



Non-AIDS defining cancer in HIV-1 infected patients in Japan



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COI

(in the past 3 years)

1. Research Grant: from MSD, CSL Berhling, ViiV Healthcare

Research materials: from Trii Pharmaceutical/Japan Tobacco

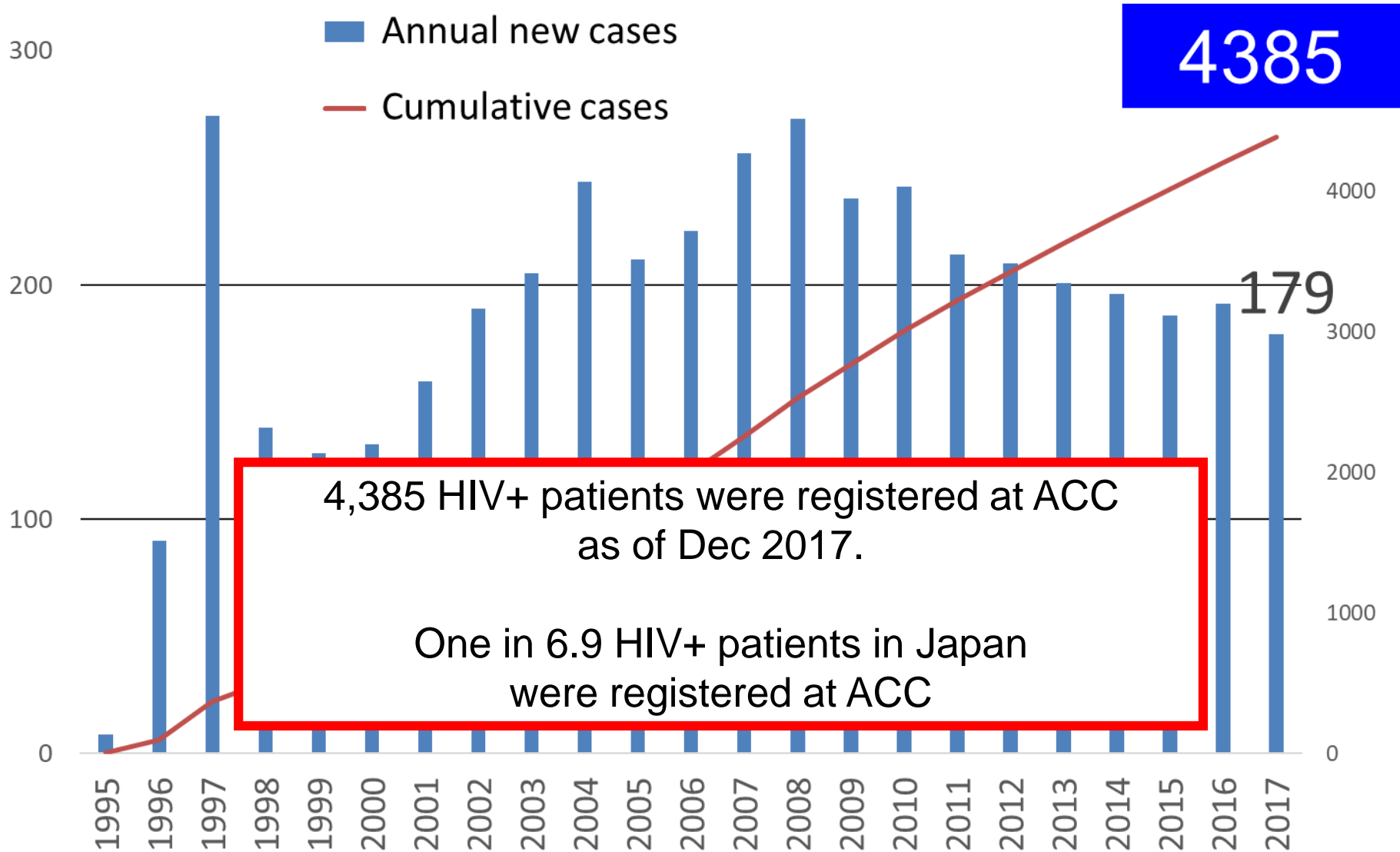
2. Honorarium for lectures: from MSD, Torii Pharmaceutical, Janssen Pharmaceutical, ViiV Healthcare, Gilead Sciences

Including COI irrespective of the today's lecture

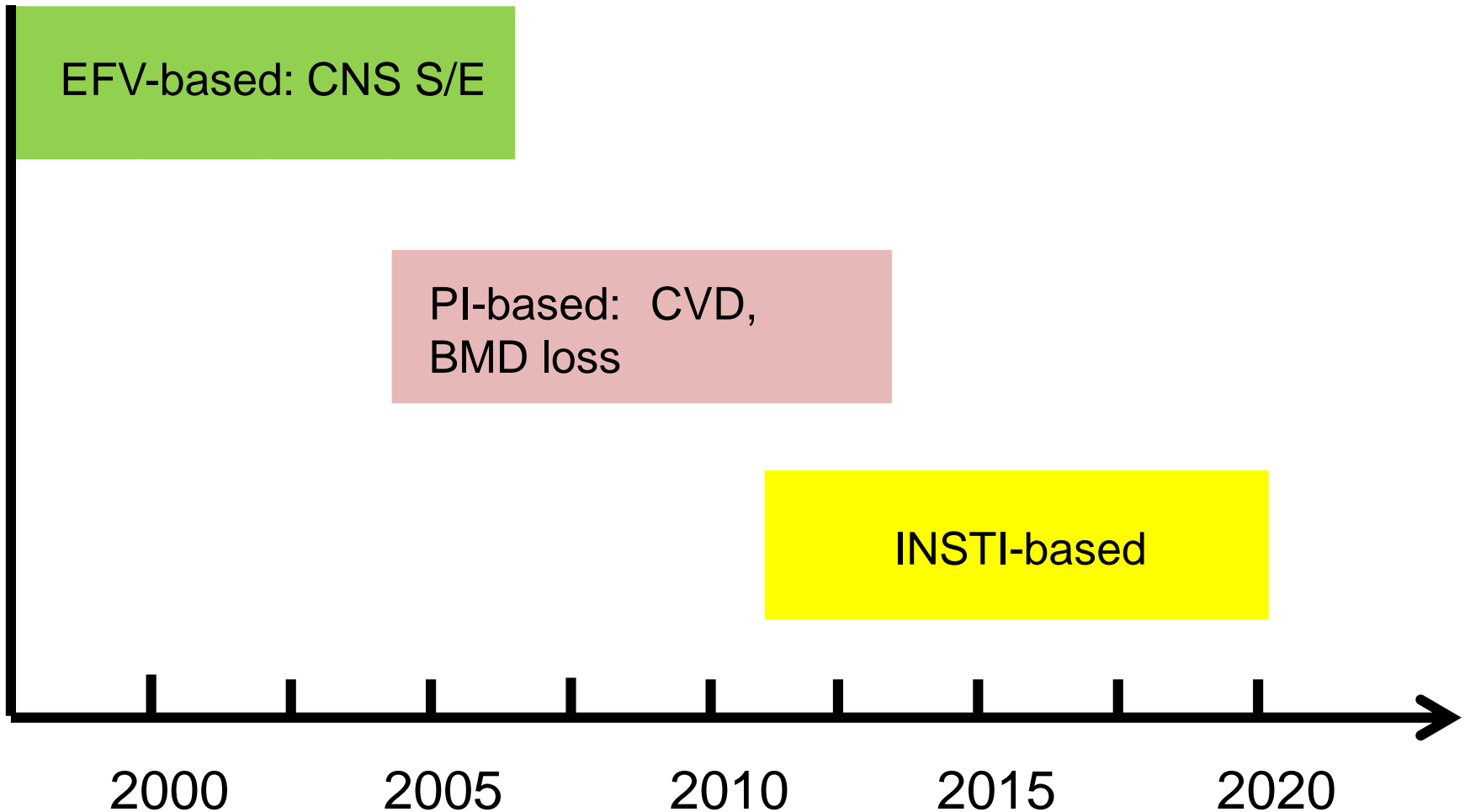
HIV/AIDS in Japan as of Dec 31, 2017

	male	female	total
total	27,013	3,258	30,271
HIV	17,470	2,426	19,896
AIDS	8,122	814	8,936
(hemophilia	1,421	18	1,439)
Route of Inf.			
heterosexual	6,022	2,136	8,158
homosexual	15,495	10	15,505
Injecting drug	127	12	139
MTCT	33	28	61
others	634	111	745
unknown	3,281	943	4,224

Annual new and cumulative HIV cases in ACC



Trend of cART in ACC over time



CD4 counts at the first ACC visit in 2017

■ AIDS ■ AC

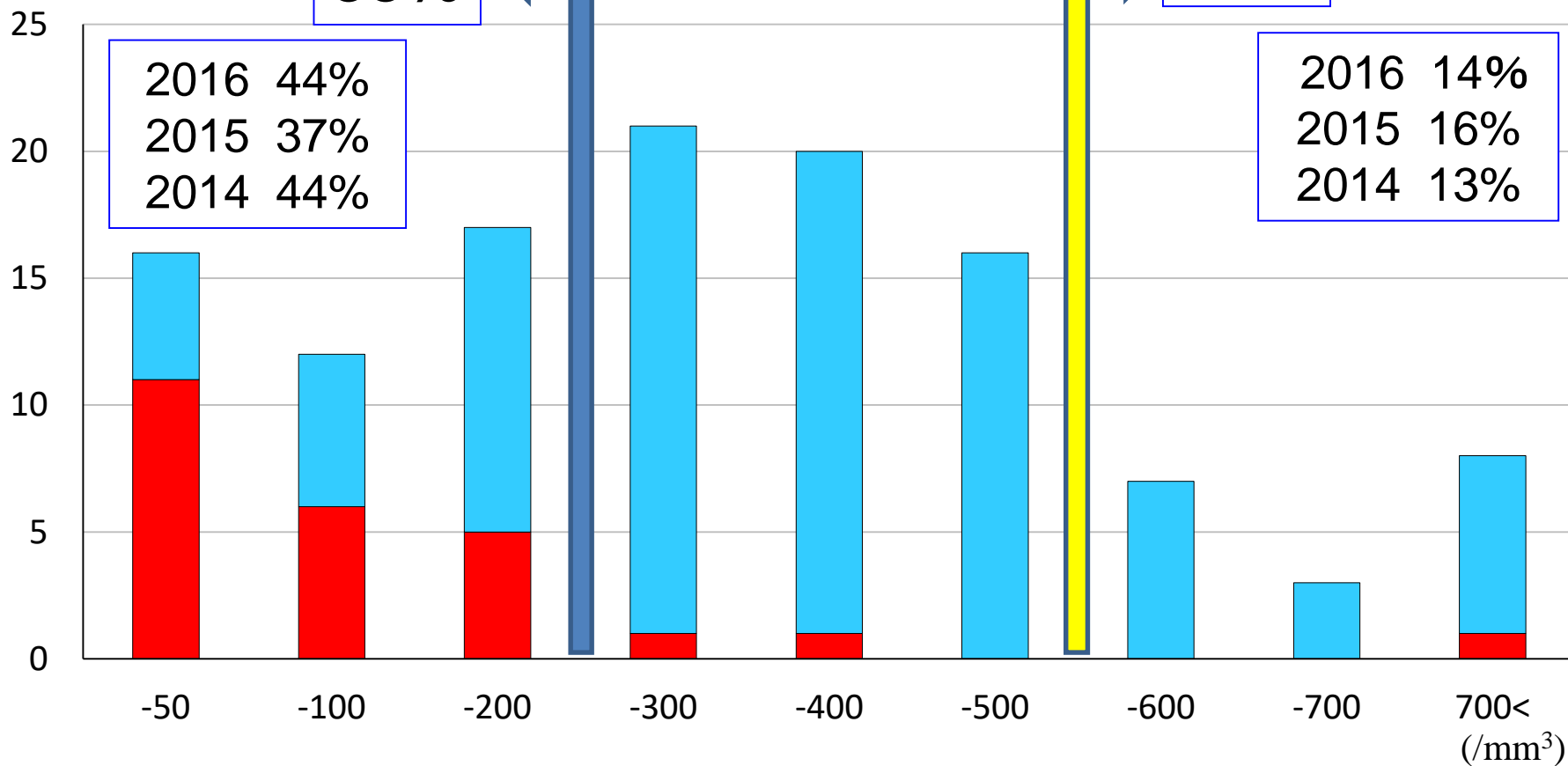
<person>

38%

15%

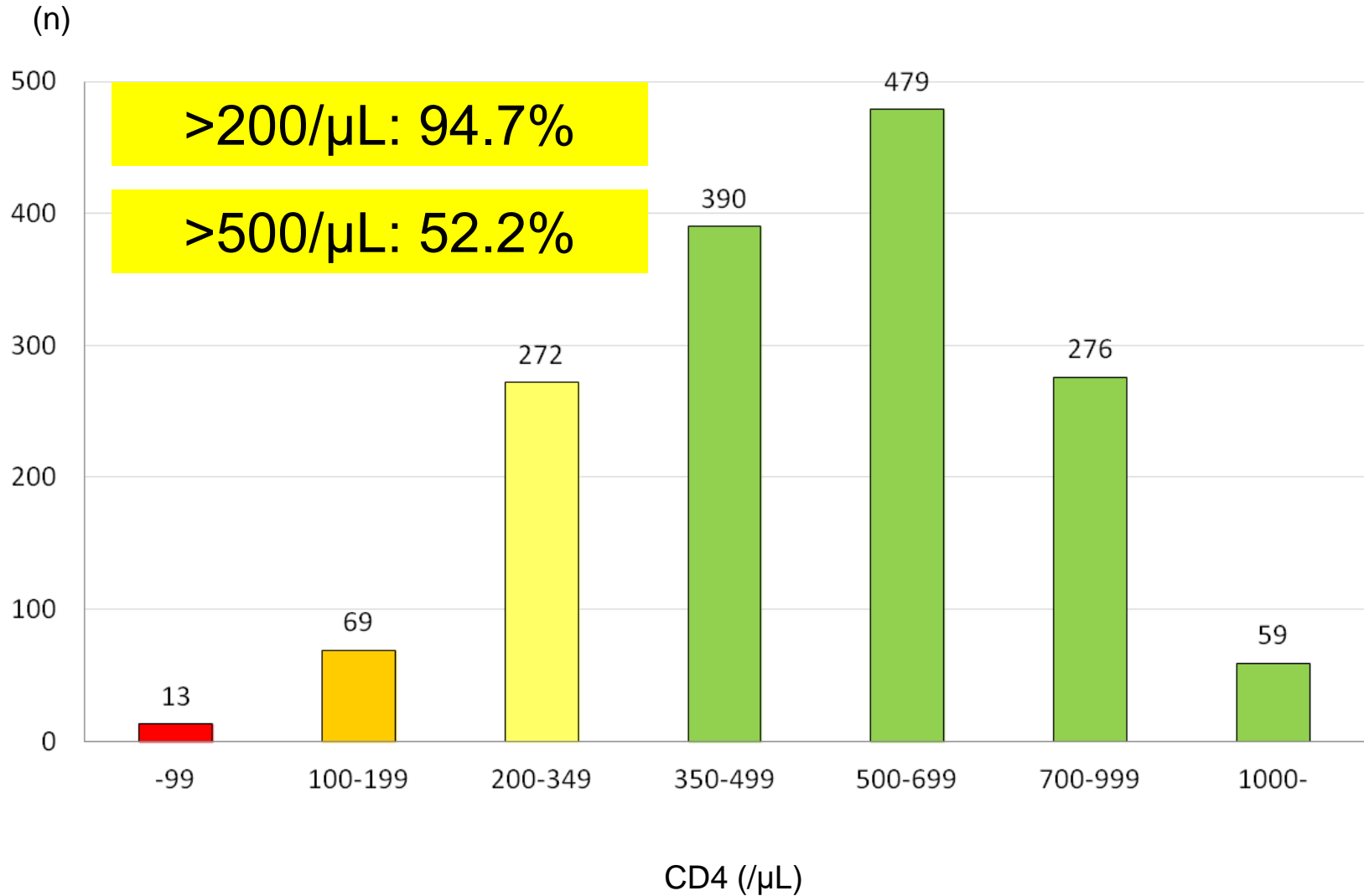
2016	44%
2015	37%
2014	44%

2016	14%
2015	16%
2014	13%

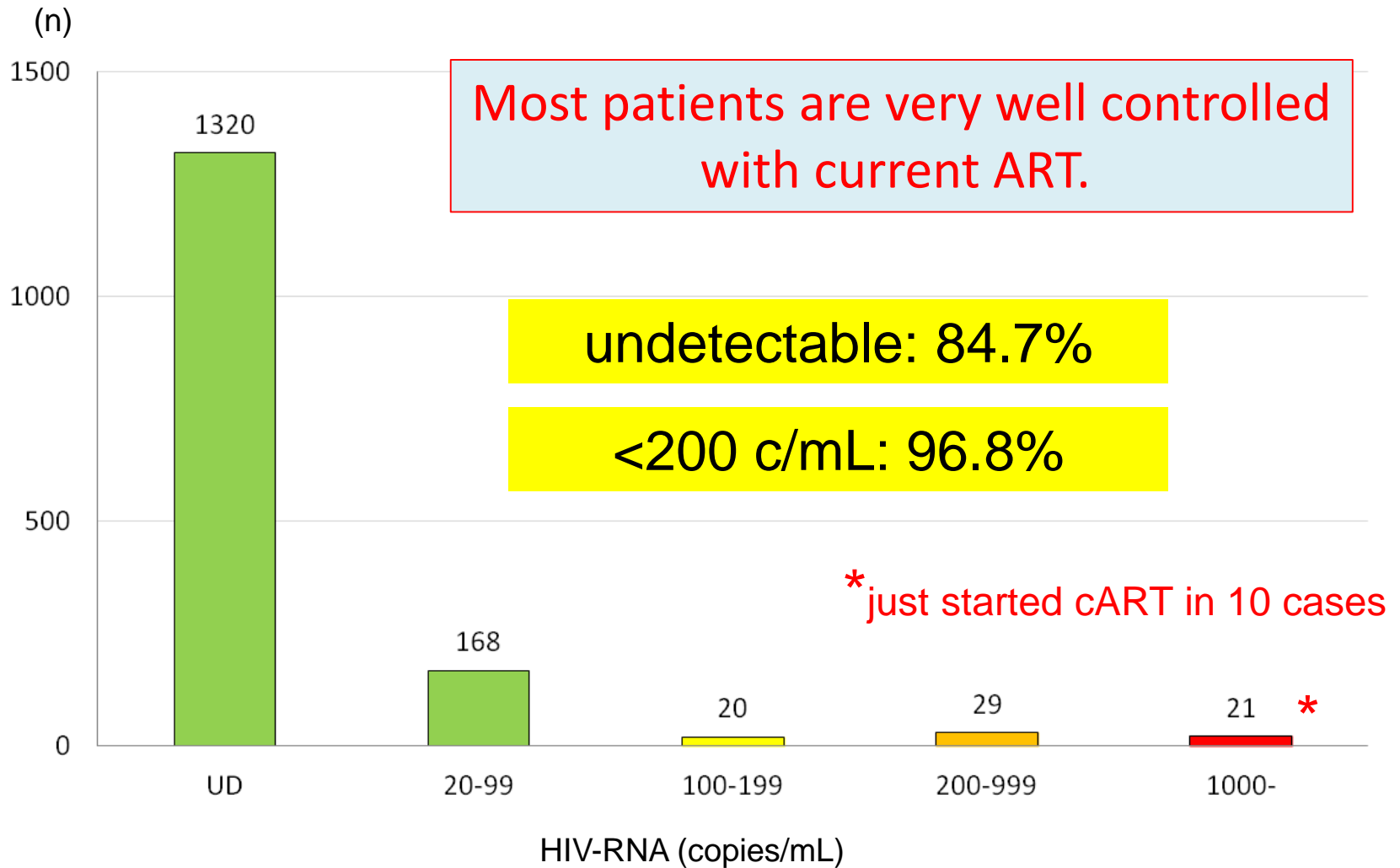


- ACC data -

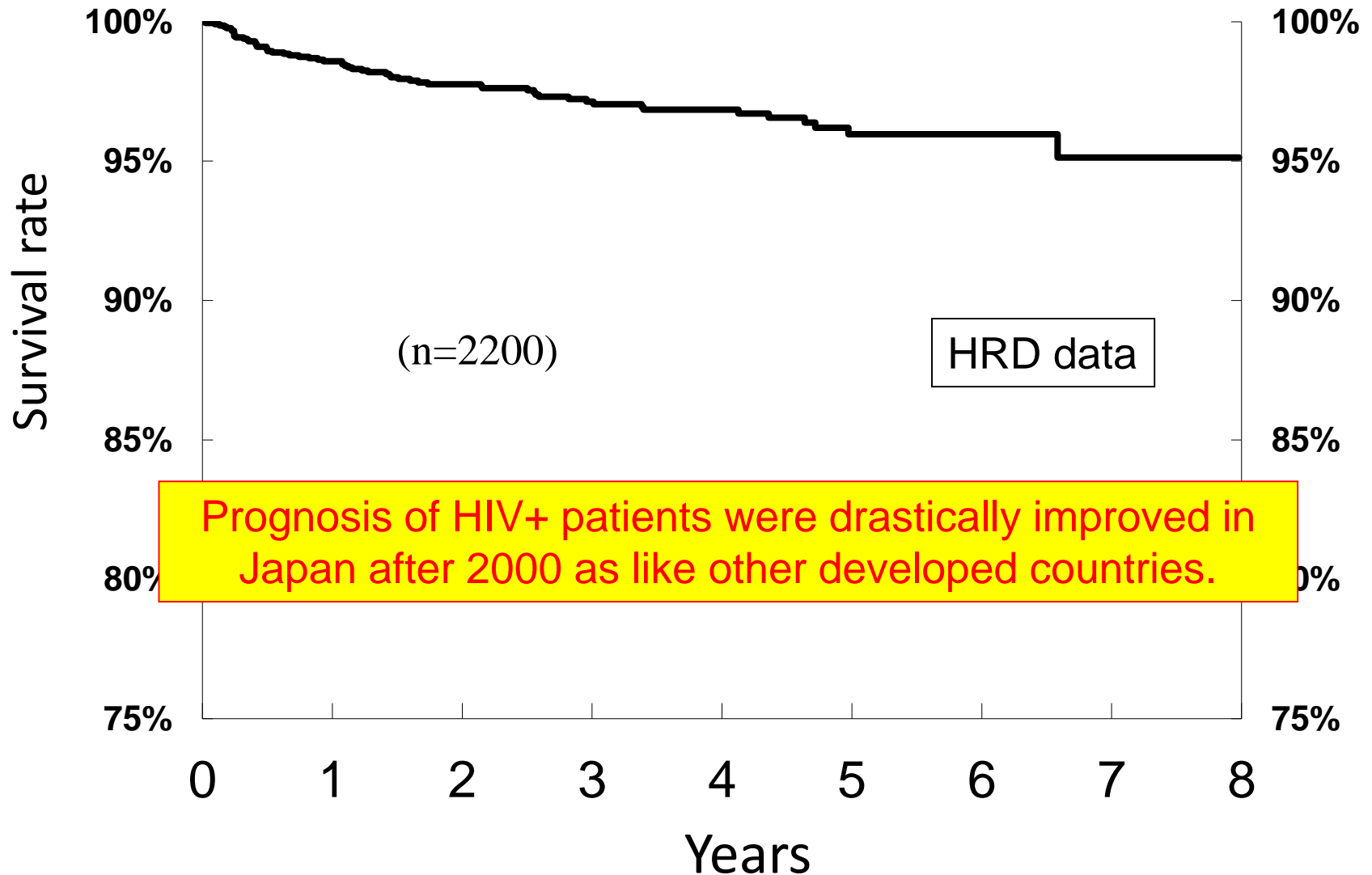
CD4 counts in patients on cART in ACC



HIV-RNA in patients on cART in ACC

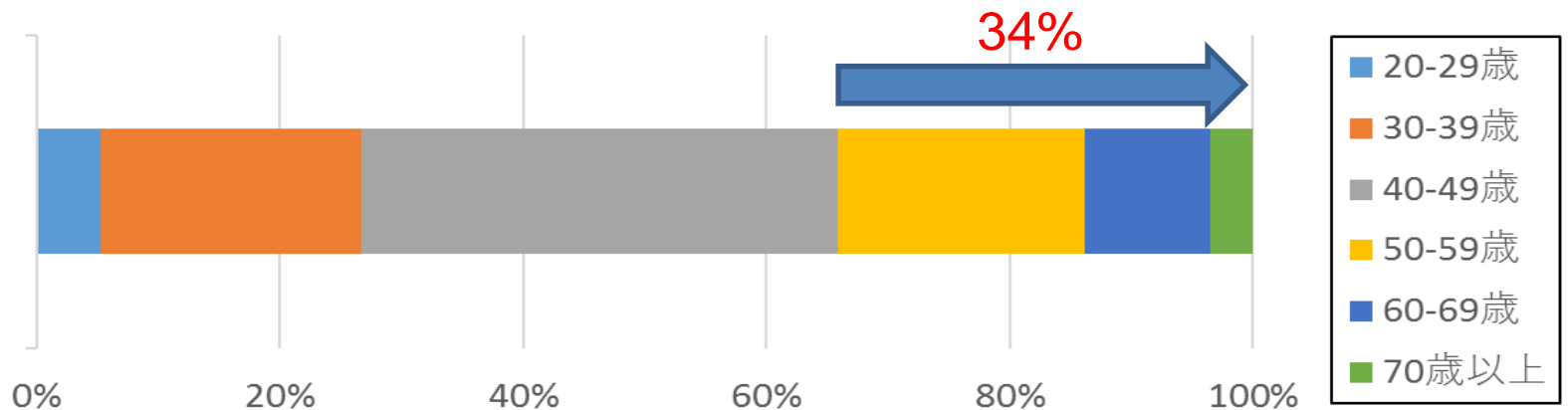
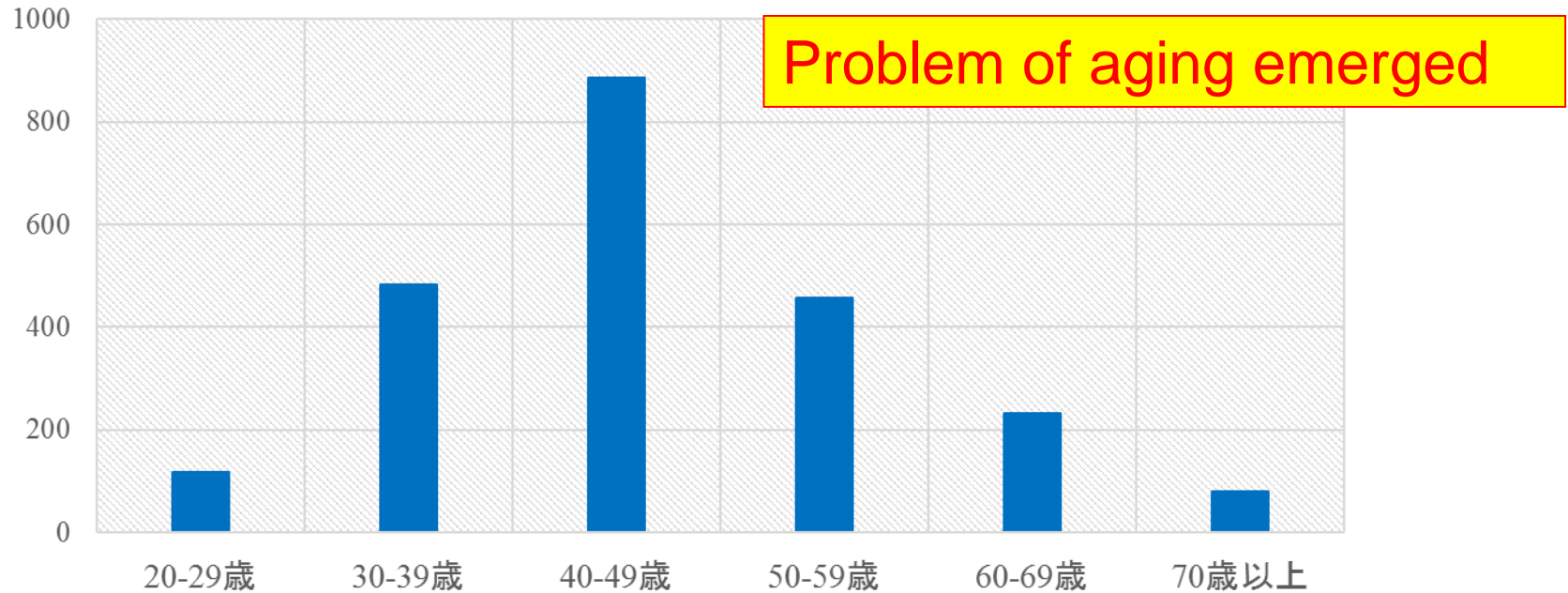


Survival of HIV-patients on cART initiated after 2001 in Japan



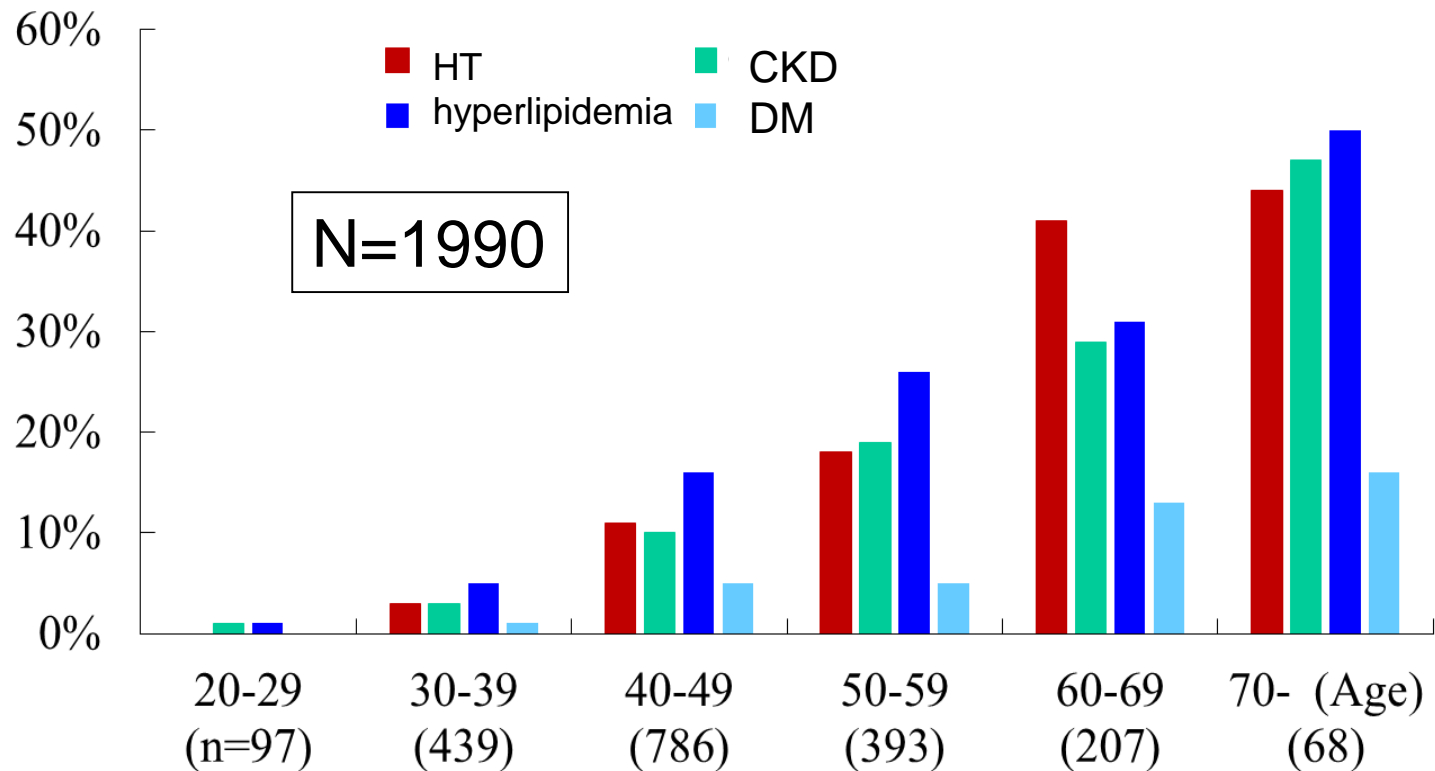
Age of patients in ACC at the end of 2016

34% of out patients were >50 yrs



Comorbidities observed in HIV+ patients

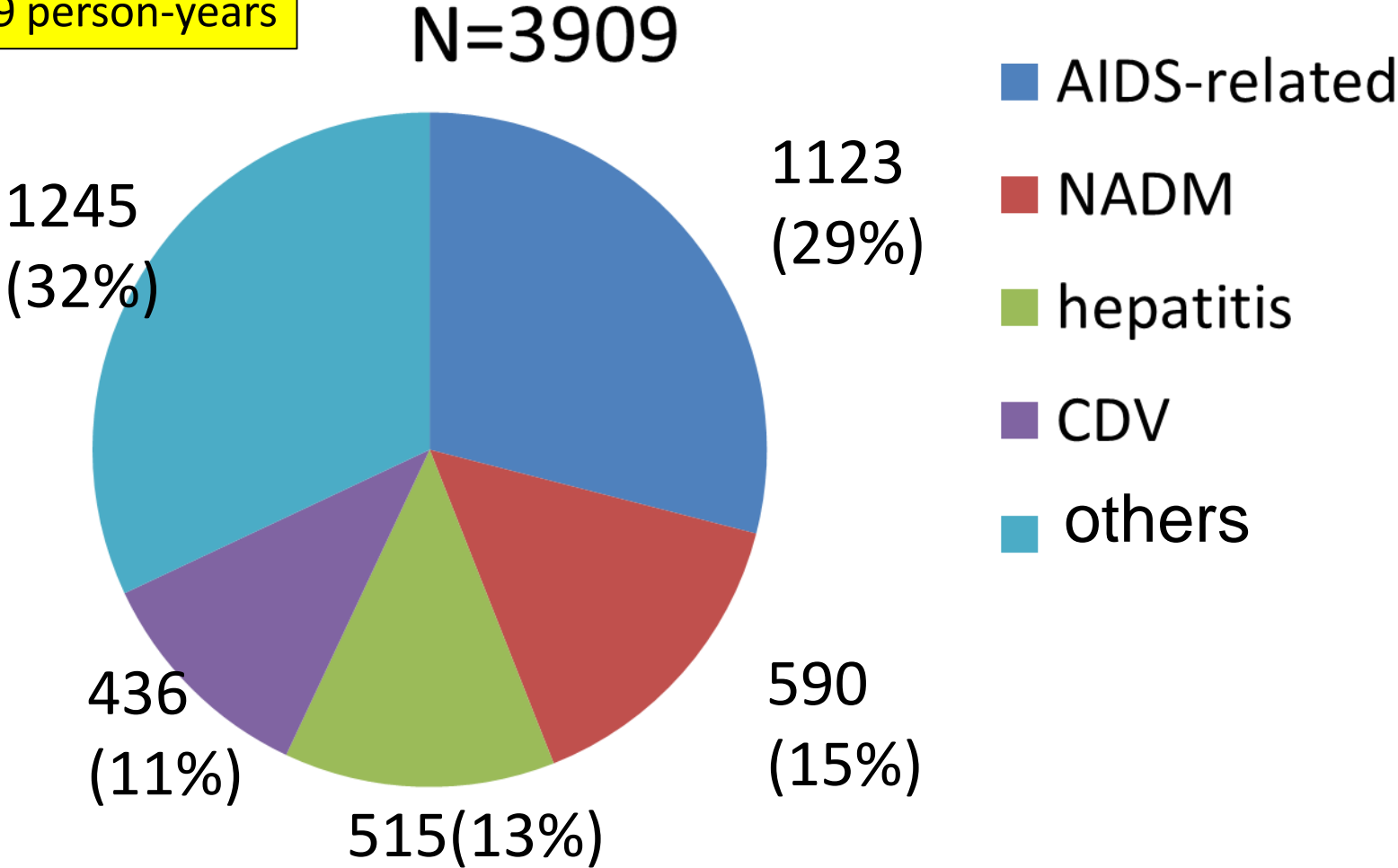
Along with aging, HIV+ patients have high rate of life-style related diseases. In addition to these comorbidities, we should consider cancer in HIV+ Pts.



Journal Review: D:A:D study

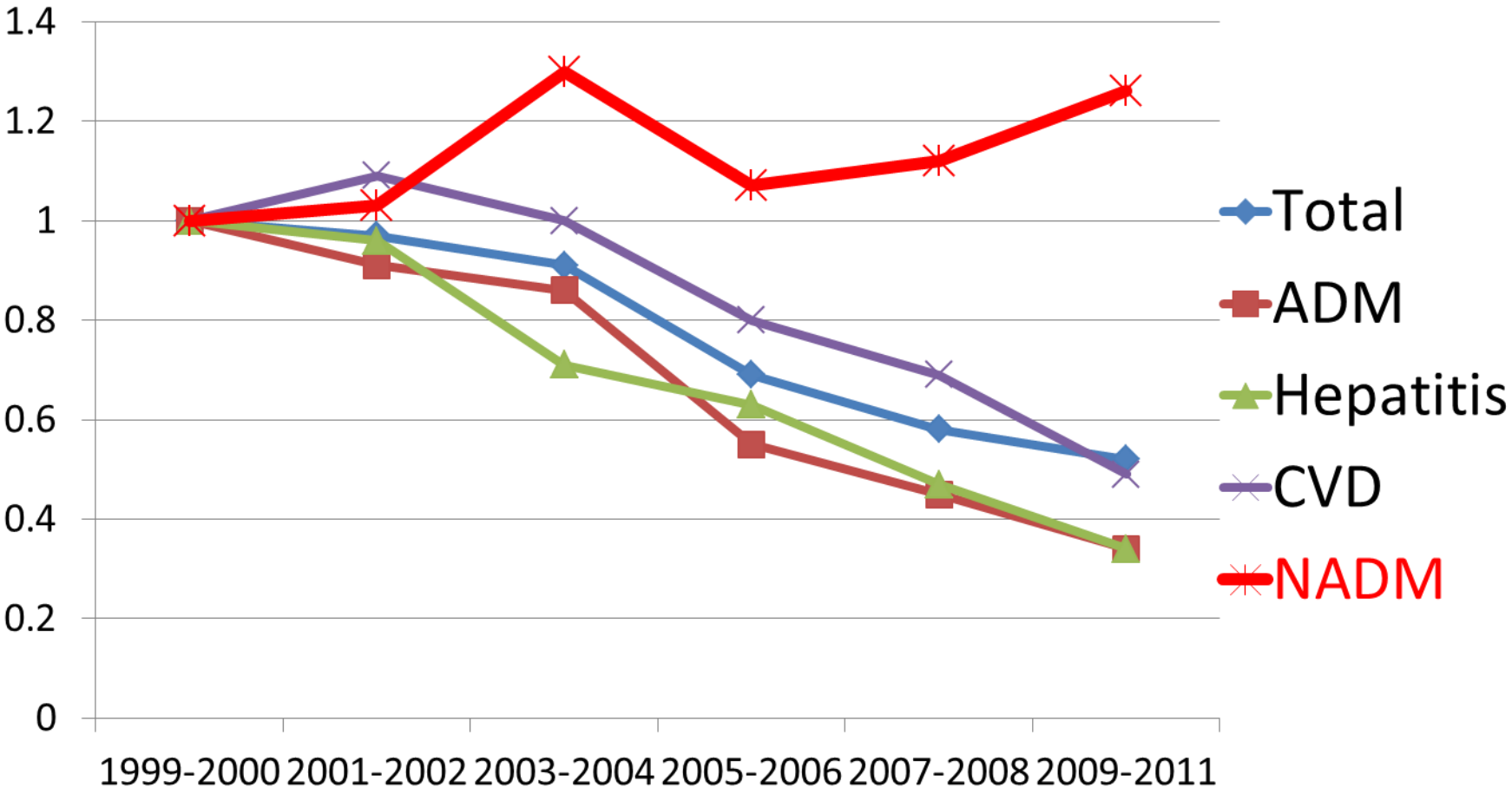
Causes of death since 1999

N=49,731
308,719 person-years



Journal Review: D:A:D study

Annual change of mortality since 1999-2000



Causes of death in Pts registered at ACC in 2016

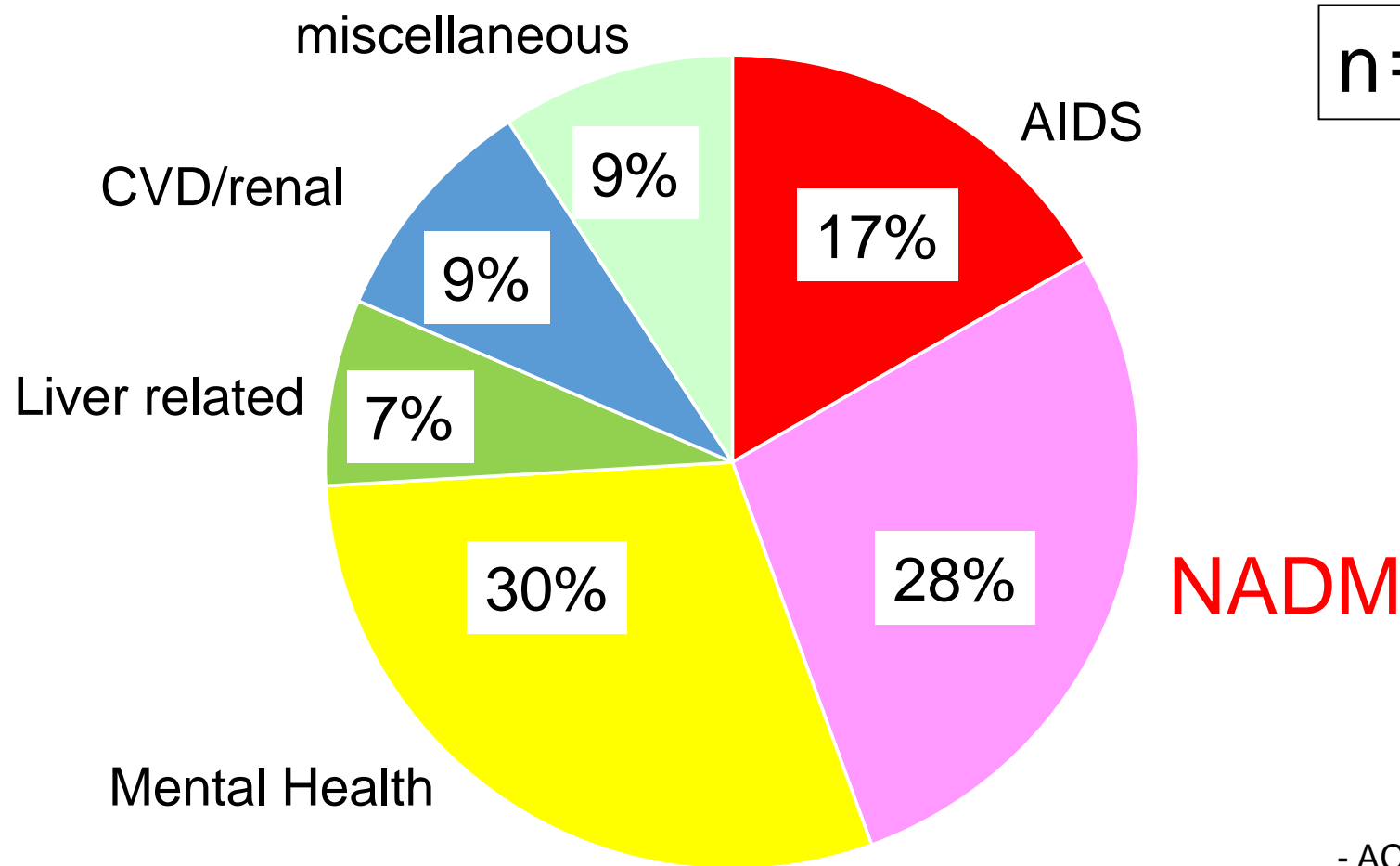
Case	age	stage	route	place	Causes of death
1	30	AIDS	MSM	ACC	AIDS (cryptococcus meningitis)
2	30	AC	MSM	home	Mental health
3	40	AIDS	MSM	ACC	NADM (gallbladder Ca)
4	40	AIDS	MSM	ACC	NADM (ALL)
5	40	AIDS	MSM	Other HP	unknown
6	40	AIDS	MSM	home	Accidental death
7	40	AIDS	MSM	home	Mental health
8	40	AC	MSM	home	Mental health (suicide)
9	40	AC	MSM	ACC	NADM (Colon Ca)
10	40	AIDS	MSM	home	Mental health
11	40	AC	MSM	home	LC
12	50	AIDS	MSM	ACC	AIDS (Lymphoma)
13	50	AC	MSM	Other HP	Heart Failure
14	60	AIDS	MSM	Other HP	NADM (Esophageal Ca)
15	60	AIDS	MSM	Other HP	NADM (Lung Ca)
16	70	AIDS	Hetero	home	Renal Failure
17	70	AIDS	MSM	ACC	AIDS
18	70	AIDS	Hetero	home	AMI
19	70	AC	MSM	Other HP	Senility

5 out of 19 cases (26.3%) died of NADM

- ACC data -

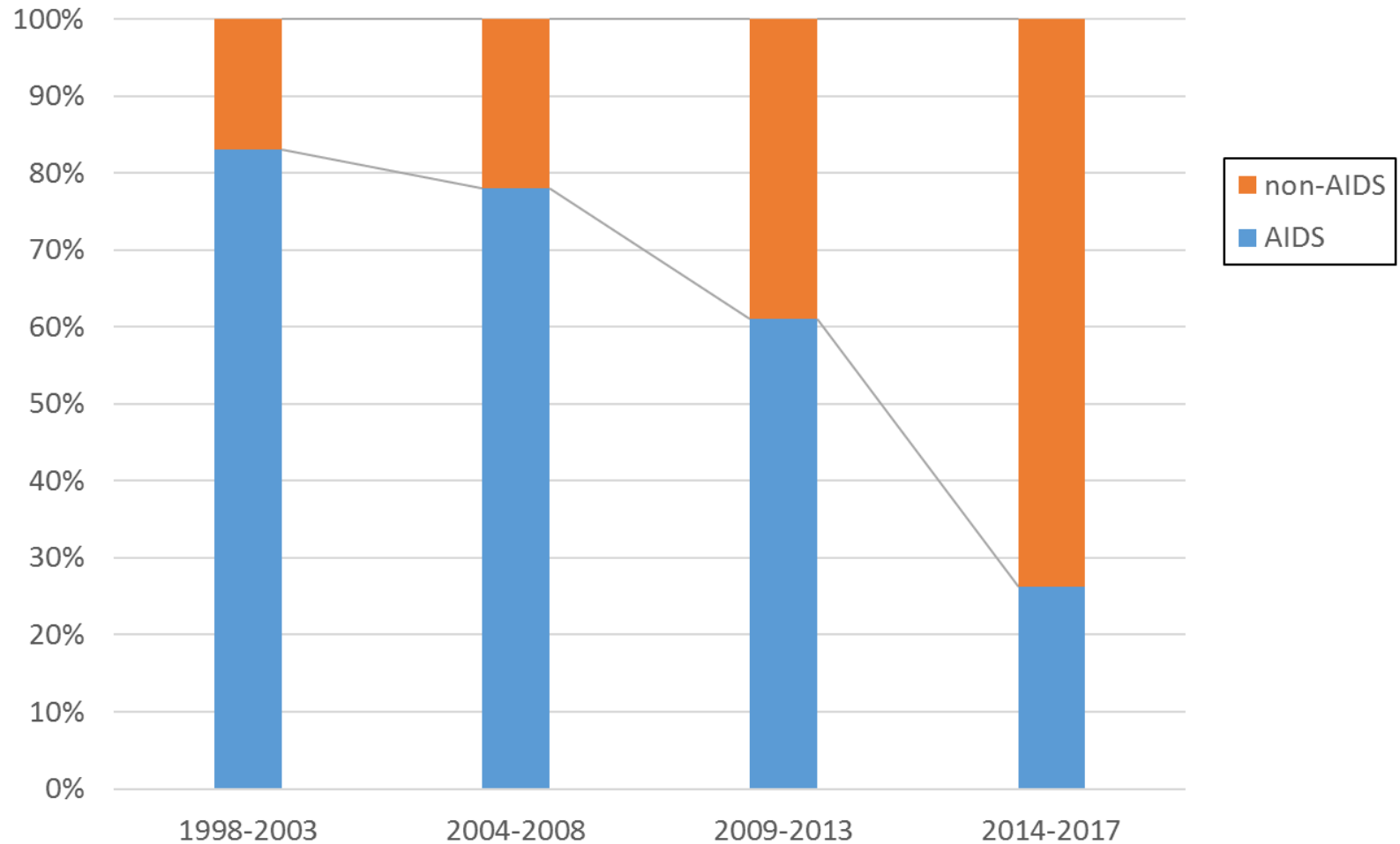
Causes of death in HIV+ Pts in ACC in the last 3 years

Causes of death have been changing from AIDS to NADM or mental health

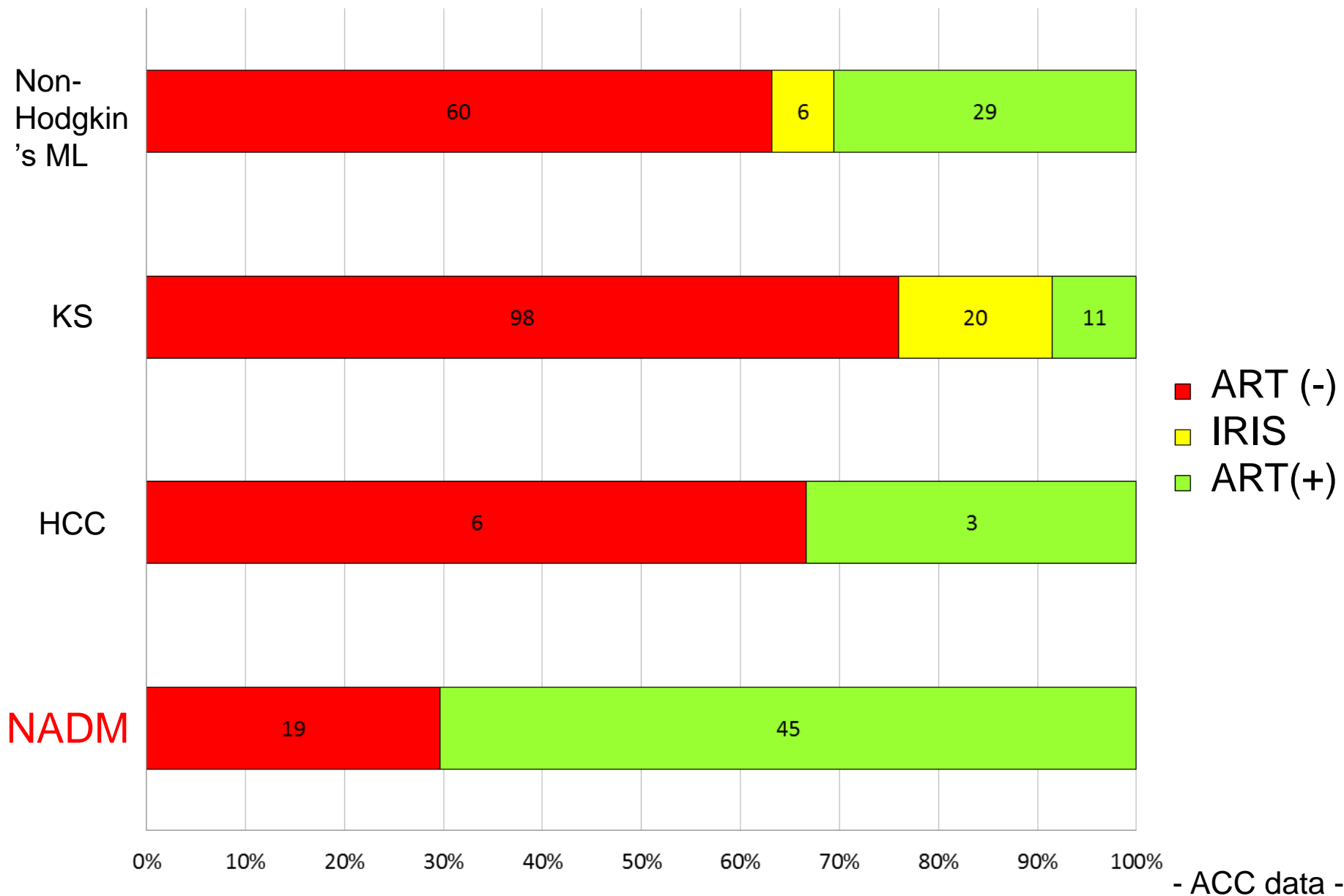


- ACC data -

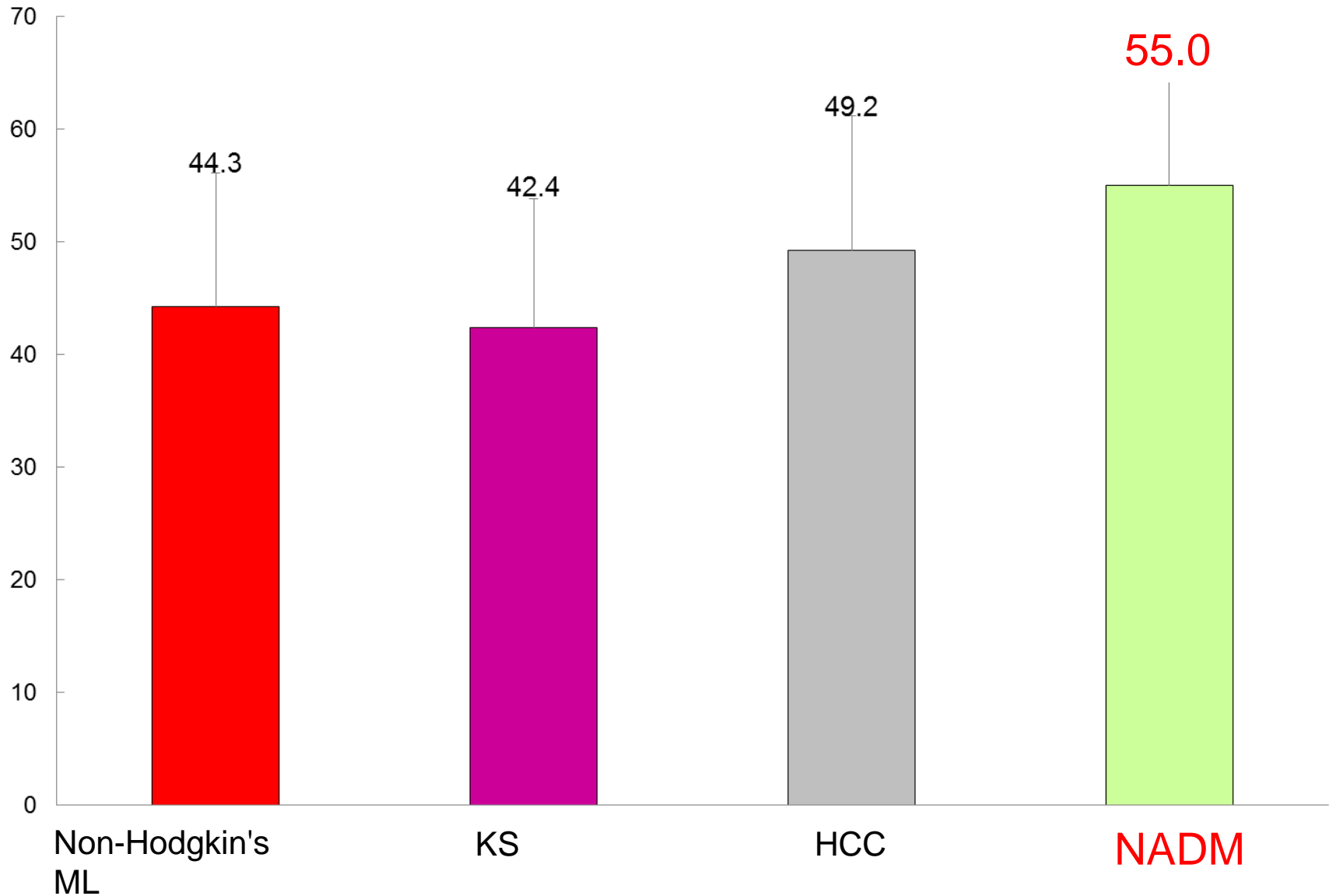
Relative increase of NADM in ACC



cART at Diagnosis of Malignancies in ACC

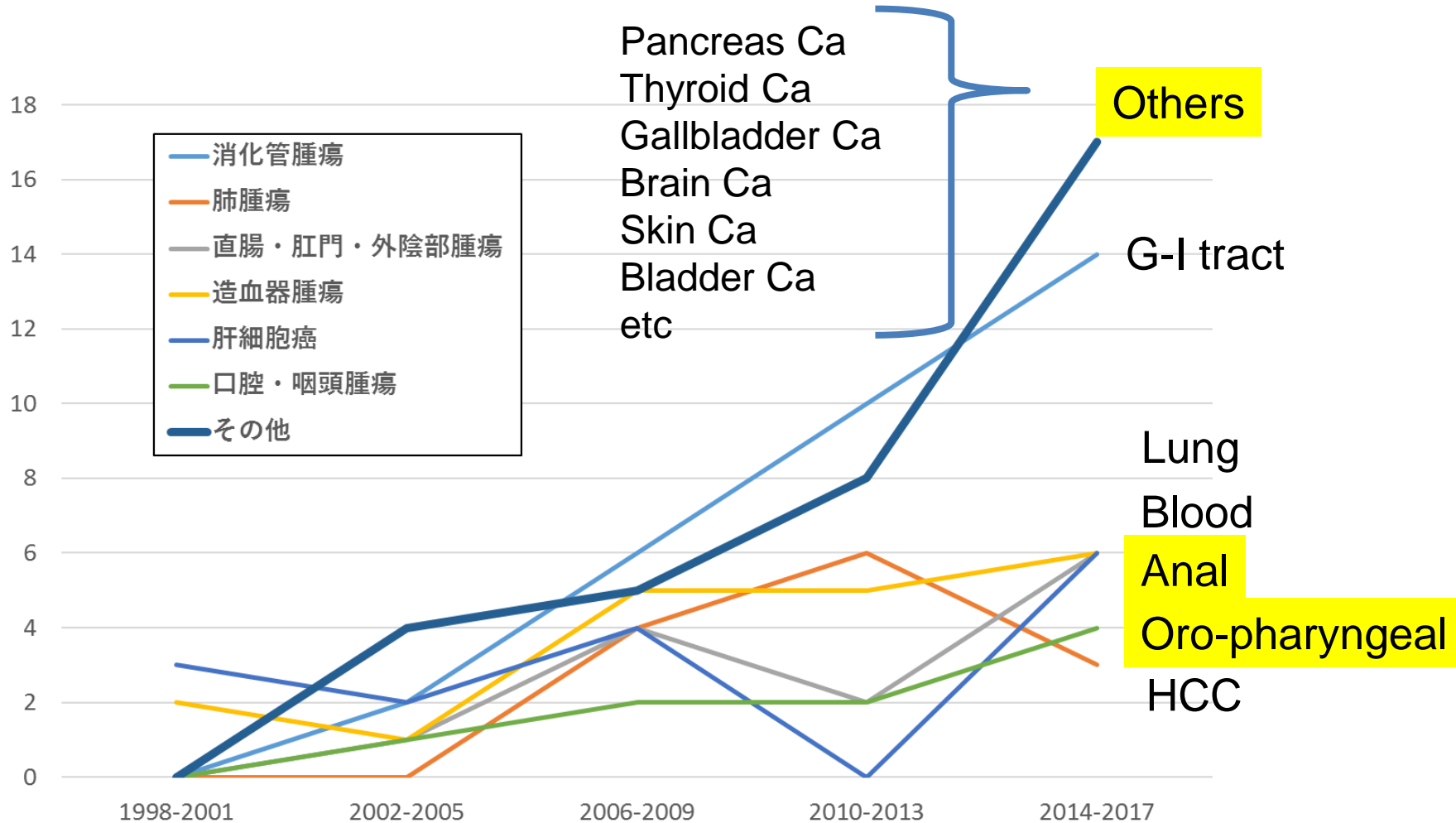


Age at diagnosis of malignancies in ACC

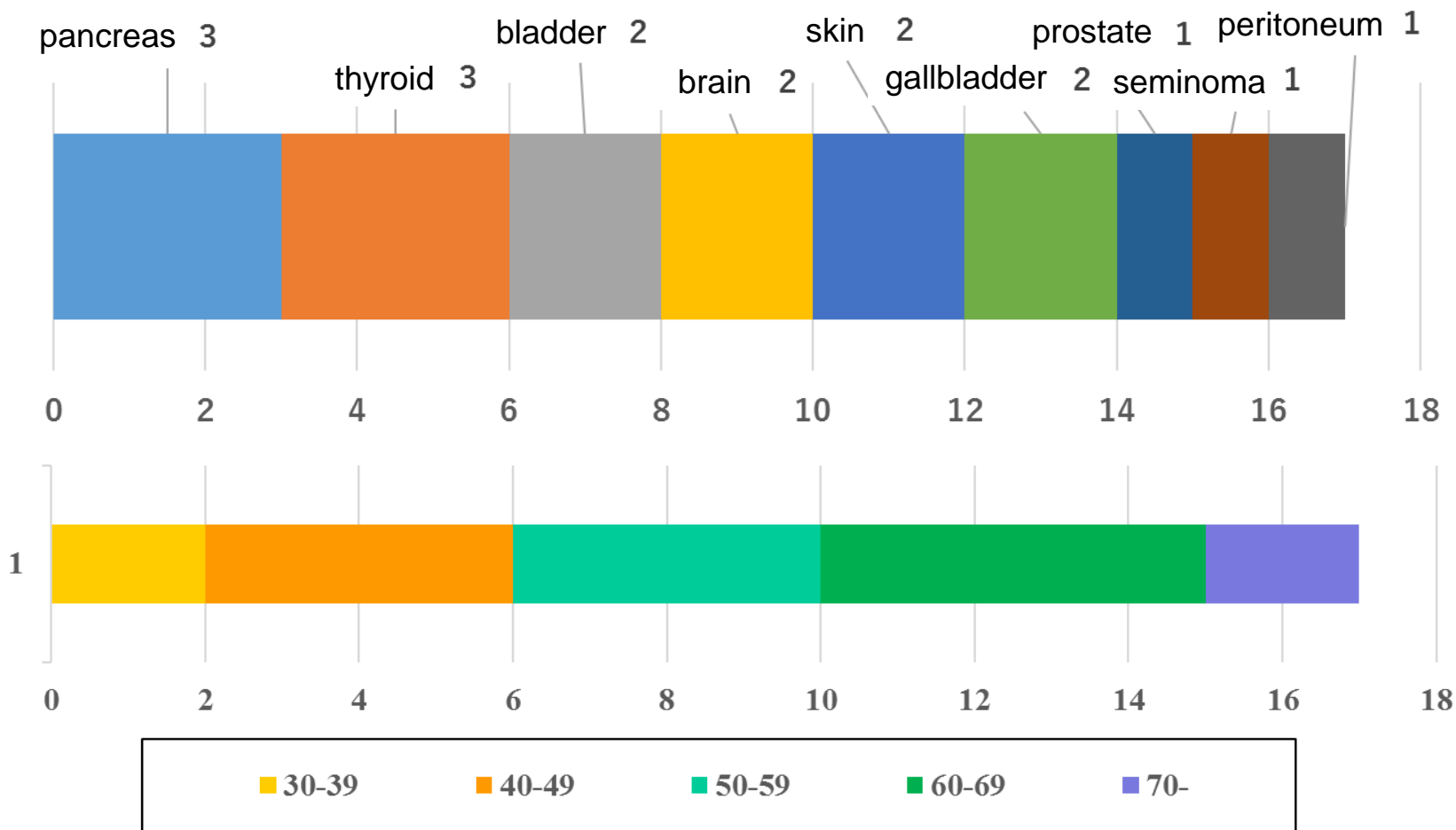


Cases of NADM in ACC

Many rare cancers were diagnosed recently



Other cancers diagnosed in 2014~2017



Many rare cancers occurred in each age group

- ACC data -

Anorectal HPV infection and pre-cancer status in MSM

< subjects and methods >

Anal pap smear test and anal high risk (HR) HPV test were conducted cross-sectionally in HIV+ MSM at ACC-OPC and HIV- MSM at Sexual Health Clinic, NCGM.

	HIV+ MSM (n=206)	HIV- MSM (n=252)	total (n=458)	P value
Mean age (years)	46.9 (SD 10.6)	35.5 (SD 10.2)	39.3 (SD 11.9)	P<0.001
Anorectal HPV infection	152 (73.8%)	100 (39.7%)	252 (55.0%)	P<0.001
Pre-cancer (LSIL or HSIL*)	72 (34.9%)	38 (15.1%)	110 (24.0%)	P<0.001

*LSIL (Low grade squamous intraepithelial lesion), HSIL (High grade squamous intraepithelial lesion)

Both rates of HIV+ MSM were nearly twice as high as those of HIV- MSM. Reasons of differences, accumulation or clearance, are to be elucidated in a longitudinal study.

Oropharyngeal and anorectal HPV-related cancers in MSM

age	Oropharyngeal cancer	Anorectal cancer	total
30s	-	4	4
40s	1	4	5
50s	2	2	4
60s	2	-	2
70s	-	2	2
total	5	12	17

52.9 % of HPV-related cancer occurred in 30s and 40s.

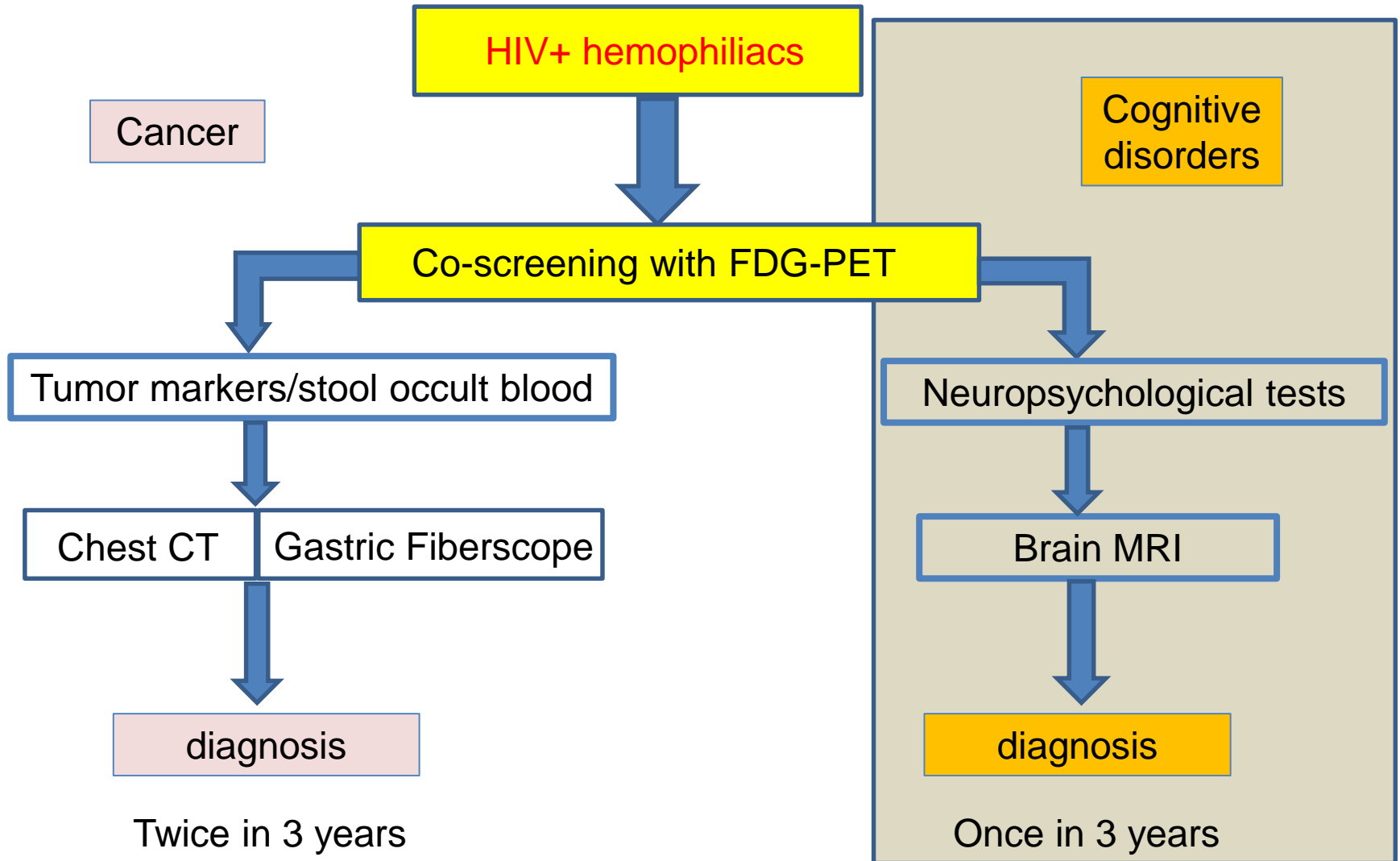
Summary of NADM

1. NADM has become one of the major causes of death in HIV-infected patients in cART era.
2. NADM occurs during on cART.
3. NADM occurs earlier than those in general population.
4. Many rare cancers have been increasing recently.

In the next step, how to get early diagnoses of these rare cancers are an important clinical issue.

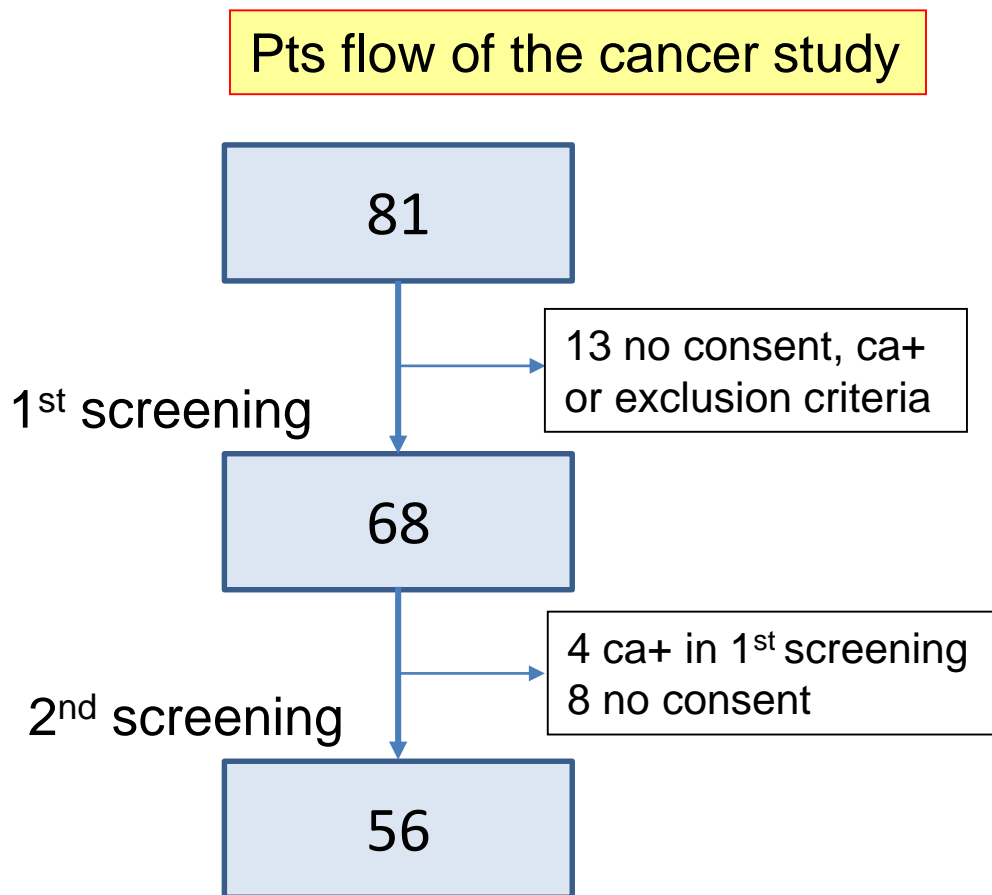
5. We should be aware that HPV-related cancers must be increasing.

Study of co-screening for cancer and cognitive disorders with FDG-PET in HIV-infected Japanese hemophiliacs



Background of hemophiliac/HIV+ Pts

1. Infected with HIV at least before 1985 (>34 years of HIV infection)
2. Median age of 48.7 years old
3. Almost all infected with HCV (all cured HCV)
4. Long histories of ART (esp. with NRTIs)
5. NADM has been increasing



Screening methods

If, positive findings by FDG-PET and/or chest CT
stool occult blood positive
tumor markers* positive

(*tumor markers examined; CEA, AFP, CA19-9, DUPAN-1, Span-1, PSA, CYFRA, ProGRP)



Responsible specific examinations to confirm diagnosis
such as colon fiberscope, abdominal CT, MRI, echograph, etc

Result of the first screening

- Cancer positive in 4 patients among 68 study participants (Prevalence; 5.9%)
mean age; 45.8 years
1. 50s, Thyroid papillary ca: T1, N1, M0
Diagnosed with eho + biopsy => operation
 2. 40s, Thyroid follicular ca: T1, N0, M0
Diagnosed with eho + biopsy => operation
 3. 40s, Thyroid papillary ca suspected with eho: refused further examination
 4. 30s, Neuroendocrine tumor: T1, N0, M0
Diagnosed with CT, MRI, and EUS-FNA => operation

FDG-PET false positive in 12 cases (18.8%)

Tumor markers had no diagnostic value in this study.

Result of the second screening

- During a mean **follow-up of 1.2 years** (67.2 PY), cancer was diagnosed in **2** cases among **56** study participants (**2.99/100PY**)
 1. 70s, Pancreas ca (invasive ductal ca); TS2, N0, PCM1 diagnosed by CT and MRI => operation
 2. 60s, Hepatocellular ca; 22x21x19mm in S6, meta (-) diagnosed by CT and MRI => operation

The incidence strongly suggests the necessity of the cancer screening in this population.

Conclusion of the cancer screening study for HIV+ Japanese hemophiliacs

1. FDG-PET was conducted in 68 HIV+ hemophiliacs with the mean age of **48.7 years old**.
2. Abnormal accumulation was found in 16 cases. Among them, cancer was diagnosed in 4 cases (**prevalence; 5.9%**, false positive rate 18.8%), although the early diagnosis of thyroid cancer is still under arguments.
3. During a mean follow-up of 1.2 years, cancer was diagnosed in 2 cases among 56 study participants (**incidence; 2.99/100PY**).

According to results above,

We recommend the cancer screening, at least, to HIV+ hemophiliacs in other hospitals.

acknowledgements

- Thanks to all staff members of ACC and HIV+ hemophiliac participants in the cancer screening study.
- Special thanks to Mikiko Ogata, RN for her support to the cancer screening study and Daisuke Mizushima, MD for giving data of his HPV-related study.
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