

Monitoring Report 2011

Human Immunodeficiency Virus (HIV) Infection in the Netherlands

Appendix



Contributing to the quality of HIV care

Stichting HIV Monitoring (SHM), the Dutch HIV monitoring foundation, was founded in 2001. Based in Amsterdam, SHM was appointed by the Dutch Minister of Health, Welfare and Sports (Ministerie van Volksgezondheid, Welzijn en Sport) as the national executive organization for the registration and monitoring of HIV-infected patients in follow-up in one of the Dutch HIV Treatment Centres.

Our Mission:

To further the knowledge and understanding of the epidemiology and the course of the treated and untreated HIV infection.

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Colophon

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Appendix

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Appendix Table 1.1: Characteristics of the 14,610 HIV-infected patients in follow-up as of June 2011.

	MSM	Heterosexual		IDU		Blood or blood products		Other / unknown		Total	
	Men N=8523	Men N=1902	Women N=2589	Men N=240	Women N=102	Men N=111	Women N=71	Men N=838	Women N=234	Men N=11614	Women N=2996
Current age [years]											
0-12	0 0.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	1 0.9%	0 0.0%	50 6.0%	43 18.4%	51 0.4%	43 1.4%
13-17	2 0.0%	0 0.0%	2 0.1%	0 0.0%	0 0.0%	1 0.9%	0 0.0%	24 2.9%	32 13.7%	27 0.2%	34 1.1%
18-24	147 1.7%	23 1.2%	69 2.7%	0 0.0%	0 0.0%	5 4.5%	1 1.4%	49 5.8%	20 8.5%	224 1.9%	90 3.0%
25-34	1061 12.4%	215 11.3%	650 25.1%	16 6.7%	3 2.9%	12 10.8%	9 12.7%	119 14.2%	33 14.1%	1423 12.3%	695 23.2%
35-44	2489 29.2%	608 32.0%	998 38.5%	47 19.6%	16 15.7%	23 20.7%	27 38.0%	200 23.9%	48 20.5%	3367 29.0%	1089 36.3%
45-54	3084 36.2%	661 34.8%	604 23.3%	126 52.5%	61 59.8%	42 37.8%	21 29.6%	241 28.8%	41 17.5%	4154 35.8%	727 24.3%
55-64	1347 15.8%	287 15.1%	195 7.5%	49 20.4%	21 20.6%	17 15.3%	7 9.9%	110 13.1%	14 6.0%	1810 15.6%	237 7.9%
≥65	393 4.6%	108 5.7%	71 2.7%	2 0.8%	1 1.0%	10 9.0%	6 8.5%	45 5.4%	3 1.3%	558 4.8%	81 2.7%
Current age 50 years or older											
No	5507 64.6%	1218 64.0%	2084 80.5%	133 55.4%	55 53.9%	65 58.6%	47 66.2%	562 67.1%	197 84.2%	7485 64.4%	2383 79.5%
Yes	3016 35.4%	684 36.0%	505 19.5%	107 44.6%	47 46.1%	46 41.4%	24 33.8%	276 32.9%	37 15.8%	4129 35.6%	613 20.5%
Region of origin											
Netherlands	6309 74.0%	816 42.9%	686 26.5%	147 61.3%	54 52.9%	73 65.8%	16 22.5%	418 49.9%	104 44.4%	7763 66.8%	860 28.7%
Sub-Saharan Africa	105 1.2%	620 32.6%	1204 46.5%	4 1.7%	0 0.0%	22 19.8%	31 43.7%	187 22.3%	65 27.8%	938 8.1%	1300 43.4%
Western Europe	590 6.9%	58 3.0%	58 2.2%	26 10.8%	30 29.4%	4 3.6%	2 2.8%	45 5.4%	32 13.7%	723 6.2%	122 4.1%
Latin America	533 6.3%	181 9.5%	240 9.3%	9 3.8%	3 2.9%	2 1.8%	10 14.1%	48 5.7%	5 2.1%	773 6.7%	258 8.6%
Caribbean	258 3.0%	93 4.9%	153 5.9%	7 2.9%	1 1.0%	1 0.9%	3 4.2%	35 4.2%	5 2.1%	394 3.4%	162 5.4%

	MSM	Heterosexual		IDU		Blood or blood products		Other / unknown		Total	
	Men N=8523	Men N=1902	Women N=2589	Men N=240	Women N=102	Men N=111	Women N=71	Men N=838	Women N=234	Men N=11614	Women N=2996
Years aware of HIV infection											
<1	494 5.8%	106 5.6%	105 4.1%	2 0.8%	0 0.0%	3 2.7%	0 0.0%	35 4.2%	14 6.0%	640 5.5%	119 4.0%
1-2	1373 16.1%	266 14.0%	274 10.6%	6 2.5%	1 1.0%	4 3.6%	3 4.2%	67 8.0%	20 8.5%	1716 14.8%	298 9.9%
3-4	1297 15.2%	256 13.5%	347 13.4%	11 4.6%	5 4.9%	5 4.5%	11 15.5%	81 9.7%	19 8.1%	1650 14.2%	382 12.8%
5-10	2219 26.0%	630 33.1%	924 35.7%	35 14.6%	15 14.7%	24 21.6%	16 22.5%	225 26.8%	61 26.1%	3133 27.0%	1016 33.9%
>10	3117 36.6%	638 33.5%	901 34.8%	184 76.7%	81 79.4%	75 67.6%	41 57.7%	232 27.7%	98 41.9%	4246 36.6%	1121 37.4%
Unknown	23 0.3%	6 0.3%	38 1.5%	2 0.8%	0 0.0%	0 0.0%	0 0.0%	198 23.6%	22 9.4%	229 2.0%	60 2.0%
Current CD4 count [cells/mm³], median / IQR	540 410-700	480 340-660	540 400-730	430 280-610	530 310-790	508 290-690	570 374-740	486 330-680	620 410-940	526 390-699	540 390-740
Current CD8 count [cells/mm³], median / IQR	910 661-1237	850 601-1170	800 580-1090	825 510-1070	860 544-1214	760 550-1107	750 530-1010	810 590-1190	761 540-1090	890 650-1220	800 570-1097
Current HIV RNA <500 copies/ml	6824 80.1%	1571 82.6%	2058 79.5%	210 87.5%	87 85.3%	104 93.7%	68 95.8%	548 65.4%	176 75.2%	9257 79.7%	2389 79.7%
Ever AIDS	1701 20.0%	602 31.7%	551 21.3%	86 35.8%	46 45.1%	35 31.5%	22 31.0%	240 28.6%	59 25.2%	2664 22.9%	678 22.6%
AIDS at diagnosis	874 10.3%	400 21.0%	317 12.2%	22 9.2%	11 10.8%	14 12.6%	11 15.5%	173 20.6%	30 12.8%	1483 12.8%	369 12.3%
Current treatment											
cART	7162 84.0%	1669 87.7%	2300 88.8%	229 95.4%	94 92.2%	103 92.8%	69 97.2%	593 70.8%	196 83.8%	9756 84.0%	2659 88.8%
Non-cART	22 0.3%	3 0.2%	12 0.5%	1 0.4%	1 1.0%	0 0.0%	0 0.0%	5 0.6%	1 0.4%	31 0.3%	14 0.5%
Not started	1340 15.7%	230 12.1%	277 10.7%	10 4.2%	7 6.9%	8 7.2%	2 2.8%	240 28.6%	37 15.8%	1828 15.7%	323 10.8%
Coinfection											
HBV	597 7.0%	150 7.9%	119 4.6%	27 11.3%	6 5.9%	6 5.4%	2 2.8%	44 5.3%	15 6.4%	824 7.1%	142 4.7%
HCV	707 8.3%	87 4.6%	105 4.1%	213 88.8%	91 89.2%	39 35.1%	8 11.3%	73 8.7%	48 20.5%	1119 9.6%	252 8.4%

Legend: MSM=men who have sex with men; IDU=injecting drug use; IQR=interquartile range; cART=combination antiretroviral therapy; HBV=hepatitis B virus; HCV=hepatitis C virus.

Appendix Table 2.1: Annual number of cases of death and first AIDS-defining events amongst 18,229 HIV-1-infected patients in the Netherlands recorded up to June 2011.

Year	AIDS			Death	
	Total	More than six weeks after HIV diagnosis	After the start of cART	Total	After the start of cART
≤1995	757	478	1	24	-
1996	365	289	86	46	29
1997	301	183	118	87	69
1998	244	132	107	85	72
1999	236	133	112	90	88
2000	246	113	88	83	78
2001	260	145	95	82	79
2002	294	147	107	122	84
2003	293	147	111	141	119
2004	283	174	114	144	129
2005	340	190	131	140	123
2006	277	165	118	120	104
2007	281	162	110	149	126
2008	255	162	126	146	132
2009	244	135	102	155	141
2010	240	117	95	121	114
2011	36	21	17	45	43
Total	4952	2893	1638	1780	1530

Appendix Table 2.2: The demographic characteristics and cause of death of the 1530 patients who died after starting cART according to calendar year.

	Total	Year of death																Median last CD4 count	IQR last CD4 count
		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011		
Total	1530	29	69	72	88	78	79	84	119	129	123	104	126	132	141	114	43	180	(60 - 370)
Male	1316	28	62	60	79	65	70	72	98	116	105	84	106	110	123	99	39	180	(60 - 380)
Female	213	1	7	12	9	13	9	11	21	13	18	20	20	22	18	15	4	190	(60 - 354)
HBV co-infection at death	129	1	6	4	6	7	4	7	8	15	18	6	9	13	16	6	3	210	(70 - 390)
No HBV co-infection at death	1228	15	40	47	68	64	62	67	95	104	95	88	113	116	119	101	34	180	(60 - 380)
HBV status unknown at death	173	13	23	21	14	7	13	10	16	10	10	10	4	3	6	7	6	110	(30 - 280)
HCV co-infection at death	278	3	11	11	16	16	9	20	31	14	23	17	21	26	24	27	9	185	(70 - 380)
No HCV co-infection at death	947	9	26	32	45	41	45	45	64	96	81	62	96	98	104	74	29	190	(60 - 380)
HCV status unknown at death	305	17	32	29	27	21	25	19	24	19	19	25	9	8	13	13	5	130	(40 - 360)
200 or more CD4 cells per ml at start cART	465	1	10	11	18	24	22	24	36	37	42	46	45	46	51	39	13	349	(180 - 551)
Less than 200 CD4 cells per ml at start cART	902	28	48	53	61	48	47	56	71	77	65	50	72	73	74	57	22	100	(30 - 250)
Unknown CD4 count at start cART	163	0	11	8	9	6	10	4	12	15	16	8	9	13	16	18	8	190	(80 - 373)
Mode of transmission																			
Homosexual contact	808	22	45	37	53	45	41	41	47	79	57	48	69	70	74	61	19	190	(60 - 400)
Heterosexual contact	334	4	9	11	13	14	12	21	28	30	34	23	26	35	34	23	17	136	(35 - 360)
Intravenous drug use	210	2	10	11	13	13	15	11	29	13	13	14	15	20	16	12	3	170	(70 - 370)
Blood, needle accident	30	0	0	1	5	0	1	4	4	1	1	2	3	1	3	4	0	165	(98 - 213)
Other or unknown	147	1	5	12	4	6	10	6	11	6	18	17	13	6	14	14	4	180	(60 - 325)
Region of birth																			
The Netherlands	1071	21	45	55	73	56	60	55	85	92	76	71	88	90	96	77	31	189	(60 - 380)
The Netherlands Antilles	31	0	0	2	0	0	1	4	0	3	5	2	1	4	4	4	1	155	(28 - 420)
Suriname	65	0	2	0	0	3	1	5	6	6	5	6	7	7	9	7	1	186	(40 - 400)
Sub-Saharan Africa	110	1	5	4	3	7	5	6	8	9	12	10	9	12	7	8	4	123	(30 - 300)
Other	252	7	17	11	12	12	12	13	20	19	25	15	21	19	25	18	6	140	(56 - 350)
Cause of death																			
AIDS defining causes*																			
Total AIDS	521	24	46	38	40	28	37	31	36	48	48	31	35	34	33	12	0	60	(20 - 170)
Infection	172	8	15	10	11	11	12	10	16	19	15	8	9	16	9	3	0	50	(18 - 140)
Malignancy	180	5	17	9	15	8	12	9	9	14	22	16	13	9	15	7	0	111	(37 - 210)
Not specified	169	11	14	19	14	9	13	12	11	15	11	7	13	9	9	2	0	40	(16 - 120)

	Total	Year of death																	Median last CD4 count	IQR last CD4 count
		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011			
Non-AIDS defining malignancy	214	0	5	5	9	7	9	5	26	18	23	17	19	31	24	15	1	220	(100 - 420)	
Cardiovascular diseases																				
Total cardiovascular	109	2	2	4	2	5	6	13	4	15	7	12	18	10	6	2	1	307	(180 - 466)	
Myocardial infarction	42	1	1	3	0	3	3	3	2	7	1	4	7	2	3	2	0	264	(160 - 500)	
Stroke	15	1	0	0	0	1	0	4	0	3	1	2	2	1	0	0	0	270	(180 - 530)	
Other ischemic heart disease	3	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	210	(190 - 574)	
Other cardiovascular diseases	15	0	1	1	2	1	3	5	2	5	5	6	8	6	3	0	1	340	(210 - 450)	
Non-AIDS defining infection	96	0	6	3	4	3	3	8	18	7	4	9	6	8	9	8	0	140	(70 - 320)	
Liver failure, cirrhosis and HBV or HCV co-infection at death	71	0	6	3	4	4	3	2	2	5	10	7	9	10	7	5	0	250	(150 - 350)	
Lung related**	41	1	0	1	1	2	2	4	2	1	1	7	6	8	2	3	0	210	(91 - 415)	
Non-natural death																				
Total non-natural death	74	1	3	5	7	5	4	6	8	7	4	7	5	2	7	3	0	331	(120 - 570)	
Accident or other violent death	26	0	0	1	4	1	2	3	2	0	1	4	1	1	5	1	0	406	(230 - 660)	
Suicide	35	1	2	2	2	1	1	3	5	4	3	3	3	1	2	2	0	354	(215 - 600)	
Euthanasia	13	0	1	2	1	3	1	0	1	3	0	0	1	0	0	0	0	80	(30 - 130)	
Substance abuse	32	0	1	3	1	4	2	0	4	1	1	0	4	3	6	2	0	235	(95 - 483)	
Other causes***	84	0	2	6	3	7	4	3	4	5	12	8	12	6	7	4	1	285	(100 - 537)	
Unknown or unclassifiable causes	288	1	2	6	17	13	9	12	15	22	13	6	12	2	40	60	40	271	(100 - 488)	
Median last CD4 count		30	75	65	81	140	170	175	170	140	120	228	190	229	260	310	290			
IQR last CD4 count		(10 - 80)	(20 - 160)	(20 - 155)	(30 - 250)	(50 - 450)	(70 - 360)	(72 - 280)	(60 - 350)	(40 - 335)	(40 - 310)	(90 - 420)	(96 - 430)	(100 - 420)	(100 - 465)	(150 - 490)	(106 - 490)			

* According to the clinical part of the 1993 revised classification system of the U.S. Centres for Disease Control and Prevention

** Includes: primary pulmonary hypertension; lung embolus; chronic obstructive lung disease; and other types of respiratory diseases.

*** Includes: complications of diabetes mellitus; pancreatitis; lactic acidosis; liver failure without HBV or HCV at death; renal failure; haematological disease; endocrine disease; psychiatric disease; diseases of the central nervous system; diseases of the digestive system; diseases of the skin and motor system; urogenital disease; and other causes.

Legend: IQR = interquartile range; HBV = hepatitis B virus; HCV = hepatitis C virus.

Appendix Table 2.3: Number of specific AIDS-defining diseases and serious non-AIDS-defining diseases per calendar year (only the first event of each category is counted).

	Total diagnoses	Number of diagnoses																	
		1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
Any AIDS	2087	6	129	141	121	132	119	121	126	142	144	177	145	138	158	141	132	15	
AIDS dementia complex / HIV encephalopathy	138	0	1	5	5	12	8	13	4	10	9	17	8	11	17	11	7	0	
Cryptococcosis	53	0	0	2	2	4	4	4	8	3	6	4	2	6	3	3	2	0	
Cryptosporidiosis	28	0	1	7	3	2	4	1	1	2	3	2	1	0	0	0	1	0	
Herpes simplex virus	128	0	8	6	9	9	4	7	3	10	10	12	17	11	6	7	8	1	
Histoplasmosis	20	0	2	1	0	3	2	0	0	0	2	3	2	2	1	1	1	0	
Kaposi sarcoma	282	0	4	25	15	17	15	17	13	19	14	22	33	20	22	18	24	4	
Disseminated mycobacterium disease	131	2	14	12	10	10	7	9	3	3	6	9	9	12	6	8	11	0	
Other mycobacterium	75	1	5	6	6	11	10	6	5	2	3	4	1	3	6	4	2	0	
Pneumocystis jiroveci (carinii) pneumonia	223	2	6	12	16	17	15	14	21	13	14	14	13	10	22	20	14	0	
Recurrent pneumonia	231	0	4	5	8	9	12	19	12	22	19	21	13	27	27	17	12	4	
Progressive multifocal leucoencephalopathy	71	0	3	4	1	3	10	5	5	3	4	5	6	6	5	7	3	1	
Cerebral toxoplasmosis	119	0	10	6	11	12	8	11	4	13	10	12	6	7	1	3	5	0	
HIV wasting syndrome	91	0	5	5	5	10	5	3	7	4	4	11	7	8	8	5	4	0	
Candidiasis	470	0	30	33	26	28	27	33	31	34	25	39	42	33	34	27	24	4	
Cytomegalovirus infection	222	1	39	18	7	13	17	11	10	14	20	12	14	11	11	10	13	1	
Non-Hodgkin's lymphoma	218	0	13	16	15	10	10	7	10	15	14	25	16	14	20	19	13	1	
Tuberculosis	231	0	3	8	13	11	12	12	21	20	19	26	21	14	18	15	17	1	
Any other CDC-C- defining disease	70	0	8	7	4	5	8	7	4	6	2	5	4	1	3	4	2	0	
Any serious non-AIDS-defining disease	1658	60	133	131	187	183	191	202	261	275	35	
Renal insufficiency	429	5	32	30	48	51	54	58	67	75	9	
Liver disease	430				17	17	16	20	32	26	30	43	33	36	33	56	63	8	
Diabetes mellitus	440				20	31	22	24	32	35	25	33	39	33	40	58	43	5	
Myocardial infarction	222						8	11	24	22	20	20	23	25	30	17	20	2	
Osteoporosis	193								3	14	10	16	15	23	23	33	44	12	
Stroke	193						5	9	12	13	14	22	14	17	20	18	24	1	
Non-AIDS-defining malignancy	500				6	12	20	18	35	29	37	43	51	49	55	73	63	9	

* Included are events with 20 or fewer diagnoses: invasive cervical carcinoma (13), microsporidiosis (16), isosporiasis (7), leishmaniasis (5), salmonella septicaemia (1), extrapulmonary pneumocystis (2), penicilliosis (1), and unspecified events (25 diagnoses).

Type-specific AIDS diseases were combined into a single category with use of the 1993 CDC classification. For example, cytomegalovirus retinitis and cytomegalovirus infection of other sites were combined into one category. Only the first diagnosis of each type of disease after the start of cART was noted. Incidence figures for the serious non-AIDS-defining diseases are shown only from the start of routine recording of the disease in question. Centers for Disease Control and Prevention (CDC)-C events were collected beginning in 1996, whilst routine collection of diagnoses of non-AIDS-defining malignancies and diabetes mellitus started in 1998. Collection of data on myocardial infarction and CVA was started in 2000, and it was begun for renal insufficiency and osteoporosis in 2002.

Appendix Table 2.4: The incidence of individual AIDS-defining illnesses and serious non-AIDS-defining diseases per 1000 person-years of follow-up per calendar year.

	Total diagnoses	Incidence per 1000 person-years of follow-up																	
		1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
Any AIDS	24.0	203.4	175.4	63.9	41.0	36.9	29.0	25.7	23.7	24.1	22.6	25.5	19.5	17.2	17.9	14.6	14.2	14.8	
AIDS dementia complex / HIV encephalopathy	1.4	0.0	1.3	2.1	1.6	3.1	1.8	2.5	0.7	1.5	1.3	2.2	1.0	1.2	1.7	1.0	0.7	0.0	
Cryptococcosis	0.5	0.0	0.0	0.8	0.6	1.0	0.9	0.8	1.4	0.5	0.8	0.5	0.2	0.7	0.3	0.3	0.2	0.0	
Cryptosporidiosis	0.3	0.0	1.3	3.0	0.9	0.5	0.9	0.2	0.2	0.3	0.4	0.3	0.1	0.0	0.0	0.0	0.1	0.0	
Herpes simplex virus	1.3	0.0	10.4	2.5	2.8	2.3	0.9	1.4	0.5	1.5	1.4	1.6	2.0	1.2	0.6	0.7	0.8	0.9	
Histoplasmosis	0.2	0.0	2.6	0.4	0.0	0.8	0.4	0.0	0.0	0.0	0.3	0.4	0.2	0.2	0.1	0.1	0.1	0.0	
Kaposi sarcoma	2.9	0.0	5.2	10.6	4.7	4.4	3.4	3.3	2.2	2.9	2.0	2.9	4.0	2.2	2.3	1.7	2.4	3.6	
Disseminated mycobacterium disease	1.4	67.2	18.3	5.1	3.1	2.6	1.6	1.7	0.5	0.5	0.8	1.2	1.1	1.3	0.6	0.7	1.1	0.0	
Other mycobacterium	0.8	33.6	6.5	2.5	1.9	2.8	2.2	1.2	0.8	0.3	0.4	0.5	0.1	0.3	0.6	0.4	0.2	0.0	
Pneumocystis jiroveci (carinii) pneumonia	2.3	66.7	7.8	5.1	5.0	4.4	3.4	2.7	3.6	2.0	2.0	1.8	1.6	1.1	2.2	1.9	1.4	0.0	
Recurrent pneumonia	2.4	0.0	5.2	2.1	2.5	2.3	2.7	3.7	2.0	3.4	2.7	2.7	1.6	3.0	2.8	1.6	1.2	3.6	
Progressive multifocal leucoencephalopathy	0.7	0.0	3.9	1.7	0.3	0.8	2.2	1.0	0.8	0.5	0.6	0.6	0.7	0.7	0.5	0.6	0.3	0.9	
Cerebral toxoplasmosis	1.2	0.0	13.0	2.5	3.5	3.1	1.8	2.1	0.7	2.0	1.4	1.6	0.7	0.8	0.1	0.3	0.5	0.0	
HIV wasting syndrome	0.9	0.0	6.5	2.1	1.6	2.6	1.1	0.6	1.2	0.6	0.6	1.4	0.8	0.9	0.8	0.5	0.4	0.0	
Candidiasis	5.0	0.0	39.2	14.2	8.3	7.3	6.1	6.5	5.4	5.3	3.6	5.1	5.1	3.7	3.5	2.5	2.4	3.6	
Cytomegalovirus infection	2.3	33.3	51.3	7.7	2.2	3.4	3.8	2.1	1.7	2.2	2.8	1.6	1.7	1.2	1.1	0.9	1.3	0.9	
Non-Hodgkin's lymphoma	2.3	0.0	16.9	6.8	4.7	2.6	2.2	1.4	1.7	2.3	2.0	3.2	1.9	1.6	2.0	1.8	1.3	0.9	
Tuberculosis	2.4	0.0	3.9	3.4	4.1	2.8	2.7	2.3	3.6	3.1	2.7	3.4	2.5	1.6	1.8	1.4	1.7	0.9	
Any other CDC-C- defining disease	0.9	0.0	10.4	3.0	1.3	1.3	1.8	1.4	0.7	0.9	0.3	0.6	0.5	0.1	0.3	0.4	0.2	0.0	
Any serious non-AIDS-defining disease	24.7	21.1	21.9	19.9	26.2	24.0	23.4	22.6	27.0	29.9	35.5	
Renal insufficiency	5.9	1.7	4.9	4.3	6.3	6.2	6.1	6.0	6.3	7.4	8.2	
Liver disease	4.7	.	.	.	5.4	4.4	3.6	3.9	5.5	4.0	4.3	5.6	4.0	4.1	3.4	5.3	6.2	7.3	
Diabetes mellitus	4.8	.	.	.	6.3	8.0	4.9	4.7	5.5	5.4	3.6	4.3	4.8	3.7	4.1	5.5	4.3	4.6	
Myocardial infarction	2.7	3.4	2.1	4.1	3.4	2.8	2.6	2.8	2.8	3.1	1.6	2.0	1.8	
Osteoporosis	2.6	1.0	2.1	1.4	2.1	1.8	2.6	2.3	3.1	4.3	10.8	
Stroke	2.6	2.1	1.7	2.0	2.0	2.0	2.8	1.7	1.9	2.0	1.7	2.3	0.9	
Non-AIDS-defining malignancy	5.5	.	.	.	3.5	3.1	4.4	3.5	6.0	4.5	5.2	5.6	6.2	5.5	5.6	6.9	6.2	8.1	

* Included are events with 20 or fewer diagnoses: invasive cervical carcinoma (13), microsporidiosis (16), isosporiasis (7), leishmaniasis (5), salmonella septicaemia (1), extrapulmonary pneumocystis (2), penicilliosis (1), and unspecified events (25 diagnoses).

Type-specific AIDS-defining diseases were combined into a single category with use of the 1993 CDC classification. For example, cytomegalovirus retinitis and cytomegalovirus infection of other sites were combined into one category. Only the first diagnosis of each type of disease after the start of cART was noted. Incidence figures for the serious non-AIDS-defining diseases are shown only from the start of routine recording of the disease in question. Centers for Disease Control and Prevention (CDC)-C events were collected beginning in 1996, whilst routine collection of diagnoses of non-AIDS-defining malignancies and diabetes mellitus started in 1998. Collection of data on myocardial infarction and cerebrovascular accident was started in 2000, and it was begun for renal insufficiency and osteoporosis in 2002.

Appendix Table 2.5: The incidence per 1,000 person years of follow-up of newly diagnosed, routinely collected serious co-morbidities and AIDS per age group for male and female patients after starting cART. The confidence intervals reported are based on the Poisson distribution.

	Age in years	Male					Female				
		Number of diagnoses	Person years of follow-up	Incidence per 1,000 person years of follow-up	Confidence interval		Number of diagnoses	Person years of follow-up	Incidence per 1,000 person years of follow-up	Confidence interval	
					Lower	Upper				Lower	Upper
Any AIDS	<30	111	3646	30.4	25.0	36.7	89	3632	24.5	19.7	30.2
	30-40	524	19128	27.4	25.1	29.8	196	7618	25.7	22.3	29.6
	40-50	610	27079	22.5	20.8	24.4	100	4963	20.1	16.4	24.5
	50-60	320	14010	22.8	20.4	25.5	22	1456	15.1	9.5	22.9
	≥60	102	4895	20.8	17.0	25.3	13	650	20.0	10.7	34.2
Any serious non-AIDS defining disease	<30	20	2499	8.0	4.9	12.4	21	2849	7.4	4.6	11.3
	30-40	183	13060	14.0	12.1	16.2	85	6298	13.5	10.8	16.7
	40-50	518	21622	24.0	21.9	26.1	111	4396	25.2	20.8	30.4
	50-60	407	11021	36.9	33.4	40.7	53	1205	44.0	32.9	57.5
	≥60	234	3747	62.5	54.7	71.0	26	513	50.6	33.1	74.2
Renal insufficiency	<30	7	2520	2.8	1.1	5.7	7	2901	2.4	1.0	5.0
	30-40	47	13431	3.5	2.6	4.7	14	6539	2.1	1.2	3.6
	40-50	109	23378	4.7	3.8	5.6	30	4813	6.2	4.2	8.9
	50-60	105	12556	8.4	6.8	10.1	20	1354	14.8	9.0	22.8
	≥60	83	4700	17.7	14.1	21.9	7	617	11.4	4.6	23.4
Liver disease	<30	9	3649	2.5	1.1	4.7	6	3715	1.6	0.6	3.5
	30-40	72	19637	3.7	2.9	4.6	35	8190	4.3	3.0	5.9
	40-50	180	28696	6.3	5.4	7.3	31	5432	5.7	3.9	8.1
	50-60	75	15241	4.9	3.9	6.2	10	1547	6.5	3.1	11.9
	≥60	11	5471	2.0	1.0	3.6	1	710	1.4	0.0	7.8
Diabetes mellitus	<30	2	3663	0.5	0.1	2.0	11	3691	3.0	1.5	5.3
	30-40	50	19699	2.5	1.9	3.3	31	8231	3.8	2.6	5.3
	40-50	127	28788	4.4	3.7	5.2	31	5445	5.7	3.9	8.1
	50-60	108	14901	7.2	5.9	8.8	11	1525	7.2	3.6	12.9
	≥60	60	5109	11.7	9.0	15.1	9	662	13.6	6.2	25.8
Myocardial infarction	<30	0	3072	0.0	.	1.2	0	3364	0.0	.	1.1
	30-40	12	16596	0.7	0.4	1.3	4	7567	0.5	0.1	1.4
	40-50	73	26437	2.8	2.2	3.5	5	5312	0.9	0.3	2.2
	50-60	78	13978	5.6	4.4	7.0	0	1517	0.0	.	2.4
	≥60	45	5034	8.9	6.5	12.0	5	667	7.5	2.4	17.5

	Age in years	Male					Female				
		Number of diagnoses	Person years of follow-up	Incidence per 1,000 person years of follow-up	Confidence interval		Number of diagnoses	Person years of follow-up	Incidence per 1,000 person years of follow-up	Confidence interval	
					Lower	Upper				Lower	Upper
Osteoporosis	<30	1	2535	0.4	0.0	2.2	2	2910	0.7	0.1	2.5
	30-40	11	13546	0.8	0.4	1.5	3	6603	0.5	0.1	1.3
	40-50	62	23600	2.6	2.0	3.4	14	4858	2.9	1.6	4.8
	50-60	47	12787	3.7	2.7	4.9	15	1379	10.9	6.1	17.9
	≥60	28	4865	5.8	3.8	8.3	10	605	16.5	7.9	30.4
Stroke	<30	3	3065	1.0	0.2	2.9	2	3364	0.6	0.1	2.1
	30-40	15	16594	0.9	0.5	1.5	9	7544	1.2	0.5	2.3
	40-50	37	26631	1.4	1.0	1.9	10	5310	1.9	0.9	3.5
	50-60	46	14215	3.2	2.4	4.3	4	1503	2.7	0.7	6.8
	≥60	38	5138	7.4	5.2	10.2	5	676	7.4	2.4	17.3
Non-AIDS malignancy	<30	5	3665	1.4	0.4	3.2	1	3724	0.3	0.0	1.5
	30-40	46	19709	2.3	1.7	3.1	16	8314	1.9	1.1	3.1
	40-50	148	29009	5.1	4.3	6.0	29	5554	5.2	3.5	7.5
	50-60	147	15258	9.6	8.1	11.3	10	1545	6.5	3.1	11.9
	≥60	97	5246	18.5	15.0	22.6	7	708	9.9	4.0	20.4

Appendix Table 2.6: The incidence per 1000 person-years of newly diagnosed, routinely collected, serious co-morbidities and any AIDS-defining disease according to the latest CD4 cell count after the start of cART. Follow-up of each patient was split into periods of three months, and for each period the latest CD4 cell count was selected. The confidence intervals are based on the Poisson distribution.

	Latest CD4 cell count (cells/mm ³)	Number of diagnoses	Person years of follow-up	Incidence per 1,000 person years of follow-up	95% confidence interval	
Any AIDS	<50	526	910	577.9	529.6	629.5
	50 - 200	635	7318	86.8	80.2	93.8
	200 - 350	386	16385	23.6	21.3	26.0
	350 - 500	230	20711	11.1	9.7	12.6
	≥500	223	39684	5.6	4.9	6.4
Any serious non-AIDS-defining disease	<50	79	618	127.8	101.2	159.3
	50 - 200	266	4801	55.4	48.9	62.5
	200 - 350	348	12288	28.3	25.4	31.5
	350 - 500	335	16611	20.2	18.1	22.4
	≥500	619	31856	19.4	17.9	21.0
Renal insufficiency	<50	49	661	74.1	54.8	97.9
	50 - 200	121	5365	22.6	18.7	26.9
	200 - 350	81	13352	6.1	4.8	7.5
	350 - 500	62	17832	3.5	2.7	4.5
	≥500	114	34555	3.3	2.7	4.0
Liver disease	<50	17	1171	14.5	8.5	23.2
	50 - 200	73	7954	9.2	7.2	11.5
	200 - 350	104	17518	5.9	4.9	7.2
	350 - 500	80	21993	3.6	2.9	4.5
	≥500	151	41786	3.6	3.1	4.2
Diabetes mellitus	<50	17	1158	14.7	8.5	23.5
	50 - 200	56	8047	7.0	5.3	9.0
	200 - 350	91	17510	5.2	4.2	6.4
	350 - 500	88	21871	4.0	3.2	5.0
	≥500	184	41264	4.5	3.8	5.2
Myocardial infarction	<50	4	892	4.5	1.2	11.5
	50 - 200	20	6736	3.0	1.8	4.6
	200 - 350	45	15596	2.9	2.1	3.9
	350 - 500	53	20126	2.6	2.0	3.4
	≥500	98	38772	2.5	2.1	3.1

	Latest CD ₄ cell count (cells/mm ³)	Number of diagnoses	Person years of follow-up	Incidence per 1,000 person years of follow-up	95% confidence interval	
Osteoporosis	<50	3	695	4.3	0.9	12.6
	50 - 200	21	5539	3.8	2.3	5.8
	200 - 350	45	13548	3.3	2.4	4.4
	350 - 500	49	18007	2.7	2.0	3.6
	≥500	75	34854	2.2	1.7	2.7
Stroke	<50	7	898	7.8	3.1	16.1
	50 - 200	33	6775	4.9	3.4	6.8
	200 - 350	41	15652	2.6	1.9	3.6
	350 - 500	38	20262	1.9	1.3	2.6
	≥500	50	39028	1.3	1.0	1.7
Non-AIDS malignancy	<50	20	1121	17.8	10.9	27.5
	50 - 200	85	7774	10.9	8.7	13.5
	200 - 350	121	17220	7.0	5.8	8.4
	350 - 500	109	21773	5.0	4.1	6.0
	≥500	162	41560	3.9	3.3	4.5

Appendix Table 2.7: Estimates of odds ratios obtained from two time-updated logistic regression models on non-AIDS morbidity and mortality.

		Non-AIDS morbidity			Non-AIDS mortality				
		Odds ratio	95% Confidence interval	P-value	Odds ratio	95% Confidence interval	P-value		
Treatment status at start cART	Anti-retroviral therapy naive	0.77	0.68	0.88	<.0001	0.78	0.62	0.99	0.0432
	Anti-retroviral therapy experienced	1.00				1.00			
Age in years during follow-up	<30	0.13	0.09	0.18	<.0001	0.19	0.10	0.36	<.0001
	30-40	0.22	0.18	0.26	<.0001	0.24	0.16	0.35	<.0001
	40-50	0.35	0.30	0.41	<.0001	0.31	0.22	0.44	<.0001
	50-60	0.56	0.48	0.66	<.0001	0.66	0.47	0.94	0.0215
	≥60	1.00				1.00			
Latest CD4 count (cells/mm ³)	<50	3.88	2.98	5.05	<.0001	5.31	3.60	7.83	<.0001
	50-200	1.83	1.55	2.15	<.0001	2.85	2.13	3.81	<.0001
	200-350	1.00				1.00			
	350-500	0.76	0.65	0.88	0.0004	0.77	0.55	1.07	0.1234
	≥500	0.74	0.64	0.85	<.0001	0.58	0.42	0.81	0.0012
Years between HIV diagnosis and start of cART (per year longer)		1.02	1.01	1.03	0.0029	1.04	1.01	1.06	0.0041
Hepatitis B virus co-infection	-	1.00				1.00			
	+	1.32	1.13	1.55	0.0006	1.06	0.74	1.52	0.7369
Hepatitis C virus co-infection	-	1.00				1.00			
	+	2.25	1.99	2.55	<.0001	1.97	1.50	2.59	<.0001
Cumulative time (per year longer) after starting cART with HIV RNA _{≥1000} copies/ml		1.03	0.99	1.07	0.2058	1.13	1.02	1.24	0.0169

Appendix Table 3.1: Unadjusted and adjusted results from a Cox regression analysis of time from start of cART to initial virologic suppression to ≤ 50 copies/ml. Models were also adjusted for laboratory (results not shown).

	Unadjusted			Adjusted				
	HR	95% CI	P-value	HR	95% CI	P-value		
Gender								
Male	1.00			1.00				
Female	1.00	0.94	1.06	0.92	1.10	1.30	<0.0001	
CD4 at the start of cART (cells/mm³)							<0.0001*	
<50	0.84	0.77	0.90	<0.0001	0.97	0.88	1.06	0.46
50-200	0.88	0.82	0.93	<0.0001	0.94	0.88	1.00	0.06
200-350	1.00				1.00			
350-500	0.89	0.82	0.97	0.009	0.89	0.82	0.98	0.01
≥ 500	0.78	0.70	0.87	<0.0001	0.79	0.70	0.89	0.0002
HIV RNA at the start of cART (copies/ml)								<0.0001*
<10000	1.26	1.16	1.37	<0.0001	1.58	1.45	1.73	<0.0001
10000-100000	1.00				1.00			
≥ 100000	0.70	0.66	0.74	<0.0001	0.65	0.61	0.69	<0.0001
Transmission risk group								0.006*
MSM	1.00				1.00			
Heterosexual	0.93	0.88	0.98	0.004	0.95	0.88	1.03	0.22
IDU	0.76	0.67	0.87	0.0001	0.75	0.64	0.88	0.0005
Other	0.90	0.81	0.99	0.03	0.97	0.86	1.08	0.55
Region of origin								0.04*
Netherlands	1.00				1.00			
Caribbean/South America	0.84	0.77	0.91	<0.0001	0.99	0.91	1.09	0.87
Sub Sahara Africa	0.88	0.83	0.94	0.0002	0.94	0.86	1.03	0.21
W-Europe/N-America	0.79	0.72	0.87	<0.0001	0.84	0.76	0.94	0.002
Other	0.91	0.83	1.00	0.04	0.96	0.87	1.07	0.47
Age at the start of cART (years)								<0.0001*
16-29	0.89	0.83	0.95	0.0009	0.89	0.82	0.96	0.003
30-39	1.00				1.00			
40-49	1.10	1.03	1.16	0.002	1.08	1.02	1.16	0.01
≥ 50	1.03	0.96	1.11	0.37	1.07	0.99	1.16	0.09
Calendar year of starting cART								<0.0001*
1999	0.74	0.64	0.86	0.0001	0.78	0.66	0.94	0.0077
2000	0.75	0.66	0.86	<0.0001	0.72	0.61	0.84	<0.0001
2001	0.89	0.78	1.02	0.09	1.00	0.86	1.16	0.99
2002	0.86	0.77	0.98	0.02	0.91	0.79	1.04	0.17
2003	0.88	0.78	0.99	0.04	0.90	0.78	1.03	0.12

	Unadjusted				Adjusted			
	HR	95% CI	P-value	HR	95% CI	P-value		
2004	1.08	0.96	1.21	0.21	1.08	0.95	1.23	0.22
2005	1.00				1.00			
2006	0.97	0.86	1.08	0.55	0.97	0.85	1.10	0.65
2007	0.99	0.89	1.11	0.88	0.88	0.78	0.99	0.04
2008	0.99	0.90	1.10	0.92	0.87	0.77	0.97	0.01
2009	0.91	0.82	1.01	0.09	0.91	0.80	1.02	0.11
2010	0.81	0.72	0.91	0.0006	0.83	0.72	0.96	0.01
AIDS diagnosis at the start of cART								
No	1.00							
Yes	0.98	0.93	1.04	0.59				
Hepatitis B diagnosis at the start of cART								
-	1.00				1.00			
+	1.11	1.00	1.22	0.04	1.14	1.03	1.26	0.01
Hepatitis C diagnosis at the start of cART								
-	1.00							
+	0.99	0.90	1.09	0.8413				
cART started during primary infection								
No	1.00				1.00			
Yes	0.83	0.75	0.91	0.0001	0.89	0.80	0.99	0.03
Daily dosing								
NNRT-based regimen								
1	1.00				1.00			
2	0.84	0.78	0.91		0.81	0.74	0.89	
PI-based regimen								
1	1.00				1.00			
2	1.08	0.96	1.21	0.13	1.09	0.96	1.24	0.15
3	0.43	0.29	0.64		0.64	0.42	0.97	0.04
Pregnant at the start of cART								
No	1.00							
Yes	1.01	0.91	1.13	0.85				
Integrase inhibitor included in initial regimen								
No	1.00				1.00			
Yes	1.46	1.11	1.91	0.006	1.87	1.40	2.50	<0.0001
Assay used for HIV RNA determination								
TaqMan2	0.78	0.69	0.87	0.0000	0.72	0.62	0.83	<0.0001
Other assay	1.00				1.00			

Legend: cART= combination antiretroviral therapy; HR=hazard ratio; CI=confidence interval; MSM=men having sex with men; IDU=injecting drug use; W-Europe=Western Europe; N-America=North America.

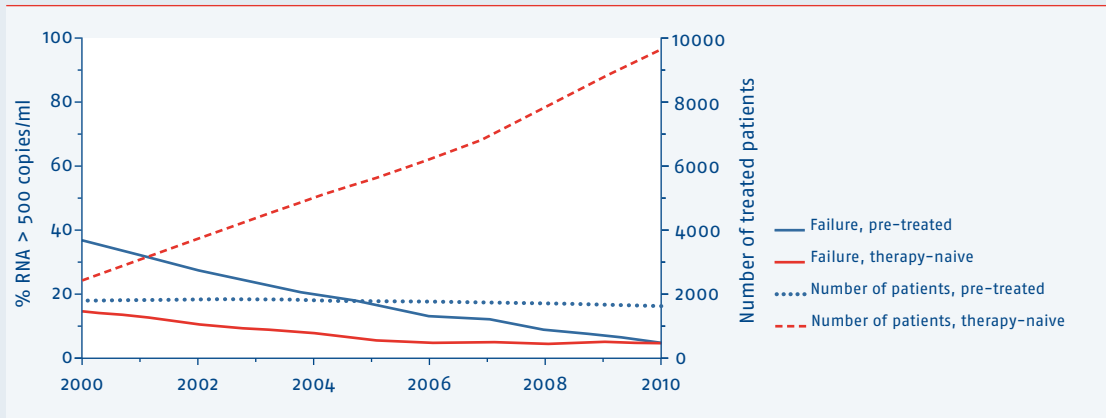
Appendix Table 4.1: Number of patients with evidence of various levels of resistance to specific antiretroviral drugs, according to the Stanford algorithm for scoring mutations. Altogether, out of 14,610 patients still in follow-up as of June 2011, 1773 (12%) patients were included.

	Susceptible		Potential low-level		Low-level		Intermediate		High-level	
	N	%	N	%	N	%	N	%	N	%
Protease inhibitors (PIs)^a										
FPV	1251	71	112	6	130	7	152	9	123	7
IDV	1246	70	101	6	18	1	181	10	222	13
NFV	1154	65	29	2	18	1	114	6	453	26
SQV	1307	74	54	3	45	3	158	9	204	12
LOP	1260	71	160	9	81	5	172	10	95	5
ATV	1182	67	106	6	142	8	149	8	189	11
TPV	1514	86	63	4	135	8	44	2	12	1
DRV	1605	91	88	5	61	4	13	1	1	0
Any PI	1132	64	47	3	15	1	111	6	463	26
Nucleoside RT inhibitors (NRTIs)										
ABC	317	18	527	30	195	11	427	24	307	17
AZT	791	45	24	1	260	15	306	17	392	22
d4T	681	38	87	5	336	19	346	20	323	18
ddI	655	37	231	13	203	11	411	23	273	15
TDF	791	45	243	14	251	14	451	25	37	2
Any NRTI	266	15	359	20	257	14	364	21	527	30
3TC/FTC	606	34	42	2	45	3	48	3	1032	58
Non-nucleoside RT inhibitors (NNRTIs)										
EFV	866	49	44	2	18	1	238	13	607	34
NVP	841	47	59	3	16	1	17	1	840	47
ETR	1069	60	150	8	185	10	314	18	55	3
Any NNRTI	841	47	59	3	15	1	18	1	840	47

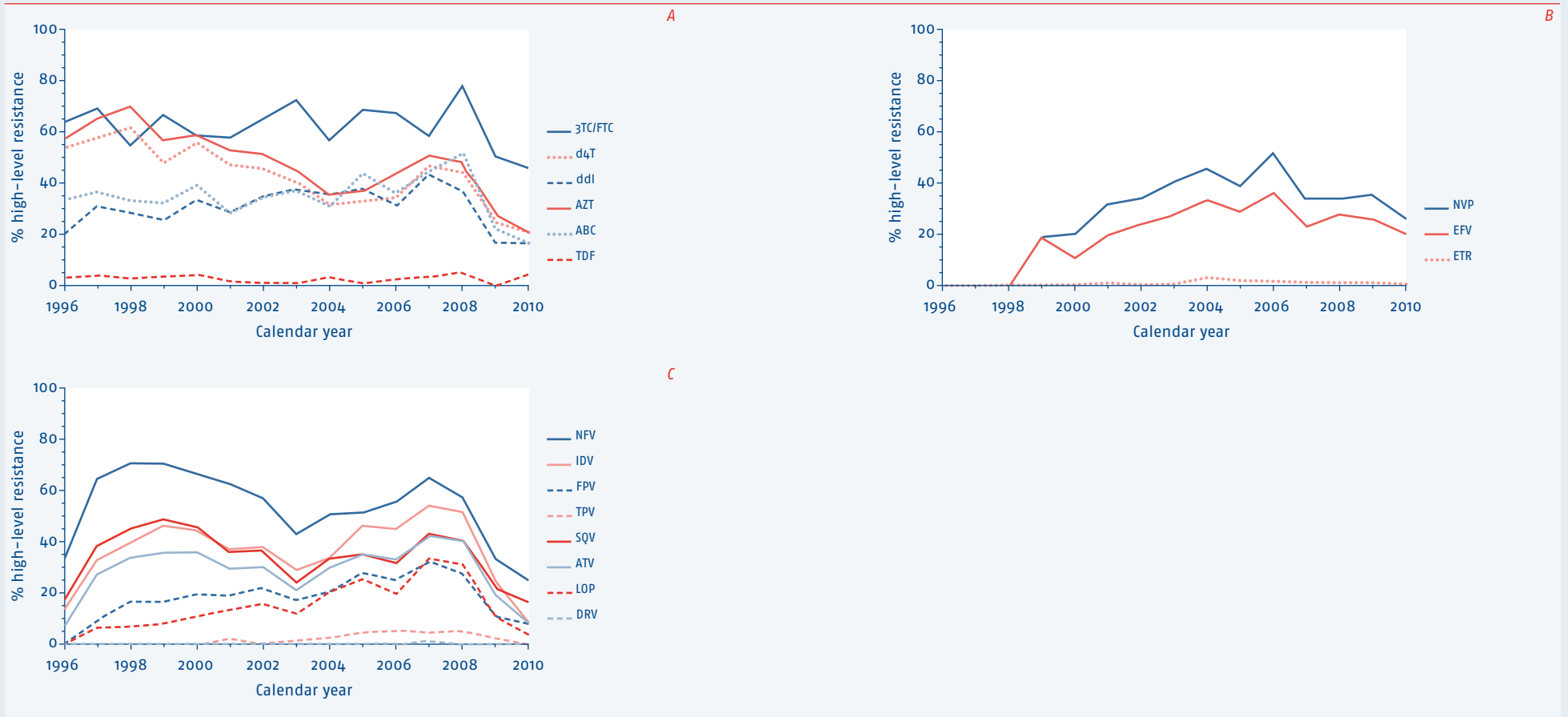
Legend: FPV=fosamprenavir; IDV=indinavir; NFV=nelfinavir; SQV=saquinavir; LOP=lopinavir; ATV= atazanavir; TPV=tipranavir; DRV=darunavir; ABC=abacavir; AZT=azidothymidine; d4T=stavudine; ddI=didanosine; TDF=tenofovir; 3TC/FTC=lamivudine/emtricitabine; EFV=efavirenz; NVP=nevirapine; ETR=etravirine.

^a protease not available for 5 patients.

Appendix Figure 4.1: Annual number of treated patients and the proportion of patients with virologic failure, i.e., a viral load above 500 copies/ml whilst the patient was being treated that was measured at least four months after the start of cART or four months after resumption of treatment following an interruption. Amongst approximately 1800 pre-treated patients, the proportion with failure decreased from 37% in 2000 to 5% in 2010. Amongst previously therapy-naïve patients, failure was less common and decreased from 15% to 5% during the same period, whilst the number of naïve patients increased from approximately 2500 to 9700.

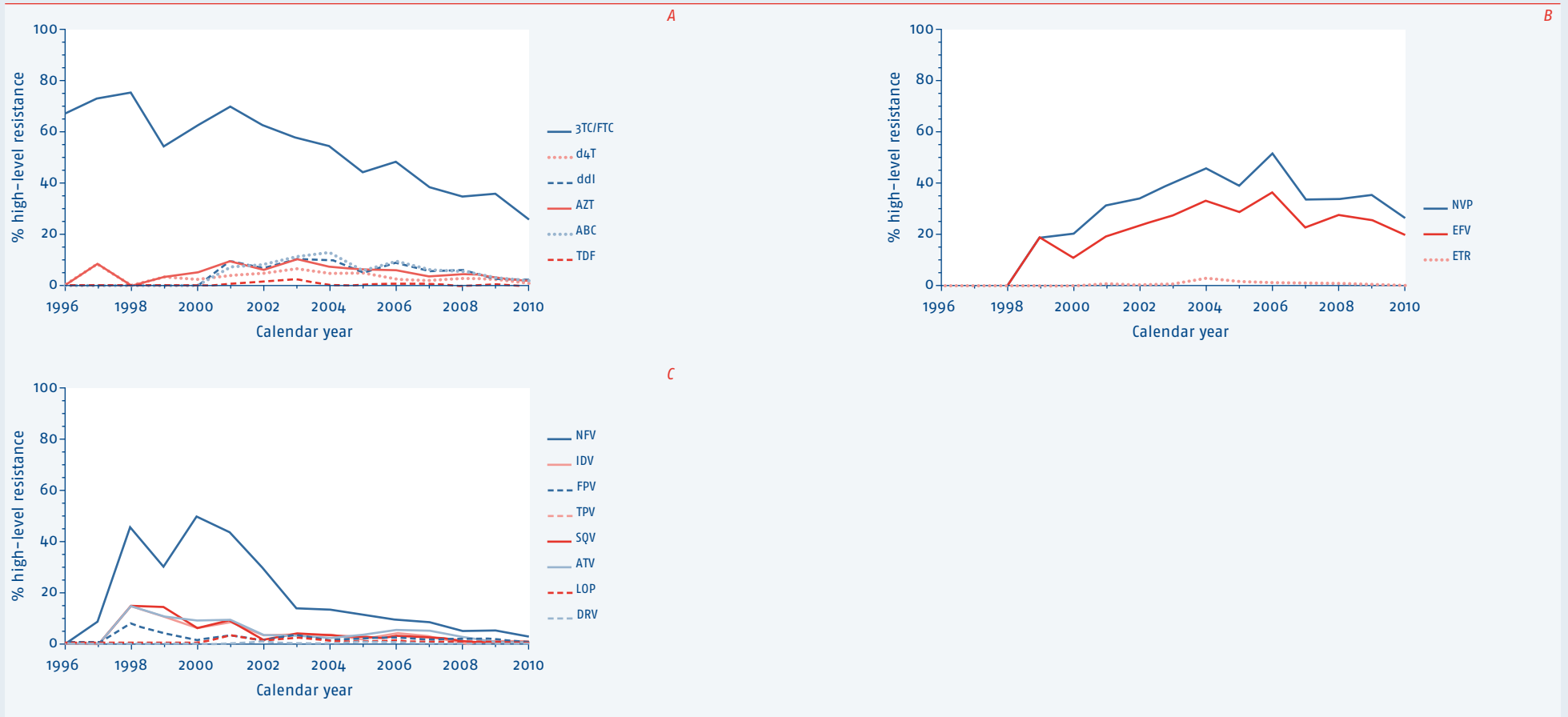


Appendix Figure 4.2: Annual proportion of sequences from treated patients with evidence of high-level resistance, according to the Stanford mutation interpretation algorithm, in patients who had received treatment regimens not considered combination antiretroviral treatment. Resistance is shown to individual drugs from the three original drug classes including (A) nucleoside reverse transcriptase inhibitors, (B) non-nucleoside reverse transcriptase inhibitors, and (C) protease inhibitors.



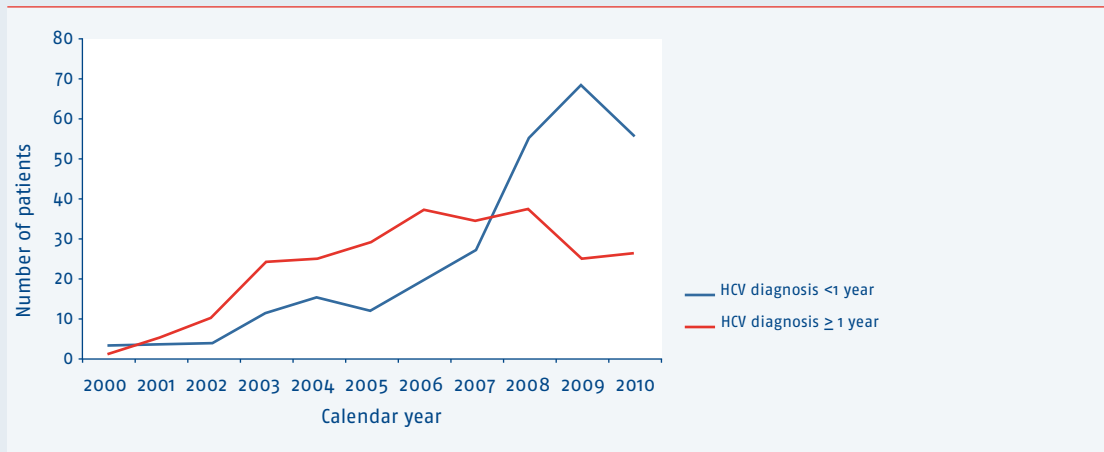
Legend: 3TC/FTC=lamivudine/emtricitabine; d4T=stavudine; ddI=didanosine; AZT=azidothymidine; ABC=abacavir; TDF=tenofovir; NVP=nevirapine; EFV=efavirenz; ETR=etravirine; NFV=nelfinavir; IDV=indinavir; FPV=fosamprenavir; TPV=tipranavir; SQV=saquinavir; ATV=atazanavir; LOP=lopinavir; DRV=darunavir.

Appendix Figure 4.3: Annual proportion of sequences from treated patients with evidence of high-level resistance, according to the Stanford mutation interpretation algorithm, in previously therapy-naïve patients whose first treatment regimen was combination antiretroviral treatment. Resistance is shown to individual drugs from the three original drug classes including (A) nucleoside reverse transcriptase inhibitors, (B) non-nucleoside reverse transcriptase inhibitors, and (C) protease inhibitors.



Legend: 3TC/FTC=lamivudine/emtricitabine; d4T=stavudine; ddi=didanosine; AZT=zidovudine; ABC=abacavir; TDF=tenofovir; NVP=nevirapine; EFV=efavirenz; ETR=etravirine; NFV=nelfinavir; IDV=indinavir; FPV=fosamprenavir; TPV=tipranavir; SQV=saquinavir; ATV=atazanavir; LOP=lopinavir; DRV=darunavir.

Appendix Figure 5.1: Calendar year of the start of anti-hepatitis C virus (HCV) treatment according to time since HCV diagnosis.



Appendix Table 7.1: Annual number of diagnoses in Curaçao stratified by sex and survival status as of June 2011.

	Alive, in follow-up		Alive, lost to follow-up		Dead		Total	
	Men	Women	Men	Women	Men	Women	Men	Women
≤1999	76	47	21	13	50	16	147	76
2000	14	11	2	4	6	4	22	19
2001	7	8	4	4	5	4	16	16
2002	14	9	9	7	5	2	28	18
2003	19	11	6	4	11	2	36	17
2004	12	8	6	6	10	2	28	16
2005	25	5	0	8	3	4	28	17
2006	19	11	4	3	3	2	26	16
2007	18	5	4	5	5	1	27	11
2008	16	13	12	5	2	1	30	19
2009	21	12	5	4	0	2	26	18
2010	15	13	3	0	2	0	20	13
2011	3	4	0	0	0	0	3	4
Total	259	157	76	63	102	40	437	260
Unknown	10	6	13	6	6	8	29	20

