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# Temporal Changes in the Epidemiology of Transmission of Drug-Resistant HIV-1 across the World

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## Abstract

***A substantial number of studies have been performed across the world to determine transmitted drug resistance. Large variations between different parts of the world can be expected because of differences in availability over time of treatment. Time trend analyses are often not possible because of small numbers of included patients. In this review, we present the available data on the transmission of drug-resistant HIV, with a major emphasis on the time trends of drug resistance prevalences. We identified relevant literature by searching in PubMed through September 2009. Studies were grouped, according to the year of data collection, into the following time periods: < 2001, 2001-2003, > 2003. We selected a total of 215 studies, which included 43,170 patients. The following prevalences of transmission of drug-resistant HIV were found, in rank order: North America (12.9%), Europe (10.9%), Latin America (6.3%), Africa (4.7%), and Asia (4.2%). Changes over time in particular drugs classes were found in all parts of the world. Nucleoside reverse transcriptase inhibitor resistance declined over time in North America (p = 0.03), Europe (p < 0.001), and Latin America (p < 0.001). The decline in nucleoside reverse transcriptase inhibitor resistance reflects the improvement of treatment regimens in resource-rich settings. In contrast the resistance prevalence increased in Asia (p = 0.047) and Africa (p < 0.001). This can be explained by the antiretrovirals becoming more available during recent years in these continents. Nonnucleoside reverse transcriptase inhibitor resistance rose over time in North America (p < 0.001), Europe (p < 0.001), Latin America (p < 0.001), and Asia (p = 0.01). This paper gives a complete overview of the epidemiology of resistance of antiretroviral drugs in drug-naive patients worldwide. The time trends that were observed seem to reflect changes in describing prescriptions over time. Changes include the more wide-spread use of antiretroviral drugs in developing countries and the development of therapies from low-active mono-therapies to highly active antiretroviral regimens in the industrialized countries.*** **(AIDS Rev. 2012;14:17-27)**

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## Key words

***HIV-1. Drug resistance mutations. Resistance prevalence. Transmitted drug resistance.***

## Introduction

The use of HAART has substantially improved survival among patients infected with HIV-1. But the success of antiretroviral treatment can be limited by the emergence of HIV drug resistance, which in turn can be transmitted to newly infected individuals. Transmission of drug resistance is associated with an increased risk for virologic failure 12 months after start of treatment[1].

A large number of studies reported on transmitted drug resistance across the world. These studies report a prevalence of transmitted drug resistance that ranges between 0-25%[2-4].

The prevalence is lowest in resource-limited settings[5]. But the prevalence in resource-limited countries may have increased in recent years as access to antiretroviral drugs has been expanding.

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Substantial differences in resistance to particular classes of antiretroviral drugs may exist over time in different parts of the world. For example, the use of nevirapine in Africa to prevent mother-to-child transmission could have increased the prevalence of transmitted resistance to nonnucleoside reverse transcriptase inhibitors (NNRTI) in Africa[6]. Similarly, in resource-rich settings zidovudine was given as monotherapy before 1996, resulting in transmitted nucleoside reverse transcriptase inhibitor (NRTI) drug resistance[7,8]. In recent years, other classes of antiretrovirals have become popular, which could have changed the epidemic of transmission of drug resistance. We conducted a systematic review of the literature to compare temporal changes in the prevalence of transmission of drug-resistant HIV-1 across different continents.

## Selection of studies on transmitted drug resistance

PubMed was used to identify studies written in English on the epidemiology of transmission of drug-resistant HIV-1 until September 1, 2009 (key words "HIV" and "resistance" or "HIV" and "transmission"). Primary research studies that investigated the prevalence of HIV drug resistance in antiretroviral-naive HIV-1-infected persons were eligible for inclusion.

Transmitted drug resistance was reported in 215 papers, including 43,170 patients (Table 1).

Most studies came from Europe (82 studies; 25,446 patients), followed by Africa (47; 3,096), North America (36; 8,718), Latin America (26; 3,218), Asia (23; 2,507), and Australia (1; 185). The characteristics of included patients varied between continents. The proportion of risk groups per continent in the included studies followed the regional mode of HIV-1 transmission across the world. For example, in North America and Europe, patients were predominantly infected through men who have sex with men (41 and 47%, respectively), whereas in other continents this did not exceed 20%, as described in literature[9].

## Definition of transmission of drug resistance

We compiled transmitted drug resistance as reported in the studies. Resistance to NRTI, NNRTI, and protease inhibitors (PI) was defined as the presence of at least one drug resistance-associated mutation to that particular drug class. Multiclass resistance was defined as the presence of resistance-associated mutations to at least two different classes of antiretroviral drugs. The list used to define transmitted drug resistance was extracted from the studies.

## Statistical analysis

Time trends were analyzed by grouping the studies according to the year of data collection: before 2001, 2001-2003, and 2004 or later. We used these cutoffs so that we could include time periods with comparable numbers of patients. Taking different time periods did not result in different trends over time (data not shown). Studies reporting the epidemiology of transmission of resistance over a range of years were grouped according to the average of the years.

Sixteen studies did not report the year of data collection. The average difference between year of data collection and year of publication was four years. We therefore calculated the missing data collection years by subtracting four years from the year of publication. Exclusion of these studies or subtraction of 0, 2, or 6 years from the year of publication did not change the results (data not shown).

Prevalence estimates are presented with 95% confidence intervals calculated according to the Wilson score interval. Poisson regression analysis was used to calculate the time trend analyses for each continent.

## Epidemiology of transmission of drug resistance Europe

The studies were predominantly performed in Western Europe (n = 75). A smaller number of studies (n = 7) came from Central Europe and the former Soviet Union. Studies from the former Soviet Union are of particular interest as this part of the world has the strongest growing epidemic worldwide due to an explosive outbreak of HIV-1 infections among intravenous drug users[10-12].

The prevalence of transmission of drug resistance across Europe was 10.9% (95% CI: 10.6-11.3%). Transmission of drug resistance most frequently involved NRTI, with a prevalence of 7.4% (7.1-7.7%). The prevalence of resistance to NNRTI was with a prevalence of 3.4% (3.2-3.6%), slightly higher than the prevalence of 2.9% (2.7-3.2%) found for PI.

Transmission of drug resistance declined over time in Europe. The prevalence was around 11.5% before 2003 and reduced to 7.7% after that year ($p < 0.001$). A closer examination of the classes showed that this decrease was ascribed to the decline in resistance to NRTI (from 8.0 to 4.3%) and PI (from 3.3 to 1.4%) ($p < 0.001$).

Resistance to NNRTI increased from 2.9% to a small peak in 2001-2002 of 4.4%, after which it decreased again to 3.2% (p = 0.004).

Two European studies that reported on the epidemiology of transmitted drug resistance over time confirm our results. First, the pan-European SPREAD program also reported a decrease in the prevalence of transmitted NRTI resistance and an increase in the prevalence of transmitted NNRTI resistance over time (2002-2006). These changes were, however, not statistically significant, which could be ascribed to a smaller sample size in the SPREAD program[13]. The second study confirming the decline in transmitted drug resistance over time was performed in the United Kingdom. This study reported a small increase in NRTI resistance, with some evidence of a leveling off from 1996 to 2003. This British study also reported an increase in transmission of NNRTI resistance[14].

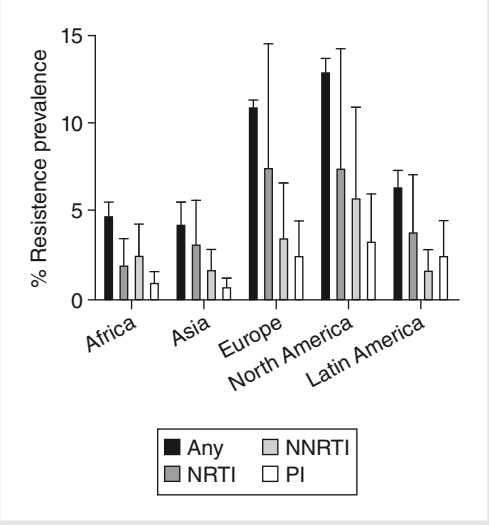


**Figure 1.** *Prevalence of transmitted drug resistance to any of the drug classes, nucleoside reverse transcriptase inhibitors, nonnucleoside reverse transcriptase inhibitors, and protease inhibitors in Africa, Asia, Europe, North America, and Latin America. Any: any class of drugs; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: nonnucleoside reverse transcriptase inhibitor; PI: protease inhibitor.*

## North America

Europe and North America have had the longest access to antiretrovirals across the world. There were, however, several differences between the two continents. In North America, the prevalence of transmission of drug resistance was higher, with a proportion of 12.9% (12.2-13.7%) (Fig. 1). Similar to Europe, transmission of drug resistance was for the largest part ascribed to NRTI; prevalence 7.4% (6.8-8.0%). But transmission of NNRTI resistance in North America was 5.7% (5.2-6.2%), higher than the prevalence of 3.4% found in Europe. Similar to Europe, resistance to PI was also uncommon in North America, with a prevalence of 3.2% (2.8-3.6%) as compared to 2.9% in Europe.

Contrary to Europe, the prevalence of resistance showed an increase over time from 11.6% (10.7-12.7%) in studies performed before 2001 to 14.3% (12.8-16.1%) in studies performed after 2003 (p = 0.003) (Fig. 2). This increase in overall transmitted resistance was ascribed to the increase in NNRTI resistance (from 4.1 to 8.3%; p < 0.001), whereas the NRTI resistance decreased from 8.0 to 6.4% (p = 0.032).

Studies that included longitudinal data confirm the time trends we observed. A study performed in San Francisco showed a decrease in transmitted NRTI resistance from 21% in 1996-1997 to 3.3% in 1998-1999 and a subsequent increase to 6.2% in 2000-2001[8].

The decline in NRTI resistance in resource-rich settings reflects the improvement of treatment regimens. Before 1996, antiretroviral therapy consisted of monotherapy or dual-therapy of NRTI, which lead to the appearance of drug-resistant HIV-1 in many patients[15,16]. After 1996, HAART was introduced, which is virologically more active and is associated with a substantially lower risk of resistance. As a consequence, NRTI resistance was initially high and then decreased in recent years.

The increase of NNRTI resistance in Europe and North America coincides with the more frequent use of this drug class in the developed world in the previous years. NNRTI were approved in 1996 and clinical trials in 1999 indicated that virologic outcomes during treatment with this drug class were better compared with those of PI-based treatment[17].

## Latin America

Large Latin American countries, such as Argentina and Brazil, have sponsored a policy of universal access to antiretroviral drugs since the 1990s. Interestingly, transmission of drug resistance was reported in 6.3% (5.5-7.3%) of HIV-1 patients from Latin American studies, suggesting that universal access did not result in high levels of resistance.

Studies from Latin America reported a low prevalence of transmission of drug resistance to the different drug classes: 3.8% (3.2-4.6%) for NRTI, 1.6% (1.2-2.1%) for

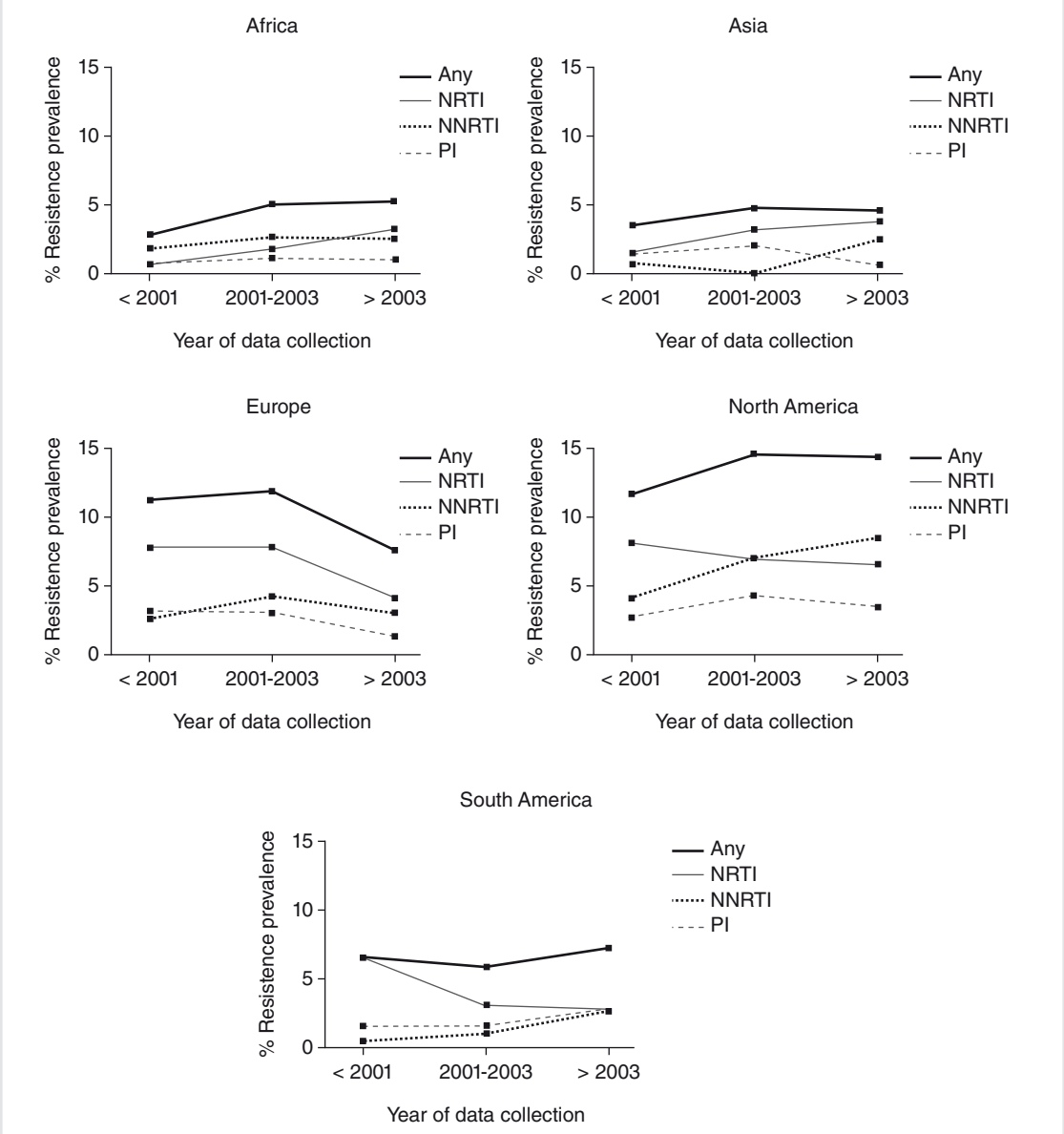


**Figure 2.** *Prevalence over time of transmitted drug resistance to any of the drug classes, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors in Africa, Asia, Europe, North America, and Latin America. Any: any class of drugs; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: nonnucleoside reverse transcriptase inhibitor; PI: protease inhibitor.*

NNRTI, and 2.4% (2.0-2.8%) for PI. The time trends for resistance to particular classes followed the same trend as in Europe and North America. Resistance to NRTI decreased over time (from 6.6 to 2.8%; $p < 0.001$). The prevalence of transmission of NNRTI increased from 0.6 to 2.7% ($p < 0.001$). Resistance to PI increased, but remained limited (from 1.6 to 2.7%; $p = 0.01$).

Transmitted drug resistance to PI was uncommon in all parts of the world (< 3.2%). This may be explained by the high genetic threshold for resistance to boosted PI. Moreover, PI are not used in treatment of all patients as they are frequently reserved for second-line therapy.

## Africa

Transmission of drug resistance was variable in Africa and 30 out of 47 studies reported a prevalence < 5%. The combined prevalence of transmission of drug

resistance in studies from Africa was low with a proportion of 4.7% (4.0-5.5%). However, many parts of Africa still do not have access to antiretrovirals. Epidemiological studies on transmitted resistance will not be performed in these areas as resistance is unlikely. Therefore, the transmitted resistance prevalence that we calculated from the available studies performed in Africa is an overestimation of the real prevalence in this continent.

Importantly, transmission of drug-resistant HIV increased over time. The prevalence was 2.8% (1.7-4.5%) before 2001 and almost doubled to 5.3% (4.0-6.9%) after 2003. This increase was, however, not statistically significant ($p = 0.06$). The increase can be explained by the increase in NRTI drug resistance over time from 0.6% before 2001 to 3.0% after 2003 ($p < 0.001$). The prevalence of PI resistance was low (0.9%; 95% CI: 0.6-1.3%) and NNRTI prevalence showed a non-significant increase from 1.7 to 2.5%.

In Africa, different patterns of resistance to particular antiretroviral drug classes were seen than in other parts of the world. Contrary to the Americas and Europe, the prevalence of NRTI resistance increased over time. This increase can be explained by the antiretrovirals becoming more widely available during recent years (e.g. due to the efforts of the Global Fund and PEPFAR, the President's Emergency Plan for AIDS Relief). Due to the increased use of HAART, which includes NRTI as the backbone, resistant mutations have developed, and as a consequence transmitted NRTI resistance in Africa has been rising.

A high proportion of NNRTI resistance was initially observed and is decreasing over time. This high contribution reflects the prophylactic use of a single dose of NNRTI monotherapy for prevention of mother-to-child-transmission[6,18]. Due to the low genetic threshold for resistance to NNRTI, viral resistance could be induced[19]. Currently, the WHO recommends combinations of different antiretroviral drugs, including NRTI, to prevent vertical transmission, instead of using the simplest regimen of single-dose nevirapine[20]. Furthermore, universal access to HAART has been scaled up in developing countries[21,22].

As a consequence, transmitted NRTI resistance has increased and the contribution of NNRTI resistance to the total resistance has decreased.

## Asia

We found a lack of data on transmission of drug resistance in Asia. Data from Asia should therefore be interpreted with caution. Only a low number of studies and patients could be extracted from literature. Consequently, time trend analyses showed less significant results.

For example, the overall resistance prevalence of 4.2% (3.4-5.4%) was stable over time ($p = 0.496$). However, NRTI and NNRTI resistance were slightly increasing from 1.3 to 3.5% ($p = 0.047$) and 0.6 to 2.2% ($p = 0.01$), respectively. Transmitted resistance to PI declined over time from 1.3 to 0.4% ($p = 0.02$).

## Oceania

Only one study was included from Australia in this review. This study reported a high prevalence of 23.2% (17.7-29.8%). No further analyses were performed with this data.

## Discussion

In this review, we examined all literature available on HIV-1 transmitted drug resistance epidemiology. Reviewing all literature on this subject allowed us to calculate the change over time in the prevalence of transmission of drug-resistant HIV-1 for the different drug classes in each continent.

The prevalence of transmitted resistance ranged between 0%[23-26] and 27%[8]. This means that most HIV infections are with a virus that is susceptible to antiretrovirals. There were, however, clear differences across the world. The highest prevalence of transmitted resistance was found in North America (12.9%) and Europe (10.9%), where antiretroviral drugs have been available for prolonged periods of time. Lower proportions of transmitted resistance were found in Latin America (6.3%), Africa (4.7%), and in Asia (4.2%).

Time trends observed in this study may be caused by true differences in temporal changes in treatment regimens between continents, or by other sources of variability. An important factor may be the inclusion of recently or chronically infected patients, a distinction sometimes made in studies performed in resource-rich countries. Resistance in recently infected patients has been reported to be higher than resistance in patients infected > 1 year[27]. This can be explained by several factors. First, the difference partly reflects the variation of resistance prevalence among different HIV risk groups. The majority of the recently infected patients are men who have sex with men (MSM)[28]. Transmitted drug resistance is often much higher in MSM HIV-infected patients compared to the heterosexual risk group because most HIV patients who acquired HIV

through heterosexual contact are more likely to come from regions with limited access to antiretroviral drugs[13,29]. In addition, the lower prevalence of transmitted drug resistance in chronic patients can be explained by the outgrowth of the wild-type or the reversion of the transmitted drug resistance mutations. Remarkably, some resistance viruses remain present in patients, despite the negative effect on replication capacity, due to the appearance of compensatory mutations and the reduced replication capacity of the required intermediate viruses[30]. In this review, the effect of differences between studies in including recently or chronically infected patients on the time trends is probably limited, as most differences in studies were seen between continents and not over time.

Another source of variation in resistance prevalence between studies may be the use of different methods to define drug resistance. The majority of the studies we included have defined resistance either with the IAS USA or the Stanford genotypic resistance interpretation algorithm. However, the use of different algorithms to score resistance may not have a large impact. This is supported by a previous study reporting that scoring resistance using the IAS USA mutation list of 2006[31], or the Stanford HIVdb (version 4.3.0, 2007) or the Shafer list of 2007[32] was associated with comparable levels of transmitted drug resistance in 8,272 genotypic resistance tests of drug-naive patients conducted during 1997-2005[33].

This review is limited by the data that could be extracted from published reports. Convenience sampling (i.e. an over-representation of patients suspected to carry a drug-resistant virus) may have an impact on the prevalence estimates. Although we cannot rule out that convenience sampling occurred, the vast majority of included studies used well-defined sampling strategies to identify relevant patients.

Heterogeneity is another bias that can occur within reviews. Heterogeneity applies to differences in the strategies used to sample patients and in research methodology. We reduced the heterogeneity by taking into account the year of data collection and performing analyses per continent.

The studies that were collected used population sequence analysis. This method fails to detect minor populations of drug-resistant quasispecies[34]. As resistance variants in the absence of drug-selection pressure in the antiretroviral-naive host may be present in minority viral variants, population sequence analysis will underestimate the prevalence of drug-resistant HIV-1.

Despite these shortcomings, this review is the first, to our knowledge, to summarize all the published articles on transmitted drug resistance.

## Conclusion

In this paper, we gave an overview of the epidemiology of resistance to antiretroviral drugs in drug-naive patients worldwide. The resistance profiles of the three antiretroviral drug classes seem to be different among continents and reflect changes in prescribing behavior of antiretroviral drugs. Although the prevalence of resistance to antiretroviral drugs decreases, resistance can become a larger problem in third world continents, where antiretroviral drug therapy is becoming more widespread. Continuous global surveillance is needed to monitor the circulating HIV strains and ensure that the development of treatment is adjusted to the evolution of drug resistance.

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## Supplementary Data

Supplementary data is available at AIDS Reviews journal online (http://www.aidsreviews.com). This data is provided by the author and published online to benefit the reader. The contents of all supplementary data are the sole responsibility of the authors. *(See last pages of this file.)*

## References

1. Wittkop L, Gunthard H, de Wolf F, et al. Effect of transmitted drug resistance on virological and immunological response to initial combination antiretroviral therapy for HIV (EuroCoord-CHAIN joint project): a European multicohort study. Lancet Infect Dis. 2011;11:363-71.
2. Wensing A, Boucher C. Worldwide transmission of drug-resistant HIV. AIDS Rev. 2003;5:140-55.
3. Geretti A. Epidemiology of antiretroviral drug resistance in drug-naive persons. Curr Opin Infect Dis. 2007;20:22-32.
4. Van de Vijver D, Wensing A, Boucher C. The epidemiology of transmission of drug resistant HIV-1. HIV Sequence Compendium. 2007;2006/2007:17-36.
5. Vergne L, Diagbouga S, Kouanfack C, et al. HIV-1 drug-resistance mutations among newly diagnosed patients before scaling-up programmes in Burkina Faso and Cameroon. Antivir Ther. 2006;11:575-9.
6. Lockman S, Shapiro R, Smeaton L, et al. Response to antiretroviral therapy after a single, peripartum dose of nevirapine. N Engl J Med. 2007;356:135-47.
7. SPREAD Program. Transmission of drug-resistant HIV-1 in Europe remains limited to single classes. AIDS. 2008;22:625-35.
8. Grant R, Hecht F, Warmerdam M, et al. Time trends in primary HIV-1 drug resistance among recently infected persons. JAMA. 2002;288:181-8.
9. UNAIDS WHO. AIDS epidemic update, December 2009.
10. European Centre for Disease Prevention and Control/WHO Regional Office for Europe. HIV/AIDS surveillance in Europe 2009. Stockholm: European Centre for Disease Prevention and Control, 2010.

11. UNAIDS. Report on the global HIV/AIDS epidemic, July 2002.
12. Mathers B, Degenhardt L, Phillips B, et al. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. Lancet. 2008;372:1733-45.
13. Vercauteren J, Wensing A, van de Vijver D, et al. Transmission of drug-resistant HIV-1 is stabilizing in Europe. J Infect Dis. 2009;200:1503-8.
14. Cane P, Chrystie I, Dunn D, et al. Time trends in primary resistance to HIV drugs in the United Kingdom: multicentre observational study. BMJ. 2005;331:1368.
15. Schuurman R, Nijhuis M, van Leeuwen R, et al. Rapid changes in human immunodeficiency virus type 1 RNA load and appearance of drug-resistant virus populations in persons treated with lamivudine (3TC). J Infect Dis. 1995;171:1411-9.
16. Boucher C, O'Sullivan E, Mulder J, et al. Ordered appearance of zidovudine resistance mutations during treatment of 18 human immunodeficiency virus-positive subjects. J Infect Dis. 1992;165:105-10.
17. Staszewski S, Morales-Ramirez J, Tashima K, et al. Efavirenz plus zidovudine and lamivudine, efavirenz plus indinavir, and indinavir plus zidovudine and lamivudine in the treatment of HIV-1 infection in adults. Study 006 Team. N Engl J Med. 1999;341:1865-73.
18. Arrive E, Newell M, Ekouevi D, et al. Prevalence of resistance to nevirapine in mothers and children after single-dose exposure to prevent vertical transmission of HIV-1: a meta-analysis. Int J Epidemiol. 2007;36:1009-21.
19. Stringer J, McConnell M, Kiarie J, et al. Effectiveness of non-nucleoside reverse transcriptase inhibitor-based antiretroviral therapy in women previously exposed to a single intrapartum dose of nevirapine: a multicountry, prospective cohort study. PLoS Med. 2010;7:e1000233.
20. World Health Organisation. Treat 3 million by 2005: Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. 2004.
21. Holmes C, Coggin W, Jamieson D, et al. Use of generic antiretroviral agents and cost savings in PEPFAR treatment programs. JAMA. 2010;304:313-20.
22. World Health Organisation. Treating 3 million by 2005: '3 by 5' Progress report, June 2005.
23. Agwale S, Zeh C, Paxinos E, et al. Genotypic and phenotypic analyses of human immunodeficiency virus type 1 in antiretroviral drug-naive Nigerian patients. AIDS Res Hum Retroviruses. 2006;22:22-6.
24. Dumans A, Soares M, Pieniazek D, et al. Prevalence of protease and reverse transcriptase drug resistance mutations over time in drug-naive human immunodeficiency virus type 1-positive individuals in Rio de Janeiro, Brazil. Antimicrob Agents Chemother. 2002;46:3075-9.
25. Paraschiv S, Otelea D, Dinu M, Maxim D, Tinischi M. Polymorphisms and resistance mutations in the protease and reverse transcriptase genes of HIV-1 F subtype Romanian strains. Int J Infect Dis. 2007;11:123-8.
26. Eshleman S, Hudelson S, Gupta A, et al. Limited evolution in the HIV type 1 pol region among acute seroconverters in Pune, India. AIDS Res Hum Retroviruses. 2005;21:93-7.
27. Wensing A, van de Vijver D, Angarano G, et al. Prevalence of drug-resistant HIV-1 variants in untreated individuals in Europe: implications for clinical management. J Infect Dis. 2005;192:958-66.
28. Leaity S, Sherr L, Wells H, et al. Repeat HIV testing: high-risk behaviour or risk reduction strategy? AIDS. 2000;14:547-52.
29. Booth C, Garcia-Diaz A, Youle M, Johnson M, Phillips A, Geretti A. Prevalence and predictors of antiretroviral drug resistance in newly diagnosed HIV-1 infection. J Antimicrob Chemother. 2007;59:517-24.
30. van Maarseveen N, Wensing A, de Jong D, et al. Persistence of HIV-1 variants with multiple protease inhibitor (PI)-resistance mutations in the absence of PI therapy can be explained by compensatory fixation. J Infect Dis. 2007;195:399-409.
31. Johnson V, Brun-Vezinet F, Clotet B, et al. Update of the drug resistance mutations in HIV-1: Fall 2006. Top HIV Med. 2006;14:125-30.
32. Shafer R, Rhee S, Pillay D, et al. HIV-1 protease and reverse transcriptase mutations for drug resistance surveillance. AIDS. 2007;21:215-23.
33. Green H, Tilston P, Fearnhill E, Pillay D, Dunn DT. The impact of different definitions on the estimated rate of transmitted HIV drug resistance in the United Kingdom. J Acquir Immune Defic Syndr. 2008;49:196-204.
34. Metzner K, Rauch P, Walter H, et al. Detection of minor populations of drug-resistant HIV-1 in acute seroconverters. AIDS. 2005;19:1819-25.
35. Vergne L, Peeters M, Mpoudi-Ngole E, et al. Genetic diversity of protease and reverse transcriptase sequences in non-subtype-B human immunodeficiency virus type 1 strains: evidence of many minor drug resistance mutations in treatment-naive patients. J Clin Microbiol. 2000;38:3919-25.
36. Vergne L, Malonga-Mouellet G, Mistoul I, et al. Resistance to antiretroviral treatment in Gabon: need for implementation of guidelines on antiretroviral therapy use and HIV-1 drug resistance monitoring in developing countries. J Acquir Immune Defic Syndr. 2002;29:165-8.
37. Toni T, Masquelier B, Bonard D, et al. Primary HIV-1 drug resistance in Abidjan (Cote d'Ivoire): a genotypic and phenotypic study. AIDS. 2002;16:488-91.
38. Fonjungo P, Mpoudi E, Torimiro J, et al. Human immunodeficiency virus type 1 group m protease in Cameroon: genetic diversity and protease inhibitor mutational features. J Clin Microbiol. 2002;40:837-45.
39. Pillay C, Bredell H, McIntyre J, Gray G, Morris L. HIV-1 subtype C reverse transcriptase sequences from drug-naive pregnant women in South Africa. AIDS Res Hum Retroviruses. 2002;18:605-10.
40. Toni T, Recordon-Pinson P, Minga A, et al. Presence of key drug resistance mutations in isolates from untreated patients of Abidjan, Cote d'Ivoire: ANRS 1257 study. AIDS Res Hum Retroviruses. 2003;19:713-17.
41. Gordon M, De Oliveira T, Bishop K, et al. Molecular characteristics of human immunodeficiency virus type 1 subtype C viruses from KwaZulu-Natal, South Africa: implications for vaccine and antiretroviral control strategies. J Virol. 2003;77:2587-99.
42. Handema R, Terunuma H, Kasolo F, et al. Prevalence of drug-resistance-associated mutations in antiretroviral drug-naive Zambians infected with subtype C HIV-1. AIDS Res Hum Retroviruses. 2003;19:151-60.
43. Hirsch M, Conway B, D'Aquila R, et al. Antiretroviral drug resistance testing in adults with HIV infection: implications for clinical management. International AIDS Society--USA Panel. JAMA. 1998;279:1984-91.
44. Vergne L, Kane C, Laurent C, et al. Low rate of genotypic HIV-1 drug-resistant strains in the Senegalese government initiative of access to antiretroviral therapy. AIDS. 2003;17(Suppl 3):S31-8.
45. Adje-Toure C, Bile CE, Borget M, et al. Polymorphism in protease and reverse transcriptase and phenotypic drug resistance of HIV-1 recombinant CRF02_AG isolates from patients with no prior use of antiretroviral drugs in Abidjan, Cote d'Ivoire. J Acquir Immune Defic Syndr. 2003;34:111-13.
46. Konings F, Zhong P, Agwara M, et al. Protease mutations in HIV-1 non-B strains infecting drug-naive villagers in Cameroon. AIDS Res Hum Retroviruses. 2004;20:105-9.
47. Birk M, Sonnerborg A. Variations in HIV-1 pol gene associated with reduced sensitivity to antiretroviral drugs in treatment-naive patients. AIDS. 1998;12:2369-75.
48. Bessong P, Larry Obi C, Cilliers T, et al. Characterization of human immunodeficiency virus type 1 from a previously unexplored region of South Africa with a high HIV prevalence. AIDS Res Hum Retroviruses. 2005;21:103-9.
49. Bussmann H, Novitsky V, Wester W, et al. HIV-1 subtype C drug-resistance background among ARV-naive adults in Botswana. Antivir Chem Chemother. 2005;16:103-15.
50. Shafer R. Genotypic testing for human immunodeficiency virus type 1 drug resistance. Clin Microbiol Rev. 2002;15:247-77.
51. Bellocchi M, Forbici F, Palombi L, et al. Subtype analysis and mutations to antiviral drugs in HIV-1-infected patients from Mozambique before initiation of antiretroviral therapy: results from the DREAM programme. J Med Virol. 2005;76:452-8.
52. Petch L, Hoffman I, Jere C, et al. Genotypic analysis of the protease and reverse transcriptase of HIV type 1 subtype C isolates from antiretroviral drug-naive adults in Malawi. AIDS Res Hum Retroviruses. 2005;21:799-805.
53. Maslin J, Rogier C, Caron M, Grandadam M, Koeck J, Nicand E. Short communication. Antiretroviral drug resistance among drug-naive HIV-1-infected individuals in Djibouti (Horn of Africa). Antivir Ther. 2005;10:855-9.
54. Johnson V, Brun-Vezinet F, Clotet B, et al. Update of the Drug Resistance Mutations in HIV-1: 2005. Top HIV Med. 2005;13:51-7.
55. Koizumi Y, Ndembi N, Miyashita M, et al. Emergence of antiretroviral therapy resistance-associated primary mutations among drug-naive HIV-1-infected individuals in rural western Cameroon. J Acquir Immune Defic Syndr. 2006;43:15-22.
56. Vergne L, Stuyver L, Van Houtte M, Butel C, Delaporte E, Peeters M. Natural polymorphism in protease and reverse transcriptase genes and in vitro antiretroviral drug susceptibilities of non-B HIV-1 strains from treatment-naive patients. J Clin Virol. 2006;36:43-9.
57. Vidal N, Mulanga C, Bazepeo S, et al. HIV type 1 pol gene diversity and antiretroviral drug resistance mutations in the Democratic Republic of Congo (DRC). AIDS Res Hum Retroviruses. 2006;22:202-6.
58. Vessiere A, Nerrienet E, Kfutwah A, et al. HIV-1 pol gene polymorphism and antiretroviral resistance mutations in drug-naive pregnant women in Yaounde, Cameroon. J Acquir Immune Defic Syndr. 2006;42:256-8.
59. Tebit D, Ganame J, Sathiandee K, Nagabila Y, Coulibaly B, Krausslich H. Diversity of HIV in rural Burkina Faso. J Acquir Immune Defic Syndr. 2006;43:144-52.
60. Ojesina A, Sankale J, Odaibo G, et al. Subtype-specific patterns in HIV Type 1 reverse transcriptase and protease in Oyo State, Nigeria: implications for drug resistance and host response. AIDS Res Hum Retroviruses. 2006;22:770-9.
61. Nadembega W, Giannella S, Simpore J, et al. Characterization of drug-resistance mutations in HIV-1 isolates from non-HAART and HAART treated patients in Burkina Faso. J Med Virol. 2006;78:1385-91.
62. Razafindratsimandresy R, Rajaonatahina D, Soares J, Rousset D, Reynes JM. High HIV type 1 subtype diversity and few drug resistance mutations among seropositive people detected during the 2005 second generation HIV surveillance in Madagascar. AIDS Res Hum Retroviruses. 2006;22:595-7.
63. Marechal V, Jauvin V, Selekon B, et al. Increasing HIV type 1 polymorphic diversity but no resistance to antiretroviral drugs in untreated patients from Central African Republic: a 2005 study. AIDS Res Hum Retroviruses. 2006;22:1036-44.
64. Johnson V, Brun-Vezinet F, Clotet B, et al. Update of the drug resistance mutations in HIV-1: Fall 2005. Top HIV Med. 2005;13:125-31.

65. Bessong P, Mphahlele J, Choge I, et al. Resistance mutational analysis of HIV type 1 subtype C among rural South African drug-naive patients prior to large-scale availability of antiretrovirals. AIDS Res Hum Retroviruses. 2006;22:1306-12.
66. Parreira R, Piedade J, Domingues A, et al. Genetic characterization of human immunodeficiency virus type 1 from Beira, Mozambique. Microbes Infect. 2006;8:2442-51.
67. Vidal N, Niyongabo T, Nduwimana J, et al. HIV Type 1 Diversity and Antiretroviral Drug Resistance Mutations in Burundi. AIDS Res Hum Retroviruses. 2007;23:175-80.
68. Derache A, Traore O, Koita V, et al. Genetic diversity and drug resistance mutations in HIV type 1 from untreated patients in Bamako, Mali. Antivir Ther. 2007;12:123-9.
69. Toni T, Masquelier B, Minga A, et al. HIV-1 Antiretroviral Drug Resistance in Recently Infected Patients in Abidjan, Cote d'Ivoire: A 4-Year Survey, 2002-2006. AIDS Res Hum Retroviruses. 2007;23:1155-60.
70. Galluzzo C, Germinario E, Bassani L, et al. Antiretroviral resistance mutations in untreated pregnant women with HIV infection in Uganda and Rwanda. AIDS Res Hum Retroviruses. 2007;23:1449-51.
71. Ndembi N, Abraha A, Pilch H, et al. Molecular characterization of human immunodeficiency virus type 1 (HIV-1) and HIV-2 in Yaounde, Cameroon: evidence of major drug resistance mutations in newly diagnosed patients infected with subtypes other than subtype B J Clin Microbiol. 2008;46:177-84.
72. Deho L, Walwema R, Cappelletti A, et al. Subtype assignment and phylogenetic analysis of HIV type 1 strains in patients from Swaziland. AIDS Res Hum Retroviruses. 2008;24:323-5.
73. Ndembi N, Lyagoba F, Nanteza B, et al. Transmitted antiretroviral drug resistance surveillance among newly HIV type 1-diagnosed women attending an antenatal clinic in Entebbe, Uganda. AIDS Res Hum Retroviruses. 2008;24:889-95.
74. Johnson V, Brun-Vezinet F, Clotet B, et al. Update of the drug resistance mutations in HIV-1: 2007. Top HIV Med. 2007;15:119-25.
75. Somi G, Kibuka T, Diallo K, et al. Surveillance of transmitted HIV drug resistance among women attending antenatal clinics in Dar es Salaam, Tanzania. Antivir Ther. 2008;13(Suppl 2):77-82.
76. Pillay V, Ledwaba J, Hunt G, et al. Antiretroviral drug resistance surveillance among drug-naive HIV-1-infected individuals in Gauteng Province, South Africa in 2002 and 2004. Antivir Ther. 2008;13(Suppl 2):101-7.
77. Kamoto K, Aberle-Grasse J. Surveillance of transmitted HIV drug resistance with the World Health Organization threshold survey method in Lilongwe, Malawi. Antivir Ther. 2008;13(Suppl 2):83-7.
78. Abegaz W, Grossman Z, Wolday D, et al. Threshold survey evaluating transmitted HIV drug resistance among public antenatal clinic clients in Addis Ababa, Ethiopia. Antivir Ther. 2008;13(Suppl 2):89-94.
79. Maphalala G, Okello V, Mndzebele S, et al. Surveillance of transmitted HIV drug resistance in the Manzini-Mbabane corridor, Swaziland, in 2006. Antivir Ther. 2008;13(Suppl 2):95-100.
80. Bartolo I, Casanovas J, Bastos R, et al. HIV-1 genetic diversity and transmitted drug resistance in health care settings in Maputo, Mozambique. J Acquir Immune Defic Syndr. 2009;51:323-31.
81. Shafer R, Rhee S, Bennett D. Consensus drug resistance mutations for epidemiological surveillance: basic principles and potential controversies. Antivir Ther. 2008;13(Suppl 2):59-68.
82. Bartolo I, Rocha C, Bartolomeu J, et al. Antiretroviral drug resistance surveillance among treatment-naive HIV-1-infected individuals in Angola: evidence for low level of transmitted drug resistance. Antimicrob Agents Chemother. 2009;53:3156-8.
83. Eshleman S, Laeyendecker O, Parkin N, et al. Antiretroviral drug susceptibility among drug-naive adults with recent HIV infection in Rakai, Uganda. AIDS. 2009;27:845-52.
84. Tebit D, Sangare L, Tiba F, et al. Analysis of the diversity of the HIV-1 pol gene and drug resistance associated changes among drug-naive patients in Burkina Faso. J Med Virol. 2009;81:1691-701.
85. Johnson VA, Brun-Vezinet F, Clotet B, et al. Update of the drug resistance mutations in HIV-1. Top HIV Med. 2008;16:138-45.
86. Aghokeng A, Vergne L, Mpoudi-Ngole E, et al. Evaluation of transmitted HIV drug resistance among recently-infected antenatal clinic attendees in four Central African countries. Antivir Ther. 2009;14:401-11.
87. Brodine S, Shaffer R, Starkey M, et al. Drug resistance patterns, genetic subtypes, clinical features, and risk factors in military personnel with HIV-1 seroconversion. Ann Intern Med. 1999;131:502-6.
88. Alexander C, Dong W, Schechter M, et al. Prevalence of primary HIV drug resistance among seroconverters during an explosive outbreak of HIV infection among injecting drug users. AIDS. 1999;13:981-5.
89. Wegner S, Brodine S, Mascola J, et al. Prevalence of genotypic and phenotypic resistance to anti-retroviral drugs in a cohort of therapy-naive HIV-1 infected US military personnel. AIDS. 2000;14:1009-15.
90. Weinstock H, Respess R, Heneine W, et al. Prevalence of mutations associated with reduced antiretroviral drug susceptibility among human immunodeficiency virus type 1 seroconverters in the United States, 1993-1998. J Infect Dis. 2000;182:330-3.
91. Alexander C, Dong W, Chan K, et al. HIV protease and reverse transcriptase variation and therapy outcome in antiretroviral-naive individuals from a large North American cohort. AIDS. 2001;15:601-7.
92. Verbiest W, Brown S, Cohen C, et al. Prevalence of HIV-1 drug resistance in antiretroviral-naive patients: a prospective study. AIDS. 2001;15:647-50.
93. Nannini E, Han X, O'Brien W, Arduino R. Genotypic HIV-1 drug resistance testing in antiretroviral-naive subjects in Houston, Texas. J Acquir Immune Defic Syndr. 2002;29:317-19.
94. Ristig M, Arens M, Kennedy M, Powderly W, Tebas P. Increasing prevalence of resistance mutations in antiretroviral-naive individuals with established HIV-1 infection from 1996-2001 in St. Louis. HIV Clin Trials. 2002;3:155-60.
95. Hirsch M, Brun-Vezinet F, D'Aquila R, et al. Antiretroviral drug resistance testing in adult HIV-1 infection: recommendations of an International AIDS Society-USA Panel. JAMA. 2000;283:2417-26.
96. D'Aquila R, Schapiro J, Brun-Vezinet F, et al. Drug resistance mutations in HIV-1. Top HIV Med. 2002;10:21-5.
97. Little S, Holte S, Routy J, et al. Antiretroviral-drug resistance among patients recently infected with HIV. N Engl J Med. 2002;347:385-94.
98. Sullivan P, Buskin S, Turner J, et al. Low prevalence of antiretroviral resistance among persons recently infected with human immunodeficiency virus in two US cities. Int J STD AIDS. 2002;13:554-8.
99. Stone D, Corcoran C, Wurcel A, et al. Antiretroviral drug resistance mutations in antiretroviral-naive prisoners. Clin Infect Dis. 2002;35:883-6.
100. Hanna G, D'Aquila R. Antiretroviral drug resistance in HIV-1. Curr Infect Dis Rep. 1999;1:289-97.
101. Juethner S, Williamson C, Ristig M, Tebas P, Seyfried W, Aberg JA. Nonnucleoside reverse transcriptase inhibitor resistance among antiretroviral-naive HIV-positive pregnant women. J Acquir Immune Defic Syndr. 2003;32:153-6.
102. Hanna G, Balaguera H, Freedberg K, et al. Drug-selected resistance mutations and non-B subtypes in antiretroviral-naive adults with established human immunodeficiency virus infection. J Infect Dis. 2003;188:986-91.
103. Weinstock H, Zaidi I, Heneine W, et al. The epidemiology of antiretroviral drug resistance among drug-naive HIV-1-infected persons in 10 US cities. J Infect Dis. 2004;189:2174-80.
104. Holodniy M, Charlebois E, Bangsberg D, Zolopa A, Schulte M, Moss A. Prevalence of antiretroviral drug resistance in the HIV-1-infected urban indigent population in San Francisco: a representative study. Int J STD AIDS. 2004;15:543-51.
105. Turner D, Brenner B, Routy J, et al. Diminished representation of HIV-1 variants containing select drug resistance-conferring mutations in primary HIV-1 infection. J Acquir Immune Defic Syndr. 2004;37:1627-31.
106. Johnson V, Brun-Vezinet F, Clotet B, et al. Drug resistance mutations in HIV-1. Top HIV Med. 2003;11:215-21.
107. Novak R, Chen L, MacArthur R, et al. Prevalence of antiretroviral drug resistance mutations in chronically HIV-infected, treatment-naive patients: implications for routine resistance screening before initiation of antiretroviral therapy. Clin Infect Dis. 2005;40:468-74.
108. Hirsch M, Brun-Vezinet F, Clotet B, et al. Antiretroviral drug resistance testing in adults infected with human immunodeficiency virus type 1: 2003 recommendations of an International AIDS Society-USA Panel. Clin Infect Dis. 2003;37:113-28.
109. Welles S, Bauer G, Larussa P, Colgrove R, Pitt J. Time trends for HIV-1 antiretroviral resistance among antiretroviral-experienced and -naive pregnant women in New York City during 1991 to early 2001. J Acquir Immune Defic Syndr. 2007;44:329-35.
110. Jayaraman G, Archibald C, Kim J, et al. A population-based approach to determine the prevalence of transmitted drug-resistant HIV among recent versus established HIV infections: results from the Canadian HIV strain and drug resistance surveillance program. J Acquir Immune Defic Syndr. 2006;42:86-90.
111. D'Aquila R, Schapiro J, Brun-Vezinet F, et al. Drug resistance mutations in HIV-1. Top HIV Med. 2003;11:92-6.
112. Shet A, Berry L, Mohri H, et al. Tracking the prevalence of transmitted antiretroviral drug-resistant HIV-1: a decade of experience. J Acquir Immune Defic Syndr. 2006;41:439-46.
113. Grubb J, Singhatiraj E, Mondy K, Powderly W, Overton E. Patterns of primary antiretroviral drug resistance in antiretroviral-naive HIV-1-infected individuals in a midwest university clinic. AIDS. 2006;20:2115-16.
114. Truong H, Grant R, McFarland W, et al. Routine surveillance for the detection of acute and recent HIV infections and transmission of antiretroviral resistance. AIDS. 2006;20:2193-7.
115. Viani R, Peralta L, Aldrovandi G, et al. Prevalence of primary HIV-1 drug resistance among recently infected adolescents: a multicenter adolescent medicine trials network for HIV/AIDS interventions study. J Infect Dis. 2006;194:1505-9.
116. Ross L, Lim M, Liao Q, et al. Prevalence of antiretroviral drug resistance and resistance-associated mutations in antiretroviral therapy-naive HIV-infected individuals from 40 United States cities. HIV Clin Trials. 2007;8:1-8.

117. Smith D, Moini N, Pesano R, et al. Clinical utility of HIV standard genotyping among antiretroviral-naive individuals with unknown duration of infection. Clin Infect Dis. 2007;44:456-8.
118. Eshleman S, Husnik M, Hudelson S, et al. Antiretroviral drug resistance, HIV-1 tropism, and HIV-1 subtype among men who have sex with men with recent HIV-1 infection. AIDS. 2007;21:1165-74.
119. Parker M, Gordon D, Reilly A, et al. Prevalence of drug-resistant and nonsubtype B HIV strains in antiretroviral-naive, HIV-infected individuals in New York State. AIDS Patient Care STDS. 2007;21:644-52.
120. Brennan C, Stramer S, Holzmayer V, et al. Identification of human immunodeficiency virus type 1 non-B subtypes and antiretroviral drug-resistant strains in United States blood donors. Transfusion. 2009;49:125-33.
121. Gorbach P, Drumright L, Javanbakht M, et al. Antiretroviral drug resistance and risk behavior among recently HIV-infected men who have sex with men. J Acquir Immune Defic Syndr. 2008;47:639-43.
122. Huang H, Daar E, Sax P, et al. The prevalence of transmitted antiretroviral drug resistance in treatment-naive patients and factors influencing first-line treatment regimen selection. HIV Med. 2008;9:285-93.
123. Madsen T, Lohse N, Jensen E, et al. Short communication: high prevalence of drug-resistant human immunodeficiency virus type 1 in treatment-naive patients in Greenland. AIDS Res Hum Retroviruses. 2008;24:1073-7.
124. Brenner B, Roger M, Moisi D, et al. Transmission networks of drug resistance acquired in primary/early stage HIV infection. AIDS. 2008; 22:2509-15.
125. Johnson V, Brun-Vezinet F, Clotet B, et al. Update of the drug resistance mutations in HIV-1: Spring 2008. Top HIV Med. 2008;16:62-8.
126. Rahim S, Fredrick L, da Silva B, Bernstein B, King MS. Geographic and temporal trends of transmitted HIV-1 drug resistance among antiretroviral-naive subjects screening for two clinical trials in North America and Western Europe. HIV Clin Trials. 2009;10:94-103.
127. James C, Moffett L, Szabo S. Prevalence of antiretroviral drug resistance in antiretroviral-naive individuals. J Int Assoc Physicians AIDS Care (Chic). 2009;8:193-5.
128. Hirsch M, Gunthard H, Schapiro J, et al. Antiretroviral drug resistance testing in adult HIV-1 infection: 2008 recommendations of an International AIDS Society-USA panel. Clin Infect Dis. 2008;47:266-85.
129. Hurt C, McCoy S, Kuruc J, et al. Transmitted antiretroviral drug resistance among acute and recent HIV infections in North Carolina from 1998 to 2007. Antivir Ther. 2009;14:673-8.
130. Tanuri A, Vicente A, Otsuki K, et al. Genetic variation and susceptibilities to protease inhibitors among subtype B and F isolates in Brazil. Antimicrob Agents Chemother. 1999;43:253-8.
131. Cesaire R, Dos Santos G, Abel S, Bera O, Sobesky G, Cabie A. Drug resistance mutations among HIV-1 strains from antiretroviral-naive patients in Martinique, French West Indies. J Acquir Immune Defic Syndr. 1999;22:401-5.
132. Ruibal-Brunet I, Cuevas M, Diaz-Torres H, et al. Genotypic resistance mutations to antiretroviral drugs in HIV-1 B and non-B subtypes from Cuba. Rev Panam Salud Publica. 2001;10:174-80.
133. Kijak G, Pampuro S, Avila M, et al. Resistance profiles to antiretroviral drugs in HIV-1 drug-naive patients in Argentina. Antivir Ther. 2001;6:71-7.
134. Hammond J, Larder B, Schinazi R, Mellors J. Mutations in retroviral genes associated with drug resistance. In: Korber B, Foley B, Kuiken C, et al. (eds). A compilation and analysis of nucleic acid and amino acid sequences. Vol. III-207-49. Los Alamos National Laboratory: Human Retroviruses and AIDS, 1997.
135. Delgado E, Leon-Ponte M, Villahermosa M, et al. Analysis of HIV type 1 protease and reverse transcriptase sequences from Venezuela for drug resistance-associated mutations and subtype classification: a UNAIDS study. AIDS Res Hum Retroviruses. 2001;17:753-8.
136. Dumans A, Soares M, Pieniazek D, et al. Prevalence of protease and reverse transcriptase drug resistance mutations over time in drug-naive human immunodeficiency virus type 1-positive individuals in Rio de Janeiro, Brazil. Antimicrob Agents Chemother. 2002;46:3075-9.
137. Brindeiro R, Diaz R, Sabino E, et al. Brazilian Network for HIV Drug Resistance Surveillance (HIV-BResNet): a survey of chronically infected individuals. AIDS. 2003;17:1063-9.
138. Pires I, Soares M, Speranza F, et al. Prevalence of human immunodeficiency virus drug resistance mutations and subtypes in drug-naive, infected individuals in the army health service of Rio de Janeiro, Brazil. J Clin Microbiol. 2004;42:426-30.
139. Escoto-Delgadillo M, Vazquez-Valls E, Ramirez-Rodriguez M, et al. Drug-resistance mutations in antiretroviral-naive patients with established HIV-1 infection in Mexico. HIV Med. 2005;6:403-9.
140. Eyer-Silva W, Morgado M. A genotyping study of human immunodeficiency virus type-1 drug resistance in a small Brazilian municipality. Mem Inst Oswaldo Cruz. 2005;100:869-73.
141. Kantor R, Machekano R, Gonzales M, Dupnik K, Schapiro J, Shafer R. Human Immunodeficiency Virus Reverse Transcriptase and Protease Sequence Database: an expanded data model integrating natural language text and sequence analysis programs. Nucleic Acids Res. 2001;29:296-9.
142. Dieudonne M, Garzaro D, Torres J, et al. High prevalence of secondary resistance mutations in Venezuelan HIV-1 isolates. Invest Clin. 2006;47:27-34.
143. Rodrigues R, Scherer L, Oliveira C, et al. Low prevalence of primary antiretroviral resistance mutations and predominance of HIV-1 clade C at polymerase gene in newly diagnosed individuals from south Brazil. Virus Res. 2006;116:201-7.
144. Barreto C, Nishyia A, Araujo L, Ferreira J, Busch M, Sabino E. Trends in antiretroviral drug resistance and clade distributions among HIV-1-infected blood donors in Sao Paulo, Brazil. J Acquir Immune Defic Syndr. 2006;41:338-41.
145. Lama J, Sanchez J, Suarez L, et al. Linking HIV and antiretroviral drug resistance surveillance in Peru: a model for a third-generation HIV sentinel surveillance. J Acquir Immune Defic Syndr. 2006;42:501-5.
146. Petroni A, Deluchi G, Pryluka D, et al. Update on primary HIV-1 resistance in Argentina: emergence of mutations conferring high-level resistance to nonnucleoside reverse transcriptase inhibitors in drug-naive patients. J Acquir Immune Defic Syndr. 2006;42:506-10.
147. de Medeiros L, Lacerda H, Cavalcanti A, de Albuquerque M. Primary resistance of human immunodeficiency virus type 1 in a reference center in Recife, Pernambuco, Brazil. Mem Inst Oswaldo Cruz. 2006;101:845-9.
148. Maia Teixeira S, Bastos F, Hacker M, Guimaraes M, Morgado M. Trends in drug resistance mutations in antiretroviral-naive intravenous drug users of Rio de Janeiro. J Med Virol. 2006;78:764-9.
149. Valle-Bahena O, Ramos-Jimenez J, Ortiz-Lopez R, et al. Frequency of protease and reverse transcriptase drug resistance mutations in naive HIV-infected patients. Arch Med Res. 2006;37:1022-7.
150. Sa-Ferreira J, Brindeiro P, Chequer-Fernandez S, Tanuri A, Morgado MG. Human immunodeficiency virus-1 subtypes and antiretroviral drug resistance profiles among drug-naive Brazilian blood donors. Transfusion. 2007;47:97-102.
151. Bouchard M, Masquelier B, Moreno M, et al. HIV type 1 drug resistance among naive patients from Venezuela. AIDS Res Hum Retroviruses. 2007;23:482-5.
152. Perez L, Alvarez L, Carmona R, et al. Genotypic resistance to antiretroviral drugs in patients infected with several HIV type 1 genetic forms in Cuba. AIDS Res Hum Retroviruses. 2007;23:407-14.
153. Rios M, Delgado E, Perez-Alvarez L, et al. Antiretroviral drug resistance and phylogenetic diversity of HIV-1 in Chile. J Med Virol. 2007;79:647-56.
154. Gonsalez CR, Alcalde R, Nishiya A, et al. Drug resistance among chronic HIV-1- infected patients naive for use of anti-retroviral therapy in Sao Paulo city. Virus Res. 2007;129:87-90.
155. Rangel H, Garzaro D, Torres J, et al. Prevalence of antiretroviral drug resistance among treatment-naive and treated HIV-infected patients in Venezuela. Mem Inst Oswaldo Cruz. 2009;104:522-5.
156. Sprinz E, Netto E, Patelli M, et al. Primary antiretroviral drug resistance among HIV type 1-infected individuals in Brazil. AIDS Res Hum Retroviruses. 2009;25:861-7.
157. Cardoso L, Queiroz B, Stefani M. HIV-1 pol phylogenetic diversity and antiretroviral resistance mutations in treatment naive patients from Central West Brazil. J Clin Virol. 2009;46:134-9.
158. Fontaine E, Lambert C, Servais J, et al. Fast genotypic detection of drug resistance mutations in the HIV-1 reverse transcriptase gene of treatment-naive patients. J Hum Virol. 1998;1:451-6.
159. Stuyver L, Wyseur A, Rombout A, et al. Line probe assay for rapid detection of drugselected mutations in the human immunodeficiency virus type 1 reverse transcriptase gene. Antimicrob Agents Chemother. 1997;41:284-91.
160. Gomez-Cano M, Rubio A, Puig T, et al. Prevalence of genotypic resistance to nucleoside analogues in antiretroviral-naive and antiretroviral-experienced HIV-infected patients in Spain. AIDS. 1998;12:1015-20.
161. Tambussi G, Boeri E, Carrera P, Gianotti N, Lazzarin A. Prevalence of mutation associated to resistance with nucleoside analogues in a cohort of naive HIV-1 positive subjects during the period 1984-1997. J Biol Regul Homeost Agents. 1998;12:32-4.
162. Schnatz I, Larder B, Mellors J. Mutations in retroviral genes associated with drug resistance. Int Antiviral News. Vol. special issue, 1997.
163. Loveday C, Devereux H, Huckett L, Johnson M. High prevalence of multiple drug resistance mutations in a UK HIV/AIDS patient population. AIDS. 1999;13:627-8.
164. Magiorkinis E, Paraskevis D, Lazanas M, Kiosses V, Gargalianos P, Hatzakis A. Identification of reverse transcriptase mutations associated with HIV-1 drug resistance mainly against non-nucleoside reverse transcriptase inhibitors in treatment-naive patients. AIDS. 1999;13:1276-8.
165. Yerly S, Kaiser L, Race E, Bru J, Clavel F, Perrin L. Transmission of antiretroviral drug-resistant HIV-1 variants. Lancet. 1999;354:729-33.
166. Schinazi R, Larder B, Mellors J. Resistance table: mutations in retroviral genes associated with drug resistance. Int Antiviral News. 1997;5:129-42.
167. Balotta C, Berlusconi A, Pan A, et al. Prevalence of transmitted nucleoside analogue-resistant HIV-1 strains and pre-existing mutations in pol reverse transcriptase and protease region: outcome after treatment in recently infected individuals. Antivir Ther. 2000;5:7-14.

168. Cenci A, Bertoli A, Tambussi G, et al. Viral dynamics and mutations in the pol gene during primary HIV-1 infection. J Biol Regul Homeost Agents. 2000;14:7-10.
169. Barber A, Hizi A, Maizel JV, Hughes S. HIV-1 reverse transcriptase: structure predictions for the polymerase domain. AIDS Res Hum Retroviruses. 1990;6:1061-72.
170. Romano L, Venturi G, Ferruzzi R, et al. Detection of genotypically drug-resistant HIV-1 variants and non-B subtypes in recently infected antiretroviral-naive adults in Italy. AIDS. 2000;14:2204-6.
171. Zazzi M, Riccio M, Venturi G, et al. Long-read direct infrared sequencing of crude PCR products for prediction of resistance to HIV-1 reverse transcriptase and protease inhibitors. Mol Biotechnol. 1998;10:1-8.
172. Puig T, Perez-Olmeda M, Rubio A, et al. Prevalence of genotypic resistance to nucleoside analogues and protease inhibitors in Spain. The ERASE-2 Study Group. AIDS. 2000;14:727-32.
173. Pillay D, Cane P, Shirley J, Porter K. Detection of drug resistance associated mutations in HIV primary infection within the UK. AIDS. 2000;14:906-8.
174. Shafer R, Stevenson D, Chan B. Human Immunodeficiency Virus Reverse Transcriptase and Protease Sequence Database. Nucleic Acids Res. 1999;27:348-52.
175. Perez-Alvarez L, Villahermosa M, Cuevas M, et al. Single- and multidrug resistance mutations to reverse transcriptase and protease inhibitors: human immunodeficiency virus type 1-infected patients from two geographical areas in Spain. Spanish Groups for Antiretroviral Resistance Studies. J Hum Virol. 2000;3:150-6.
176. Van Vaerenbergh K, Debaisieux L, De Cabooter N, et al. Prevalence of genotypic resistance among antiretroviral drug-naive HIV-1-infected patients in Belgium. Antivir Ther. 2001;6:63-70.
177. Tamalet C, Pasquier C, Yahi N, et al. Prevalence of drug resistant mutants and virological response to combination therapy in patients with primary HIV-1 infection. J Med Virol. 2000;61:181-6.
178. Perez-Olmeda M, Del Romero J, Rubio A, et al. Primary HIV-1 drug resistance in Spain before and after the introduction of protease inhibitors. J Med Virol. 2001;63:85-7.
179. de Ronde A, van Dooren M, van der Hoek L, et al. Establishment of new transmissible and drug-sensitive human immunodeficiency virus type 1 wild types due to transmission of nucleoside analogue-resistant virus. J Virol. 2001;75:595-602.
180. Duwe S, Brunn M, Altmann D, et al. Frequency of genotypic and phenotypic drug-resistant HIV-1 among therapy-naive patients of the German Seroconverter Study. J Acquir Immune Defic Syndr. 2001;26: 266-73.
181. Re M, Monari P, Borderi M, et al. Presence of genotypic resistance to antiretroviral drugs in a cohort of therapy-naive HIV-1-infected Italian patients. J Acquir Immune Defic Syndr. 2001;27:315-16.
182. UK Collaborative Group on Monitoring the Transmission of HIV Drug Resistance. Analysis of prevalence of HIV-1 drug resistance in primary infections in the United Kingdom. BMJ. 2001;322:1087-8.
183. Geretti A, Smith M, Osner N, et al. Prevalence of antiretroviral resistance in a South London cohort of treatment-naive HIV-1-infected patients. AIDS. 2001;15:1082-4.
184. Descamps D, Calvez V, Izopet J, et al. Prevalence of resistance mutations in antiretroviral-naive chronically HIV-infected patients in 1998: a French nationwide study. AIDS. 2001;15:1777-82.
185. Gallego O, Ruiz L, Vallejo A, et al. Changes in the rate of genotypic resistance to antiretroviral drugs in Spain. AIDS. 2001;15:1894-6.
186. Yerly S, Vora S, Rizzardi P, et al. Acute HIV infection: impact on the spread of HIV and transmission of drug resistance. AIDS. 2001;15: 2287-92.
187. Schinazi R, Larder BA, Mellors J. Resistance table: mutations in retroviral genes associated with drug resistance: 2000-2001 update. Int Antiviral News. 2000;8:65-91.
188. Fidler S, Frater J, Clarke J, Weber J. HIV-1 drug resistance in primary infections in the UK. BMJ. 2001;323:632-3.
189. Clevenbergh P, Cua E, Dam E, et al. Prevalence of nonnucleoside reverse transcriptase inhibitor (NNRTI) resistance-associated mutations and polymorphisms in NNRTI-naive HIV-infected patients. HIV Clin Trials. 2002;3:36-44.
190. Violin M, Forbici F, Cozzi-Lepri A, et al. Primary HIV-1 resistance in recently and chronically infected individuals of the Italian Cohort Naive for Antiretrovirals. J Biol Regul Homeost Agents. 2002;16:37-43.
191. Magiorkinis E, Paraskevis D, Magiorkinis G, et al. Mutations associated with genotypic resistance to antiretroviral therapy in treatment naive HIV-1 infected patients in Greece. Virus Res. 2002;85:109-15.
192. Hertogs K, Bloor S, De Vroey V, et al. A novel human immunodeficiency virus type 1 reverse transcriptase mutational pattern confers phenotypic lamivudine resistance in the absence of mutation 184V. Antimicrob Agents Chemother. 2000;44:568-73.
193. Easterbrook P, Hertogs K, Waters A, Wills B, Gazzard B, Larder B. Low prevalence of antiretroviral drug resistance among HIV-1 seroconverters in London, 1984-1991. J Infect. 2002;44:88-91.
194. Eiros J, Labayru C, Hernandez B, Ortega M, Bachiller P, Ortiz de Lejarazu R. Prevalence of genotypic resistance in untreated HIV patients in Spain. Eur J Clin Microbiol Infect Dis. 2002;21:310-13.
195. Harzic M, Pellegrin I, Deveau C, et al. Genotypic drug resistance during HIV-1 primary infection in France (1996-1999): frequency and response to treatment. AIDS. 2002;16:793-6.
196. Delfraissy JF. Prise en charge thérapeutique des personnes infectées par le VIH 2000. Paris: Médicine - Sciences, Flammarion 2000:17-28.
197. de Mendoza C, del Romero J, Rodriguez C, Corral A, Soriano V. Decline in the rate of genotypic resistance to antiretroviral drugs in recent HIV seroconverters in Madrid. AIDS. 2002;16:1830-2.
198. Antiretroviral Resistance Mutations (revised April 2001). HIV Clin Trials. 2001;2:346-55.
199. Geretti A, Smith M, Watson C, et al. Primary antiretroviral resistance in newly diagnosed patients with established heterosexually acquired HIV-1. AIDS. 2002;16:2358-60.
200. Gallego O, Corral A, De Mendoza C, Gonzalez-Lahoz J, Soriano V. High rate of resistance to antiretroviral drugs among HIV-infected prison inmates. Med Sci Monit. 2003;9:CR217-21.
201. Maljkovic I, Wilbe K, Solver E, Alaeus A, Leitner T. Limited transmission of drug-resistant HIV type 1 in 100 Swedish newly detected and drug-naive patients infected with subtypes A, B, C, D, G, U, and CRF01_AE. AIDS Res Hum Retroviruses. 2003;19:989-97.
202. Chaix M, Descamps D, Harzic M, et al. Stable prevalence of genotypic drug resistance mutations but increase in non-B virus among patients with primary HIV-1 infection in France. AIDS. 2003;17:2635-43.
203. Jorgensen L, Christensen M, Gerstoft J, et al. Prevalence of drug resistance mutations and non-B subtypes in newly diagnosed HIV-1 patients in Denmark. Scand J Infect Dis. 2003;35:800-7.
204. Re M, Monari P, Bon I, Borderi M, Chiodo F. Conflicting interpretations of the prevalence of mutations associated with drug resistance in antiviral naive HIV-1 patients with acute and chronic infection. Int J Antimicrob Agents. 2004;23:164-8.
205. Perez-Alvarez L, Carmona R, Munoz M, et al. High incidence of non-B and recombinant HIV-1 strains in newly diagnosed patients in Galicia, Spain: study of genotypic resistance. Antivir Ther. 2003;8:355-60.
206. Violin M, Velleca R, Cozzi-Lepri A, et al. Prevalence of HIV-1 primary drug resistance in seroconverters of the ICoNA cohort over the period 1996-2001. J Acquir Immune Defic Syndr. 2004;36:761-4.
207. Derdelinckx I, Van Laethem K, Maes B, et al. Current levels of drug resistance among therapy-naive HIV-infected patients have significant impact on treatment response. J Acquir Immune Defic Syndr. 2004;37:1664-6.
208. Yerly S, Jost S, Telenti A, et al. Infrequent transmission of HIV-1 drug-resistant variants. Antivir Ther. 2004;9:375-84.
209. Bezemer D, Jurriaans S, Prins M, et al. Declining trend in transmission of drug-resistant HIV-1 in Amsterdam. AIDS. 2004;18:1571-7.
210. Oette M, Kaiser R, Daumer M, et al. Primary drug-resistance in HIV-positive patients on initiation of first-line antiretroviral therapy in Germany. Eur J Med Res. 2004;9:273-8.
211. Roudinskii N, Sukhanova A, Kazennova E, et al. Diversity of human immunodeficiency virus type 1 subtype A and CRF03_AB protease in Eastern Europe: selection of the V77I variant and its rapid spread in injecting drug user populations. J Virol. 2004;78:11276-87.
212. Eiros J, Blanco R, Labayru C, et al. Prevalence of genotypic resistance in untreated HIV-infected patients. Rev Esp Quimioter. 2004;17:250-6.
213. Filippini P, Liguori G, Scolastico C, et al. Prevalence of genotypic resistance to nucleoside analogues and protease inhibitors in antiretroviral-naive HIV patients in Campania, Italy. J Chemother. 2004;16:534-9.
214. Clarke J, Kaye S, Babiker A, Hooker M, Tedder R, Weber J. Comparison of a point mutation assay with a line probe assay for the detection of the major mutations in the HIV-1 reverse transcriptase gene associated with reduced susceptibility to nucleoside analogues. J Virol Methods. 2000;88:117-24.
215. Grossman Z, Lorber M, Maayan S, et al. Drug-resistant HIV infection among drug-naive patients in Israel. Clin Infect Dis. 2005;40:294-302.
216. Vazquez de Parga E, Rakhmanova A, Perez-Alvarez L, et al. Analysis of drug resistance-associated mutations in treatment-naive individuals infected with different genetic forms of HIV-1 circulating in countries of the former Soviet Union. J Med Virol. 2005;77:337-44.
217. Paraskevis D, Magiorkinis E, Katsoulidou A, et al. Prevalence of resistance-associated mutations in newly diagnosed HIV-1 patients in Greece. Virus Res. 2005;112:115-22.
218. Johnson V, Brun-Vezinet F, Clotet B, et al. Update of the drug resistance mutations in HIV-1: 2004. Top HIV Med. 2004;12:119-24.
219. Descamps D, Chaix M, Andre P, et al. French national sentinel survey of antiretroviral drug resistance in patients with HIV-1 primary infection and in antiretroviral-naive chronically infected patients in 2001-2002. J Acquir Immune Defic Syndr. 2005;38:545-52.
220. de Mendoza C, Rodriguez C, Colomina J, et al. Resistance to nonnucleoside reverse transcriptase inhibitors and prevalence of HIV type 1 non-B subtypes are increasing among persons with recent infection in Spain. Clin Infect Dis. 2005;41:1350-4.
221. Masquelier B, Bhaskaran K, Pillay D, et al. Prevalence of transmitted HIV-1 drug resistance and the role of resistance algorithms: data from seroconverters in the CASCADE collaboration from 1987 to 2003. J Acquir Immune Defic Syndr. 2005;40:505-11.

222. Corvasce S, Violin M, Romano L, et al. Evidence of differential selection of HIV-1 variants carrying drug-resistant mutations in seroconverters. Antivir Ther. 2006;11:329-34.
223. Oette M, Kaiser R, Daumer M, et al. Primary HIV drug resistance and efficacy of firstline antiretroviral therapy guided by resistance testing. J Acquir Immune Defic Syndr. 2006;41:573-81.
224. Zarandia M, Tsertsvadze T, Carr J, Nadai Y, Sanchez J, Nelson A. HIV-1 genetic diversity and genotypic drug susceptibility in the Republic of Georgia. AIDS Res Hum Retroviruses. 2006;22:470-6.
225. Fox J, Dustan S, McClure M, Weber J, Fidler S. Transmitted drug-resistant HIV-1 in primary HIV-1 infection; incidence, evolution and impact on response to antiretroviral therapy. HIV Med. 2006;7:477-83.
226. Lindstrom A, Ohlis A, Huigen M, et al. HIV-1 transmission cluster with M41L 'singleton' mutation and decreased transmission of resistance in newly diagnosed Swedish homosexual men. Antivir Ther. 2006;11: 1031-9.
227. Garcia-Guerrero J, Saiz de la HP, Portilla J, Marco A, Sanchez-Paya J, Moreno S. Prevalence of HIV-1 drug resistance mutations among Spanish prison inmates. Eur J Clin Microbiol Infect Dis. 2006;25:695-701.
228. Babic D, Zelnikar M, Seme K, et al. Prevalence of antiretroviral drug resistance mutations and HIV-1 non-B subtypes in newly diagnosed drug-naive patients in Slovenia, 2000-2004. Virus Res. 2006;118:156-63.
229. Palma A, Araujo F, Duque V, Borges F, Paixao M, Camacho R. Molecular epidemiology and prevalence of drug resistance-associated mutations in newly diagnosed HIV-1 patients in Portugal. Infect Genet Evol. 2007;7:391-8.
230. Bon I, Gibellini D, Borderi M, et al. Genotypic resistance in plasma and peripheral blood lymphocytes in a group of naive HIV-1 patients. J Clin Virol. 2007;38:313-20.
231. UK Collaborative Group on HIV Drug Resistance; UK Collaborative HIV Cohort Study; UK Register of HIV Seroconverters. Evidence of a decline in transmitted HIV-1 drug resistance in the United Kingdom. AIDS. 2007;21:1035-9.
232. Poggensee G, Kucherer C, Werning J, et al. Impact of transmission of drug-resistant HIV on the course of infection and the treatment success. Data from the German HIV-1 Seroconverter Study. HIV Med. 2007;8:511-19.
233. Yerly S, von WV, Ledergerber B, et al. Transmission of HIV-1 drug resistance in Switzerland: a 10-year molecular epidemiology survey. AIDS. 2007;21:2223-9.
234. Sagir A, Oette M, Kaiser R, et al. Trends of prevalence of primary HIV drug resistance in Germany. J Antimicrob Chemother. 2007;60:843-8.
235. Vercauteren J, Derdelinckx I, Sasse A, et al. Prevalence and epidemiology of HIV type 1 drug resistance among newly diagnosed therapy-naive patients in Belgium from 2003 to 2006. AIDS Res Hum Retroviruses. 2008;24:355-62.
236. Bannister W, Cozzi-Lepri A, Clotet B, et al. Transmitted drug resistant HIV-1 and association with virologic and CD4 cell count response to combination antiretroviral therapy in the EuroSIDA Study. J Acquir Immune Defic Syndr. 2008;48:324-33.
237. Payne B, Nsutebu E, Hunter E, et al. Low prevalence of transmitted antiretroviral drug resistance in a large UK HIV-1 cohort. J Antimicrob Chemother. 2008;62:464-8.
238. Street E, Armstrong N, Monteiro E, Hale A. An audit of baseline HIV-1 genotypic resistance testing in a UK provincial city. Int J STD AIDS. 2008;19:416-17.
239. Kousiappa I, van de Vijver D, Demetriades I, Kostrikis L. Genetic analysis of HIV type 1 strains from newly infected untreated patients in Cyprus: high genetic diversity and low prevalence of drug resistance. AIDS Res Hum Retroviruses. 2009;25:23-35.
240. Shafer R. Rationale and uses of a public HIV drug-resistance database. J Infect Dis. 2006;194(Suppl 1):S51-8.
241. Cuevas M, Munoz-Nieto M, Thomson M, et al. HIV-1 transmission cluster with T215D revertant mutation among newly diagnosed patients from the Basque Country, Spain. J Acquir Immune Defic Syndr. 2009;51:99-103.
242. Avi R, Huik K, Sadam M, et al. Absence of genotypic drug resistance and presence of several naturally occurring polymorphisms of human immunodeficiency virus-1 CRF06_cpx in treatment-naive patients in Estonia. J Med Virol. 2009;81:953-8.
243. Yerly S, Junier T, Gayet-Ageron A, et al. The impact of transmission clusters on primary drug resistance in newly diagnosed HIV-1 infection. AIDS. 2009;23:1415-23.
244. Alteri C, Svicher V, Gori C, et al. Characterization of the patterns of drug resistance mutations in newly diagnosed HIV-1 infected patients naive to the antiretroviral drugs. BMC Infect Dis. 2009;9:111.
245. Bracciale L, Colafigli M, Zazzi M, et al. Prevalence of transmitted HIV-1 drug resistance in HIV-1-infected patients in Italy: evolution over 12 years and predictors. J Antimicrob Chemother 2009;64:607-15.
246. Bennett D, Camacho R, Otelea D, et al. Drug resistance mutations for surveillance of transmitted HIV-1 drug-resistance: 2009 update. PLoS One. 2009;4:e4724.
247. Rumyantseva O, Olkhovskiy I, Malysheva M, et al. Epidemiological networks and drug resistance of HIV type 1 in Krasnoyarsk Region, Russia. AIDS Res Hum Retroviruses 2009;25:931-6.
248. Sugiura W, Matsuda M, Abumi H, et al. Prevalence of drug resistance-related mutations among HIV-1 in Japan. Jpn J Infect Dis. 1999;52:21-2.
249. Jennifer H, Brendan A, Raymond F, John W. Mutations in retroviral genes associated with drug resistance. Hum Retrovir AIDS. 1997;III:207-49.
250. Auswinporn S, Jenwitheesuk E, Panburana P, Sirinavin S, Vibhagool A, Chantratita W. Prevalence of HIV-1 drug resistance in antiretroviral-naive pregnant Thai women. Southeast Asian J Trop Med Public Health. 2002;33:818-21.
251. Park S, Kim H, Choi Y, Kim N, Oh M, Choe K. Genotypic resistance of antiretroviral drugs among drug-naive HIV type 1 patients with the background of long-term access-easy zidovudine therapy. AIDS Res Hum Retroviruses. 2003;19:1039-43.
252. Lan N, Recordon-Pinson P, Hung P, et al. HIV type 1 isolates from 200 untreated individuals in Ho Chi Minh City (Vietnam): ANRS 1257 Study. Large predominance of CRF01_AE and presence of major resistance mutations to antiretroviral drugs. AIDS Res Hum Retroviruses. 2003;19:925-8.
253. Ibe S, Hotta N, Takeo U, et al. Prevalence of drug-resistant human immunodeficiency virus type 1 in therapy-naive patients and usefulness of genotype testing. Microbiol Immunol. 2003;47:499-505.
254. Deshpande A, Recordon-Pinson P, Deshmukh R, et al. Molecular characterization of HIV type 1 isolates from untreated patients of Mumbai (Bombay), India, and detection of rare resistance mutations. AIDS Res Hum Retroviruses. 2004;20:1032-5.
255. Ly N, Recordon-Pinson P, Phoung V, et al. Characterization of mutations in HIV type 1 isolates from 144 Cambodian recently infected patients and pregnant women naive to antiretroviral drugs. AIDS Res Hum Retroviruses. 2005;21:971-6.
256. Gatanaga H, Ibe S, Matsuda M, et al. Drug-resistant HIV-1 prevalence in patients newly diagnosed with HIV/AIDS in Japan. Antiviral Res. 2007;75:75-82.
257. Tee K, Kamarulzaman A, Ng K. Short communication: low prevalence of genotypic drug resistance mutations among antiretroviral-naive HIV type 1 patients in Malaysia. AIDS Res Hum Retroviruses. 2006;22:121-4.
258. Yam W, Chen J, Wong K, et al. Clinical utility of genotyping resistance test on determining the mutation patterns in HIV-1 CRF01_AE and subtype B patients receiving antiretroviral therapy in Hong Kong. J Clin Virol. 2006;35:454-7.
259. Jiang S, Xing H, Si X, Wang Y, Shao Y. Polymorphism of the protease and reverse transcriptase and drug resistance mutation patterns of HIV-1 subtype B prevailing in China. J Acquir Immune Defic Syndr. 2006;42:512-14.
260. Han X, Zhang M, Dai D, et al. genotypic resistance mutations to antiretroviral drugs in treatment-naive HIV/AIDS patients living in Liaoning Province, China: Baseline prevalence and subtype-specific difference. AIDS Res Hum Retroviruses. 2007;23:357-64.
261. Zhang X, Li S, Li X, et al. Characterization of HIV-1 subtypes and viral antiretroviral drug resistance in men who have sex with men in Beijing, China. AIDS. 2007;21(Suppl 8):S59-65.
262. Kojima Y, Kawahata T, Mori H, Oishi I, Otake T. Recent diversity of human immunodeficiency virus type 1 in individuals who visited sexually transmitted infection related clinics in Osaka, Japan. J Infect Chemother. 2008;14:51-5.
263. Apisarnthanarak A, Jirayasethpong T, Sa-nguansilp C, et al. Antiretroviral drug resistance among antiretroviral-naive persons with recent HIV infection in Thailand. HIV Med. 2008;9:322-5.
264. Sukasem C, Churdboonchart V, Sukeepaisarncharoen W, et al. Genotypic resistance profiles in antiretroviral-naive HIV-1 infections before and after initiation of first-line HAART: impact of polymorphism on resistance to therapy. Int J Antimicrob Agents 2008;31:277-81.
265. Sirivichayakul S, Phanuphak P, Pankam T, O-Charoen R, Sutherland D, Ruxrungtham K. HIV drug resistance transmission threshold survey in Bangkok, Thailand. Antivir Ther. 2008;13(Suppl 2):109-13.
266. Nguyen H, Duc N, Shrivastava R, et al. HIV drug resistance threshold survey using specimens from voluntary counselling and testing sites in Hanoi, Vietnam. Antivir Ther. 2008;13(Suppl 2):115-21.
267. Janin N, Sopheak N, Regis MP, et al. Low prevalence of drug resistance transmitted virus in HIV Type 1-infected ARV-naive patients in Cambodia. AIDS Res Hum Retroviruses. 2009;25:543-5.
268. Lee C, Sun Y, Barkham T, Leo Y. Primary drug resistance and transmission analysis of HIV-1 in acute and recent drug-naive seroconverters in Singapore. HIV Med. 2009;10:370-7.
269. Yu G, Li Y, Li J, et al. Genetic diversity and drug resistance of HIV type 1 circulating recombinant Form_BC among drug users in Guangdong Province. AIDS Res Hum Retroviruses. 2009;25:869-75.
270. Iqbal H, Solomon S, Madhavan V, Solomon S, Balakrishnan P. Primary HIV-1 Drug Resistance and Polymorphic Patterns Among Injecting Drug Users (IDUs) in Chennai, Southern India. J Int Assoc Physicians AIDS Care (Chic). 2009;8:323-7.
271. Ammaranond P, Cunningham P, Oelrichs R, et al. No increase in protease resistance and a decrease in reverse transcriptase resistance mutations in primary HIV-1 infection: 1992-2001. AIDS. 2003;17:264-7.

# Temporal Changes in the Epidemiology of Transmission of Drug-Resistant HIV-1 across the World

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**Table 1. Summary of studies on transmitted drug resistance per continent**

| Africa | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ref. | Region | Methodology | Years of sampling | (n) | HIV risk factor (%) | | | Resistance prevalence (%) | | | | | Population | | Sampling of patients |
| | | | | | MSM | IVDU | HSX | Any | NRTI | NNRTI | PI | MDR | Recent (time to infection) | Newly diagnosed | |
| [35] | Africa | Stanford HIVdb | 1995-1999 | 142 | | | | 3.5 | 0 | 3.5 | 0 | 0 | | | From hospital |
| [36] | Gabon | Stanford HIVdb 2001 | 2000 | 13 | | | | 0 | 0 | 0 | 0 | 0 | | | serosurveillance study |
| [37] | Cote d'Ivoire | Not reported | 1997-2000 | 99 | | | | 0 | 0 | 0 | 0 | 0 | 99 (<3 years) | | Blood donors |
| [38] | Cameroon | Not reported | 1998 | 110 | | | | | | | 1.8 | | | | Individuals attending a (military) hospital |
| [39] | South Africa | Not reported | 2000 | 37 | | | | 0 | 0 | 0 | 0 | 0 | | | Drug-naive pregnant woman enrolled in study to prevent MTCT |
| [40] | Cote d'Ivoire | IAS and ANRS, version not reported | 2001-2002 | 107 | | | 100 | 5.6 | 0.9 | 3.7 | 0.9 | 0 | | | Blood donors and pregnant from a MTCT prevention study |
| [41] | South-Africa | Stanford HIVdb | 2001 | 72 | | | | 5.4 | 0 | 5.4 | 0 | 0 | | | Representing patients attending clinics |
| [42] | Zambia | Stanford HIVdb, IAS 1998[43] | 2000 | 28 | | | 100 | 0 | 0 | 0 | 0.0 | 0 | | | Pregnant woman |
| [44] | Senegal | Stanford HIVdb | 1998-2001 | 41 | | | | 0 | 0 | 0 | 0 | 0 | | | Patients enrolled for ARV therapy |
| [45] | Cote d'Ivoire | IAS 1998[43] | Unreported | 20 | | | | 0 | 0 | 0 | 0 | 0 | | | Patients enrolled for ARV therapy |
| [46] | Cameroon | Birk 1998[47] | Unreported | 128 | | | | | | | 0 | | | | HIV-1 infected patients from 6 provinces |
| [48] | South Africa | Stanford HIVdb | 2001 | 14 | 0 | 0 | 100 | 0 | 0 | 0 | 0 | 0 | | | HIV infected outpatients at a clinic |
| [49] | Botswana | Shafer[50] | 2001 | 70 | | | | 0 | 0 | 0 | 0 | 0 | | | HIV-1 infected patients from 11 health districts |
| [51] | Mozambique | Stanford HIVdb | 2003 | 58 | | | | 0 | 0 | 0 | 0 | 0 | | | HIV patients visiting hospitals and enrolled for a therapy program |
| [52] | Malawi | Stanford HIVdb | 1996-2001 | 21 | | | | 0 | 0 | 0 | 0 | 0 | | | Patients attending to hospitals and woman participating in a breast-milk study |
| [53] | Djibouti | IAS 2005[54] | 2002 | 47 | | | | 21.3 | 2.1 | 14.9 | 6.4 | 2.1 | | | Patients randomly selected for HIV test |
| [55] | Cameroon | IAS 2005[54] | 2004 | 54 | | | | 13.0 | 3.9 | 5.9 | 7.4 | 3.7 | | | Patients attending clinics |
| [23] | Nigeria | Not reported | 2005 | 18 | | | | 0 | 0 | 0 | 0 | 0 | | | Patients enrolled for a therapy program |
| [56] | From 7 countries in Africa | ANRS Sept. 2004, Stanford 2005, Rega version 6.2 | 1996-2003 | 35 | | | | 11.4 | 0 | 11.4 | 0 | 0 | | | Patients attending hospitals |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Africa | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ref. | Region | Methodology | Years of sampling | (n) | HIV risk factor (%) | | | Resistance prevalence (%) | | | | | Population | | Sampling of patients |
| | | | | | MSM | IVDU | HSX | Any | NRTI | NNRTI | PI | MDR | Recent (time to infection) | Newly diagnosed | |
| [57] | Democratic Republic of Congo | Stanford HIVdb | 2002 | 70 | | | | 4.3 | 0 | 1.4 | 2.9 | 0 | | | Patients from a sentinel population groups |
| [58] | Cameroon | ANRS Sept. 2005 | 2001-2004 | 96 | | | | 2.1 | 1 | 0 | 1 | 0 | | | Pregnant woman |
| [59] | Burkina Faso | Stanford HIVdb | 2003-2004 | 38 | | | | 5,3 | 0 | 5,3 | 0 | 0 | | | Pregnant woman and other HIV positive patients attending the hospital |
| [5] | Cameroon | IAS, version not reported | 2001-2002 | 102 | | | | 7.8 | 2.9 | 2.0 | 2.9 | 0 | | | Patients attending hospitals and treatment centers |
| [60] | Nigeria | Stanford HIVdb | Unreported | RT: 35<br>PR: 43 | | | | 17.1 | 8.6 | 11.4 | 0 | 2.8 | | | Patients enrolled for a treatment program |
| [61] | Burkina Faso | Stanford HIVdb | 2003-2004 | 17 | | | | 0 | 0 | 0 | 0 | 0 | | | Patients from a HIV centre |
| [5] | Burkina Faso | IAS, version not reported | 2003 | 97 | | | | 8.3 | 2.1 | 4.1 | 2.1 | 0 | | | Patients attending hospitals and treatment centers |
| [62] | Madagascar | ANRS Sept. 2005 | 2005 | 28 | | | | 3.6 | 0 | 0 | 3.6 | 0 | | | HIV surveillance in sex workers, STD patients and pregnant women |
| [63] | Central African Republic (CAR) | IAS fall 2005[64], ANRS Sept. 2005 | 2005 | 53 | | | | 0 | 0 | 0 | 0 | 0 | | | PMTCT program |
| [65] | South Africa | Stanford HIVdb Algorithm | 2001-2004 | 40 | | | | 5.0 | 0 | 0 | 5.0 | 0 | | | HIV patients attending a clinic |
| [66] | Mozambique | IAS 2005[54] | 2003 | 43 | | | | 14.0 | 4.7 | 7.0 | 2.3 | 0 | | | Patients attending clinics |
| [67] | Burundi | IAS 2005[54], ANRS 2005. 7, Stanford db 4.1.7, Rega 6.4.1 | 2002 | 101 | | | | 1.0 | 0 | 1.0 | 0 | 0 | | | HIV sero-surveillance study with samples from sentinel population groups in four major cities |
| [68] | Mali | IAS fall 2005[64] | 2005 | 98 | | | 100 | 2 | 1 | 1 | 0 | 0 | | | Patients attending a clinic |
| [69] | Cote d'Ivoire | IAS fall 2006[31] | 2002-2006 | 100 | | | | 6.0 | 3.0 | 2.0 | 1.0 | 0 | | | Blood donors |
| [70] | Uganda and Rwanda | Not reported | Unreported | 97 | | | | 7.2 | 4.1 | 3.1 | 0 | 0 | | | Plasma samples from pregnant women at week 36 of gestational age |
| [71] | Cameroon | IAS fall 2006[31] | 2004 | 79 | | | | 13.9 | 7.6 | 8.8 | 2.6 | 5.1 | | | Patients attending clinics |
| [72] | Swaziland | IAS fall 2006[31] | 2002-2003 | 47 | | | | 2.1 | 0 | 2.1 | 0 | 0 | | | Randomly chosen plasma samples from HIV patients |
| [73] | Uganda | IAS 2007[74] | 2006-2007 | 46 | | | | 0 | 0 | 0 | 0 | 0 | | 46 | Patients attending a clinic |
| [75] | Tanzania | Shafer 2007[32] | 2005-2006 | 39 | | | | 0 | 0 | 0 | 0 | 0 | | | Surveillance among pregnant women |
| [76] | South Africa | Shafer 2007[32] | 2002 | 65 | | | | 0 | 0 | 0 | 0 | 0 | | | Young women with first pregnancy |
| | | | 2004 | 48 | | | | 4.2 | 4.2 | 0 | 0 | 0 | | | |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

**Africa**

| Ref. | Region | Methodology | Years of sampling | (n) | HIV risk factor (%) | | | Resistance prevalence (%) | | | | | Population | | Sampling of patients |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | MSM | IVDU | HSX | Any | NRTI | NNRTI | PI | MDR | Recent (time to infection) | Newly diagnosed | |
| [77] | Malawi | Shafer 2007[32] | 2006 | 34 | | | | 0 | 0 | 0 | 0 | 0 | | | PMTCT patients program |
| [78] | Ethiopia | Shafer 2007[32] | 2005 | 39 | | | | 0 | 0 | 0 | 0 | 0 | | | Pregnant women in surveillance study |
| [79] | Swaziland | WHO list | 2006 | 34 | | | | 0 | 0 | 0 | 0 | 0 | | | Young women with first pregnancy |
| [80] | Mozambique | Shafer 2007[32] and Shafer 2008[81] | 2002-2004 | 104 | | | | 3.8 | 3.8 | 1.0 | 0 | 1.0 | | | HIV-1 patients attending hospitals and clinics |
| [82] | Angola | Shafer 2008[81] and 2007[32] | 2001 | 122 | 4 | | 70 | 1.6 | 1.6 | 0.8 | 0 | 0.8 | | | HIV patients naive for ARV therapy |
| [83] | Uganda | Shafer 2007[32] | 1998-2003 | 104 | | | | 5.8 | 2.9 | 0 | 2.9 | 0 | | | Annual testing of individuals in a longitudinal study |
| [84] | Burkina Faso | Stanford HIVdb and IAS 2008[85] | 2004-2006 | 104 | | | | 12.5 | 10.6 | 6.1 | 0 | 3.8 | | | Patients attending a HIV hospital |
| [86] | Central Africa | Shafer 2007[32] | 2006-2007 | 102 | | | | | | | | | | | HIV infected woman with first |
| | | | | 34 | | | | 0 | 0 | 0 | 0 | 0 | | | pregnancy < 25 years |
| | | | | 34 | | | | 5.9 | 2.9 | 2.9 | 0 | 0 | | | |
| | | | | 34 | | | | 8.8 | 5.9 | 2.9 | 0 | 0 | | | |

**North America**

| Ref. | Region | Methodology | Years of sampling | (n) | HIV risk factor (%) | | | Resistance prevalence (%) | | | | | Population | | | Sampling of patients |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | MSM | IVDU | HSX | Any | NRTI | NNRTI | PI | MDR | Recent (time to seroconversion) | Recent (time between neg. and pos. test) | Chronic (time to diagnosis) | |
| [87] | USA | IAS 1998[43] | 1997-1998 | 31 | 50 | | 50 | 25.8 | 6.5 | 12.9 | 16.1 | 6.5 | 31 (< 3 years) | | | HIV patients assigned to a military bases |
| [88] | Canada | IAS 1998[43] | 1996-1998 | 57 | | 100 | | 0 | 0 | 0 | 0 | 0 | 57 (< 15 months) | | | Injection drug users infected with HIV |
| [89] | USA | VircoGEN interpretation software | 1997-1998 | 95 | | | | 22.1 | 4.2 | 14.7 | 10.5 | 3.2 | 54 (< 1 year), 37 (< 2 years), 6 (2-3 years) | | | Military personnel with HIV infection |
| [90] | USA | IAS 1998[43] | 1993-1998 | 99 | 26 | 3 | 71 | 7.1 | 6.1 | 2.0 | 1.0 | 2.0 | | 99 (< 2 years) | | HIV patients attending public STD clinics |
| [91] | USA | IAS 1998[43] | 1997-1998 | 458 | | | | 6.3 | | | 3.8 | | | | | Naive HIV patients attending the HIV/AIDS Centre |
| [92] | USA | Not reported | 1998-1999 | 199 | 74 | 3 | 15 | | 14 | 16 | 3 | | (< 3 years) | (< 3 years) | | Prospective study with ARV-naive patients |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| North America | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ref. | Region | Methodology | Years of sampling | (n) | HIV risk factor (%) | | | Resistance prevalence (%) | | | | | Population | | | Sampling of patients |
| | | | | | MSM | IVDU | HSX | Any | NRTI | NNRTI | PI | MDR | Recent (time to seroconversion) | Recent (time between neg. and pos. test) | Chronic (time to diagnosis) | |
| [93] | USA | Visible Genetic software | 1999 | 44 | 34 | 7 | 55 | 11 | 4.5 | 4.5 | 2.3 | 0 | | | 44 | HIV patients who planned to initiate ARV therapy in a HIV clinic |
| [94] | USA | Hirsch 2000[95] | 1996-2001 | 62 | 41.9 | 4.8 | 53.2 | 12.9 | 8.1 | 3.2 | 3.2 | 1.6 | | | 62 (> 6 months and < 5 years) | Drug-naive patients attending a outpatients clinic |
| [8] | USA | IAS 2001[96] | 1996-1997 | 40 | 80 | | | 25.0 | 25.0 | 0 | 2.5 | 2.5 | (0) | (< 12 months) | | Patients recruited through physicians, HIV-1 testing and counseling sites, community health centers, and self-referral |
| | | | 1998-1999 | 94 | 86 | | | 18.1 | 7.4 | 6.4 | 5.3 | 1.1 | | | | |
| | | | 2000-2001 | 91 | 89 | | | 27.4 | 20.9 | 13.2 | 7.7 | 14.3 | | | | |
| [97] | USA | IAS 2000[95] | 1995-1998 | 213 | | | | 8 | 8.5 | 1.7 | 0.9 | 3.8 | (< 12 months) | (< 12 months) | | Subjects with signs or symptoms of an acute HIV infection |
| | | | 1999-2000 | 88 | | | | 22.7 | 15.9 | 7.3 | 9.1 | 10.2 | | | | |
| [98] | USA | IAS 2000[95] | 1997-1999 | 69 | 84 | 3 | 6 | 4.3 | 1.4 | 2.9 | 0 | 0 | | 58 (< 2 years) | | Recently infected recruited from different clinics, private practitioners and by advertisement |
| [99] | USA | Hanna 1999[100] | 2000-2001 | 20 | | | | 5.0 | 5.0 | 0 | 5.0 | 5.0 | | | 20 | Voluntary testing in a prison |
| [101] | USA | IAS 2002[96] | 2000-2001 | 18 | | | | 17 | 0 | 17 | 0 | 0 | | | 18 | HIV-positive pregnant women at a university hospital |
| [102] | USA | Hanna 1999[100] and IAS 2000[95] | 1999 | 88 | 20 | 51 | 31 | 18.2 | 13.6 | 4.6 | 3.4 | 2.3 | 1 (< 6 months) | | 87 (> 6 months) | HIV-infected patients newly presenting for HIV care in a hospital |
| [103] | USA | IAS 2002[96] | 1997-2001 | 1082 | 44.5 | 10.2 | 45.3 | 8.3 | 6.4 | 1.7 | 1.9 | 1.3 | 182 (< 170 days) | | 767 (< 12 months) | Patients consecutively enrolled from HIV care clinics, HIV counseling and testing sites, and other clinical settings |
| [104] | USA | IAS 2000[95] | 1996-2000 | 152 | 64.6 | 33.1 | 35.5 | 13.8 | 2.6 | 7.1 | 4.9 | | | | | Homeless and marginally housed persons from major lunch lines and shelters and low-rent residence hotels |
| [105] | Canada | IAS 2003[106] | 1997-2003 | 305 | 54 | 34 | 12 | 19.3 | 14.8 | 7.2 | 4.6 | | 305 (< 6 months) | | | HIV-infected persons from a Montreal cohort |
| [107] | USA | IAS 2003[108] | 1999-2001 | 491 | 56 | 15 | | 11.6 | 7.8 | 3.0 | 0.7 | 0.7 | | | | Demographically diverse treatment-naive subjects from 18 encompassing 25 US communities |
| [109] | USA | IAS 2005[54] | 1991-2001 | 128 | | | | 8.6 | 8.6 | 1.6 | 1.6 | 1.6 | | | 128 | Pregnant women infected with HIV |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| North America | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Recent (time between neg. and pos. test)** | **Chronic (time to diagnosis)** | |
| [110] | Canada | IAS 2003[111] | 2000-2001 | 715 | 26 | 33 | 17 | 8.1 | 4.1 | 1.4 | 1.5 | 1.0 | 221 (< 170 days)<br>494 (> 170 days) | | | Newly diagnosed treatment-naive patients |
| [112] | USA | IAS 2005[54] | 1995-1998 | 76 | 93 | | | 13.2 | 11.8 | 2.6 | 1.3 | 2.6 | | 253 (< 6 months) | | Newly diagnosed patients self-referred or recruited through community referrals |
| | | | 1999-2000 | 71 | 97 | | | 19.7 | 15.5 | 5.5 | 5.6 | 5.6 | | | | |
| | | | 2001-2002 | 102 | 97 | | | 16.7 | 8.8 | 7.8 | 4.9 | 3.9 | | 72 (6-12 months) | | |
| | | | 2003-2004 | 112 | 97 | | | 24.1 | 16.1 | 13.4 | 7.1 | 9.8 | | | | |
| [113] | USA | IAS 2005[54] | 2003-2005 | 192 | 37.0 | 59.0 | 4.0 | 17.7 | 7.3 | 7.3 | 4.2 | 1.0 | | | 192 | Patients from a HIV outpatient care clinic |
| [114] | USA | IAS 2005[54] | 2004 | 129 | | | | 13.2 | 7,0 | 8.5 | 2.3 | 3.1 | 55 (0) | | 81 long-term infections | Consecutive sample of persons presenting for HIV counseling and testing at a STD clinic |
| [115] | USA | IAS 2005[54] | 2004 | 55 | | | | 18.2 | 3.6 | 14.6 | 3.6 | 1.8 | 55 (< 180 days) | | | HIV-infected adolescents aged 12-24 |
| [116] | USA | IAS fall 2005[64], Stanford HIV | 2003 | 317 | 74 | 6 | 28 | 9.8<br>12.0 | 3.5<br>6.6 | 6.0<br>6.3 | 1.9<br>0.6 | 1.6 | | | | ARV-naive patients enrolled for a clinical trial |
| [117] | USA | IAS 2006[31] | 2005 | 103 | | | | 25.2 | | | | 6.8 | | | | ARV-naive patients attending a public health site |
| [118] | USA | Shafer 2007[32] | 1999-2003 | 195 | 100 | | | 15.9 | 8.7 | 6.7 | 5.6 | 3.6 | | 195 (< 6 months) | | MSM with documented HIV-1 seroconversion |
| [119] | USA | IAS 2005[54] | 2000-2004 | 151 | 28.5 | 11.3 | 53 | 11.3 | 6.6 | 5.3 | 0.7 | | | | 93 (< 12 months), 57 (> 12 months) | ARV-naive patients presenting for care at clinics |
| [120] | USA | ViroSeq software | 1999-2005 | 18<br>44 | | | | 11.1<br>4.5 | 0<br>2.3 | 5.6<br>0 | 5.6<br>2.3 | 0<br>0 | 18 (0) | | 44 | Blood donors at American Red Cross centers |
| [121] | USA | Stanford algorithm | 2002-2006 | 112 | 100 | | | 12.5 | | | | | 112 (< 12 months) | | | MSM from a cohort of recently HIV-infected patients |
| [122] | USA | Stanford algorithm 2006 | 2005-2007 | 228 | 55.7 | | 35.1 | 12.1 | 4.5 | 9.8 | 1.8 | 2.2 | | | | Not recently infected ARV-naive patients attending one of 19 HIV clinics |
| [123] | Greenland | Stanford HIVdb | 1999-2007 | 60 | | | | 25 | 21.7 | 3.3 | 10.0 | 10.0 | | | | ARV-naive patients |
| [124] | USA | IAS 2008[125] | 1997-2007 | 848 | 78.3 | 13.0 | 8.7 | 14.9 | 6.8 | 7.6 | 5.0 | 2.1 | | 894 (< 6 months) | | Laboratory requisitions completed by prescribing physicians |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| North America | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Recent (time between neg. and pos. test)** | **Chronic (time to diagnosis)** | |
| [126] | North America | IAS 2007[74] | 2004-2006 | 913 | 61 | | | 13.6 | 6.1 | 7.3 | 3.6 | | | | | Naive patients attending a clinic |
| [127] | USA | IAS 2008[128] | 2006-2008 | 100 | | | 54 | 8 | 2 | 6 | 0 | 0 | | | | ARV-naive patients from a urban HIV clinic |
| [129] | USA | Shafer 2007[32] | 1998-2007 | 253 | 53.8 | | | 17.8 | 7.5 | 9.5 | 3.2 | 2.4 | | 120 (< 45 days)<br>133 (45-180 days) | | Patients from a Acute HIV and a Acute Transmission database |

| Latin America | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **n** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Newly diagnosed** | **Chronic (time to infection)** | |
| [130] | Brazil | Not reported | 1993-1997 | 81 | | | | | | | 2.5 | | | | | HIV-1 infected patients attending several hospitals and clinics |
| [131] | Martinique | Not reported | 1988-1997 | 69 | | | | | 24.6 | | | | 35 | | 34 | ARV-naive patients attending a hospital |
| [132] | Cuba | IAS 1998[43] | 1999 | 27 | | | | 7.4 | 7.4 | 0 | 0 | 0 | | | | Patients recruited for a UNAIDS study to monitor HIV resistance |
| [133] | Argentina | IAS 2000[95] | 1997, 1999, and 2000 | Chronic: 86 | | 8 | | 2.3 | 1.2 | 0 | 1.2 | 0 | 13 | | 86 | HIV patients attending the clinic and seroconversions |
| | | Hammond 1997[134] | | Recent: 13 | | | | 15.4 | 7.6 | 0 | 7.6 | 0 | | | | |
| [135] | Venezuela | IAS 2000[95] | unreported | RT: 31<br>PR: 56 | 63 | 3 | 30 | 3.2 | 3.2 | 0 | 1.8 | | | | | Patients recruited for a UNAIDS study to monitor HIV resistance |
| [136] | Brazil | IAS 2000[95] | 1998 | 47 | | | | 0 | 0 | 0 | 0 | 0 | | | | Blood donors |
| [137] | Brazil | IAS 1998[43], 2000[95] | 2001 | 339 | 26.9 | 5.0 | 61.7 | 6.5 | 2.4 | 2.1 | 2.4 | 0.3 | | | | Consecutive HIV patients from different voluntary counseling and testing centers |
| [138] | Brazil | IAS 1998[43], 2000[95] | 2000-2002 | 51 | 9.8 | 0 | 74.5 | 14.0 | 14.0 | 0.0 | 0.0 | 0.0 | | | | Patients attending an army hospital |
| [139] | Mexico | IAS 2003[108] | 2002-2003 | 96 | | | | 15.6 | 11.5 | 6.3 | 3.1 | 5.2 | | | 96 | Consecutive ARV-naive patients with evidence of disease progression in three large public medical centers |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| North America | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ref. | Region | Methodology | Years of sampling | (n) | HIV risk factor (%) | | | Resistance prevalence (%) | | | | | Population | | | Sampling of patients |
| | | | | | MSM | IVDU | HSX | Any | NRTI | NNRTI | PI | MDR | Recent (time to seroconversion) | Recent (time between neg. and pos. test) | Chronic (time to diagnosis) | |
| [140] | Brazil | Stanford HIVdb[141] | 1999-2005 | 27 | | | | 0 | 0 | 0 | 0 | 0 | | | | Patients attending a local ambulatory facility in a resource-poor setting region |
| [142] | Venezuela | Stanford HIVdb | unreported | 13 | | | | 7.7 | 7.7 | 0 | 0 | 0 | | | | ARV-naive patients |
| [143] | Brazil | Stanford HIVdb | unreported | 108 | <15 | 3 | >15 | 3.1 | 1.0 | 2.1 | 0 | 0 | | 108 | | Consecutive samples with sequence information |
| [144] | Brazil | IAS-USA 2003[54] | 1998-2002 | 341 | | | | 6.2 | 3.5 | 0.9 | 1.2 | 0.6 | 55 | | 280 | Blood donors, including paid donors and excluding HIV risk group donors |
| [145] | Peru | IAS-USA 2003[108] | 2002-2003 | 359 | 100 | | | 3.3 | 2.2 | 0.8 | 1.9 | 1.7 | 33 | | 326 | MSM referred to clinic sites through recruiters and peer educators |
| [146] | Argentina | IAS 2005[54] | 2004-2005 | 52 | 45 | 2 | 52 | 7.7 | 1.9 | 5.8 | 0 | 0 | 52 (< 9 months) | | | Recently HIV-infected subjects selected during routine clinical practice |
| [147] | Brazil | IAS 2002[96] | 2002-2003 | 84 | 41.8 | 3.5 | 58.2 | 3.6 | 3.6 | 0 | 0 | 0 | | | 84 | HIV-1-infected patients consecutive attending a hospital |
| [148] | Brazil | Stanford | 1994-1997 | 27 | | | | 22.2 | 22.2 | 3.7 | 0 | 3.7 | | | | Recruited ARV-naive injection |
| | | HIVdb 2000 and IAS 2005[54] | 1999-2001 | 38 | | | | 15.8 | 13.2 | 0 | 7.9 | 5.3 | | | | venous drug users |
| [149] | Mexico | IAS fall 2005[64] | 2001-2003 | 39 | 97 | | | 2.8 | 2.8 | 0 | 0 | 0 | | | | HIV-1 patients attending a hospital |
| [150] | Brazil | Stanford HIVdb | 2000, 2001, 2004 | 74 | | | | 1.35 | 1.35 | 0 | 0 | 0 | 16 (< 153 days) | | 58 (> 153 days) | Blood samples from the routine of blood banks |
| [151] | Venezuela | Stanford HIVdb | unreported | 20 | | | | 10.0 | 5.0 | 5.0 | 0 | 0 | | | | - |
| [152] | Cuba | Stanford HIVdb | 2003 | 250 | | | | 8.4 | 4.8 | 0.4 | 3.2 | 0 | | | | HIV-1 patients attending the Tropical Medicine Institute |
| [153] | Chile | Stanford HIVdb | 2000-2005 | 79 | | | | 2.5 | 2.5 | 0 | 0 | 0 | | | | HIV-1 patients |
| [154] | Brazil | Shafer 2007[32] | 2000-2006 | 123 | | | | 6.5 | 1.6 | 1.6 | 0.8 | 2.4 | | | | HIV patients who were followed at a HIV out-clinic |
| [155] | Venezuela | Stanford HIVdb | 2004-2007 | 63 | | | | 11.1 | 6.3 | 3.2 | 1.6 | | | | | Representative group of HIV-1-infected Venezuelan patients (mostly chronically infected) |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| North America | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Recent (time between neg. and pos. test)** | **Chronic (time to diagnosis)** | |
| [156] | Brazil | IAS 2008[85] | 2007 | 387 | 43 | 2.5 | 54 | 5.7 | 1.3 | 4.4 | 1.0 | 0.8 | | 387 | | HIV-infected patients from 20 sites in 13 cities |
| [157] | Brazil | SDRM-2009 IAS, version not reported | 2007-2008 | 97 | 25.8 | 1.9 | 48.5 | 10.3<br>8.2 | 3.1 | 1.0 | 2.1 | 4.1 | | | | Naive patients recruited at the main regional reference public hospital for HIV-1 care (mostly chronically infected) |
| **Europe** | | | | | | | | | | | | | | | | |
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Newly diagnosed (time to diagnosis)** | **Chronic (time to diagnosis)** | |
| [158] | Luxembourg | Stuyver 1997[159]<br>NRTI mutations: 41, 69, 70, 74, 184, 214, 215 | 1992-1997 | 135 | | | | | 11.9 | | | | | 135 | | Newly diagnosed patients from national reference laboratory |
| [160] | Spain | NRTI mutations: 41, 70, 74, 184, 215 | 1993<br>1997 | 74<br>75 | 29.3<br>13.3 | 52<br>50.7 | 14.7<br>22.7 | | 13.3<br>12.0 | | | | | | | Patients attending HIV reference centers |
| [161] | Italy | Schnatz 1997[162]<br>NRTI mutations: 41, 67, 70, 184, 215, 219 | 1985-1994<br>1995<br>1996<br>1997 | 44<br>28<br>15<br>11 | 44 | 23 | 33 | | 9.1<br>7.1<br>20<br>36.4 | | | | 64 | | 34 | HIV patients referred to the Division of Infectious Diseases |
| [163] | United Kingdom | Not reported | Unreported | 16 | | | | 0 | 0 | 0 | 0 | 0 | | | | Patients attending HIV centre |
| [164] | Greece | Hammond 1997[134] | Unreported | 17 | | | | 29 | 5.9 | 23.5 | | | | | | – |
| [165] | Switzerland | Schinazi 1997[166] | 1996-1998 | 82 | 40 | 20 | 40 | 11 | 10 | 1.4 | 4.3 | 1.4 | 82 (< 3 months) | | | Patients attending AIDS centre |
| [167] | Italy | Not reported | 1994-1997 | 38 | 44.7 | 26.3 | 28.9 | 21.1 | 21.1 | 2.6 | 0 | 0 | 38 (< 8 months) | | | Enrolment of seroconverters in AIDS institute |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Europe | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Newly diagnosed (time to diagnosis)** | **Chronic (time to diagnosis)** | |
| [168] | Italy | Barber 1990[169] | Unreported | 10 | | | | 0 | 0 | 0 | 0 | 0 | 10 (within a few weeks) | | | Patients with a few weeks primary infection |
| [170] | Italy | Infrared sequencing[171] | 1996-2000 | 116 | 52.6 | 6.9 | 27.6 | 12.9 | 12.9 | 0.9 | 0.9 | 1.8 | 116 (< 12 months) | | | Seroconverters at different clinics |
| [172] | Spain | Line prop assays | 1998 | 59<br>124 | | | | | 17 | NA | <br>6 | | | | | Patients attending HIV clinics |
| [173] | United Kingdom | HRP-ASAPv1.0 program[174] | 1995-1999 | 20 | | | | 5.0 | 5.0 | 0 | 0 | 0 | 20 (< 446 days) | | | Seroconverters from UK register |
| [175] | Spain | IAS 1998[43] | Unreported | 103 | | | | 4.9 | 3.9 | 0 | 0.9 | 0 | | | | Representative epidemiological sampling |
| [176] | Belgium | Line prop assays | 1995<br>1997<br>1998 | 45<br>75<br>111 | 40<br>47<br>27 | 2<br>0<br>2 | 51<br>35<br>21 | 26.6<br>26.6<br>31.5 | 15.6<br>14.7<br>10.8 | 17.6<br>13.3<br>16.5 | 4.4<br>8.0<br>9.9 | 2.2<br>4.0<br>2.7 | | 45<br>75<br>111 | | Patients visiting hospital for the first time |
| [177] | France | IAS 1998[43] | 1995-1998 | 48 | | | | 18.8 | 17 | 0 | 2.1 | | 14 (< 3 months) | | | Patients attending AIDS centers |
| [178] | Spain | Line prop assays | 1997 | Recent: 52<br>Chronic: 150 | | | | | 13.5<br>4.7 | | | | 52 (< 9 months) | | 150 | Well characterized group of individuals |
| [179] | The Netherlands | IAS 1998[43] | 1992-1999 | RT:74<br>PR:28 | | | | | 10.8 | 0 | <br>0 | | 74 | | | Monitoring MSM and IVDU |
| [180] | Germany | Los Alamos database 1998 | 1996-1999 | 64 | | | | 12.5 | 6.3 | 3.1 | 4.7 | 1.6 | 64 (< 3 years) | | | Seroconversion study |
| [181] | Italy | Visible Genetics software | Unreported | 17 | | | | 5.9 | 0 | 5.9 | 0 | 0 | 13 (< 12 months)<br>4 (> 12 years) | | | HIV-1 seropositive persons |
| [182] | United Kingdom | IAS 2000[95] | 1994-2000 | 69 | 84.1 | 2.9 | 13.0 | 14.5 | 11.6 | 4.3 | 1.4 | 2.9 | 69 (< 18 months) | | | Patients of UK register of HIV seroconverters |
| [183] | United Kingdom | Not reported | 1996-2000 | 60 | 75 | 23 | 1.7 | 8.3 | 5.0 | 1.7 | 1.7 | 0 | 39 (< 12 months) 21 (> 12 months) | | | Patients attending HIV clinics |
| [184] | France | IAS 2000[95] | 1998 | 391 | 48.5 | 12.9 | 29.8 | 3.7 | 3.3 | 0.8 | 1.9 | | | | | Patients from HIV treatment centers |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Europe | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Newly diagnosed (time to diagnosis)** | **Chronic (time to diagnosis)** | |
| [185] | Spain | IAS 2000[95] | 2000 | 351 | | | | 10.8 | 3.1 | 1.5 | 6.1 | | | | | First 8 naive consecutive patients at 18 outpatient clinics were selected |
| [186] | Switzerland | Schinazi 2000[187] | 1996-1999 | 197 | 42 | 13 | 42 | 8.8 | | | | | 197 (< 12 months) | | | HIV-1 patients from AIDS centers |
| [188] | United Kingdom | Not reported | 2000 | 15 | | | | 0 | 0 | 0 | 0 | 0 | 15 (< 6 months) | | | Acute primary HIV infection study |
| [189] | France | IAS 1999[43] | 1992<br>1997-1999 | 41<br>105 | 44<br>36 | 22<br>28 | 34<br>36 | | | 2<br>2 | | | | | | Patients prior to the initiation of NNRTI therapy |
| [190] | Italy | IAS 2000[95] | 1996-1998 | Recent: 68<br>Chronic: 347 | 25.0<br>23.3 | 19.1<br>37.2 | 41.1<br>31.4 | 19.1<br>11.5 | 14.7<br>7.8 | 0<br>4.9 | 5.9<br>1.4 | 1.5<br>2.6 | 68 (< 12 months) | | 347 | Patients enrolled in the Italian Cohort of ARV-Naive patients. |
| [191] | Greece | Hertogs 2000[192] | 1999-2000 | 24 | | | | 0 | 0 | 0 | 0 | 0 | | | | Patients recruited before ARV treatment use |
| [193] | United Kingdom | VircoGENm | 1988-1991 | 37 | 100 | | | 5.0 | 5.0 | 0 | 0 | 0 | 37 (< 6 months) | | | Seroconverted patients attending a HIV clinic |
| [194] | Spain | IAS 2000[95], and Medscape Guide | 1996-2000 | 91 | | | | 12.5 | 2.2 | 0.0 | 12.0 | 0.0 | | | | HIV-infected patients attending a center |
| [195] | France | Delfraissy 2000[196] | 1996-1999 | 204 | 60 | 3 | 34 | 8.8 | 6.8 | 1.0 | 3.9 | 0.5 | 61 (< 3 months) 152 (< 6 months) | | | HIV-infected patients |
| [197] | Spain | IAS 2000[95], 2001[198] | 1996-1999<br>2000-2001 | 31<br>26 | 70<br>67 | 10<br>0 | 20<br>28 | 25.8<br>4.3 | 23.3<br>0 | 3.3<br>0 | 6.7<br>4.3 | 6.7<br>0 | 57 (< 12 months) | | | HIV-infected patients attending a HIV centre |
| [199] | United Kingdom | IAS 2000[95] | 1999-2001 | 71 | | | 100 | 5.9 | 1.5 | 3.0 | 4.0 | 2.2 | 14 (0), 25 (< 12 months) | | | Representing new HIV-1 diagnosed in UK |
| [200] | Spain | IAS 2001[198] | 1999<br>2001 | 47<br>47 | | | | 12.7<br>15.0 | 8.5<br>2.1 | 4.2<br>12.7 | 2.1<br>2.1 | 2.1<br>2.1 | | | 94 (>3 years) | Randomly collected ARV-naive individuals |
| [201] | Sweden | IAS 2000[95] | 1998-2001 | 100 | 40 | 2 | 41 | 9.0 | 5.0 | 3.0 | 1.0 | 0 | | | | Randomly chosen from newly diagnosed and naive HIV patients |
| [202] | France | IAS 2002[96] | 1999-2000 | 249 | 57 | 2 | 32 | 10.4 | 7.6 | 4.0 | 5.6 | 4.8 | 249 (< 6 months) | | | Patients from primary infection therapeutic trial teams |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Europe | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Newly diagnosed (time to diagnosis)** | **Chronic (time to diagnosis)** | |
| [203] | Denmark | www.hivresistanceweb.com, IAS, version not reported | 2000 | 97 | | | | 2.1 | 2.1 | 0 | 0 | 0 | 12 | 91 | | Patients who were seroconverted or newly diagnosed |
| [204] | Italy | Trugene | Unreported | Recent: 38<br>Chronic: 24 | | | | 5.3<br>8.3 | 2.6<br>8.3 | 0<br>0 | 2.6<br>0 | 0<br>0 | | 38 (1-12 months) | 24 (> 3 years) | Cohort with naive patients |
| [205] | Spain | Stanford HIVdb | 2000-2002 | 85 | 18 | 32 | 47 | 7.1 | 5.9 | 0 | 1.2 | 0 | | 85 | | All newly diagnosed HIV-1 patients attending hospitals |
| [206] | Italy | IAS 2003[111] | 1996-2001 | 112 | 33.0 | 20.5 | 40.2 | 16.1 | 14.3 | 0.9 | 2.7 | 1.8 | 112 (< 12 months) | | | Cohort with naive patients |
| [207] | Belgium | IAS 2003[111] | 2000 | 83 | | | 58.1 | 7.2 | 5.0 | 2.5 | 1.2 | 1.3 | | 83 | | Recently diagnosed naive HIV patients |
| [208] | Switzerland | IAS 2000[95] | Unreported | 220 | | | | 10.5 | 8.6 | 0.9 | 2.3 | 1.4 | 220 (< 1 year) | | | Individuals attending a hospital |
| [209] | The Netherlands | IAS 2003[111] | 1994-2003 | 100 | 61 | 27 | 12 | 13.0 | 10.0 | 2.0 | 1.0 | 0.0 | 100 (< 6 months) | | | Seroconverters from a group of MSM and IVDU |
| [210] | Nordrhein-Westfalen, Germany | IAS 2001[198] and 2002[96] | 2001-2002 | 184 | 46.2 | 3.5 | 22.4 | 14.0 | 10.5 | 2.8 | 2.1 | 2.1 | | | | Patients attending clinics/ hospitals at time of first HAART administration |
| [211] | Russia Federation, Ukraine, Kazakhstan | Los Alamos national laboratory | 1996-2002 | 27 | 0 | 100 | 0 | | | | 0 | | | | | Samples from IVDU |
| [212] | Spain | Line prop assays | 1996-2003 | 145 | 10.1 | 54.1 | 5.4 | 20.3 | 4.1 | 1.4 | 16.6 | 1.4 | | | | Untreated HIV patients from different centers |
| [213] | Italy | Stuyver 1997[159] and Clarke 2000[214] | < 1996<br>> 2000 | 21<br>27 | 9.5<br>11.2 | 42.9<br>29.6 | 23.8<br>29.6 | 0<br>11.1 | 0<br>7.4 | 0<br>0 | 0<br>11.1 | 0<br>7.4 | | | | Naive patients attending clinics |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Europe | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Newly diagnosed (time to diagnosis)** | **Chronic (time to diagnosis)** | |
| [215] | Israel | IAS 2003[108] | 1999-2003 | 176 | 10 | 24 | 58 | 14.8 | 2.8 | 8.5 | 5.1 | 0.6 | | | | Random samples selected from naive patients |
| [216] | Former Soviet Union | Stanford HIVdb | 1997-2004 | 278 | 2.9 | 84.0 | 11.5 | 13.3 | 5.4 | 7.5 | 2.5 | 0.4 | | | | HIV-1-infected patients |
| [217] | Greece | IAS 2004[218] | 2002-2003 | 101 | 55 | 3 | 23 | 8.9 | 5.0 | 4.0 | 0 | 0 | 18 (< 1 year) | 83 | | Representative sample of newly HIV-patients<br>IV-1 diagnosed patients |
| [219] | France | IAS 2003[108] | 2001-2002 | Recent: 303<br>Chronic: 363 | 57.7<br>31.2 | 0.35<br>7.8 | 31.7<br>51.1 | 14<br>9.1 | 10.3<br>7.2 | 3.3<br>1.7 | 4.3<br>1.9 | 2.0<br>1.7 | 303 (< 6 months) | 218 (< 1 year), 145 (> 1 year) | | National survey |
| [27] | Europe, Israel | IAS 2003[111] | 1996-2002 | 2208 | 43 | 15 | 41 | 10.4 | 7.6 | 2.9 | 2.5 | 2.0 | 777 (< 1 year)<br>607 (> 1 year) | | | Surveillance program to collect samples of newly diagnosed HIV patients. Have been partly published elsewhere |
| [220] | Spain | IAS 2005[54] | 1997-2004 | 198 | 70 | 10 | 19.5 | 12.1 | 9.6 | 4.0 | 2.0 | 3.5 | 198 (< 12 months) | | | Consecutive newly diagnosed patients |
| [14] | United Kingdom | Stanford HIVdb version 2004.04 | 1996-2003 | 2357 | 76.4 | 2.6 | 21 | 14.2 | 9.9 | 4.5 | 4.6 | 3.3 | 172 (< 18 months) | | | Resistance database with test carried out as part of routine clinical care |
| [221] | Western Europe and Canada (CASCADE) | Stanford 3+<br>Stanford 4+<br>IAS 2004<br>ANRS | 1987-2003 | 438 | 74.9 | 10.3 | 12.3 | 10.3<br>15.1<br>15.5<br>11.2 | 5.7<br>10.3<br>10.5<br>7.8 | 3.4<br>3.9<br>3.4<br>3.0 | 3.0<br>4.1<br>3.9<br>2.3 | | 438 (< 18 months) | | | Patients belonging to the CASCADE Collaboration |
| [222] | Italy | IAS 2005[54] | 1997-2004 | 155 | 23.9 | 1.3 | 16.8 | 16.8 | 12.9 | 4.5 | 1.9 | 2.5 | 155 (≤ 12 months) | | | HIV-1 patients who received routine testing |
| [223] | Nordrheim-Westfalen, Germany | IAS 2003[106] | 2001-2003 | 269 | 48 | | | 11.2 | 8.6 | 4.1 | 1.5 | 1.5 | | | 269 | HIV-1 patients tested before first application of HAART |
| [25] | Romania | Stanford HIVdb | Unreported | 14 | | | | 0 | 0 | 0 | 0 | 0 | | | | ARV-naive HIV-1 patients |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Europe | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Newly diagnosed (time to diagnosis)** | **Chronic (time to diagnosis)** | |
| [224] | Georgia | Stanford HIVdb 2000 | 1998-2003 | 48 | 2 | 65 | 27 | 4.2 | 4.2 | 0 | 0 | 0 | | | | Naive HIV-1 patients represented different transmission modes |
| [225] | United Kingdom | IAS 2005[54] | 2000-2004 | 140 | 91 | | 9 | 6.4 | 2.1 | 4.3 | 1.4 | 1.4 | 140 (< 6 months) | | | HIV patients recruited into a therapy intervention study |
| [226] | Sweden | IAS fall 2005[64] | 1992-2002 | 201 | 100 | | | 13.9 | 13.4 | 0.5 | 0 | 0 | 87 (< 12 months) | | | HIV diagnosed patients at a MSM HIV clinic |
| [227] | Spain | ANRS and IAS 2003[106] | 2002 | 43 | | 90.7 | | 11.6 | 6.9 | 6.9 | 6.9 | 2.3 | | | | Randomly chosen prison inmates infected with HIV |
| [228] | Slovenia | IAS 2005[54] | 2000-2004 | 77 | 62.3 | 2.6 | 29.9 | 3.9 | 3.9 | 0 | 0 | 0 | | 77 (< 3 months) | | Patients with HIV confirmed at an AIDS centre |
| [29] | United Kingdom | IAS fall 2005[64] | 2004-2006 | 239 | 52.7 | 2.1 | 45.2 | 7.1 | 4.2 | 1.7 | 1.7 | 0.4 | 85 (< 164 days) | | | Patients newly diagnosed at a hospital |
| [229] | Portugal | IAS 2005[54] | 2003 | 180 | 19 | 20 | 54 | 7.8 | 3.9 | 1.7 | 0 | 1.7 | | 180 (< 3 months) | | Newly diagnosed patients in representing centre |
| [230] | Italy | IAS 2006[31] | Unreported | 29 | | | | 17.2 | 10.3 | 6.9 | | 6.9 | | | 29 | ARV-naive patients |
| [231] | United Kingdom | IAS 2005[54] | 1996-1997 | 310 | | | | 8.4 | 7.1 | 1.3 | 1.3 | | 19 (< 18 months) | 291 | | Database with samples as part of routine clinical care nationwide |
| | | | 1998 | 340 | | | | 10.0 | 8.2 | 2.1 | 2.9 | | | 312 | | |
| | | | 1999 | 358 | | | | 11.2 | 9.8 | 5.0 | 2.8 | | 28 | 329 | | |
| | | | 2000 | 458 | | | | 14.2 | 9.0 | 5.2 | 3.5 | | 29 | 413 | | |
| | | | 2001 | 517 | | | | 13.0 | 9.3 | 5.2 | 3.9 | | 45 | 458 | | |
| | | | 2002 | 519 | | | | 15.6 | 11.4 | 6.0 | 5.0 | | 59 | 470 | | |
| | | | 2003 | 767 | | | | 12.5 | 7.4 | 6.0 | 2.9 | | 49 | 730 | | |
| | | | 2004 | 1185 | | | | 9.2 | 4.6 | 4.4 | 2.1 | | 37 | 1135 | | |
| | | | | | | | | | | | | | 50 | | | |
| [232] | Germany | IAS 2004[218] | 1997-2004 | 504 | 88 | 7 | 2.3 | 16 | 9 | 2 | 2.8 | 1.4 | 294 (< 12 months), 178 (< 24 months), 23 (< 36 months, 9 (> 36 months) | | | Open cohort of HIV persons with known date of seroconversion |
| [233] | Switzerland | Shafer 2007[32] | 1996-2005 | 822 | 42 | 20 | 32 | 7.7 | 5.5 | 1.9 | 2.7 | 2 | 822 (< 1 year) | | | Representative populations of recently HIV patients |
| [234] | Germany | IAS 2003[106] | 2001-2005 | 831 | 51.5 | 5.0 | 18.5 | 9.0 | 5.4 | 3.0 | 2.4 | 1.3 | | | 831 | HIV patients from the majority of treatment centers of Germany |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Europe | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **Newly diagnosed (time to diagnosis)** | **Chronic (time to diagnosis)** | |
| [235] | Belgium | Shafer 2007[32] | 2003-2006 | 285 | 55 | 0.3 | 38 | 9.5 | 7.0 | 3.5 | 1.8 | 4.2 | | 285 (< 6 months) | | Patients from all eight Belgian AIDS Reference Centers |
| [236] | Europe, Israel and Argentina | Shafer 2007[32] and IAS 2007[74] and Stanford version 4.3.4 | 1994-2007 | 525 (510 from Europe) | | | | 11.4<br>13.5<br>16.0 | 9.3 | 1.0 | 3.0 | 1.7 | | 13 (< 1 year) | 512 (> 1 year) | HIV patients in 93 HIV centers |
| [237] | United Kingdom | IAS fall 2006[31] | 2005-2007 | 392 | | | 70.6 | 3.3 | 0.5 | 1.8 | 1.0 | 0 | | 392 | | Newly diagnosed HIV patients from a representative number of centers |
| [7] | Europe | IAS 2005[54] | 2002-2003 | 1050 | 44 | 8 | 41 | 9.1 | 5.4 | 2.6 | 3.0 | 1.3 | 235 (< 1 year) | 815 (< 3 months) | | Newly diagnosed HIV patients from 16 European countries with a standardized sampling strategy |
| [238] | United Kingdom | Stanford HIVdb 2007 | 2006 | 99 | | | | 7.0 | 5 | 1 | 1 | 0 | | 76 | | Naive patients with samples in the virology resistance test database |
| [239] | Cyprus | IAS 2007[74] and Shafer 2006[240] | 2003-2006 | 37 | 49 | | 46 | 6.5 | 4.3 | 2.2 | 0 | 0 | | 37 (< 3 months) | | Newly diagnosed patients attending an AIDS clinic |
| [241] | Spain | Stanford HIVdb | 2004-2007 | 261 | 37.9 | 11.1 | 47.5 | 11.1 | 7.6 | 2.3 | 0.5 | 0.9 | | 261 | | Newly diagnosed patients attending the public hospitals |
| [242] | Estonia | IAS 2007[74] | 2005-2006 | 115 | 0 | 34 | 65 | 0 | 0 | 0 | 0 | 0 | | | | HIV patients including from a prison |
| [243] | Switzerland | Shafer 2007[32] | 2000-2008 | 637 | | | | 8.5 | 6.3 | 3.5 | 1.9 | 2.7 | 131 (< 12 months) | 506 | | Newly diagnosed HIV patients |
| [126] | Western Europe | IAS 2007[74] | 2004-2006 | 500 | 54 | | | 6.8 | 3.8 | 3.2 | 0.8 | | | | | Naïve patients attending a clinic |
| [244] | Italy | Shafer 2007[32] | 2004-2007 | 255 | 48.6 | 4.0 | 47.6 | 5.9 | 3.9 | 3.5 | 0.4 | 0 | 58 (< 6 months) | 197 | | Newly diagnosed HIV-1 patients |
| [245] | Italy | Bennett 2009[246] | 1996-2007 | 1690 | 28.4 | 12.1 | 41.6 | 15.1 | 11 | 6 | 4 | 3.4 | | | | Naive HIV patients from ARCA database |
| [247] | Russia | Not reported | 2007-2008 | 33 | 5 | 36 | 36 | 9.1 | 0 | 9.1 | 0 | 0 | | | | HIV-infected patients from two Russian regions |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Asia | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **New diagnosed (time to diagnosis)** | |
| [248] | Japan | Jennifer 1997[249] | 1996-1998 | 21 | 17 | | 16 | 1.0 | 0 | | 1.0 | 0 | | | HIV-1 patients from 17 hospitals in various parts of Japan |
| [250] | Thailand | Los Alamos database | 2000-2001 | 22 | | | | 0 | 0 | 0 | 0 | 0 | | | ARV-naive pregnant woman |
| [251] | Korea | IAS 2000[95] | 1998-2002 | 50 | 18 | 0 | 82 | 8.0 | 6.4 | 0 | 2.6 | 2.0 | | | HIV-1-infected persons followed-up at the national hospital |
| [252] | Vietnam | IAS and ANRS, versions not reported | 2001-2002 | 200 | | 42.5 | | 6.5 | 4.5 | | 2.0 | | | | randomly included HIV-1 infected attending a HIV Center |
| [253] | Japan | IAS 2000[95] | 1999-2002 | 116 | 57 | | 28 | 9.5 | 6.0 | 0.0 | 3.4 | 0 | | | HIV-1-infected patients at their initial consultation at a hospital |
| [254] | India | IAS and ANRS, versions not reported | 2003 | 128 | | | | 1.6 | 1.6 | 0 | 0 | 0 | | | HIV-1 patients attending the outpatient clinic of a hospital |
| [26] | India | Software included in ViroSeq | 1999-2001 | 12 | | | | 0 | 0 | 0 | 0 | 0 | 12 (< 4 months) | | Patients with recent HIV infection |
| [255] | Cambodia | ANRS algorithm Update Sept. 2004 | 2003-2004 | 144 | | | | 4.9 | 2.8 | 0.7 | 1.5 | 0 | | 22 (< 1 year) | Consecutive patients recruited through voluntary counseling and testing center and prenatal clinics |
| [256] | Japan | IAS 2006[31], Stanford HIVdb[240] | 2003-2004 | 575 | 66.6 | 0.19 | 25.9 | 4.0 | 2.8 | 0.7 | 0.7 | 0.2 | 45 (< 1 year) | 530 | Newly diagnosed HIV cases through surveillance of 8 AIDS clinical centers |
| [257] | Malaysia | IAS 2005[54] | 2003-2004 | 100 | | | 57 | 1.0 | 0 | 1.0 | 0 | 0 | | 60 (< 2 months), 10 (3-23 months), 13 (> 12 months) | HIV-1 patients attending a HIV Clinic |
| [258] | Hong Kong | Stanford HIVdb | 1995-2004 | 39 | | | | 0 | 0 | 0 | 0 | 0 | | | HIV-infected patients |
| [259] | China | Stanford HIVdb | 2004 | RT: 71 PI: 174 | | | | 4.2 | 4.2 | 0 | 0 0 | 0 | | | Patients from 4 midland provinces of China |
| [260] | China | Stanford HIVdb | Unreported | 91 | | 8 | | 4.4 | 1.1 | 0 | 3.3 | 0 | | | Mostly chronically HIV-1-infected patients attending a hospital |
| [261] | China | Stanford HIVdb | 2005 | 40 | 100 | | | 15 | 10.0 | 12.5 | 0 | 7.5 | | | patients recruited from the HIV-1 sero-positive MSM management program |

*(continue)*

**Table 1. Summary of studies on transmitted drug resistance per continent (*continued*)**

| Asia | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **Recent (time to seroconversion)** | **New diagnosed (time to diagnosis)** | |
| [262] | Japan | IAS 2005[54] | 1992-2004 | 54 | | | | 11.1 | 1.9 | 3.7 | 5.6 | 0 | | | People visiting STD-related clinics |
| [263] | Thailand | IAS 2005[54] | 2003-2006 | 305 | 9 | 11 | 75 | 4.0 | 4.0 | 4.0 | 0 | 4.0 | | | HIV patients attending HIV-related medical care at a hospital |
| [264] | Thailand | IAS 2007[74] | Unreported | 113 | 1.3 | 2.7 | 90.7 | 12.4 | 12.4 | 0 | 0 | 0 | | | ARV-naive patients |
| [265] | Thailand | Shafer 2007[32] | 2005-2006 | 46 | | | | 0 | 0 | 0 | 0 | 0 | 46 (< 12 months) | | Consecutive returning blood donors at the Red Cross National Blood Centre |
| [266] | Vietnam | Shafer 2007[32] and IAS fall 2006[31] | 2006 | 49 | | | | 2.0 | 2.0 | 2.0 | 0 | 2.0 | | | Woman in their first pregnancy attending antenatal clinics or clients at voluntary counseling and testing sites, who were < 25 years old |
| [267] | Cambodia | WHO HIV Drug resistance database | 2006-2007 | 67 | | | 65 | 1.5 | 1.5 | 1.5 | 0 | 1.5 | | | Patients of the Medecins du Monde (40), French Red Cross (14) and pregnant woman (13) enrolled at a hospital |
| [268] | Singapore | IAS 2007[74] | 2006-2007 | 60 | 73.3 | 1.7 | 23.3 | 1.7 | 0 | 1.7 | 0 | 0 | 60 (< 24 months) | | Recently infected patients recruited from the outpatient clinic at the CDC hospital |
| [269] | China | Stanford HIVdb | 2007 | Subt<br>CRF_08BC<br>32<br>CRF_07BC<br>67 | | 100 | | <br>0<br>1.5 | <br>0<br>1.5 | <br>0<br>0 | <br>0<br>0 | <br>0<br>0 | | | Patients infected through injection drug use. |
| [270] | India | Stanford HIVdb | 2005-2006 | 55 | | 100 | | 7.2 | 3.6 | 1.8 | 2.7 | 0 | | | IDU recruited by field staff |
| **Australia** | | | | | | | | | | | | | | | |
| **Ref.** | **Region** | **Methodology** | **Years of sampling** | **(n)** | **HIV risk factor (%)** | | | **Resistance prevalence (%)** | | | | | **Population** | | **Sampling of patients** |
| | | | | | **MSM** | **IVDU** | **HSX** | **Any** | **NRTI** | **NNRTI** | **PI** | **MDR** | **recent** | **Newly diagnosed (time to diagnosis)** | |
| [271] | Australia | IAS 1998[43] | 1992-2001 | 185 | 86.5 | | | 23.2 | 18.4 | 2.7 | 1.6 | 0 | | 185 (< 13 days) | Samples from a reference laboratory of newly acquired HIV |

Where several mutation lists were compared (in 3 studies), we used the prevalence numbers of the most recent IAS list.
IAS: International AIDS Society, USA; MSM: men who have sex with men; IVDU: intravenous drug users; HSX: heterosexual; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: nonnucleoside reverse transcriptase inhibitor; PI: protease inhibitor; ARV: antiretroviral; STD: sexually transmitted disease; PMTCT: preventing mother-to-child transmission; Any: at least one drug resistance mutation; MDR: multidrug resistance to at least two classes.