.0E+00 | **0.0E+00** |
| 219 | E | SDRM | 0.000 | 0.000 | 0.94 | 5.2E-01 | 1.0E+00 | 0.068 | 0.061 | 0.90 | 7.5E-04 | **3.7E-03** |
| 219 | N | SDRM | 0.000 | 0.000 | 0.34 | 1.1E-02 | 3.0E-01 | 0.034 | 0.014 | 0.42 | 4.5E-50 | **1.0E-48** |
| 219 | Q | SDRM | 0.001 | 0.001 | 0.72 | 7.8E-02 | 1.0E+00 | 0.126 | 0.069 | 0.51 | 5.9E-113 | **1.6E-111** |
| 219 | R | SDRM | 0.001 | 0.000 | 0.57 | 2.6E-02 | 6.9E-01 | 0.027 | 0.013 | 0.47 | 2.3E-33 | **4.1E-32** |
| 44 | A | Candidate | 0.000 | 0.000 | 3.59 | 2.5E-01 | 1.0E+00 | 0.017 | 0.006 | 0.33 | 1.8E-37 | **3.1E-36** |
| 65 | N | Candidate | 0.000 | 0.000 | 0.28 | 2.5E-02 | 4.2E-01 | 0.001 | 0.002 | 1.77 | 1.1E-02 | 5.2E-02 |
| 67 | H | Candidate | 0.000 | 0.000 | 3.59 | 2.5E-01 | 1.0E+00 | 0.002 | 0.001 | 0.55 | 2.8E-03 | **2.5E-02** |
| 67 | S | Candidate | 0.000 | 0.000 | 0.00 | 3.0E-01 | 1.0E+00 | 0.003 | 0.002 | 0.58 | 8.3E-04 | **9.1E-03** |
| 67 | T | Candidate | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.002 | 0.002 | 0.63 | 1.0E-02 | 5.2E-02 |
| 69 | A | Candidate | 0.002 | 0.003 | 1.24 | 4.8E-02 | 7.1E-01 | 0.011 | 0.009 | 0.79 | 3.6E-03 | **2.9E-02** |
| 69 | del | Candidate | 0.000 | 0.000 | 0.00 | 5.4E-01 | 1.0E+00 | 0.001 | 0.003 | 2.30 | 9.4E-06 | **1.1E-04** |
| 69 | G | Candidate | 0.000 | 0.000 | 0.00 | 5.4E-01 | 1.0E+00 | 0.003 | 0.001 | 0.56 | 1.7E-03 | **1.7E-02** |
| 70 | G | Candidate | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.005 | 0.003 | 0.72 | 8.6E-03 | 5.1E-02 |
| 70 | N | Candidate | 0.000 | 0.000 | 0.96 | 5.2E-01 | 1.0E+00 | 0.003 | 0.004 | 1.31 | 3.4E-02 | 1.0E-01 |
| 70 | Q | Candidate | 0.000 | 0.000 | 0.22 | 2.5E-02 | 4.2E-01 | 0.002 | 0.006 | 2.76 | 8.1E-13 | **1.3E-11** |
| 70 | T | Candidate | 0.000 | 0.000 | 1.05 | 5.1E-01 | 1.0E+00 | 0.003 | 0.007 | 2.25 | 1.6E-11 | **2.2E-10** |
| 215 | A | Candidate | 0.001 | 0.001 | 0.80 | 1.4E-01 | 1.0E+00 | 0.003 | 0.003 | 0.91 | 3.0E-01 | 4.6E-01 |
| 215 | L | Candidate | 0.001 | 0.001 | 1.05 | 4.8E-01 | 1.0E+00 | 0.002 | 0.002 | 0.84 | 2.3E-01 | 4.6E-01 |
| 215 | N | Candidate | 0.000 | 0.000 | 0.96 | 5.6E-01 | 1.0E+00 | 0.013 | 0.007 | 0.55 | 2.3E-12 | **3.4E-11** |
| 219 | H | Candidate | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.003 | 0.001 | 0.41 | 8.4E-07 | **1.1E-05** |
| 219 | W | Candidate | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.003 | 0.002 | 0.60 | 3.9E-03 | **2.9E-02** |

Estimated odds ratio (OR) by Fisher's exact test, their p-values and adjusted p values by Holm's method are shown. Significant increase or decrease in prevalence with adjusted p <0.05 is indicated in bold.

**Table S7**. NNRTI-associated SDRMs and candidate SDRMs: Comparisons of prevalence in RTI-naïve and NNRTI-experienced persons before and after 2009 using Fisher's exact test.

| Pos | AA | SDRM | RTI-Naive | | | | | NNRTI-Experienced | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | % in <2009 (n=54,910) | % in ≥2009 (n=45,940) | OR | p | Adjusted p | % in <2009 (n=27,755) | % in ≥2009 (n=22,219) | OR | p | Adjusted p |
| 100 | I | SDRM | 0.000 | 0.000 | 0.15 | 2.2E-03 | 3.5E-02 | 0.045 | 0.035 | 0.77 | 5.2E-09 | **7.7E-08** |
| 101 | E | SDRM | 0.001 | 0.002 | 1.35 | 3.2E-02 | 4.2E-01 | 0.072 | 0.093 | 1.34 | 5.3E-19 | **9.0E-18** |
| 101 | P | SDRM | 0.000 | 0.000 | 1.20 | 7.9E-01 | 1.0E+00 | 0.017 | 0.014 | 0.81 | 1.8E-03 | **1.8E-02** |
| 103 | N | SDRM | 0.013 | 0.016 | 1.24 | 2.2E-05 | 4.2E-04 | 0.358 | 0.356 | 0.99 | 3.4E-01 | 1.0E+00 |
| 103 | S | SDRM | 0.000 | 0.001 | 1.87 | 3.4E-02 | 4.2E-01 | 0.020 | 0.023 | 1.16 | 7.6E-03 | 6.1E-02 |
| 106 | A | SDRM | 0.000 | 0.000 | 0.51 | 1.2E-01 | 9.6E-01 | 0.018 | 0.014 | 0.76 | 7.1E-05 | **9.2E-04** |
| 106 | M | SDRM | 0.000 | 0.001 | 3.93 | 5.3E-04 | 9.5E-03 | 0.026 | 0.091 | 3.75 | 6.0E-224 | **1.1E-222** |
| 179 | F | SDRM | 0.000 | 0.000 | 0.30 | 9.4E-02 | 8.4E-01 | 0.003 | 0.002 | 0.76 | 8.7E-02 | 5.7E-01 |
| 181 | C | SDRM | 0.002 | 0.002 | 1.05 | 4.2E-01 | 1.0E+00 | 0.179 | 0.181 | 1.01 | 3.3E-01 | 1.0E+00 |
| 181 | I | SDRM | 0.000 | 0.000 | 2.39 | 2.6E-01 | 1.0E+00 | 0.008 | 0.006 | 0.73 | 2.4E-03 | **2.2E-02** |
| 181 | V | SDRM | 0.000 | 0.000 | Inf | 4.6E-01 | 1.0E+00 | 0.005 | 0.007 | 1.43 | 1.2E-03 | **1.3E-02** |
| 188 | C | SDRM | 0.000 | 0.000 | 0.80 | 3.9E-01 | 1.0E+00 | 0.007 | 0.010 | 1.44 | 2.0E-04 | **2.4E-03** |
| 188 | H | SDRM | 0.000 | 0.000 | 0.32 | 2.5E-02 | 3.5E-01 | 0.008 | 0.007 | 0.88 | 1.4E-01 | 6.9E-01 |
| 188 | L | SDRM | 0.000 | 0.001 | 1.56 | 5.5E-02 | 5.7E-01 | 0.045 | 0.044 | 0.98 | 3.7E-01 | 1.0E+00 |
| 190 | A | SDRM | 0.002 | 0.002 | 1.54 | 1.5E-03 | 2.6E-02 | 0.145 | 0.146 | 1.01 | 4.0E-01 | 1.0E+00 |
| 190 | E | SDRM | 0.000 | 0.001 | 2.72 | 3.3E-03 | 4.9E-02 | 0.005 | 0.006 | 1.20 | 8.2E-02 | 5.7E-01 |
| 190 | S | SDRM | 0.000 | 0.000 | 2.39 | 1.2E-01 | 9.6E-01 | 0.027 | 0.033 | 1.24 | 2.1E-05 | **2.9E-04** |
| 225 | H | SDRM | 0.000 | 0.000 | 0.36 | 5.1E-02 | 5.7E-01 | 0.043 | 0.074 | 1.79 | 6.1E-51 | **1.1E-49** |
| 230 | L | SDRM | 0.000 | 0.000 | 1.17 | 4.9E-01 | 1.0E+00 | 0.015 | 0.026 | 1.67 | 9.7E-16 | **1.6E-14** |
| 101 | H | Candidate | 0.000 | 0.000 | Inf | 4.3E-02 | 6.5E-01 | 0.013 | 0.013 | 1.00 | 5.2E-01 | 1.0E+00 |
| 101 | N | Candidate | 0.000 | 0.000 | 1.20 | 4.2E-01 | 1.0E+00 | 0.005 | 0.007 | 1.31 | 1.3E-02 | 1.0E-01 |
| 101 | T | Candidate | 0.000 | 0.000 | 1.59 | 2.7E-01 | 1.0E+00 | 0.004 | 0.002 | 0.64 | 5.3E-03 | 5.8E-02 |

| 138 | K | Candidate | 0.001 | 0.001 | 1.07 | 3.9E-01 | 1.0E+00 | 0.004 | 0.007 | 1.70 | 4.6E-06 | **6.9E-05** |
|-----|---|-----------|-------|-------|------|---------|---------|-------|-------|------|----------|-------------|
| 138 | Q | Candidate | 0.000 | 0.001 | 2.39 | 3.5E-03 | 6.3E-02 | 0.010 | 0.016 | 1.64 | 3.3E-10 | **5.3E-09** |
| 179 | L | Candidate | 0.000 | 0.000 | 0.80 | 4.9E-01 | 1.0E+00 | 0.002 | 0.003 | 1.90 | 4.2E-04 | **5.0E-03** |
| 179 | M | Candidate | 0.000 | 0.000 | 1.31 | 3.4E-01 | 1.0E+00 | 0.001 | 0.003 | 2.14 | 1.9E-04 | **2.6E-03** |
| 181 | F | Candidate | 0.000 | 0.000 | 0.85 | 5.1E-01 | 1.0E+00 | 0.002 | 0.002 | 0.90 | 3.3E-01 | 1.0E+00 |
| 188 | F | Candidate | 0.000 | 0.000 | 1.20 | 5.4E-01 | 1.0E+00 | 0.006 | 0.006 | 0.98 | 4.6E-01 | 1.0E+00 |
| 190 | C | Candidate | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.001 | 0.001 | 1.11 | 3.9E-01 | 1.0E+00 |
| 190 | Q | Candidate | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.003 | 0.004 | 1.10 | 2.8E-01 | 1.0E+00 |
| 221 | Y | Candidate | 0.001 | 0.001 | 0.95 | 4.5E-01 | 1.0E+00 | 0.065 | 0.081 | 1.27 | 5.8E-12 | **9.9E-11** |
| 227 | C | Candidate | 0.000 | 0.000 | 0.58 | 5.6E-01 | 1.0E+00 | 0.000 | 0.001 | 3.65 | 3.0E-04 | **3.9E-03** |
| 227 | L | Candidate | 0.001 | 0.000 | 0.55 | 3.4E-02 | 5.4E-01 | 0.022 | 0.035 | 1.62 | 1.1E-18 | **1.9E-17** |
| 234 | I | Candidate | 0.000 | 0.000 | 0.47 | 1.5E-01 | 1.0E+00 | 0.003 | 0.004 | 1.46 | 8.3E-03 | 7.5E-02 |
| 236 | L | Candidate | 0.000 | 0.000 | 1.30 | 2.9E-01 | 1.0E+00 | 0.001 | 0.002 | 1.95 | 6.0E-03 | 6.0E-02 |
| 238 | N | Candidate | 0.000 | 0.001 | 1.78 | 2.1E-02 | 3.6E-01 | 0.006 | 0.004 | 0.80 | 5.3E-02 | 3.2E-01 |
| 238 | T | Candidate | 0.001 | 0.000 | 0.79 | 2.5E-01 | 1.0E+00 | 0.027 | 0.030 | 1.11 | 3.1E-02 | 2.2E-01 |

Estimated odds ratio (OR) by Fisher's exact test, their p-values and adjusted p values by Holm's method are shown. Significant increase or decrease in prevalence with adjusted p <0.05 is indicated in bold.

**Table S8**. PI-associated SDRMs and candidate SDRMs: Comparisons of prevalence in PI-naïve and PI-experienced persons before and after 2009 using Fisher's exact test.

| Pos | AA | SDRM | PII-Naive | | | | | PI-Experienced | | | | |
|-----|----|------|-----------|-----------|------|---------|---------------|------------------|----------------|------|----------|--------------|
| | | | % in <2009 (n=61,067) | % in ≥2009 (n=54,813) | OR | p | Adjusted p | % in <2009 (n=22,266) | % in ≥2009 (n=10,534) | OR | p | Adjusted p |
| 23 | I | SDRM | 0.000 | 0.000 | 1.00 | 5.7E-01 | 1.0E+00 | 0.013 | 0.011 | 0.80 | 2.1E-02 | 8.5E-02 |
| 24 | I | SDRM | 0.000 | 0.000 | 0.26 | 1.9E-02 | 6.9E-01 | 0.056 | 0.025 | 0.43 | 2.6E-40 | **8.2E-39** |
| 30 | N | SDRM | 0.000 | 0.000 | 1.25 | 4.1E-01 | 1.0E+00 | 0.062 | 0.024 | 0.38 | 6.4E-54 | **2.0E-52** |
| 32 | I | SDRM | 0.000 | 0.000 | 0.37 | 1.0E-01 | 1.0E+00 | 0.050 | 0.025 | 0.49 | 1.2E-27 | **2.7E-26** |
| 46 | I | SDRM | 0.003 | 0.003 | 1.31 | 8.0E-03 | 3.0E-01 | 0.212 | 0.126 | 0.54 | 2.9E-82 | **9.7E-81** |
| 46 | L | SDRM | 0.003 | 0.004 | 1.20 | 4.2E-02 | 1.0E+00 | 0.092 | 0.034 | 0.35 | 4.5E-88 | **1.6E-86** |
| 47 | A | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.004 | 0.010 | 2.43 | 7.8E-10 | **1.2E-08** |
| 47 | V | SDRM | 0.000 | 0.000 | 0.77 | 3.5E-01 | 1.0E+00 | 0.045 | 0.020 | 0.42 | 4.7E-34 | **1.3E-32** |
| 48 | M | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.005 | 0.002 | 0.28 | 2.2E-08 | **3.0E-07** |
| 48 | V | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.037 | 0.007 | 0.18 | 1.0E-67 | **3.4E-66** |
| 50 | L | SDRM | 0.000 | 0.000 | 0.00 | 4.1E-02 | 1.0E+00 | 0.015 | 0.025 | 1.70 | 1.9E-10 | **3.0E-09** |
| 50 | V | SDRM | 0.000 | 0.000 | 0.28 | 7.6E-02 | 1.0E+00 | 0.018 | 0.012 | 0.66 | 1.9E-05 | **1.9E-04** |
| 53 | L | SDRM | 0.000 | 0.000 | 0.72 | 2.3E-01 | 1.0E+00 | 0.059 | 0.030 | 0.49 | 7.3E-32 | **1.8E-30** |
| 53 | Y | SDRM | 0.000 | 0.000 | 2.23 | 3.4E-02 | 1.0E+00 | 0.004 | 0.002 | 0.35 | 9.9E-06 | **1.1E-04** |
| 54 | A | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.013 | 0.004 | 0.27 | 1.1E-18 | **2.4E-17** |
| 54 | L | SDRM | 0.000 | 0.000 | 0.56 | 2.5E-01 | 1.0E+00 | 0.030 | 0.014 | 0.45 | 3.4E-21 | **7.6E-20** |
| 54 | M | SDRM | 0.000 | 0.000 | 1.11 | 7.1E-01 | 1.0E+00 | 0.023 | 0.006 | 0.24 | 1.5E-35 | **4.4E-34** |
| 54 | S | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.007 | 0.001 | 0.21 | 1.1E-12 | **1.9E-11** |
| 54 | T | SDRM | 0.000 | 0.000 | 0.64 | 3.4E-01 | 1.0E+00 | 0.008 | 0.002 | 0.19 | 7.1E-16 | **1.4E-14** |
| 54 | V | SDRM | 0.000 | 0.000 | 1.67 | 3.1E-01 | 1.0E+00 | 0.231 | 0.120 | 0.46 | 1.2E-131 | **4.4E-130** |
| 73 | A | SDRM | 0.000 | 0.000 | 1.11 | 6.5E-01 | 1.0E+00 | 0.006 | 0.002 | 0.34 | 8.1E-08 | **1.1E-06** |
| 73 | C | SDRM | 0.000 | 0.000 | 1.67 | 4.5E-01 | 1.0E+00 | 0.011 | 0.003 | 0.30 | 7.5E-15 | **1.4E-13** |
| 73 | S | SDRM | 0.000 | 0.000 | 1.67 | 1.1E-01 | 1.0E+00 | 0.083 | 0.027 | 0.31 | 4.6E-92 | **1.6E-90** |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 73 | T | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.024 | 0.006 | 0.25 | 6.0E-35 | **1.7E-33** |
| 76 | V | SDRM | 0.000 | 0.000 | 1.34 | 4.3E-01 | 1.0E+00 | 0.033 | 0.033 | 1.00 | 4.9E-01 | 4.9E-01 |
| 82 | A | SDRM | 0.000 | 0.000 | 0.96 | 5.1E-01 | 1.0E+00 | 0.220 | 0.122 | 0.49 | 2.7E-106 | **1.0E-104** |
| 82 | C | SDRM | 0.000 | 0.000 | Inf | 2.2E-01 | 1.0E+00 | 0.006 | 0.004 | 0.66 | 8.7E-03 | **4.3E-02** |
| 82 | F | SDRM | 0.000 | 0.000 | 12.25 | 1.8E-03 | 7.0E-02 | 0.018 | 0.011 | 0.59 | 1.9E-07 | **2.3E-06** |
| 82 | L | SDRM | 0.000 | 0.000 | 1.35 | 2.5E-01 | 1.0E+00 | 0.003 | 0.002 | 0.69 | 7.6E-02 | 2.3E-01 |
| 82 | M | SDRM | 0.000 | 0.000 | Inf | 2.2E-01 | 1.0E+00 | 0.003 | 0.004 | 1.28 | 1.2E-01 | 2.4E-01 |
| 82 | S | SDRM | 0.000 | 0.000 | 0.56 | 5.4E-01 | 1.0E+00 | 0.013 | 0.005 | 0.40 | 6.0E-12 | **1.0E-10** |
| 82 | T | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.028 | 0.008 | 0.27 | 8.2E-38 | **2.5E-36** |
| 83 | D | SDRM | 0.000 | 0.000 | 1.62 | 1.5E-01 | 1.0E+00 | 0.009 | 0.006 | 0.69 | 4.1E-03 | **2.5E-02** |
| 84 | A | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.001 | 0.000 | 0.08 | 2.8E-04 | **1.9E-03** |
| 84 | C | SDRM | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.001 | 0.000 | 0.00 | 6.2E-05 | **5.0E-04** |
| 84 | V | SDRM | 0.000 | 0.000 | 1.98 | 7.0E-02 | 1.0E+00 | 0.122 | 0.038 | 0.28 | 6.8E-151 | **2.7E-149** |
| 85 | V | SDRM | 0.002 | 0.002 | 0.95 | 4.1E-01 | 1.0E+00 | 0.046 | 0.021 | 0.44 | 6.9E-33 | **1.8E-31** |
| 88 | D | SDRM | 0.000 | 0.000 | 0.67 | 2.3E-01 | 1.0E+00 | 0.054 | 0.027 | 0.50 | 3.4E-29 | **8.0E-28** |
| 88 | S | SDRM | 0.000 | 0.000 | 0.00 | 1.3E-04 | 5.1E-03 | 0.016 | 0.010 | 0.64 | 2.1E-05 | **1.9E-04** |
| 90 | M | SDRM | 0.002 | 0.002 | 0.97 | 4.2E-01 | 1.0E+00 | 0.296 | 0.096 | 0.25 | 0.0E+00 | **0.0E+00** |
| 10 | F | Candidate | 0.002 | 0.002 | 1.01 | 4.9E-01 | 1.0E+00 | 0.086 | 0.067 | 0.76 | 1.5E-09 | **2.0E-08** |
| 10 | R | Candidate | 0.000 | 0.000 | 0.74 | 3.8E-01 | 1.0E+00 | 0.004 | 0.002 | 0.59 | 1.1E-02 | **4.2E-02** |
| 11 | L | Candidate | 0.000 | 0.000 | 0.67 | 1.4E-01 | 1.0E+00 | 0.007 | 0.002 | 0.36 | 2.7E-07 | **2.7E-06** |
| 20 | T | Candidate | 0.001 | 0.001 | 0.91 | 3.4E-01 | 1.0E+00 | 0.053 | 0.041 | 0.77 | 1.8E-06 | **1.6E-05** |
| 24 | F | Candidate | 0.000 | 0.000 | 0.15 | 2.1E-05 | 3.6E-04 | 0.006 | 0.003 | 0.47 | 5.0E-05 | **3.0E-04** |
| 34 | Q | Candidate | 0.001 | 0.001 | 1.01 | 5.2E-01 | 1.0E+00 | 0.026 | 0.013 | 0.49 | 1.8E-15 | **2.7E-14** |
| 41 | T | Candidate | 0.000 | 0.000 | 1.11 | 4.0E-01 | 1.0E+00 | 0.001 | 0.001 | 1.27 | 3.2E-01 | 5.4E-01 |
| 43 | T | Candidate | 0.001 | 0.001 | 0.92 | 3.4E-01 | 1.0E+00 | 0.056 | 0.030 | 0.52 | 3.9E-27 | **6.6E-26** |
| 46 | V | Candidate | 0.000 | 0.001 | 1.44 | 9.4E-02 | 1.0E+00 | 0.005 | 0.004 | 0.84 | 1.8E-01 | 5.4E-01 |
| 48 | A | Candidate | 0.000 | 0.000 | 2.23 | 4.6E-01 | 1.0E+00 | 0.005 | 0.002 | 0.36 | 9.4E-06 | **7.5E-05** |
| 66 | V | Candidate | 0.001 | 0.001 | 0.87 | 2.8E-01 | 1.0E+00 | 0.011 | 0.004 | 0.40 | 4.5E-10 | **6.3E-09** |
| 71 | I | Candidate | 0.001 | 0.001 | 1.34 | 7.6E-02 | 1.0E+00 | 0.032 | 0.017 | 0.51 | 4.4E-17 | **7.0E-16** |
| 71 | L | Candidate | 0.000 | 0.000 | 0.00 | 2.8E-01 | 1.0E+00 | 0.004 | 0.002 | 0.58 | 7.7E-03 | **3.8E-02** |

| 74 | P | Candidate | 0.001 | 0.000 | 0.07 | 9.3E-08 | 1.7E-06 | 0.019 | 0.013 | 0.67 | 1.5E-05 | **1.1E-04** |
| 88 | G | Candidate | 0.000 | 0.000 | 0.00 | 1.0E+00 | 1.0E+00 | 0.002 | 0.001 | 0.78 | 2.6E-01 | 5.4E-01 |
| 89 | T | Candidate | 0.000 | 0.000 | 1.86 | 3.1E-01 | 1.0E+00 | 0.004 | 0.009 | 2.21 | 3.0E-08 | **3.3E-07** |
| 89 | V | Candidate | 0.001 | 0.000 | 0.70 | 8.9E-02 | 1.0E+00 | 0.037 | 0.014 | 0.37 | 1.9E-34 | **3.4E-33** |
| 93 | M | Candidate | 0.001 | 0.001 | 1.10 | 3.1E-01 | 1.0E+00 | 0.007 | 0.002 | 0.33 | 1.0E-08 | **1.2E-07** |

Estimated odds ratio (OR) by Fisher's exact test, their p-values and adjusted p values by Holm's method are shown. Significant increase or decrease in prevalence with adjusted $p < 0.05$ is indicated in bold.

**(A) NRTI-SDRMs**

significant increase • significant decrease • no change

215Y
41L
70R
67N
210W
219Q
215F
69D
74V

184V
65R
184I
115F
70E

**(B) NNRTI-SDRMs**

%ART−Experienced

106A
100I

101E
225H
190S
106M
230L
181V
188C

**(C) PI-SDRMs**

90M
82A
54V
46I
84V
73S
30N
46L
24I

50L
47A

Sample Year
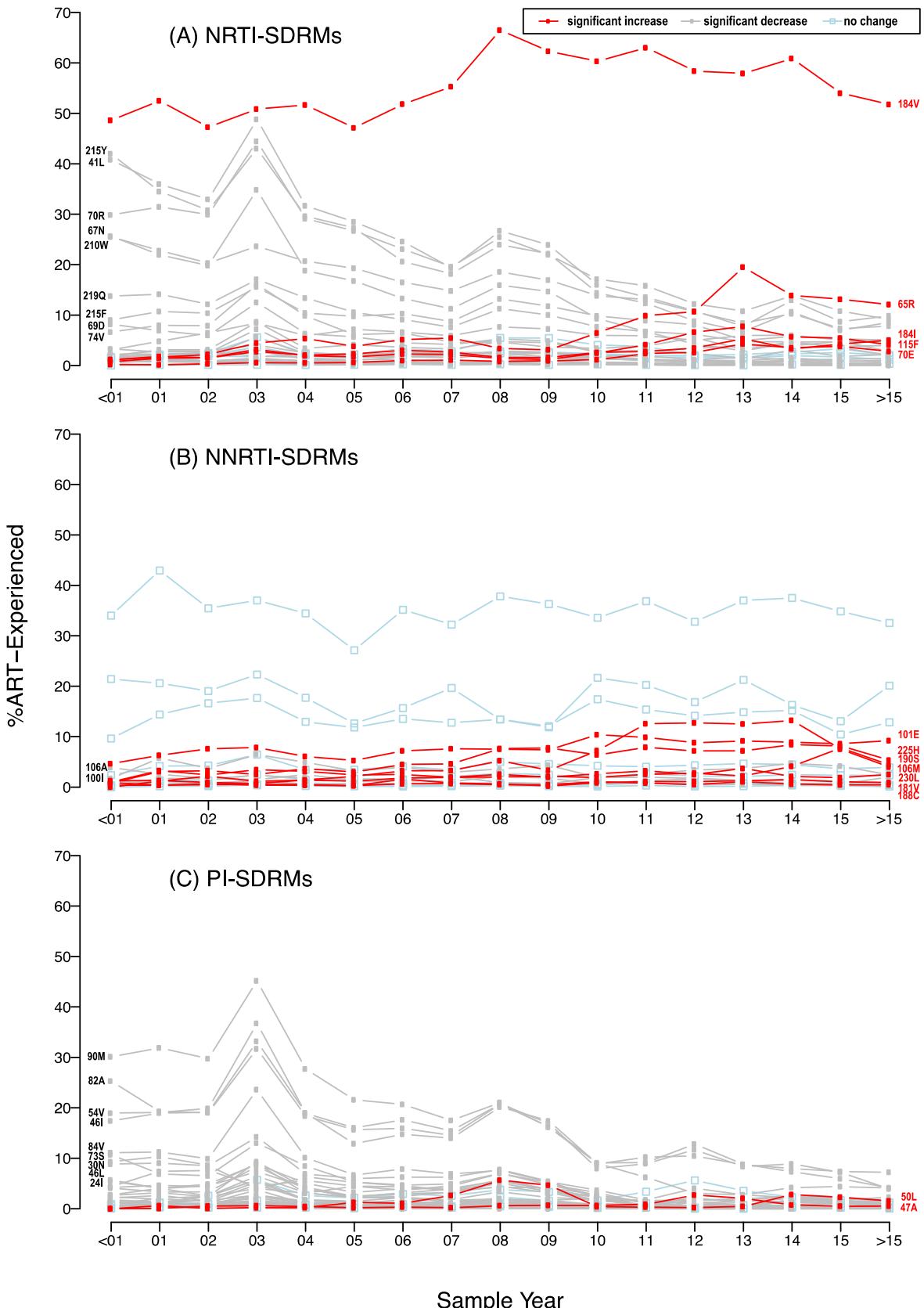
**Figure S1**. Yearly prevalence of (A) NRTI-SDRMs in NRTI-experienced persons, (B) NNRTI-SDRMs in NNRTI-experienced persons and (C) PI-SDRMs in PI-experienced persons. SDRMs significantly increased in prevalence are shown in red and indicated in red font on the right of the plotted lines. SDRMs significantly decreased in prevalence are shown in grey and indicated in black font on the left of the plotted lines. SDRMs did not change significantly in prevalence are shown in light blue. For SDRMs that decreased with a very low overall prevalence or did not change in prevalence, the labels are not shown. Full lists of NRTI-SDRMs, NNRTI-SDRMs and PI-SDRMs according to the change in prevalence are shown in Table 1, 3, and 5, respectively.

**(A) Candidate NRTI-SDRMs**

significant increase · significant decrease · no change

215N
44A
69A

70T
70Q
69del

**(B) Candidate NNRTI-SDRMs**

%ART−Experienced

221Y

227L
138Q
138K
179M
179L
227C

**(C) Candidate PI-SDRMs**

10F

43T
77I
20T

89T

Sample Year
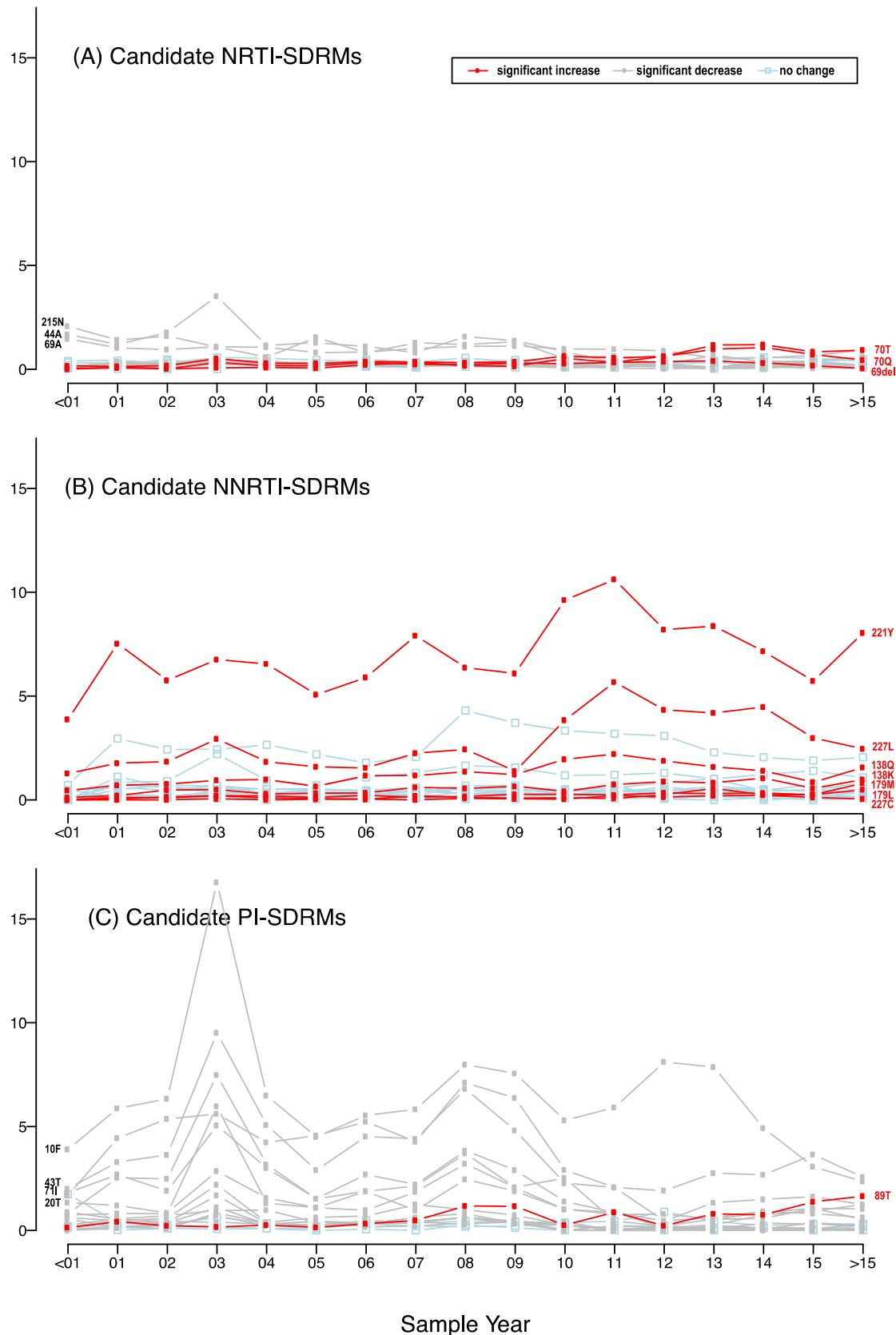
**Figure S2**. Yearly prevalence of (A) candidate NRTI-SDRMs in NRTI-experienced persons, (B) candidate NNRTI-SDRMs in NNRTI-experienced persons and (C) candidate PI-SDRMs in PI-experienced persons. Candidate SDRMs significantly increased in prevalence are shown in red and indicated in red font on the right of the plotted lines. Candidate SDRMs significantly decreased in prevalence are shown in grey and indicated in black font on the left of the plotted lines. Candidate SDRMs did not change significantly in prevalence are shown in light blue. For candidate SDRMs that decreased with a very low overall prevalence or did not change in prevalence, the labels are not shown. Full lists of candidate NRTI-SDRMs, NNRTI-SDRMs and PI-SDRMs according to the change in prevalence are shown in Table 2, 4, and 6, respectively.