Monitoring Report 2013

Human Immunodeficiency Virus (HIV) Infection in the Netherlands

HIV Monitoring

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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HIV Monitoring

Colophon

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Monitoring of Human Immunodeficiency Virus (HIV)
Infection in the Netherlands

Appendix

List of tables and figures

The Web Appendix contains tables and figures supplementary to SHM's Monitoring Report 2013. The first number in the table or figure numbering below relates to the relevant chapter of the report.

Web Appendix Table 1.1: Characteristics of the 17,006 HIV-infected patients in follow-up as of June 2013.

	MSM	Heterosexual		IDU		Blood or blood products		Other / unknown		Total	
	Men	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
	N=10,161	N=2,208	N=2,953	N=260	N=95	N=132	N=83	N=849	N=265	N=13,610	N=3,396
Current age [years]											
0–12	0	0	0	0	0	0	0	64	60	64	60
	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	7.5%	22.6%	0.5%	1.8%
13–17	0	0	2	0	0	1	1	31	34	32	37
	0.0%	0.0%	0.1%	0.0%	0.0%	0.8%	1.2%	3.7%	12.8%	0.2%	1.1%
18–24	202	20	62	1	0	2	1	51	30	276	93
	2.0%	0.9%	2.1%	0.4%	0.0%	1.5%	1.2%	6.0%	11.3%	2.0%	2.7%
25–34	1,276	247	662	18	3	12	13	108	36	1,661	714
	12.6%	11.2%	22.4%	6.9%	3.2%	9.1%	15.7%	12.7%	13.6%	12.2%	21.0%
35–44	2,653	598	1,082	42	11	31	26	166	45	3,490	1,164
	26.1%	27.1%	36.6%	16.2%	11.6%	23.5%	31.3%	19.6%	17.0%	25.6%	34.3%
45–54	3,693	782	771	124	55	47	23	239	39	4,885	888
	36.3%	35.4%	26.1%	47.7%	57.9%	35.6%	27.7%	28.2%	14.7%	35.9%	26.1%
55–64	1,745	384	269	72	24	25	12	128	16	2,354	321
	17.2%	17.4%	9.1%	27.7%	25.3%	18.9%	14.5%	15.1%	6.0%	17.3%	9.5%
≥65	592	177	105	3	2	14	7	62	5	848	119
	5.8%	8.0%	3.6%	1.2%	2.1%	10.6%	8.4%	7.3%	1.9%	6.2%	3.5%
Current age 50 years or older											
No	6,137	1,272	2,265	120	33	75	52	544	228	8,148	2,578
	60.4%	57.6%	77.7%	46.2%	34.7%	56.8%	62.7%	64.1%	86.0%	59.9%	75.9%
Yes	4,024	936	688	140	62	57	31	305	37	5,462	818
	39.6%	42.4%	23.3%	53.8%	65.3%	43.2%	37.3%	35.9%	14.0%	40.1%	24.1%
Region of origin											
Netherlands	7,485	967	802	160	50	84	19	412	112	9,108	983
	73.7%	43.8%	27.2%	61.5%	52.6%	63.6%	22.9%	48.5%	42.3%	66.9%	28.9%
Sub-Saharan Africa	123	657	1327	4	0	26	37	211	85	1,021	1,449
	1.2%	29.8%	44.9%	1.5%	0.0%	19.7%	44.6%	24.9%	32.1%	7.5%	42.7%
Western Europe	666	74	71	29	28	6	2	41	28	816	129
	6.6%	3.4%	2.4%	11.2%	29.5%	4.5%	2.4%	4.8%	10.6%	6.0%	3.8%
Latin America	631	209	284	9	1	4	9	47	7	900	301
	6.2%	9.5%	9.6%	3.5%	1.1%	3.0%	10.8%	5.5%	2.6%	6.6%	8.9%
Caribbean	359	124	166	6	1	3	4	26	2	518	173
	3.5%	5.6%	5.6%	2.3%	1.1%	2.3%	4.8%	3.1%	0.8%	3.8%	5.1%
Other	859	172	301	52	15	9	12	107	29	1,199	357
	8.5%	7.8%	10.2%	20.0%	15.8%	6.8%	14.5%	12.6%	10.9%	8.8%	10.5%
Unknown	38	5	2	0	0	0	0	5	2	48	4
	0.4%	0.2%	0.1%	0.0%	0.0%	0.0%	0.0%	0.6%	0.8%	0.4%	0.1%

	MSM	Heterosexual		IDU		Blood or blood products		Other / unknown		Total	
	Men	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
	N=10,161	N=2,208	N=2,953	N=260	N=95	N=132	N=83	N=849	N=265	N=13,610	N=3,396
Years aware of HIV infection											
<1	527	93	100	2	1	6	2	21	9	649	112
	5.2%	4.2%	3.4%	0.8%	1.1%	4.5%	2.4%	2.5%	3.4%	4.8%	3.3%
1–2	1,380	281	276	7	1	9	6	87	27	1,764	310
	13.6%	12.7%	9.3%	2.7%	1.1%	6.8%	7.2%	10.2%	10.2%	13.0%	9.1%
3–4	1,448	270	300	8	1	5	3	79	32	1,810	336
	14.3%	12.2%	10.2%	3.1%	1.1%	3.8%	3.6%	9.3%	12.1%	13.3%	9.9%
5–10	2,872	686	942	33	13	17	21	258	67	3,866	1,043
	28.3%	31.1%	31.9%	12.7%	13.7%	12.9%	25.3%	30.4%	25.3%	28.4%	30.7%
>10	3,925	874	1,307	208	79	94	51	287	118	5,388	1,555
	38.6%	39.6%	44.3%	80.0%	83.2%	71.2%	61.4%	33.8%	44.5%	39.6%	45.8%
Unknown	9	4	28	2	0	1	0	117	12	133	40
	0.1%	0.2%	0.9%	0.8%	0.0%	0.8%	0.0%	13.8%	4.5%	1.0%	1.2%
Current CD4 count [cells/mm³],	580	520	575	470	645	485	654	520	695	570	580
median / IQR	443–754	370–697	410–762	320–700	360–840	286–716	490–890	350–750	463–985	430–747	420–780
Current CD8 count [cells/mm³],	920	870	830	860	881	799	840	860	820	910	830
median / IQR	680–1,250	610–1,240	600–1,140	580–1,180	660–1,200	580–1,076	569–1,049	610–1,180	535–1,115	660–1,250	600–1,135
Current HIV RNA <500 copies/ml	8,328	1,844	2,377	230	82	112	71	625	209	11,139	2,739
	82.0%	83.5%	80.5%	88.5%	86.3%	84.8%	85.5%	73.6%	78.9%	81.8%	80.7%
Current HIV RNA <100 copies/ml	8,066	1,757	2,256	224	80	108	71	603	204	10,758	2,611
	79.4%	79.6%	76.4%	86.2%	84.2%	81.8%	85.5%	71.0%	77.0%	79.0%	76.9%
Ever AIDS	1,926	670	636	87	45	44	24	261	67	2,988	772
	19.0%	30.3%	21.5%	33.5%	47.4%	33.3%	28.9%	30.7%	25.3%	22.0%	22.7%
AIDS at diagnosis	996	448	364	22	12	20	13	192	28	1,678	417
	9.8%	20.3%	12.3%	8.5%	12.6%	15.2%	15.7%	22.6%	10.6%	12.3%	12.3%
Current treatment											
cART	8,726	1,972	2,644	249	94	121	81	694	236	11,762	3,055
	85.9%	89.3%	89.5%	95.8%	98.9%	91.7%	97.6%	81.7%	89.1%	86.4%	90.0%
Non-cART	46	5	8	3	0	0	0	3	1	57	9
	0.5%	0.2%	0.3%	1.2%	0.0%	0.0%	0.0%	0.4%	0.4%	0.4%	0.3%
Not started	1,389	231	301	8	1	11	2	152	28	1,791	332
	13.7%	10.5%	10.2%	3.1%	1.1%	8.3%	2.4%	17.9%	10.5%	13.2%	9.8%
Co-infection											
HBV	823	204	182	36	3	18	4	60	22	1,141	211
	8.1%	9.2%	6.2%	13.8%	3.2%	13.6%	4.8%	7.1%	8.3%	8.4%	6.2%
HCV	919	110	134	240	88	42	8	84	49	1,395	279
	9.0%	5.0%	4.5%	92.3%	92.6%	31.8%	9.6%	9.9%	18.5%	10.2%	8.2%

Legend: *MSM=men who have sex with men; IDU=injection drug use; IQR=interquartile range; HBV=hepatitis B; HCV=hepatitis C.*

Web Appendix Table 1.2: *Annual number of HIV-1 diagnoses amongst adults per transmission risk group, including men who have sex with men (MSM), patients infected via heterosexual contact, injection drug use (IDU), contact with contaminated blood, or other or unknown modes of transmission. Note: data collection for 2011 and 2012 is not yet finalised. *: projected numbers of diagnoses when the backlog in registration of HIV cases (3% in 2011, 11% in 2012) is taken into account.*

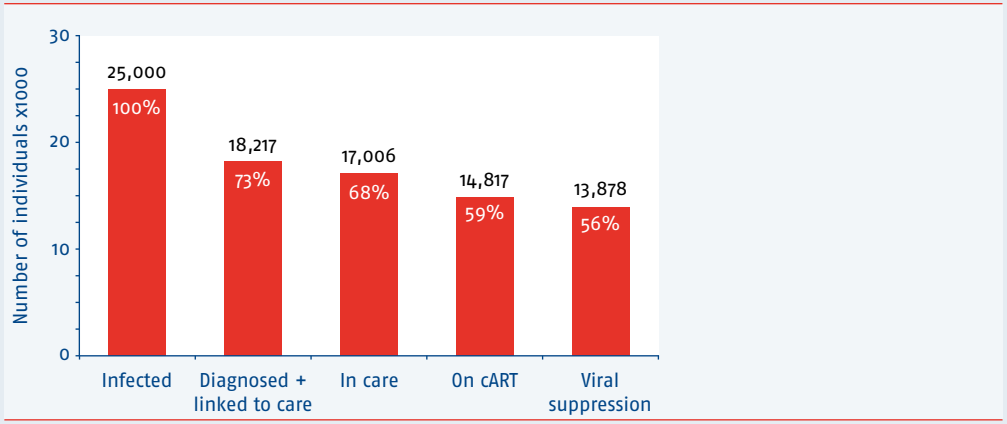
	MSM	Heterosexual		IDU		Blood or blood products		Other/unknown		Total
Year of diagnosis	**Men**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	
≤1995	2,195	261	386	286	133	58	21	155	50	3,545
1996	386	92	82	32	11	4	4	36	4	651
1997	436	110	129	43	10	7	3	45	7	790
1998	332	107	113	22	5	6	5	30	9	629
1999	354	107	138	18	7	8	4	21	5	662
2000	375	159	189	18	3	3	4	34	6	791
2001	441	169	210	14	5	7	4	40	8	898
2002	460	164	249	15	3	11	7	61	4	974
2003	452	180	271	22	5	9	2	62	15	1,018
2004	575	194	262	9	4	4	3	72	11	1,134
2005	635	195	254	14	2	3	5	64	11	1,183
2006	655	160	190	10	5	4	7	53	5	1,089
2007	758	153	204	9	3	2	6	49	7	1,191
2008	832	176	173	6	1	3	2	52	5	1,250
2009	751	153	170	6	0	1	1	47	9	1,138
2010	742	171	152	4	1	5	2	36	8	1,121
2011	703	139	136	2	1	5	5	50	6	1,047
2011*	724	143	140	2	1	5	5	52	6	1078
2012	630	134	126	6	1	3	3	36	8	947
2012*	699	149	140	7	1	3	3	40	9	1051
2013	151	21	27	0	0	4	0	8	3	214
Total	11,863	2,845	3,461	536	200	147	88	951	181	20,272

Web Appendix Table 1.3: *Region of origin of the 20,272 adult HIV-1-infected patients with a recorded date of diagnosis. For men who have sex with men (MSM) and for heterosexual men and women, numbers are stratified according to year of HIV diagnosis.*

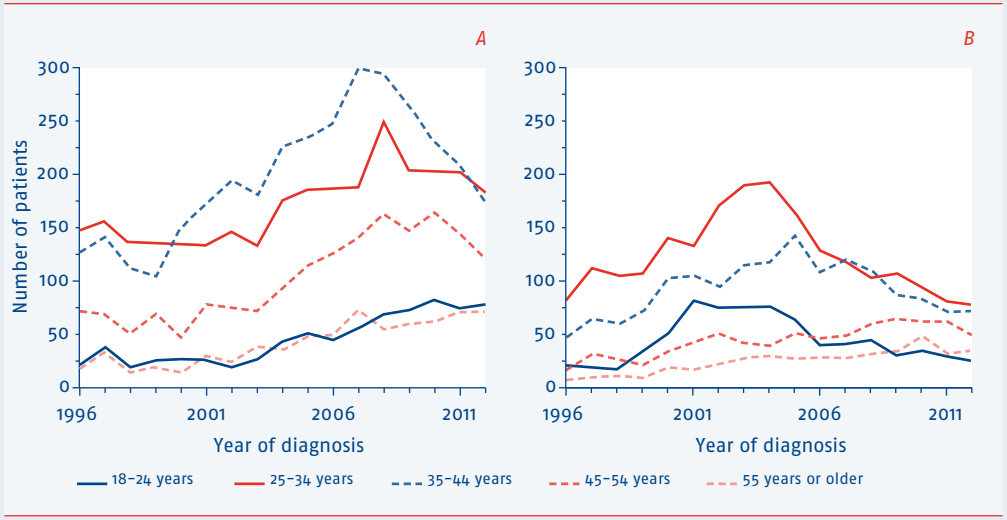
	MSM			Heterosexual men			Heterosexual women			IDU	Other
	<2011	≥2011	Total	<2011	≥2011	Total	<2011	≥2011	Total	Total	Total
The Netherlands	7,400	1,124	8,524	1,019	134	1,153	768	83	851	442	608
	71.3%	75.7%	71.9%	40.0%	45.6%	40.5%	24.2%	28.7%	24.6%	60.1%	44.5%
Sub-Saharan Africa	142	19	161	852	60	912	1,525	110	1,635	8	341
	1.4%	1.3%	1.4%	33.4%	20.4%	32.1%	48.1%	38.1%	47.2%	1.1%	24.9%
Western Europe	843	75	918	92	9	101	88	7	95	143	107
	8.1%	5.1%	7.8%	3.6%	3.1%	3.6%	2.8%	2.4%	2.7%	19.4%	7.8%
Central Europe	173	40	213	65	15	80	40	12	52	26	45
	1.7%	2.7%	1.8%	2.5%	5.1%	2.8%	1.3%	4.2%	1.5%	3.5%	3.3%
Eastern Europe	54	10	64	10	1	11	19	5	24	25	19
	0.5%	0.7%	0.5%	0.4%	0.3%	0.4%	0.6%	1.7%	0.7%	3.4%	1.4%
Latin America	701	63	764	258	33	291	301	34	335	24	79
	6.8%	4.2%	6.4%	10.1%	11.2%	10.2%	9.5%	11.8%	9.7%	3.3%	5.8%
Caribbean	328	66	394	128	21	149	190	12	202	13	35
	3.2%	4.4%	3.3%	5.0%	7.1%	5.2%	6.0%	4.2%	5.8%	1.8%	2.6%
South and Southeast Asia	291	47	338	45	6	51	191	22	213	19	51
	2.8%	3.2%	2.8%	1.8%	2.0%	1.8%	6.0%	7.6%	6.2%	2.6%	3.7%
Other/unknown	447	40	487	82	15	97	50	4	54	36	82
	4.3%	2.7%	4.1%	3.2%	5.1%	3.4%	1.6%	1.4%	1.6%	4.9%	6.0%

Legend: *MSM=men who have sex with men; IDU=injection drug use.*

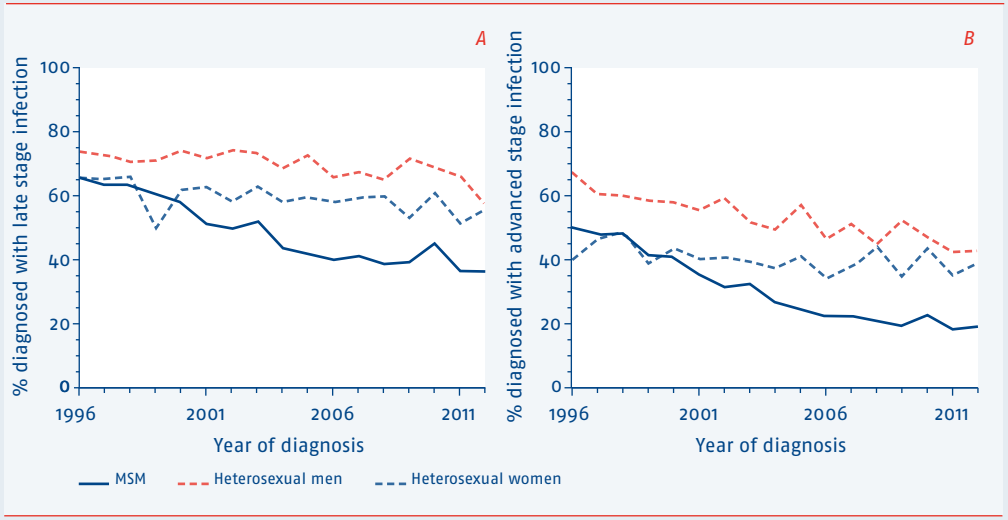
Web Appendix Figure 1.1: *Cascade of HIV care for the total HIV-infected population in the Netherlands as of June 2013. According to UNAIDS, 25,000 were living with HIV in the Netherlands in 2012. In total, 18,217 patients were ever linked to care and registered by SHM and still alive and not reported as having moved abroad (21,157 registered patients minus 2,104 patients who died minus 836 patients who moved abroad). Of these patients, 17,006 were still in care, whilst 14,817 had started combination antiretroviral treatment (cART). Altogether, 13,878 patients of the patients in care had a most recent RNA measurement below the limit of quantification or below 500 copies/ml.*



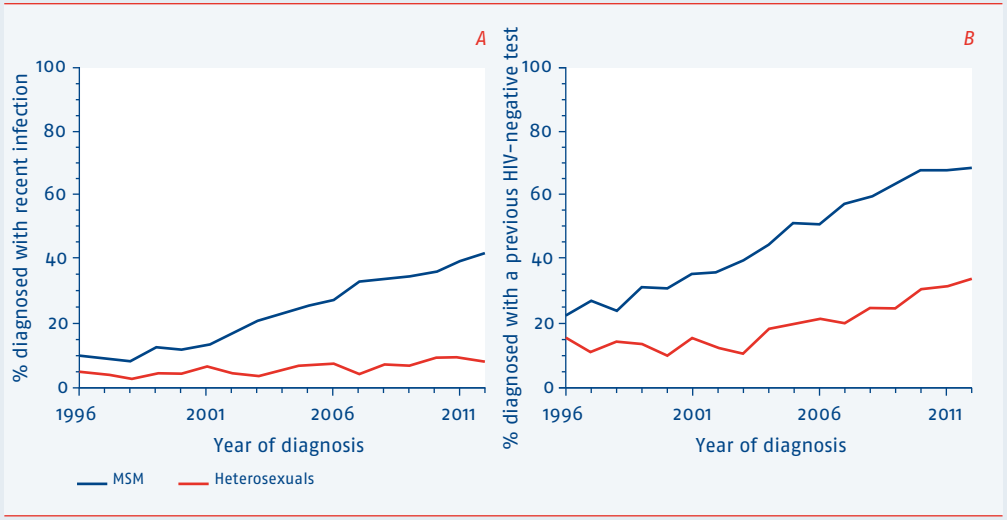
Web Appendix Figure 1.2: *Age distribution at the time of diagnosis amongst HIV-1-infected adult men who have sex with men (A) and heterosexual men and women (B). Note: data collection for 2011 and 2012 is not yet finalised.*



Web Appendix Figure 1.3: *Proportion of patients classified as presenting with (A) late or (B) advanced HIV infection at the time of HIV diagnosis. From 1996 onwards, 54% were diagnosed with late-stage HIV: men who have sex with men (MSM) 46%, heterosexual men 70%, heterosexual women 59%, injection drug users (IDU) 67%. Overall, 36% were advanced presenters: MSM 27%, heterosexual men 52%, heterosexual women 39%, and IDU 50%. Late stage infection: CD4 counts below 350 cells/mm³ or having AIDS, regardless of CD4 count. Advanced stage infection: CD4 counts below 200 cells/mm³ or having AIDS.*



Web Appendix Figure 1.4: *Proportion of patients diagnosed with a recent HIV infection (A) or with a previous HIV-negative test (B). A diagnosed infection was considered to be recent if the time between the last negative HIV test and the first positive test was at most 1.5 years. The proportion diagnosed with a recent infection increased from 10% in 1996 to 42% in 2012 amongst men who have sex with men (MSM) and varied between 5% and 10% during the same period for heterosexual men and women. Median CD4 counts in those diagnosed with a recent infection were 500 (370-670) cells/mm³ in MSM and 459 (290-650) cells/mm³ in heterosexual men and women. Amongst those diagnosed with a non-recent infection, CD4 counts were 210 (76-398) cells/mm³ in 1996 and 370 (190-548) cells/mm³ in 2012 in MSM, whilst in heterosexuals CD4 counts increased from 190 (50-400) cells/mm³ to 263 (65-470) cells/mm³ during the same period. Altogether, 69% of MSM and 34% of heterosexuals (men 28%, women 41%) diagnosed in 2012 had a previous HIV-negative test.*



Web Appendix Table 2.1: Baseline characteristics of 17,443 patients starting combination antiretroviral therapy (cART) between 1 January 1995 and 31 December 2012 by gender and region of origin.

Year of starting cART	1995-2000		2001-2006		2007-2011		2012	
	N	%	N	%	N	%	N	%
Total (N, %)	5,228	100	5,071	100	6,111	100	924	100
Male	4,292	82.1	3,651	72.0	5,070	83.0	810	87.7
Female	936	17.9	1,420	28.0	1,041	17.0	114	12.3
Region of origin in men								
Netherlands	2,903	67.6	2,104	57.6	3,436	67.8	578	71.4
W-Europe/N-America/Australia	514	12.0	315	8.6	376	7.4	38	4.7
Caribbean/S-America	367	8.6	433	11.9	506	10.0	78	9.6
Sub-Saharan Africa	255	5.9	517	14.2	351	6.9	41	5.1
Other	253	5.9	282	7.7	401	7.9	75	9.3
Region of origin in women								
Netherlands	343	36.6	270	19.0	272	26.1	30	26.3
W-Europe/N-America/Australia	94	10.0	57	4.0	39	3.7	1	0.9
Caribbean/S-America	124	13.2	205	14.4	151	14.5	25	21.9
Sub-Saharan Africa	312	33.3	756	53.2	454	43.6	40	35.1
Other	63	6.7	132	9.3	125	12.0	18	15.8

Web Appendix Table 2.2: *Overview of the most frequently recorded adverse events leading to a toxicity driven therapy stop 2005–2011. Multiple adverse events in a patient during the same year are counted once. For every toxicity driven therapy stop up to 3 adverse events could be recorded. Therefore percentages do not add up to 100%.*

	2005		2006		2007		2008		2009		2010		2011		2012	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Patients with at least 1 toxicity driven therapy stop	882		883		911		1,000		989		1,041		998		986	
Body composition and serum lipids																
Lipodystrophy, any	172	19.5	151	17.1	132	14.5	136	13.6	102	10.3	54	5.2	52	5.2	80	8.1
Lipoatrophy, peripheral fat loss	125	14.2	112	12.7	103	11.3	104	10.4	79	8.0	58	5.6	35	3.5	32	3.2
Lipohpertrophy – central fat accumulation	41	4.6	37	4.2	26	2.9	29	2.9	21	2.1	19	1.8	17	1.7	16	1.6
Lipodystrophy unspecified	7	0.8	4	0.5	3	0.3	3	0.3	3	0.3	4	0.4		0.0	6	0.6
Elevated triglycerides	22	2.5	12	1.4	9	1.0	17	1.7	17	1.7	16	1.5	24	2.4	6	0.6
Elevated cholesterol	14	1.6	18	2.0	17	1.9	19	1.9	11	1.1	12	1.2	14	1.4	19	1.9
Liver																
Elevated gamma GT	13	1.5	8	0.9	13	1.4	11	1.1	26	2.6	23	2.2	22	2.2	21	2.1
Icterus	8	0.9	13	1.5	8	0.9	6	0.6	8	0.8	24	2.3	23	2.3	20	2.0
Elevated ASAT	3	0.3	9	1.0	11	1.2	8	0.8	15	1.5	14	1.3	12	1.2	11	1.1
Elevated bilirubin	6	0.7	8	0.9	12	1.3	9	0.9	10	1.0	14	1.3	12	1.2	8	0.8
Elevated ALAT	7	0.8	4	0.5	3	0.3	5	0.5	10	1.0	11	1.1	5	0.5	9	0.9
Hepatic steatosis	4	0.5	4	0.5	1	0.1	2	0.2	3	0.3		0.0	6	0.6		0.0
Lactate acidosis	2	0.2	7	0.8	5	0.5	2	0.2	1	0.1	2	0.2	1	0.1		0.0
Renal																
Renal insufficiency	23	2.6	21	2.4	35	3.8	45	4.5	41	4.1	47	4.5	52	5.2	73	7.4
Elevated creatinine	5	0.6	16	1.8	19	2.1	21	2.1	24	2.4	23	2.2	31	3.1	40	4.1
Nephrolithiasis	9	1.0	5	0.6	4	0.4	2	0.2	2	0.2	5	0.5	10	1.0	3	0.3
Neurological / psychosocial																
Depression	23	2.6	23	2.6	21	2.3	39	3.9	45	4.6	43	4.1	62	6.2	56	5.7
Dizziness	22	2.5	26	2.9	35	3.8	27	2.7	46	4.7	42	4.0	30	3.0	37	3.8
Sleeplessness	11	1.2	22	2.5	19	2.1	23	2.3	29	2.9	39	3.7	60	6.0	53	5.4
Non-HIV related neuropathy	39	4.4	34	3.9	30	3.3	22	2.2	14	1.4	12	1.2	10	1.0	6	0.6
Mood changes	10	1.1	10	1.1	20	2.2	25	2.5	30	3.0	45	4.3	42	4.2	42	4.3
Nightmares	17	1.9	17	1.9	16	1.8	25	2.5	23	2.3	34	3.3	30	3.0	33	3.3
Headache	7	0.8	9	1.0	15	1.6	7	0.7	8	0.8	27	2.6	23	2.3	15	1.5
Concentration disorders	6	0.7	4	0.5	8	0.9	9	0.9	10	1.0	8	0.8	10	1.0	13	1.3
Fear	3	0.3	5	0.6	3	0.3	4	0.4	9	0.9	10	1.0	4	0.4	4	0.4
Paresthesia (transient numbness or tingling)	4	0.5		0.0	3	0.3	7	0.7	5	0.5	2	0.2	3	0.3	1	0.1
Erection disorders	3	0.3	2	0.2	5	0.5	2	0.2	1	0.1	8	0.8	3	0.3	3	0.3
Psychosis	2	0.2		0.0		0.0	1	0.1	4	0.4	2	0.2	7	0.7	2	0.2
Loss of libido	4	0.5	2	0.2	1	0.1	3	0.3	1	0.1	2	0.2	3	0.3	7	0.7
Confusion	3	0.3	1	0.1	1	0.1	1	0.1	3	0.3	2	0.2	1	0.1		0.0
Loss of memory		0.0	2	0.2	1	0.1	2	0.2		0.0	4	0.4	1	0.1	6	0.6

	2005		2006		2007		2008		2009		2010		2011		2012	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Gastrointestinal																
Diarrhoea	66	7.5	77	8.7	81	8.9	97	9.7	98	9.9	101	9.7	97	9.7	60	6.1
Nausea	41	4.6	48	5.4	70	7.7	48	4.8	40	4.0	42	4.0	38	3.8	32	3.2
Vomiting	24	2.7	22	2.5	14	1.5	23	2.3	24	2.4	28	2.7	19	1.9	12	1.2
Abdominal pain	13	1.5	11	1.2	12	1.3	20	2.0	12	1.2	18	1.7	15	1.5	14	1.4
Flatulence	2	0.2	1	0.1	2	0.2	4	0.4	8	0.8	4	0.4	12	1.2	7	0.7
Weight loss	4	0.5	2	0.2	4	0.4	6	0.6	2	0.2	1	0.1	2	0.2		0.0
Loss of appetite	1	0.1	3	0.3	5	0.5	1	0.1	3	0.3	2	0.2	3	0.3	4	0.4
Change in taste	3	0.3	1	0.1	1	0.1	3	0.3	3	0.3	3	0.3	2	0.2	1	0.1
Constipation	1	0.1	3	0.3	1	0.1	1	0.1	1	0.1	3	0.3		0.0	2	0.2
Dermatological																
Rash	58	6.6	61	6.9	61	6.7	86	8.6	68	6.9	80	7.7	62	6.2	43	4.4
Itchiness	11	1.2	12	1.4	13	1.4	9	0.9	13	1.3	12	1.2	14	1.4	13	1.3
Systemic																
Fatigue	35	4.0	40	4.5	35	3.8	32	3.2	29	2.9	42	4.0	43	4.3	39	4.0
General discomfort	10	1.1	3	0.3	10	1.1	12	1.2	11	1.1	11	1.1	15	1.5	13	1.3
Fever	7	0.8	8	0.9	3	0.3	4	0.4	3	0.3	1	0.1	2	0.2	5	0.5
Night sweats	1	0.1	3	0.3	1	0.1	2	0.2	1	0.1	2	0.2	2	0.2	3	0.3
Haematological																
Anaemia	34	3.9	41	4.6	25	2.7	29	2.9	31	3.1	24	2.3	11	1.1	19	1.9
Leucopenia	17	1.9	15	1.7	8	0.9	5	0.5	7	0.7	3	0.3	4	0.4	6	0.6
Pancytopenia	3	0.3	5	0.6	2	0.2	5	0.5	2	0.2	2	0.2	2	0.2	3	0.3
Thrombocytopenia	3	0.3	3	0.3		0.0	3	0.3	1	0.1	3	0.3	3	0.3	2	0.2
Neutropenia		0.0	3	0.3		0.0		0.0	2	0.2	2	0.2	4	0.4	5	0.5
Neuromuscular																
Myalgia	1	0.1	5	0.6	4	0.4	7	0.7	8	0.8	7	0.7	4	0.4	3	0.3
Myopathy	5	0.6	4	0.5	11	1.2	3	0.3	1	0.1	2	0.2		0.0	3	0.3
Arthralgia		0.0	2	0.2	2	0.2	3	0.3	4	0.4	11	1.1	1	0.1	1	0.1
Skeletal																
Osteoporosis	1	0.1	2	0.2		0.0	5	0.5	1	0.1	3	0.3	2	0.2	4	0.4
Osteopenia		0.0	1	0.1		0.0	3	0.3	1	0.1	3	0.3	1	0.1	4	0.4

	2005		2006		2007		2008		2009		2010		2011		2012	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Cardiovascular																
Hypertension	2	0.2	2	0.2	3	0.3	3	0.3	4	0.4	3	0.3	4	0.4	5	0.5
Myocardial infarction	1	0.1	1	0.1	1	0.1	4	0.4	1	0.1	2	0.2	1	0.1	1	0.1
Elevated creatine phosphokinase	2	0.2		0.0		0.0		0.0	3	0.3	2	0.2	3	0.3		0.0
Cardiomyopathy	1	0.1	1	0.1		0.0	2	0.2	1	0.1	3	0.3	1	0.1		0.0
Other																
Cough	2	0.2		0.0	2	0.2	2	0.2	1	0.1	2	0.2	3	0.3	1	0.1
Pancreatitis	2	0.2	2	0.2	1	0.1	4	0.4	1	0.1			1	0.1	2	0.2
Abacavir hypersensitivity	4	0.5	9	1.0	6	0.7	2	0.2	2	0.2	1	0.1		0.0	1	0.1
Diabetes mellitus (both I and II)	3	0.3	3	0.3	3	0.3	1	0.1	6	0.6	7	0.7	4	0.4	4	0.4

Web Appendix Table 3.1: *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 17,006 patients still in follow-up as of June 2013, 2,062 (12%) patients with at least one major resistance-associated mutation from the March 2013 International Antiviral Society-USA (IAS-USA) list were included.*

	Susceptible		Potential low-level		Low-level		Intermediate		High-level	
	N	%	N	%	N	%	N	%	N	%
Protease inhibitors (PIs)[a]										
FPV	1,510	73	127	6	94	5	115	6	211	10
IDV	1,526	74	99	5	81	4	113	5	238	12
NFV	1,211	59	179	9	159	8	49	2	459	22
SQV	1,633	79	20	1	22	1	120	6	262	13
LPV	1,535	75	159	8	81	4	137	7	145	7
ATV	1,491	72	119	6	80	4	107	5	260	13
TPV	1,729	84	47	2	132	6	126	6	23	1
DRV	1,890	92	78	4	51	2	32	2	6	0
Any PI	1,188	58	199	10	155	8	46	2	469	23
Nucleoside RT inhibitors (NRTIs)										
ABC	644	31	31	2	594	29	313	15	480	23
AZT	1,041	50	36	2	189	9	208	10	588	29
d4T	921	45	41	2	219	11	302	15	579	28
ddI	612	30	414	20	253	12	332	16	451	22
TDF	1,094	53	53	3	262	13	390	19	263	13
Any NRTI	482	23	21	1	562	27	232	11	765	37
3TC/FTC	783	38	54	3	69	3	49	2	1,107	54
Non-nucleoside RT inhibitors (NNRTIs)										
EFV	1,061	51	29	1	46	2	244	12	682	33
NVP	993	48	57	3	51	2	28	1	933	45
ETR	1,376	67	163	8	143	7	302	15	78	4
RPV	1,376	67	117	6	138	7	304	15	127	6
Any NNRTI	976	47	54	3	55	3	44	2	933	45

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

[a] *protease not available for 5 patients.*

Web Appendix Table 3.2: *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 17,006 patients still in follow-up as of June 2013, 7,155 (42%) patients with at least one genotypic sequence were included. Note that due to small differences in resistance-associated mutations between the Stanford algorithm and the International Antiviral Society-USA (IAS-USA) list, the number of patients with resistance may be different from those reported in Web Appendix Table 3.1.*

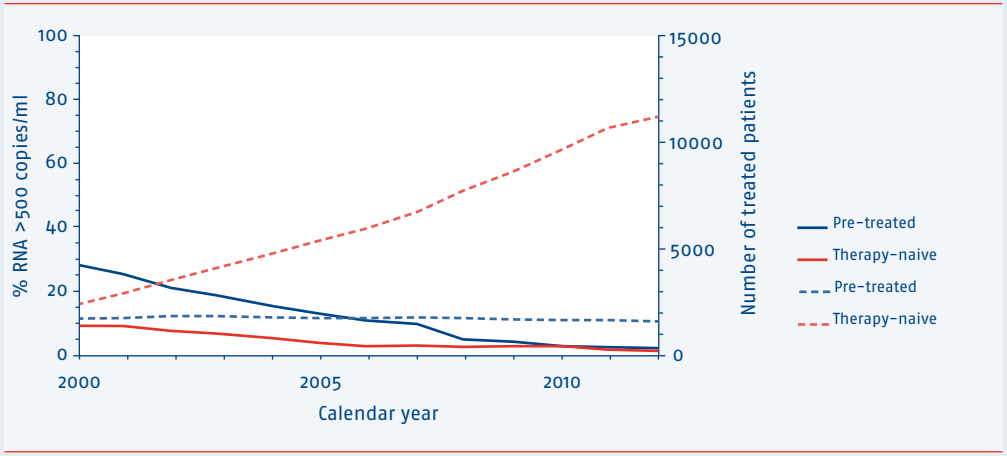
	Susceptible		Potential low-level		Low-level		Intermediate		High-level	
	N	%	N	%	N	%	N	%	N	%
Protease inhibitors (PIs)[a]										
FPV	6,557	92	167	2	96	1	115	2	211	3
IDV	6,612	93	100	1	83	1	113	2	238	3
NFV	5,645	79	656	9	330	5	56	1	459	6
SQV	6,717	94	23	0	24	0	120	2	262	4
LPV	6,622	93	161	2	81	1	137	2	145	2
ATV	6,573	92	124	2	82	1	107	1	260	4
TPV	6,815	95	48	1	134	2	126	2	23	0
DRV	6,979	98	78	1	51	1	32	0	6	0
Any PI	5,607	78	691	10	326	5	53	1	469	7
Nucleoside RT inhibitors (NRTIs)[b]										
ABC	5,610	78	149	2	595	8	314	4	480	7
AZT	5,992	84	44	1	315	4	209	3	588	8
d4T	5,864	82	55	1	347	5	303	4	579	8
ddI	5,527	77	571	8	261	4	338	5	451	6
TDF	6,176	86	57	1	262	4	390	5	263	4
Any NRTI	5,386	75	64	1	695	10	238	3	765	11
3TC/FTC	5,867	82	56	1	69	1	49	1	1107	15
Non-nucleoside RT inhibitors (NNRTIs)[b]										
EFV	6,049	85	117	2	55	1	244	3	683	10
NVP	5,970	84	142	2	66	1	34	0	936	13
ETR	6,389	89	233	3	146	2	302	4	78	1
RPV	6,389	89	187	3	141	2	304	4	127	2
Any NNRTI	5,953	83	138	2	71	1	50	1	936	13

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

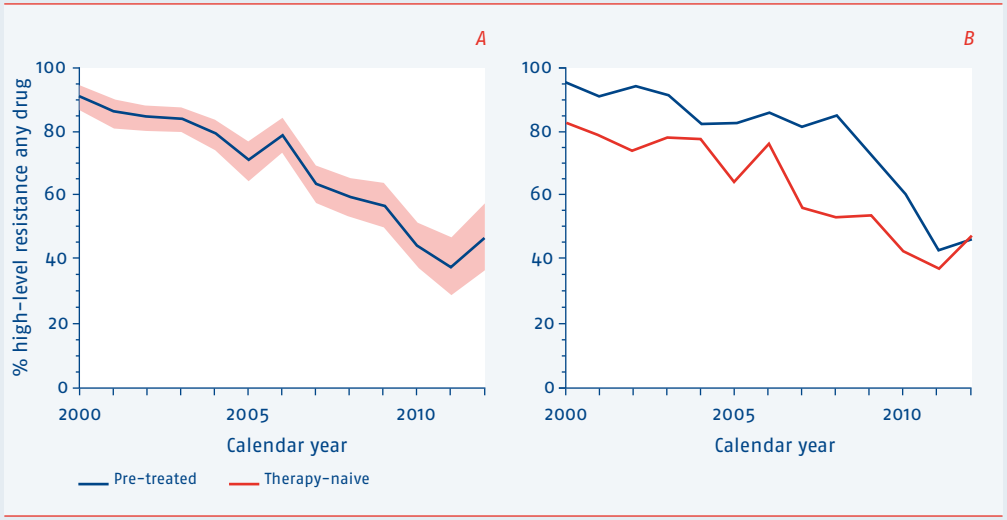
[a] *protease not available for 9 patients;*

[b] *RT not available for 7 patients.*

Web Appendix Figure 3.1: *Annual number of treated patients with a viral load measurement (dashed lines) and the proportion of patients with virological failure (solid lines), i.e., a viral load above 500 copies/ml whilst on treatment and measured at least 4 months after start of cART or 4 months after resuming treatment following a treatment interruption. Amongst approximately 1,700 pre-treated patients, the proportion with failure with use of a threshold of 500 copies/ml decreased from 28% in 2000 to 2% in 2012. Amongst previously therapy-naïve patients, failure was less common and decreased from 10% to 2% during the same period, whilst the number of naïve patients increased from approximately 2,350 to 11,250.*



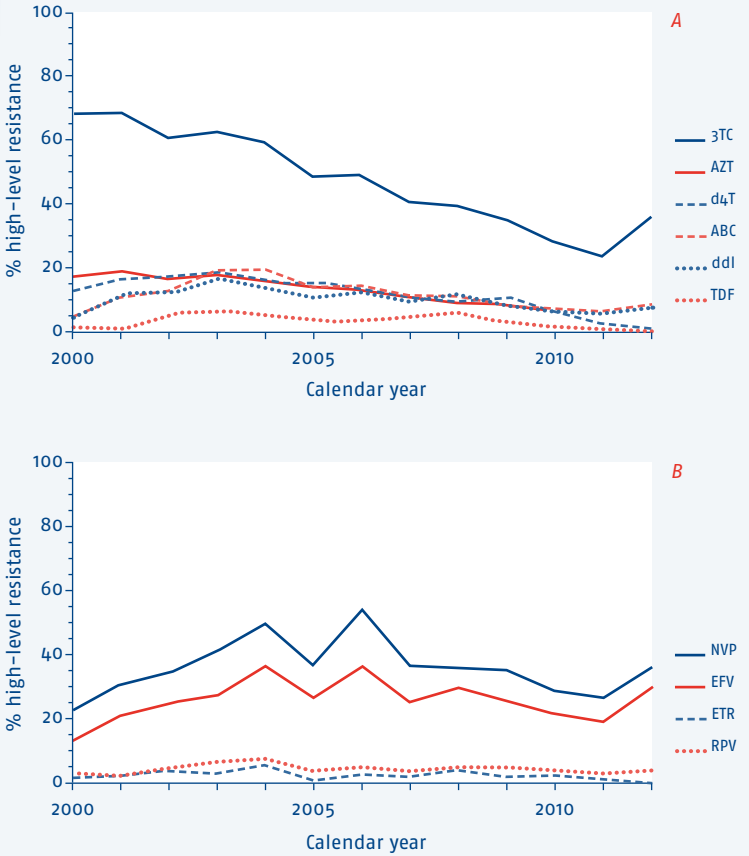
Web Appendix Figure 3.2: *(A) The proportion of sequences obtained at the time of virological failure with evidence of high-level resistance to any antiretroviral drug decreased from 91% in 2000 to 47% in 2012. The shaded area is the 95% confidence interval. (B) Resistance to any antiretroviral drug was found more often in patients pre-treated with mono- or dual therapy before commencing combination antiretroviral therapy (cART).*

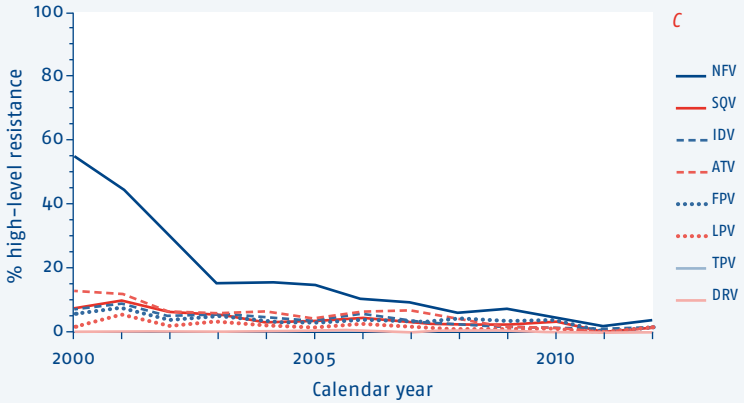


Web Appendix Figure 3.3: *Annual proportion of sequences from treated patients with evidence of high-level resistance, according to the Stanford mutation interpretation algorithm, in patients who received treatment regimens that were not considered combination antiretroviral treatment (cART). Resistance is shown to individual drugs from the four original drug classes including (A) nucleoside reverse transcriptase inhibitors and lamivudine/emtricitabine, (B) non-nucleoside reverse transcriptase inhibitors, and (C) protease inhibitors.*

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

Web Appendix Figure 3.4: *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 who started with combination antiretroviral treatment (cART) as their first treatment regimen. Resistance is shown to individual drugs from the four original drug classes including (A) nucleoside reverse transcriptase inhibitors and lamivudine/emtricitabine, (B) non-nucleoside reverse transcriptase inhibitors, and (C) protease inhibitors.*





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

Web Appendix Table 4.1: *The characteristics of the 13,761 men and 3,404 women who had a recorded date of HIV-1 diagnosis, but were not known to be HIV-2 positive as of 1 June 2012, had started combination antiretroviral therapy when they were at least 18 years old and had their last recorded contact with HIV-related care in the Netherlands.*

Patient characteristics		**Total**	**Men**		**Women**		**P-value**
		n=17,165	n = 13,761		n = 3,404		
			Number	**Percentage***	**Number**	**Percentage***	
Region of birth	The Netherlands	9,869	8,992	(65%)	877	(26%)	< 0.0001
	Other or unknown	7,272	4,769	(35%)	2,503	(74%)	
HIV-1 transmission route	Homosexual contact	9,939	9,939	(72%)	0	(0%)	< 0.0001
	Heterosexual contact	5,424	2,433	(18%)	2,991	(88%)	
	IDU or blood contact	857	598	(4%)	259	(8%)	
	Other or unknown	945	791	(6%)	154	(5%)	
Age at the start of cART	Under 45 years	12,209	9,320	(68%)	2,889	(85%)	< 0.0001
	45 to 64 years	4,684	4,201	(30%)	483	(14%)	
	Over 65 years	272	240	(2%)	32	(1%)	
CD4 cell count**	Less than 200 cells/mm^3	6,568	5,240	(39%)	1,328	(39%)	< 0.0001
	200 to 500 cells/ mm^3	5,831	4,471	(45%)	1,360	(41%)	
	More than 500 cells/ mm^3	1,342	1,005	(7%)	337	(10%)	
	Unknown	1,569	1,208	(9%)	361	(11%)	
HIV RNA load **	Less than 100 particles/ml	272	189	1%	83	2%	< 0.0001
	100-1,000 particles/ml	2,188	1,465	11%	723	21%	
	More than 1,000 particles	12,356	10,246	(75%)	2,110	(62%)	
	Unknown	2,349	1,861	(14%)	488	(14%)	
Body mass index**	Less than 18.5 kg/m^2 (underweight)	736	591	(4%)	145	(4%)	< 0.0001
	Between 18.5 and 25 kg/m^2 (normal)	7,494	6,370	(46%)	1,124	(33%)	
	More than 25 kg/m^2 (overweight)	2,940	2,171	(16%)	769	(23%)	
	Unknown	5,995	4,629	(34%)	1,366	(40%)	
Hepatitis B virus status***	Positive	846	737	(5%)	109	(3%)	< 0.0001
	Negative	7,625	5,892	(43%)	1,733	(51%)	
	Unknown	8,694	7,132	(52%)	1,562	(46%)	
Hepatitis C virus status***	Positive	1,005	765	(6%)	240	(7%)	< 0.0001
	Negative	8,692	7,316	(53%)	1,376	(40%)	
	Unknown	7,468	5,680	(41%)	1,788	(53%)	

** Percentages may not sum to 100 due to rounding; ** Last known before the start of combination antiretroviral therapy, but within a year of this date; *** At the start of cART.*

Legend: *cART=combination antiretroviral therapy, ART=antiretroviral therapy, IDU=injecting drug use*

Web Appendix Table 4.2: *Annual number of cases of death and first AIDS events amongst 20,761 HIV-1-infected patients in the Netherlands recorded up to June 2013. Note: data collection for 2011, 2012, and 2013 is not yet finalised.*

		AIDS		Death	
Year	**Total**	≥6 weeks after diagnosis	**≥4 weeks after start of cART**	**Total**	**After start of cART**
≤1995	768	486	1	34	–
1996	366	293	89	48	31
1997	303	183	115	87	68
1998	242	133	111	84	72
1999	234	131	108	89	87
2000	245	112	87	84	79
2001	261	145	96	82	79
2002	296	147	109	119	82
2003	293	147	109	140	120
2004	282	174	114	144	128
2005	353	199	137	140	123
2006	285	167	117	121	104
2007	292	168	115	149	126
2008	268	163	127	149	134
2009	259	139	102	159	145
2010	274	145	121	129	122
2011	217	126	94	146	138
2012	208	112	93	136	130
2013	31	14	8	27	27
Total	5,477	3,184	1,853	2,067	1,795

Legend: *cART=combination antiretroviral therapy*

Web Appendix Table 4.3: The causes of death for patients after the start of cART in the periods 1996 to 2001, 2002 to 2006 and 2007 to 2012.

Cause of death	1996–2001 Total	2002–2006 Total	2007–2012 Total
All AIDS-defining causes*	206	191	141
Infection	65	68	49
Malignancy	65	69	51
Not specified	76	54	41
Non-AIDS defining malignancy	35	89	113
All cardiovascular diseases	21	51	51
Myocardial infarction	11	17	21
Stroke	2	10	9
Other ischemic heart disease	0	1	2
Other cardiovascular diseases	8	23	19
Non-AIDS defining infection	19	44	36
Liver failure, cirrhosis and hepatitis B or C virus infection at death	21	33	40
Lung related	7	15	24
Non-natural death	26	32	22
Accident or other violent death	8	11	10
Suicide	10	17	10
Euthanasia	8	4	2
Substance abuse	11	6	19
Other causes	12	24	29
Unknown or unclassifiable causes	51	67	80
Total	409	552	555

Web Appendix Table 4.4: Hazard ratios for time to death and AIDS from the start of cART.

Patient characteristics		Mortality		AIDS	
		Hazard ratio	95% CI	Hazard ratio	95% CI
Gender	**Female**			**1.03**	**0.85–1.25**
Region of birth	The Netherlands	1		1	
	Other/unknown	0.758	0.667–0.861	1.06	0.93–1.22
HIV-1 transmission route	Homosexual contact	0.851	0.728–0.994	1	
	Heterosexual contact	1		1.08	0.90–1.30
	IDU or blood contact	1.235	0.978–1.560	1.59	1.20–2.10
Age at the start of cART	Under 45 years	1		1	
	45 to 64 years	2.031	1.816–2.271	0.99	0.86–1.15
	Over 65 years	5.467	4.190–7.133	1.22	0.84–1.76
HIV-1 diagnosis to cART	Less than one year	1		3.42	2.64–4.45
	One to five years	1.454	1.269–1.667	1.24	0.95–1.63
	More than five years	2.075	1.811–2.377	1	
CD4 cell count*	Less than 200 cells/mm^3	2.272	1.735–2.975	2.58	2.13–3.13
	200 to 500 cells/mm^3	1.053	0.798–1.389	1	
	More than 500 cells/mm^3	1		0.47	0.39–0.55
HIV RNA load *	Less than 1,000 particles/ml	1		1	
	More than 1,000 particles/ml	1.046	0.827–1.323	0.85	0.60–1.22
Body mass index*	Less than 18.5 kg/m^2 (underweight)	1.397	1.130–1.727	1.51	1.11–2.06
	Between 18.5 and 25 kg/m^2 (normal)	1		1	
	More than 25 kg/m^2 (overweight)	0.672	0.560–0.807	0.89	0.75–1.06
Hepatitis B virus status**	Positive	1.510	1.229–1.856	1.06	0.82–1.39
	Negative	1		1	
Hepatitis C virus status**	Positive	2.868	2.313–3.557	1.18	0.92–1.51
	Negative	1		1	

** Last known before the start of combination antiretroviral therapy, but within a year of this date; ** At the start of cART.*

***Legend:** cART=combination antiretroviral therapy, IDU=injecting drug use, CI=confidence interval*

Web Appendix Table 4.5: The number and incidence (in parentheses) per 1,000 years of patient follow-up of the first occurrence per patient of any and individual AIDS-defining events per time period.

Event	1996-2001	2002-2006	2007-2012
Any AIDS-defining event	755 (42.7)	734 (23.4)	736 (15.1)
AIDS dementia complex / HIV encephalopathy	44 (2.3)	48 (1.4)	61 (1.1)
Cryptococcosis	15 (0.8)	23 (0.7)	15 (0.3)
Cryptosporidiosis	17 (0.9)	10 (0.3)	1 (0.0)
Herpes simplex virus	42 (2.2)	50 (1.4)	49 (0.9)
Disseminated or extrapulmonary histoplasmosis	8 (0.4)	7 (0.2)	5 (0.1)
Kaposi's sarcoma	85 (4.4)	104 (3.0)	109 (2.0)
Mycobacterium avium complex or kansasii clade, disseminated or extra pulmonary	71 (3.7)	33 (0.9)	40 (0.7)
Other or unidentified mycobacterium	37 (1.9)	15 (0.4)	17 (0.3)
Pneumocystis jiroveci (carinii) pneumonia	83 (4.3)	80 (2.3)	86 (1.6)
Recurrent pneumonia	58 (3.0)	90 (2.6)	107 (2.0)
Progressive multifocal leucoencephalopathy	27 (1.4)	22 (0.6)	31 (0.6)
Cerebral toxoplasmosis	55 (2.8)	46 (1.3)	25 (0.5)
HIV wasting syndrome	32 (1.7)	36 (1.0)	31 (0.6)
Oesophageal or pulmonary candidiasis	175 (9.2)	171 (5.0)	153 (2.9)
Cytomegalovirus infection	104 (5.4)	72 (2.1)	64 (1.2)
Non-Hodgkin's lymphoma	58 (3.0)	74 (1.8)	82 (1.5)
Tuberculosis	57 (3.1)	107 (3.1)	76 (1.4)
Any other CDC-C-defining disease*	81 (2.5)	37 (0.8)	46 (0.4)

** Including primary lymphoma of the central nervous system (23 cases), chronic intestinal microsporidiosis lasting more than 1 month (15 cases) and invasive cervical cancer (14 cases).*

Web Appendix Table 4.6: The number and incidence (in parentheses) per 1,000 years of patient follow-up from 2002, of the first occurrence per patient of diabetes mellitus, invasive cardiac procedures, myocardial infarction, stroke, renal insufficiency, and non-AIDS defining malignancies, after starting cART, per time period.

	n	2002-2006	2007-2012	p-value
Diabetes mellitus	475	168 (4.8)	307 (4.7)	ns
Cardiovascular diseases*	532	191 (5.5)	341 (5.3)	ns
Renal insufficiency	410	-	410 (6.4)	-
Non-AIDS-defining malignancies	796	269 (8.0)	527 (8.3)	ns
Myocardial infarction	279	109 (3.1)	170 (2.7)	ns
Stroke	214	78 (2.2)	133 (2.1)	ns

** Includes myocardial infarction, stroke, coronary artery by-pass grafting, coronary angioplasty/stenting and carotic endarterectomy.*

Web Appendix Table 4.7a: Odds ratios for factors associated with the incidence of diabetes mellitus.

Patient characteristics		Diabetes Mellitus	
		Odds ratio	95% CI
Gender	Male	1.30	1.00–1.69
Region of birth	The Netherlands	1	
	Other/unknown	1.37	1.12–1.68
HIV-1 transmission route	Homosexual contact	1	
	Heterosexual contact	1.86	1.44–2.40
	IDU or blood contact	1.80	1.23–2.63
Age at the start of cART	Under 30 years	0.53	0.30–0.96
	30–40 years	1	
	40–50 years	1.26	0.97–1.65
	50 to 60 years	1.80	1.34–2.43
	Over 60 years	2.77	1.97–3.90
CD4 cell count*	Less than 200 cells/mm^3	1.34	0.90–1.99
	200 to 500 cells/mm^3	1	
	More than 500 cells/mm^3	1.14	0.92–1.42
HIV RNA load *	Less than 1,000 particles/ml	1	
	More than 1,000 particles/ml	0.75	0.41–1.36
Body mass index*	Less than 18.5 kg/m^2 (underweight)	1.13	1.60–2.14
	Between 18.5 and 25 kg/m^2 (normal)	1	
	More than 25 kg/m^2 (overweight)	1.83	1.44–2.33
CDC-C prior to cART	AIDS event	1.48	1.21–1.82
	No AIDS event	1	
Hepatitis B virus status**	Positive	0.87	0.59–1.28
	Negative	1	
Hepatitis C virus status**	Positive	1.30	0.91–1.84
	Negative	1	
Hypertension	Yes	2.45	1.99–3.02
	No		

** Last known before the start of combination antiretroviral therapy, but within a year of this date; ** At the start of cART.*

***Legend:** IDU=injecting drug use; cART=combination antiretroviral therapy; CDC=Centers for Disease Control and Prevention*

Web Appendix Table 4.7b: Hazard ratios for factors potentially associated with the incidence of cardiovascular disease.

Patient characteristics		Cardiovascular disease	
		Odds ratio	95% CI
Gender	Male	1.58	1.15–2.18
Region of birth	The Netherlands	1	
	Other/unknown	0.76	0.61–0.95
HIV-1 transmission route	Homosexual contact	1	
	Heterosexual contact	1.27	0.99–1.62
	IDU or blood contact	1.12	0.76–1.65
Age at the start of cART	Under 30 years	0.34	0.12–0.95
	30–40 years	1	
	40–50 years	1.94	1.41–2.68
	50–60 years	3.96	2.85–5.53
	Over 60 years	7.70	5.43–10.9
CD4 cell count*	Less than 200 cells/mm^3	0.95	0.61–1.47
	200 to 500 cells/mm^3	1	
	More than 500 cells/mm^3	1.05	0.85–1.29
HIV RNA load *	Less than 1,000 particles/ml	0.75	0.38–1.48
	More than 1,000 particles/ml	1	
Body mass index*	Less than 18.5 kg/m^2 (underweight)	1.30	0.78–2.16
	Between 18.5 and 25 kg/m^2 (normal)	1	
	More than 25 kg/m^2 (overweight)	0.93	0.74–1.18
CDC-C prior to cART	AIDS event	1.51	1.25–1.83
	No AIDS event	1	
Hepatitis B virus status**	Positive	1.13	0.83–1.56
	Negative	1	
Hepatitis C virus status**	Positive	0.90	0.66–1.24
	Negative	1	
Hypertension	Yes	1.65	1.36–2.01
	No		

** Last known before the start of combination antiretroviral therapy, but within a year of this date; ** At the start of cART.*

***Legend:** IDU=injecting drug use; cART=combination antiretroviral therapy; CDC=Centers for Disease Control and Prevention*

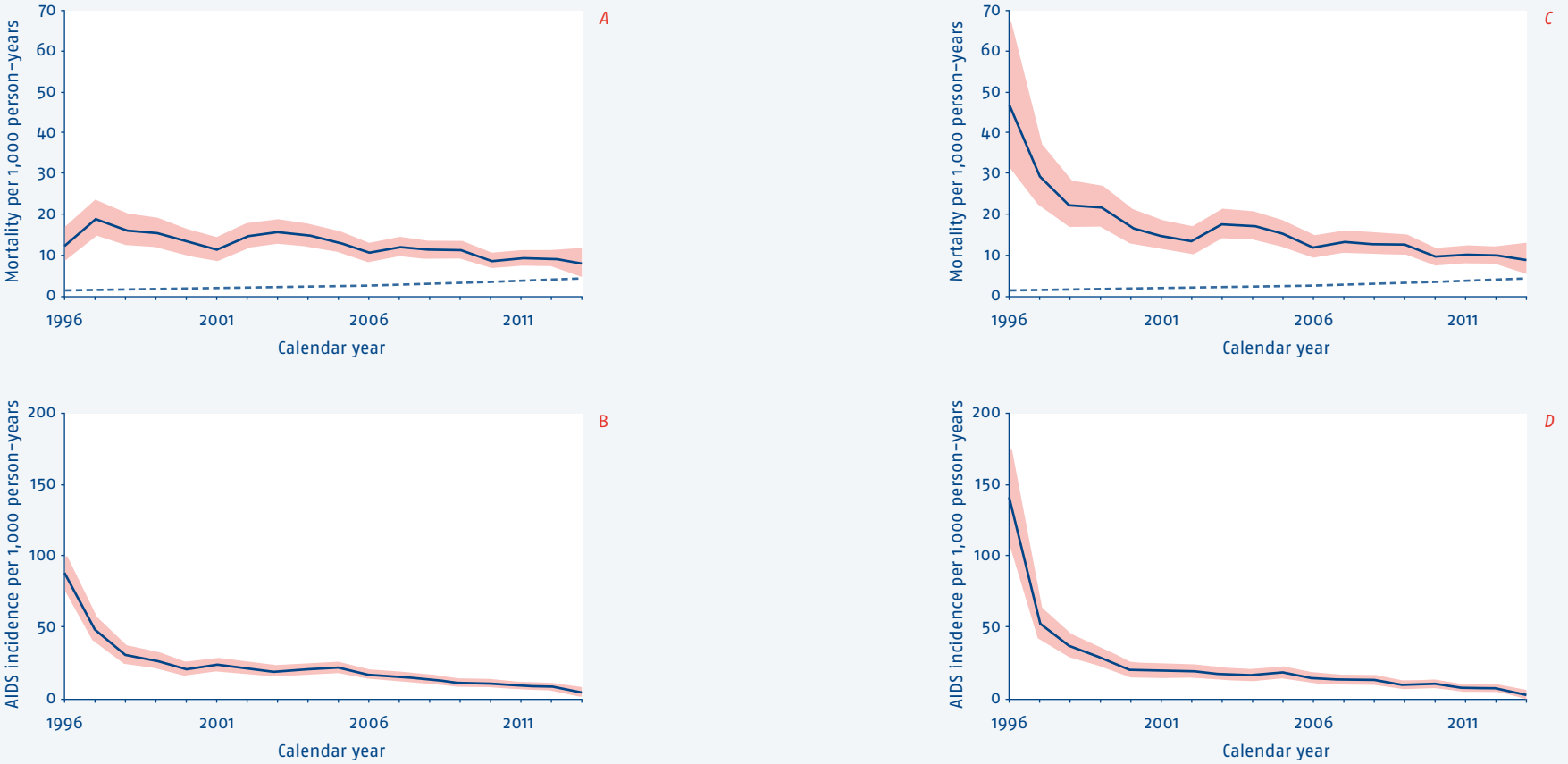
Web Appendix Table 4.7c: Odds ratios for factors associated with the incidence of non-AIDS-defining malignancies.

Patient characteristics		Non-AIDS-defining malignancies	
		Odds ratio	95% CI
Gender	Male	1.01	0.77-1.33
Region of birth	The Netherlands	1	
	Other/unknown	0.82	0.59-1.14
HIV-1 transmission route	Homosexual contact	1	
	Heterosexual contact	0.79	0.63-0.99
	IDU or blood contact	0.66	0.44-0.98
Age at the start of cART	Under 30 years	0.49	0.24-1.03
	30-40 years	1	
	40-50 years	2.36	1.80-3.09
	50-60 years	4.31	3.27-5.69
	Over 60 years	7.59	5.65-10.19
CD4 cell count*	Less than 200 cells/mm^3	2.52	1.95-3.26
	200 to 500 cells/mm^3	1	
	More than 500 cells/mm^3	0.62	0.51-0.74
HIV RNA load *	Less than 1,000 particles/ml	1	
	More than 1,000 particles/ml	1.04	0.60-1.81
CDC-C prior to cART	AIDS event	1.29	1.10-1.52
	No AIDS event	1	
Hepatitis B virus status**	Positive	1.57	1.25-1.97
	Negative	1	
Hepatitis C virus status**	Positive	1.27	0.97-1.66
	Negative	1	

** Last known before the start of combination antiretroviral therapy, but within a year of this date; ** At the start of cART.*

***Legend:** IDU=injecting drug use; cART=combination antiretroviral therapy; CDC=Centers for Disease Control and Prevention*

Web Appendix Figure 4.1: *Annual mortality (A, C) and incidence of AIDS (B, D) in 20,761 HIV-1-infected patients in the Netherlands after HIV diagnosis (upper plots) and in a subpopulation of 17,773 treated patients who started combination antiretroviral therapy (lower plots) from 1995 onwards. Solid lines represent the incidence, whilst the shaded areas are the 95% confidence intervals. The dotted line is the mortality rate for age- and sex-matched individuals from the general population in the Netherlands. A: 2,033 deaths, 169,355 person-years of follow-up; B: 2,698 AIDS cases from 6 weeks after diagnosis onwards, 146,551 person-years; C: 1,794 deaths, 129,255 person-years; D: 1,852 cases from 4 weeks after start of combination antiretroviral therapy onwards, 119,025 person-years.*



Web Appendix Table 9.1: Annual number of HIV diagnoses in Curacao stratified by sex and survival status as of June 2013.

	Alive, in clinical care		Alive, not in clinical care		Dead		Total	
	Men	Women	Men	Women	Men	Women	Men	Women
≤1995	34	16	9	7	35	10	78	33
1996	7	9	3	3	0	1	10	13
1997	7	12	2	1	7	3	16	16
1998	10	4	9	1	8	1	27	6
1999	13	5	2	2	5	2	20	9
2000	13	6	3	8	6	4	22	18
2001	8	7	3	6	6	4	17	17
2002	15	8	8	8	6	2	29	18
2003	16	11	9	5	11	2	36	18
2004	9	8	9	5	10	2	28	15
2005	21	7	2	5	5	4	28	16
2006	17	11	5	2	3	2	25	15
2007	16	5	7	5	5	1	28	11
2008	14	13	14	5	2	1	30	19
2009	20	14	10	4	0	2	30	20
2010	11	9	8	5	2	1	21	15
2011	24	17	4	4	0	0	28	21
2012	25	21	0	0	0	0	25	21
Total	280	183	107	76	111	42	498	301
Unknown	3	1	17	4	2	7	22	12


2023