

HIV Treatment and Resistance in Curaçao

Frank de Wolf

8th HIV Monitoring Update

2-3 May 2012

Curaçao



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1. Introduction HIV monitoring
2. Observational clinical HIV cohort in Curaçao
3. cART treatment and treatment effect
4. Access to care and treatment
5. Conclusions

HIV Monitoring Foundation

HIV Monitoring Foundation

- founded 11 November 2001
- appointed by Minister of Health: executive organisation for registration and monitoring of HIV-infected patients followed in the Dutch treatment centres
- part of HIV care



Activities

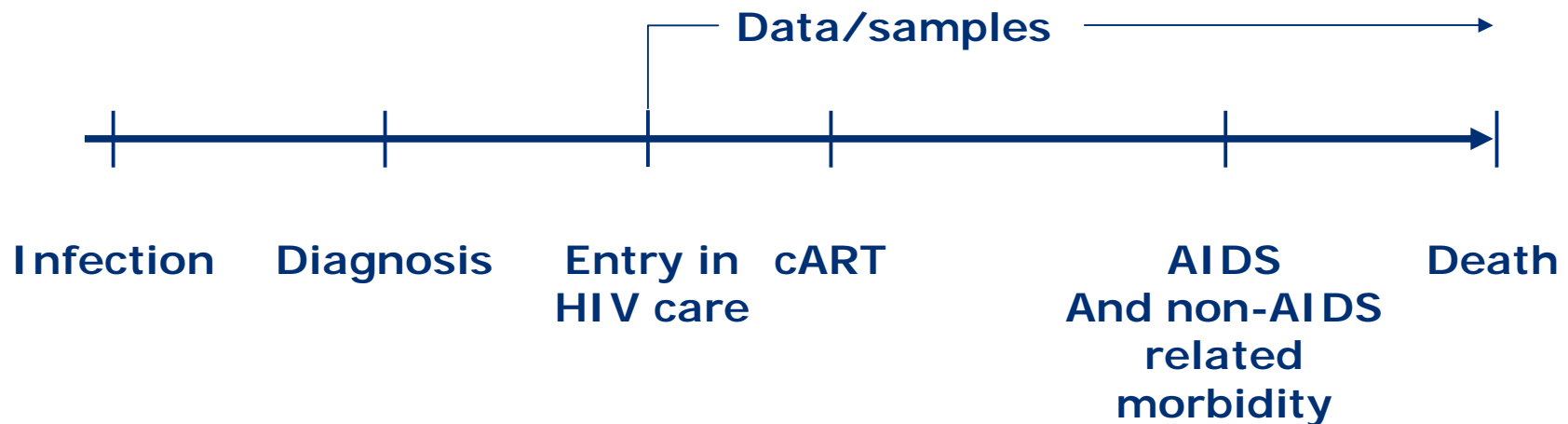
- collection and maintenance of anonymized data
- report to government, HIV treating physicians and others
- make data available for treating physicians
- provide data for research



Since 2005



Testing, care & treatment



Testing

- STD out-patient facilities
- General practitioners
- HIV treatment centres (HTC)

Together with 25 HTC's HMF:

- Collects data and plasma samples from all HIV infected patients followed in these centres
- Monitors changes in the course of HIV infection and the HIV epidemic

Basic demographics

Curaçao

- 150,000 inhabitants
- HIV prevalence 0.6% to 1.1%
- 2010: 73 new HIV diagnoses



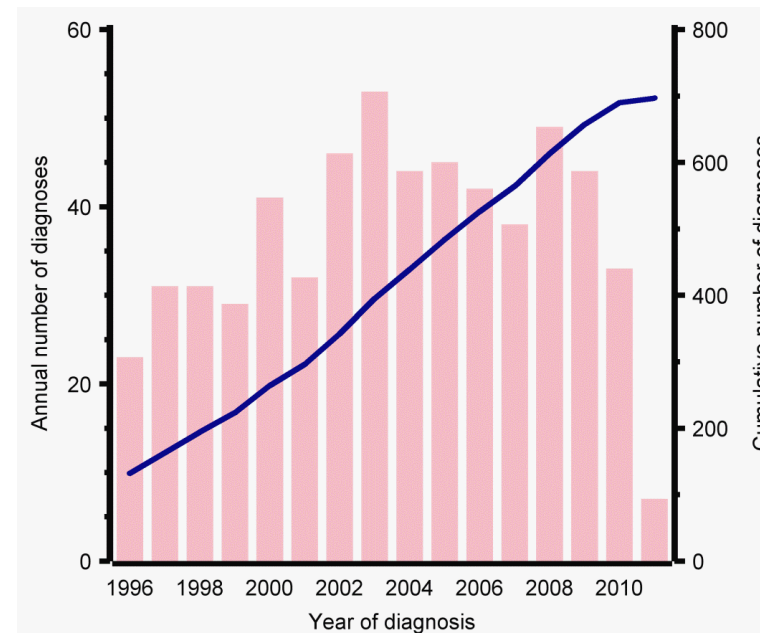
Netherlands

- 17,000,000 inhabitants
- HIV prevalence 0.2%
- 2010: 1169 new HIV diagnoses



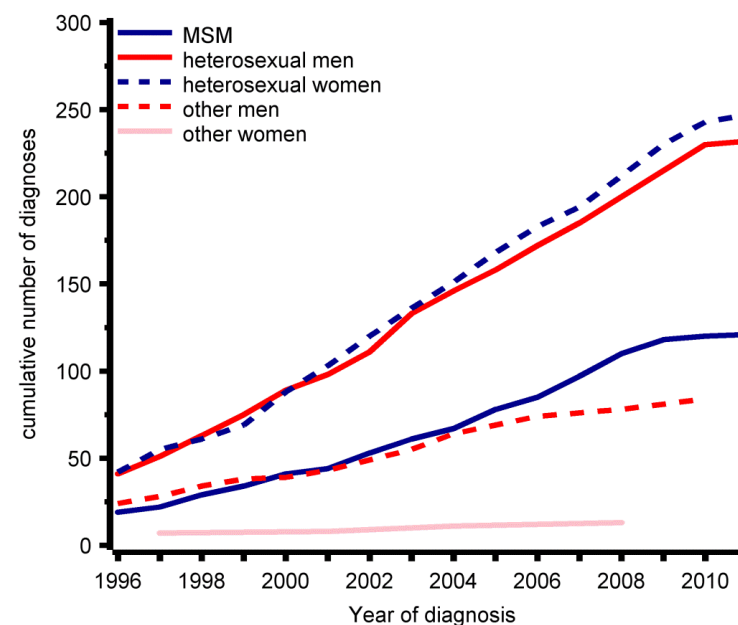
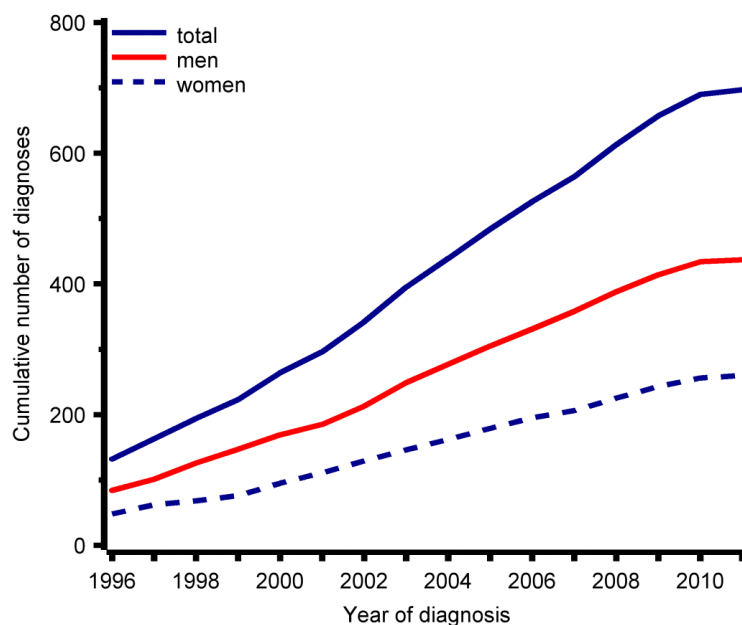
Number registered in HIV care in Curaçao

- Registration and monitoring since 2005
- Per June 2011: 746 patients registered
- 432 (58%) still in out-patient care
- 590 (78%) alive
- 156 (21%) died since start registration
- Total follow-up: 4862 py
- 233 (30%) diagnosed prior to 1996; 66(30%) died before June 2011
- 474 patients were diagnosed between 2000 and 2011
- 49 patients: unknown date of first positive sample



- Majority infected with HIV-1

Cumulative number of diagnoses by gender and risk group



	Alive, N=590		Dead, N=156		Total, N=746	
	N	%	N	%	N	%
Gender, male	358	61	108	69	466	62
Transmission						
MSM	108	18	15	10	123	16
Heterosexual	394	67	98	63	492	66
Other/unknown	88	15	43	28	131	18

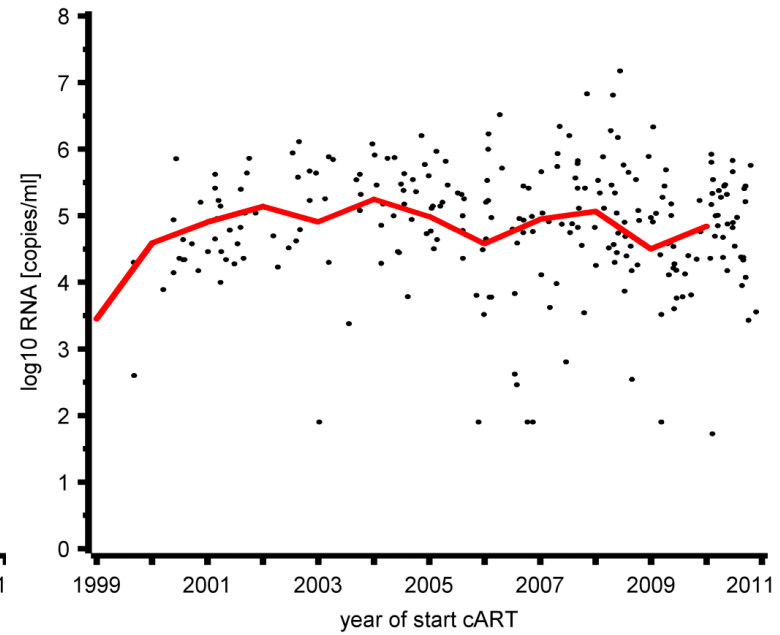
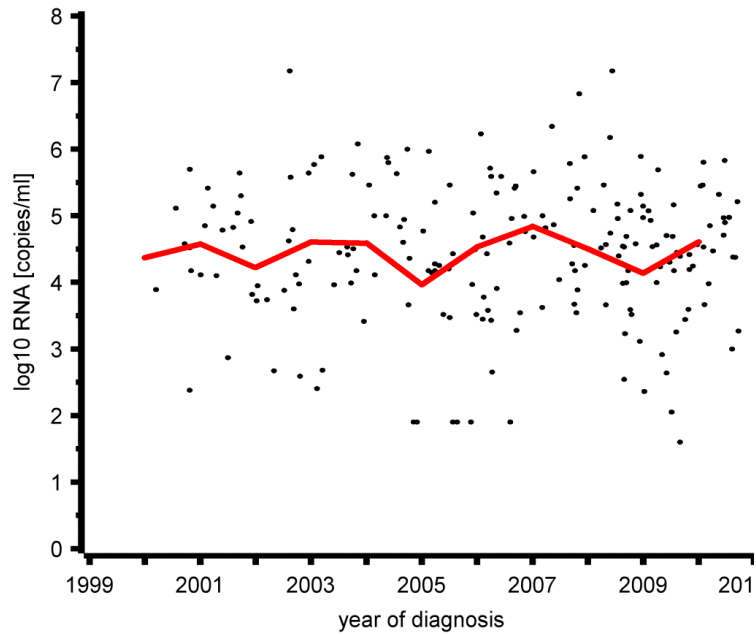
Origin

	Alive, N=590		Dead, N=156		Total, N=746	
	N	%	N	%	N	%
Country of birth						
Antilles	408	69	139	89	547	73
Haiti	76	13	7	4	83	11
Dominican Republic	48	8	6	4	54	7
Country of infection (433)						
Antilles					392	86
Haiti					14	3
Dominican Republic					9	2
Netherlands					17	4

Characteristics at diagnosis and start of cART

	Total, N= 746; Diagnosis		cART, N= 535 Start of cART	
	median	IQR	median	IQR
Age (yrs)	38	31–47	43	35–51
AIDS	66	9%	112	15%
Time to cART (yrs)	1.4	0.3–4.9		
Follow-up (years)	5.3	1.6–10.5	3.6	1.3–8.0
RNA (log ₁₀ cps/ml)	4.5	3.9–5.1	4.9	4.4–5.4
CD4 (cells/mm ³)	313	94–476	141	49–264

HIV RNA plasma levels at diagnosis and at start of cART

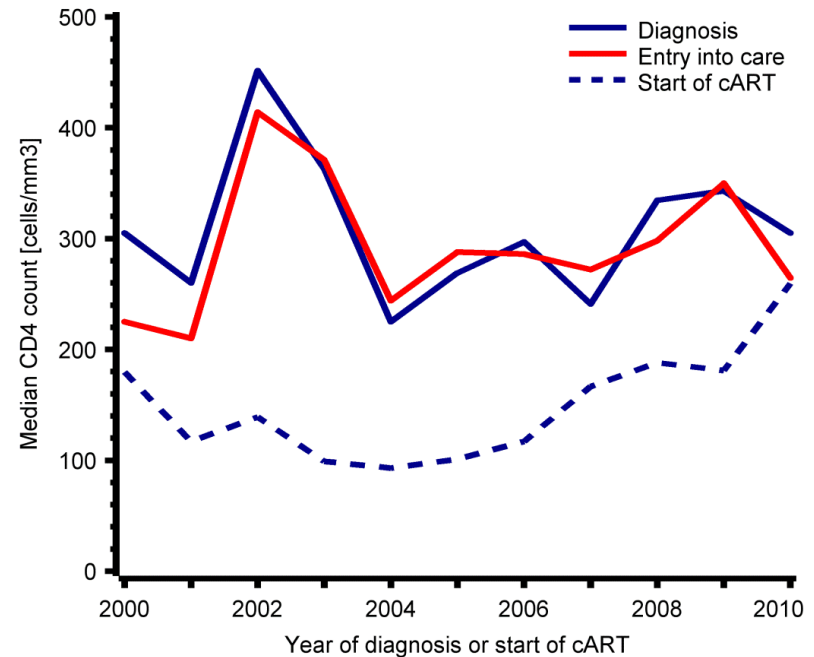


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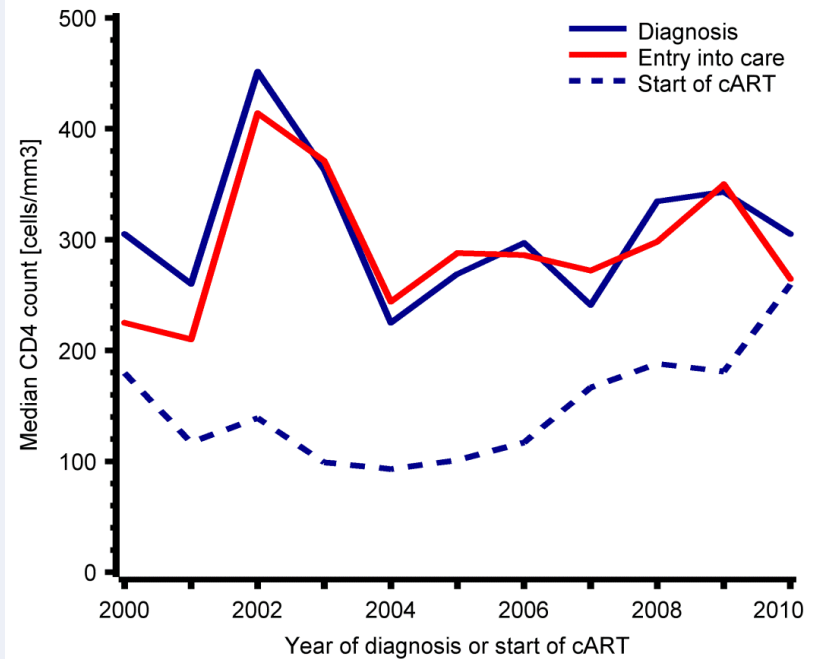
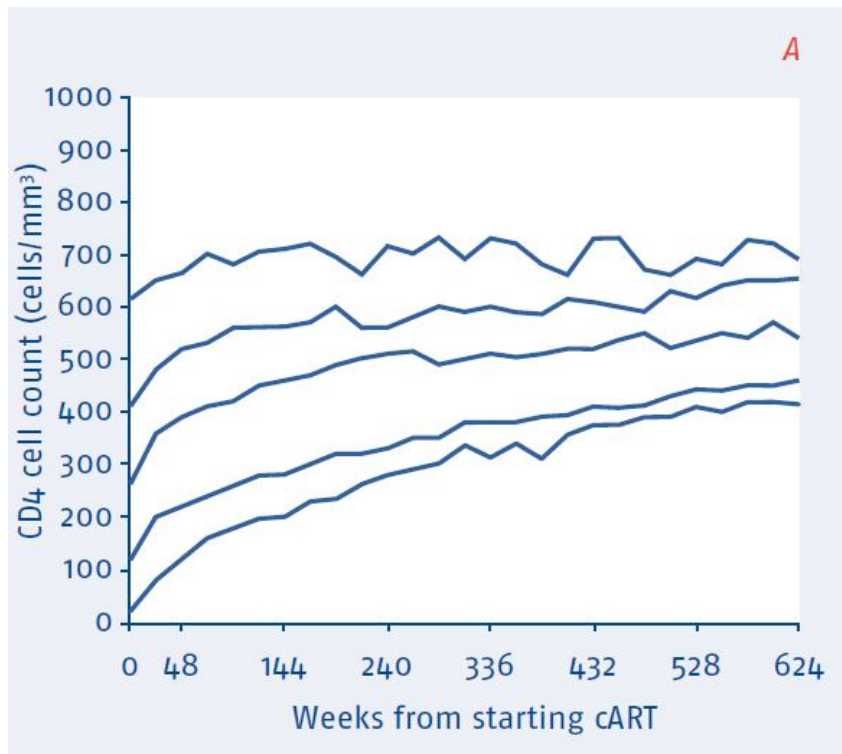
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CD4 cell counts at diagnosis, entry and start cART

- Over time late diagnosis and late entry in to care
- Delayed start of cART until 2010
- Still median CD4 cell count at start is below 300 cells/mm³



CD4 cell counts after start of cART



Gras L, et al; J Acquir Immune Defic Syndr 45 (2) 2007

Late entry into HIV care

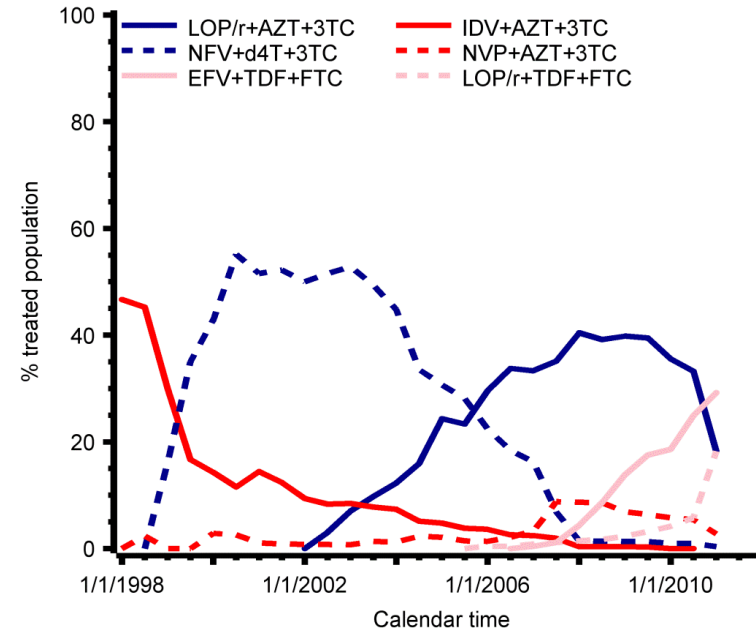
Variable	Entry into care					
	HR	95%CI	<i>p</i>	aHR	95%CI	<i>p</i>
Gender (male)	1.01	0.82-1.25	0.93			
Older age (by ten yrs)	1.09	1.00-1.19	0.06	1.16	1.09-2.19	0.07
Transmission						
Hetero women	1					
Hetero men	0.99	0.77-1.26	0.92			
MSM	1.08	0.81-1.44	0.59			
Born in Curacao	1.28	1.02-1.61	0.03	1.54	1.09-2.19	0.02
Pregnant at diagnosis	1.89	1.25-2.85	0.002	2.92	1.82-4.72	<0.001
Diagnosed primary health care setting	0.66	0.53-0.81	<0.001	0.71	0.50-1.00	0.04
Diagnosis <2005	0.54	0.43-0.67	<0.001	0.41	0.28-0.60	<0.001

Late start of cART

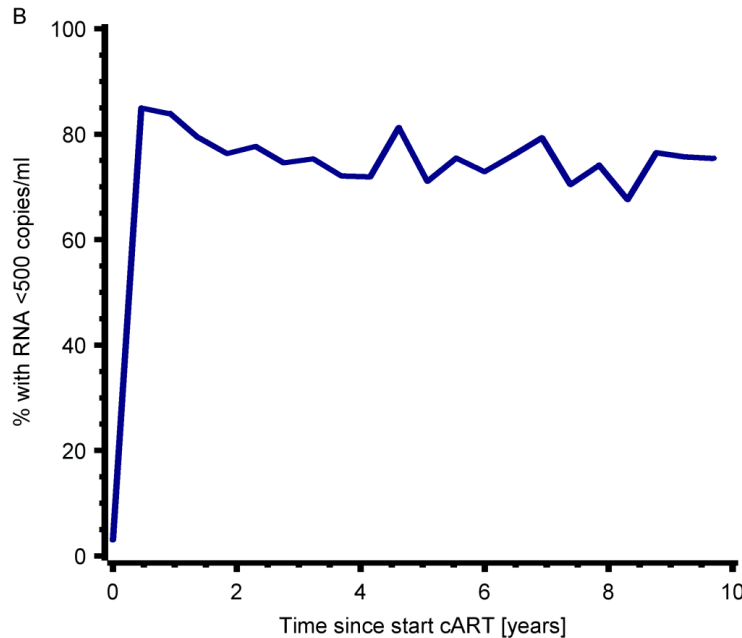
Variable	Start of cART			aHR	95%CI	<i>p</i>
	HR	95%CI	<i>p</i>			
Diagnosis <2005	0.70	0.54-0.90	0.01	0.66	0.51-0.87	0.003
CD4 cell count at entry						
CD4 <200	1			1		
CD4 200-350	0.31	0.22-0.44	<0.001	0.33	0.22-0.49	<0.001
CD4 >350	0.15	0.11-0.22	<0.001	0.15	0.10-0.23	<0.001
unknown	0.31	0.22-0.44	<0.001	0.35	0.22-0.55	<0.001
AIDS at entry	2.23	1.72-2.95	<0.001	1.48	1.10-2.00	0.01
Delayed entry (yes)	0.73	0.58-0.94	0.01	0.70	0.54-0.90	0.01

cART regimen changes over time

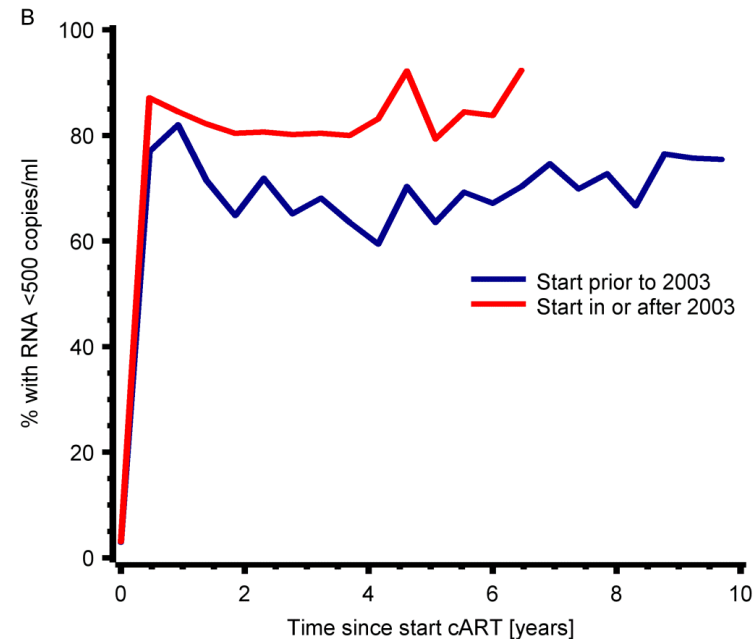
- 535 (72%) patients on cART
- 333 started between 2004 and 2011:
 - combivir plus lopinavir/r in 62%
 - tenofovir/ emtricitabine plus efavirenz in 22%
- As per June 2011 tenofovir/emtricitabine with either efavirenz or lopinavir/r



Virological success after start of cART

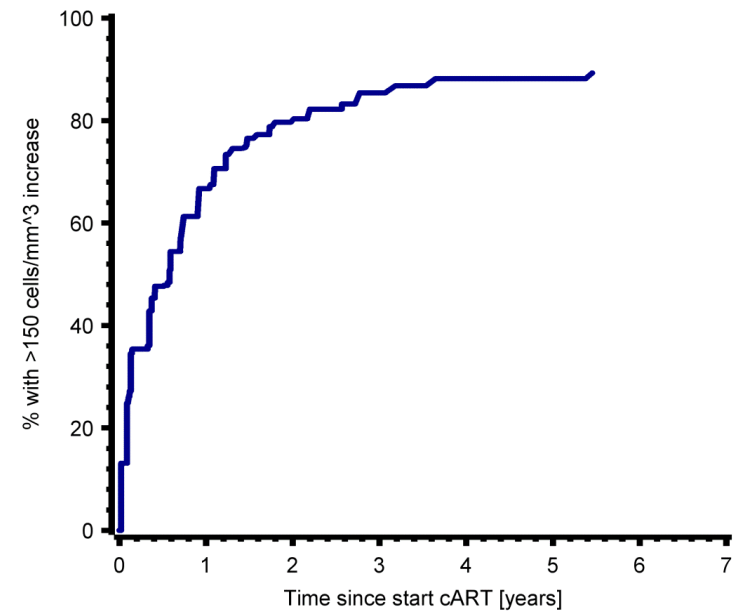
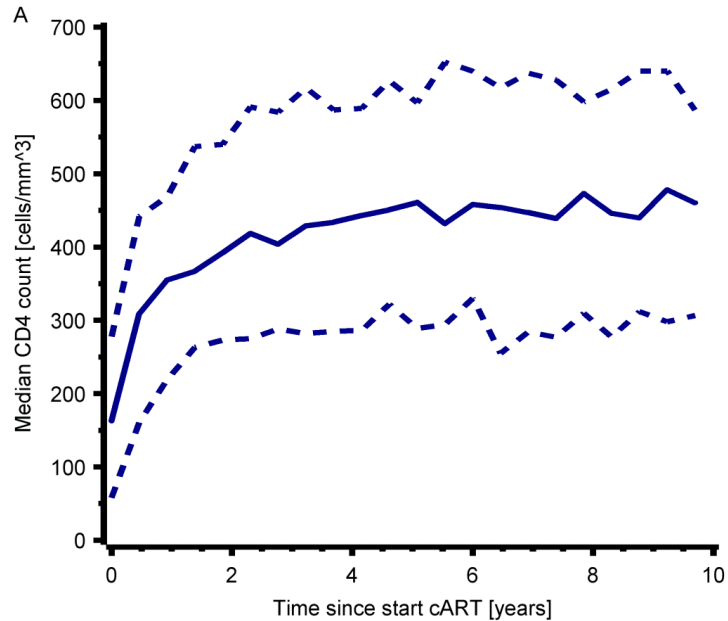


- 85% had HIV-RNA levels below 500 cps/ml after 49 weeks



- The proportion below 500 cps/ml remains at about 85% for those started after 2003
- A gradual decline to 70 % for those who started cART prior to 2003

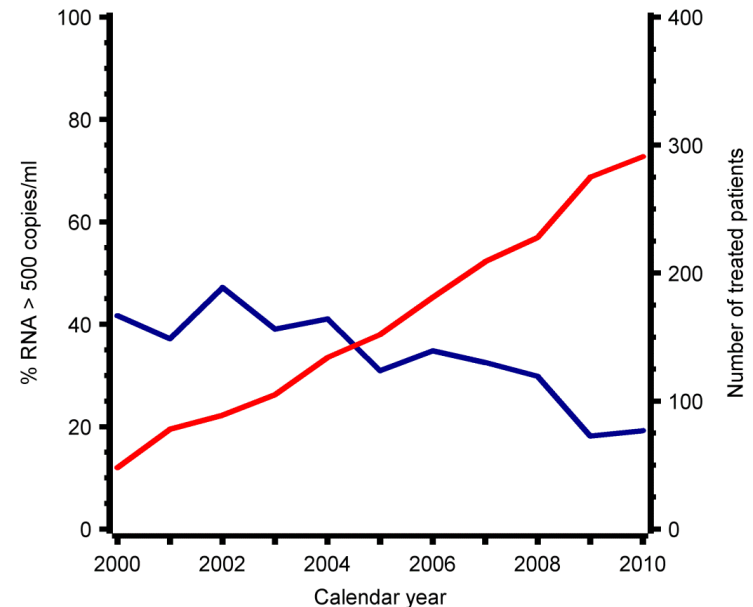
Changes in CD4 over time since start of cART



- Median CD4 cell count rose from 163 at start to 309 after 24 weeks reaching a plateau at 450 to 500 cells/mm³ after 5 years
- 48% experienced 150 CD4 cells increase within 6 months
- 80% in 2 years

Percentage failure of treated population over time

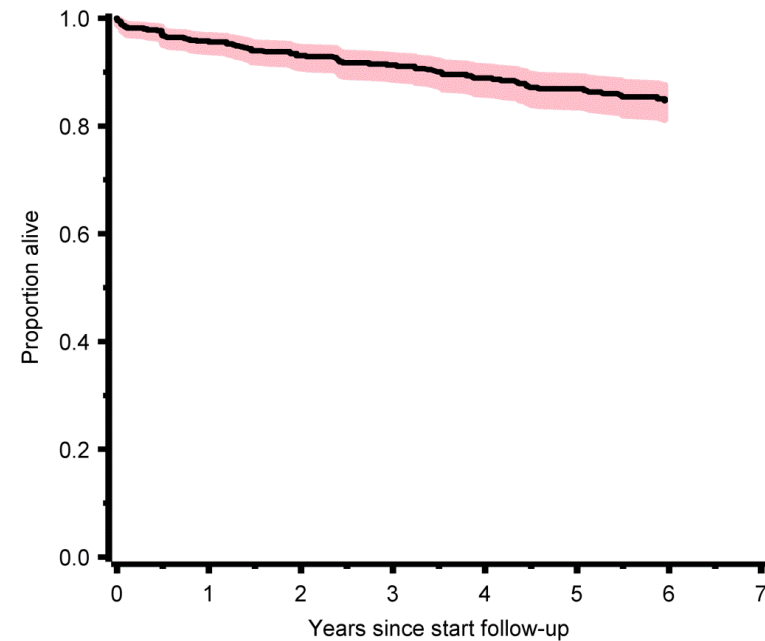
- Virological failure: HIV-RNA levels > 500 cps/ml for at least 4 months of continuous treatment.
- Proportion on therapy and experiencing virological failure declined from 40% in 2000-2004 to 20% in 2010
- 142 patients tested for resistance to (N)NRTI or PI
- 78 (56%) of those tested had high level resistance to at least one drug used
 - 51% against NRTI's
 - 32% against PI's (↓)
 - 23% against NNRTI's (↑)



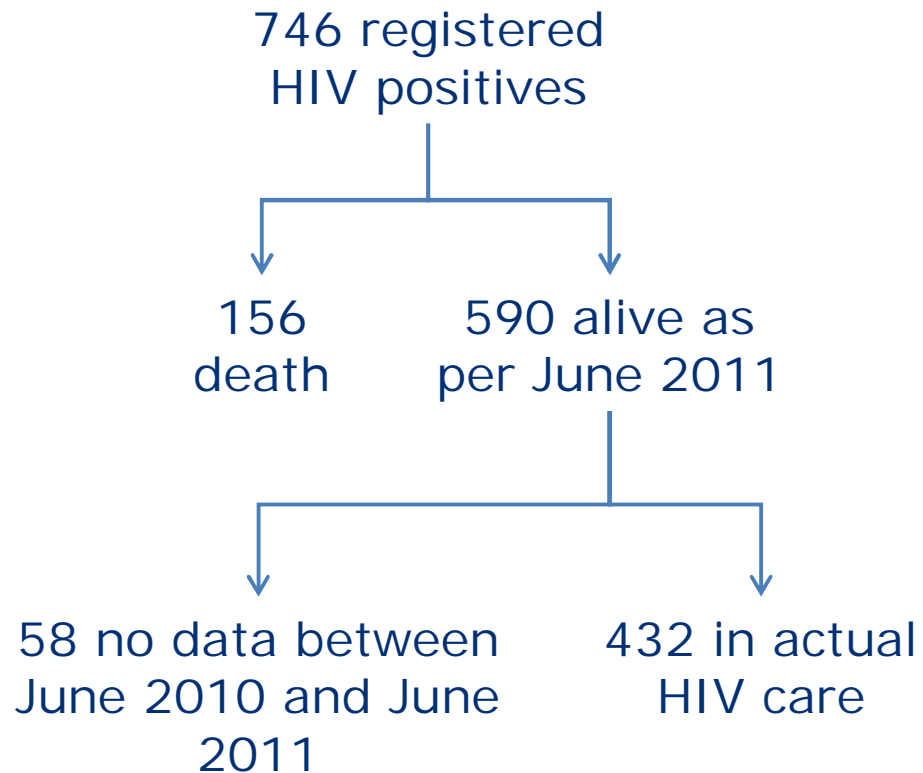
- Triple class resistance was found in 14%
- Transmission of drug resistant virus:
 - RAM in 3
 - High level resistance in 1

Survival

- 658 patients still alive in or diagnosed after 2005:
 - 21 patients died within 12 months
 - 77 patients had died by June 2011
 - Overall survival after 6 years is 85%
- 286 patients started cART in 2005:
 - 37 died
 - Survival probability 82%

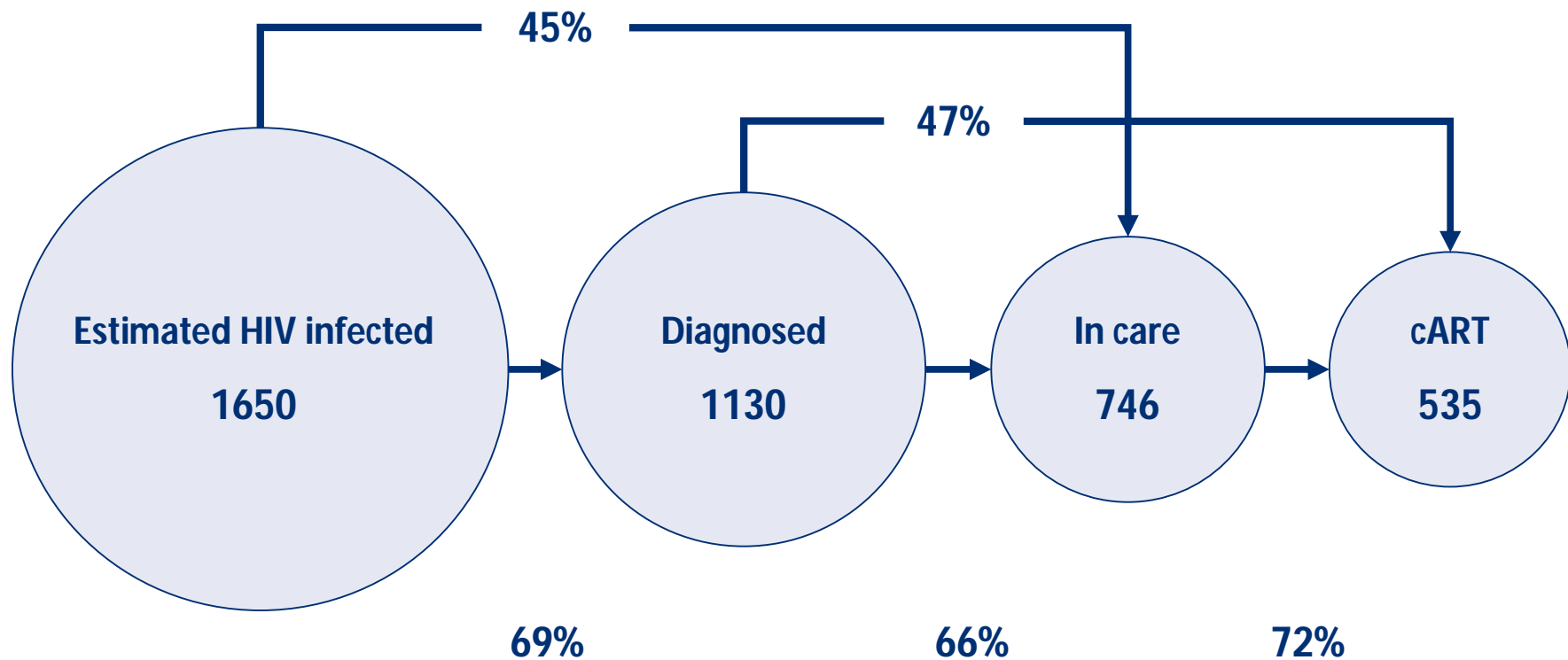


Curaçao HIV Registration 2011



- Stable yearly growth of around 40 HIV infected patients entering care
- Majority born and infected in the Netherlands Antilles
- Late diagnosis, late entry in care and late start of treatment
- Late entry is associated with diagnosis in primary health care setting
- Late start cART is associated with delayed entry

Curação



Testing, time between diagnosis and entry in care and time between entry and start treatment need improvement

Effect of treatment

- CD4 cell response to cART is as expected, given the late start of cART
- Since 2005 survival after 6 years is at a level of 85%
- Virological response has improved since 2003
- Virological failure declined, but is still around 20% of those treated
- Resistance in those tested is frequent; triple class resistance in high
- Resistance transmission is limited

Acknowledgements

- **Curaçao:**
 - Ashley Duits
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Netherlands

