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Oral Presentation

SERIOUS CLINICAL EVENTS IN HIV-POSITIVE PERSONS WITH CHRONIC KIDNEY DISEASE (CKD)

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Disclosures

Nothing to disclose

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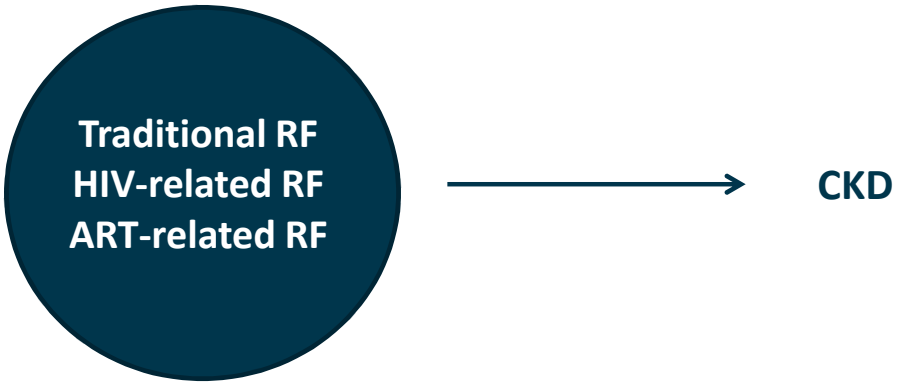
Background

- CKD is becoming increasingly common in the ageing HIV-positive population with an estimated prevalence up to 30% in high risk populations[1-3]

- Risk factors (RF) for incident CKD amongst HIV-positive persons are well established[4-9] and include
    - Traditional renal RF (i.e. older age, hypertension & diabetes)
    - HIV related RF (i.e. immunosuppression & co-infections)
    - Antiretroviral treatment related RF (i.e. tenofovir disoproxil fumarate, indinavir, boosted atazanavir & lopinavir)



1. Capeau J, CID 2011; 2. Gupta SK, Clin Nephrol 2004; 3. Fernando, AM J Med Sci 2008; 4. Mocroft A. AIDS 2010; 5. Jotwani V, Am J Kid Dis 2011; 6. Scherzer R, AIDS 2012; 7. Kalayjian RC, AIDS 2012; 8. Ryom L, JID 2013; 9. Mocroft A, Plos Med 2016

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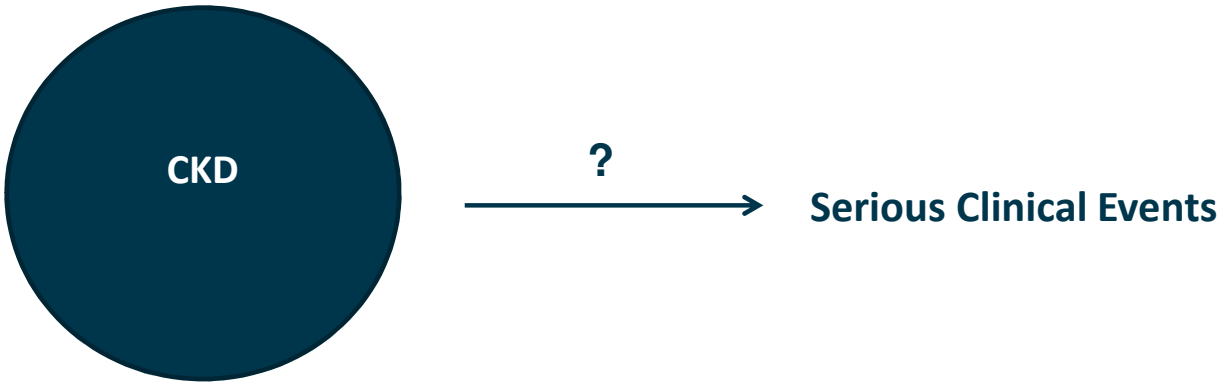
Background & Aims

- However, insights into the prognosis after CKD in persons with HIV is limited and requires a large dataset with substantial follow-up time



- Aim to determine the prognosis and incidence of serious clinical events (SCE) after a diagnosis of CKD in persons with HIV and the role of modifiable risk factors

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Methods I

- D:A:D study participants under follow-up after 2004 (baseline for creatinine collection) with data on estimated glomerular filtration rate (eGFR) were included

- Incident CKD defined as:
  - Confirmed, $\geq$ 3 months apart, eGFR $\leq$ 60 mL/min/1.73m^2 or
  - 25% eGFR decrease when baseline eGFR $\leq$ 60 mL/min/1.73m^2

- SCE, were all centrally validated, included:
  - Cardiovascular disease (CVD)
    - myocardial infarction, stroke, invasive cardiovascular procedures
  - End stage renal disease (ESRD)
  - End stage liver disease (ESLD)
  - AIDS defining malignancies (ADM)
  - Non-AIDS defining malignancies (NADM)
  - Other AIDS events (excluding malignancies)
  - Death

- Recurrent SCE of the same type were excluded

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Methods II

- Persons were followed from CKD to incident SCE, 6 months after last visit or Feb 1st 2016, whichever occurred first
- Kaplan Meier estimation calculated time to a SCE
- Poisson regression models considered associations between individual SCE and potential risk factors (time-updated when subjective to change over time)
- The population attributable risk fraction (PAF) was calculated for key identified risk factors (only those >5% presented)
- For perspectives, in a descriptive analysis, we followed participants from first eGFR to SCE and stratified follow-up time according to CKD status and compared crude rates of SCE between those with/without CKD

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Baseline Characteristics

		All CKD		No SCE		Any SCE		
		N	%	N	%	N	%	p
Total		2467	100.0	1872	75.9	595	24.1	
Gender	Male	1904	77.2	1436	76.7	468	78.7	0.32
Race	White	1249	50.6	949	50.7	300	50.4	0.88
HIV risk	MSM	1171	47.5	908	48.5	263	44.2	0.0031
	IDU	318	12.9	222	11.9	96	16.1	
HCV	Positive	555	22.5	393	21.0	162	27.2	0.002
VL < 400	Yes	2221	90.0	1725	92.1	496	83.4	<0.0001
Smoking	Current	828	33.6	596	31.8	232	39.0	0.0043
	Yes	1568	63.6	1108	59.2	460	77.3	
Diabetes	Yes	398	16.1	258	13.8	140	23.5	<0.0001
Hypertension	Yes	509	20.6	350	18.7	159	26.7	<0.0001
BMI	<18	249	10.1	169	9.0	80	13.4	0.0009

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HCV	Positive	555	22.5	393	21.0	162	27.2	0.002
VL < 400	Yes	2221	90.0	1725	92.1	496	83.4	<0.0001
Any prior SCE	Yes	1181	47.9	844	45,1	337	56,6	<0.0001
Smoking	Current	828	33.6	596	31.8	232	39.0	0.0043
Hypertension	Yes	509	20.6	350	18.7	159	26.7	<0.0001
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BMI	<18	249	10.1	169	9.0	80	13.4	0.0009
		Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**	
Age	Years	60	52 - 67	60	52 - 67	60	51 - 68	0.92
CD4	cells/mm^3	516	345 - 723	547	380-750	388	250-610	<0.0001

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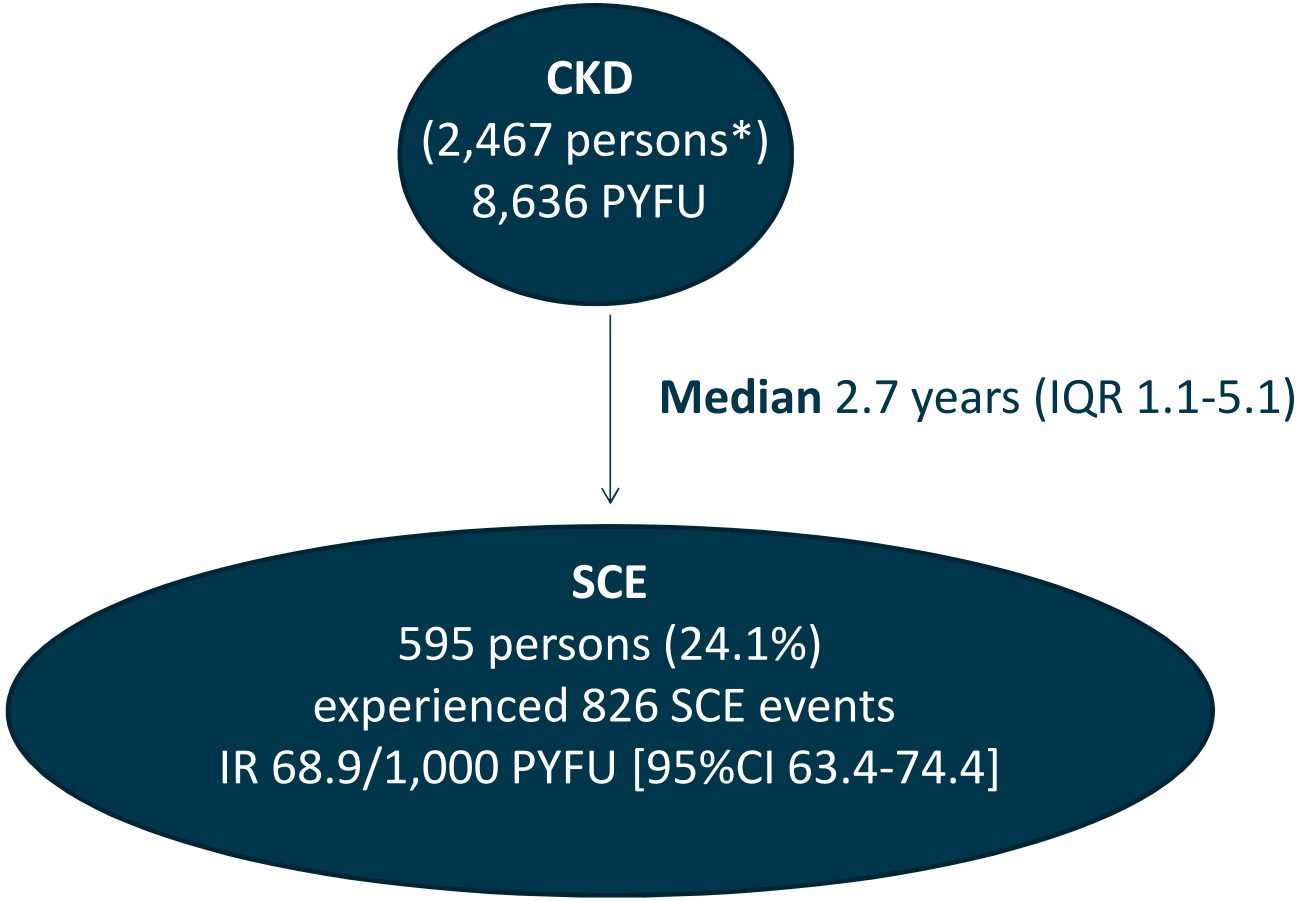
Rates of Incident SCE in HIV-Positive Persons With CKD



*2,231 persons (90.4%) with eGFR $\leq$ 60 mL/min/1.73m^2 &236 persons (9.6%) with 25% eGFR decline

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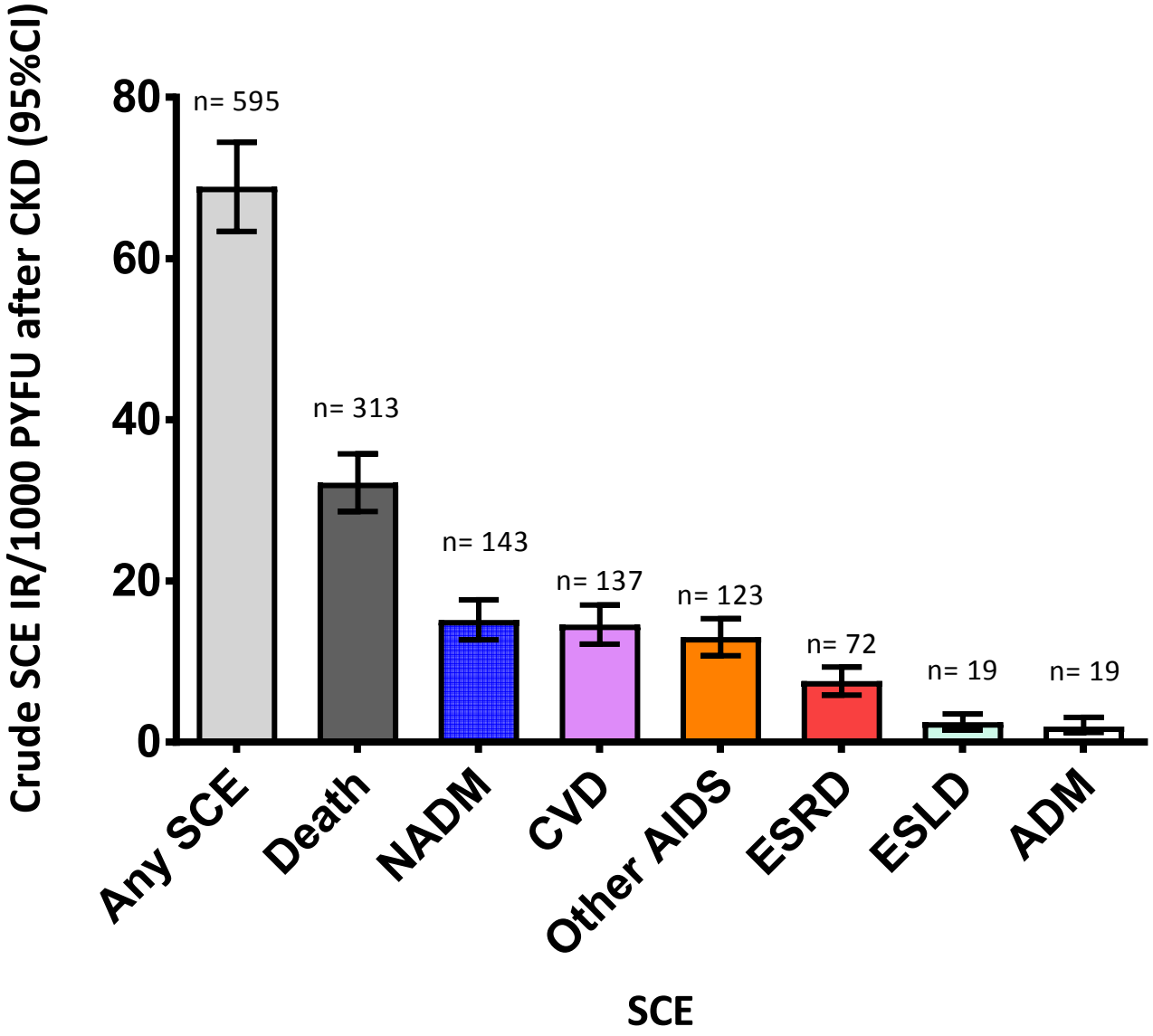
SCE Incidence Rates & Distribution After CKD



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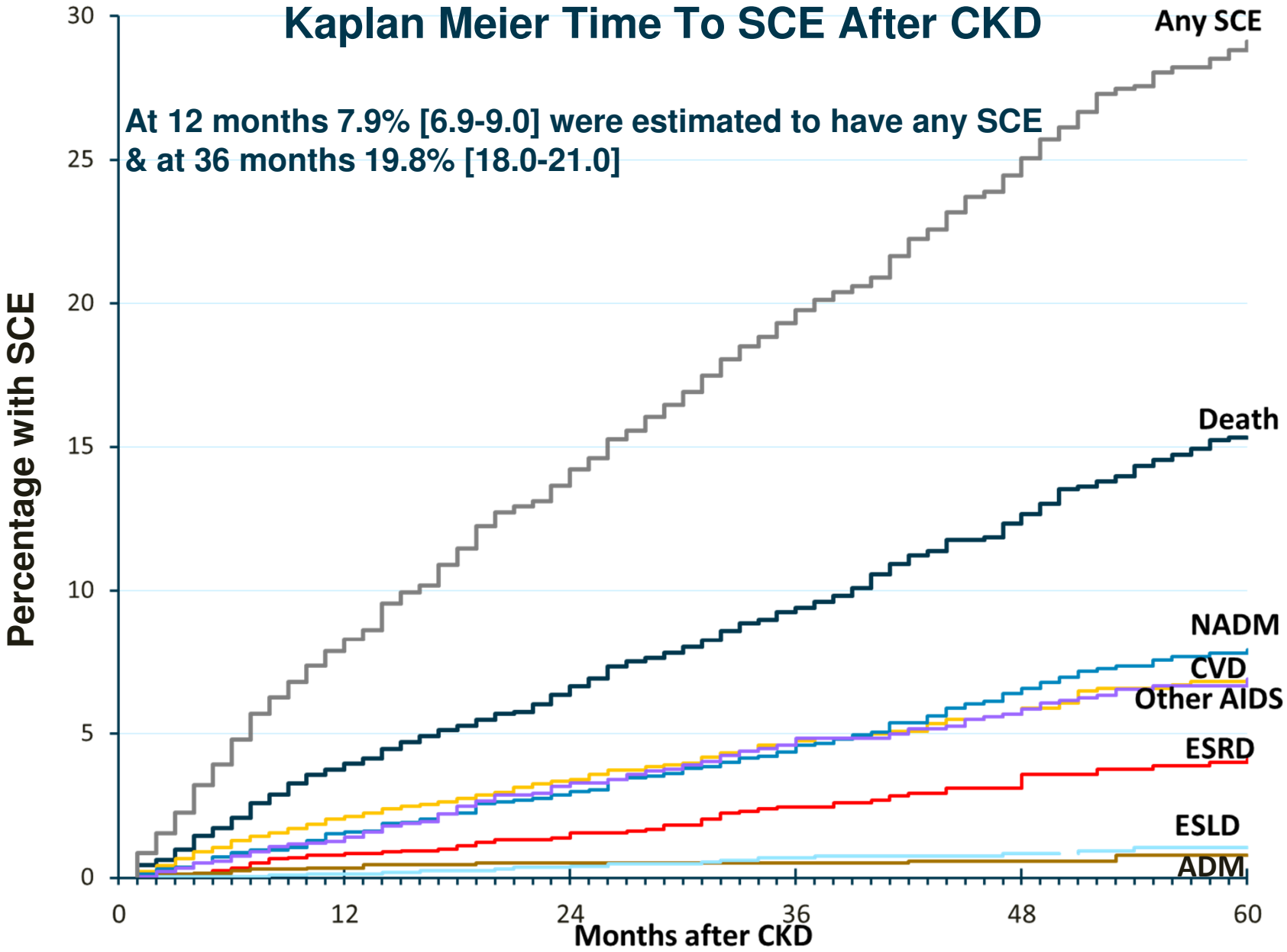
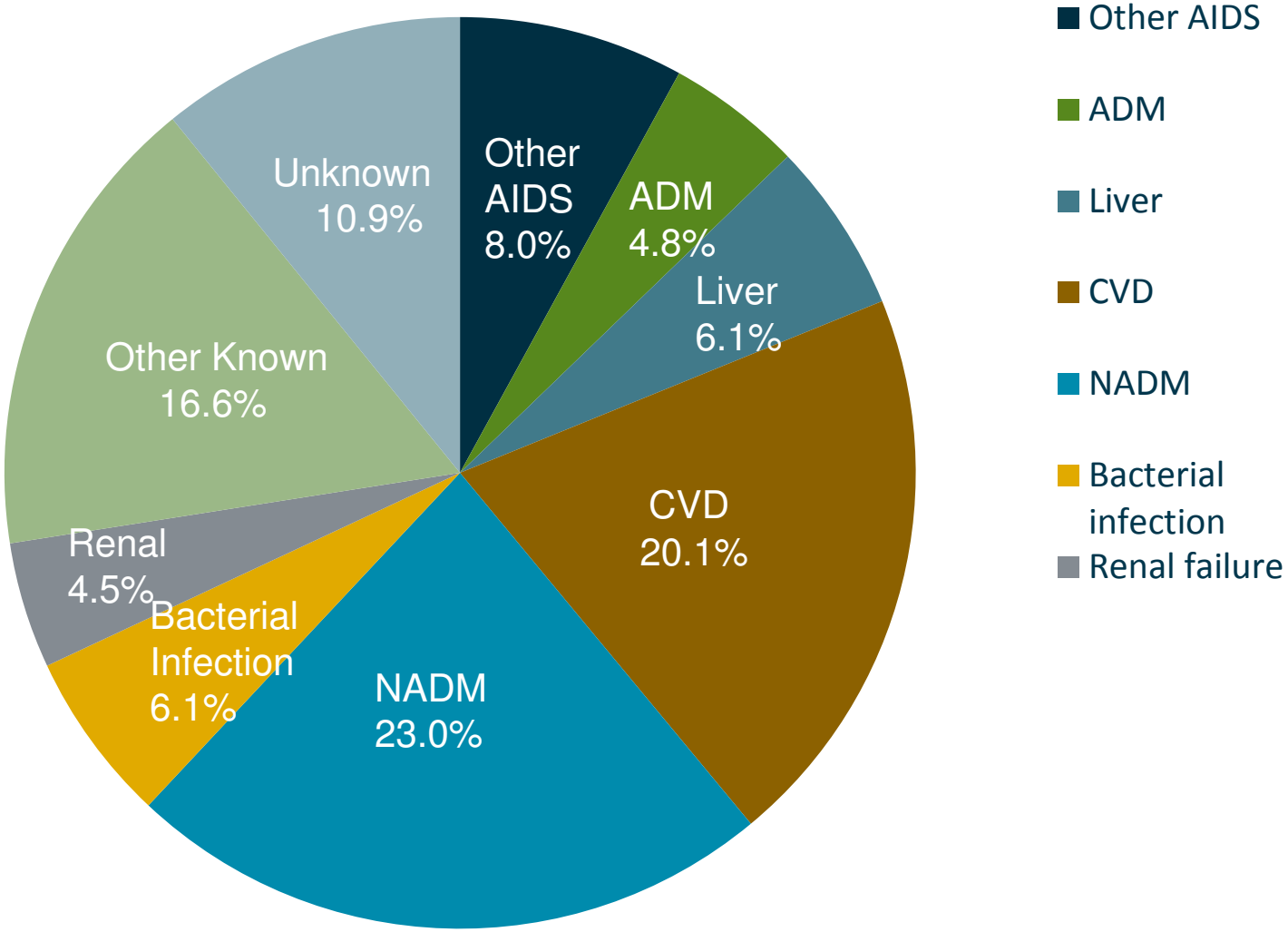

Kaplan Meier Time To SCE After CKD
At 12 months 7.9% [6.9-9.0] were estimated to have any SCE
& at 36 months 19.8% [18.0-21.0]
Any SCE
Death
NADM
CVD
Other AIDS
ESRD
ESLD
ADM
Percentage with SCE
Months after CKD
0
5
10
15
20
25
30
0
12
24
36
48
60

Underlying Cause of Death Following CKD (n=313)



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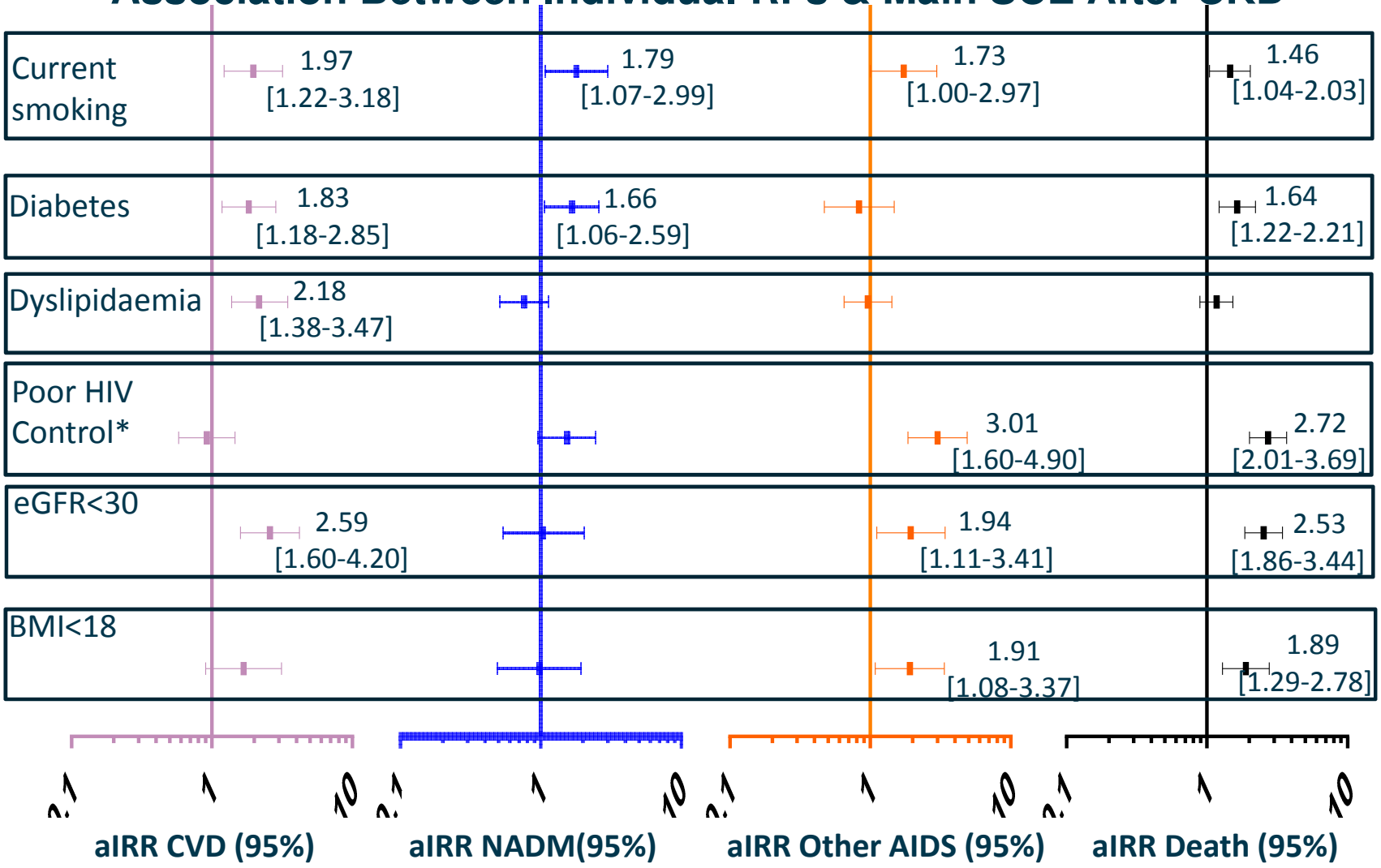
Association Between Individual RFs & Main SCE After CKD



Adjusted for age, gender, ethnicity, HIV acquisition, baseline date, smoking status, diabetes, hypertension, dyslipidaemia, eGFR, BMI, HBV and HCV status, *HIV control (poor CD4<350/VL>10000; good CD4>500/VL<400; Intermediate all other combinations), CD4 count, previous events (pre-baseline) and time-updated ESLD , ESRD, NADM, ADM other AIDS and CVD

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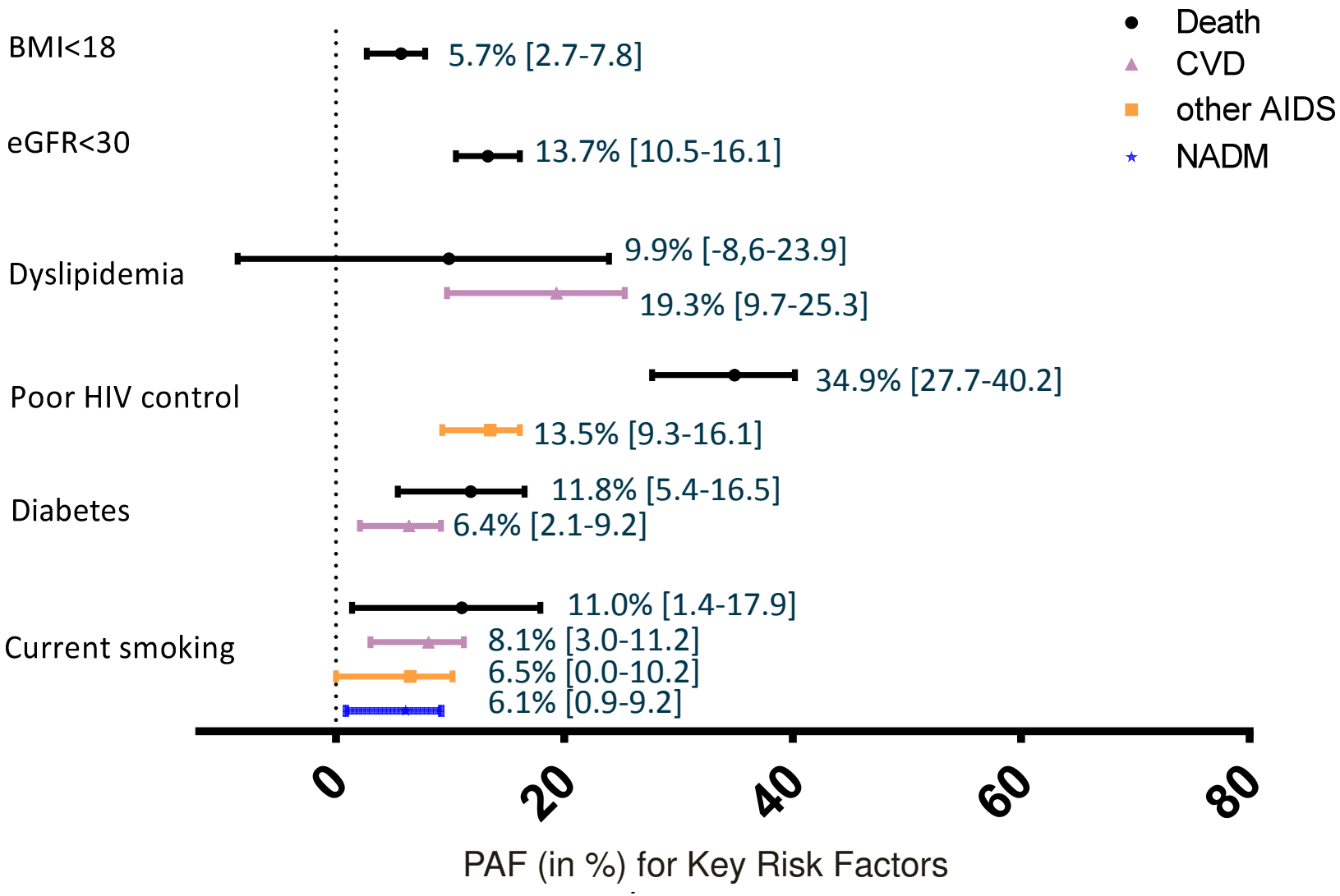
PAF (>5%) For Key Risk Factors For SCE After CKD



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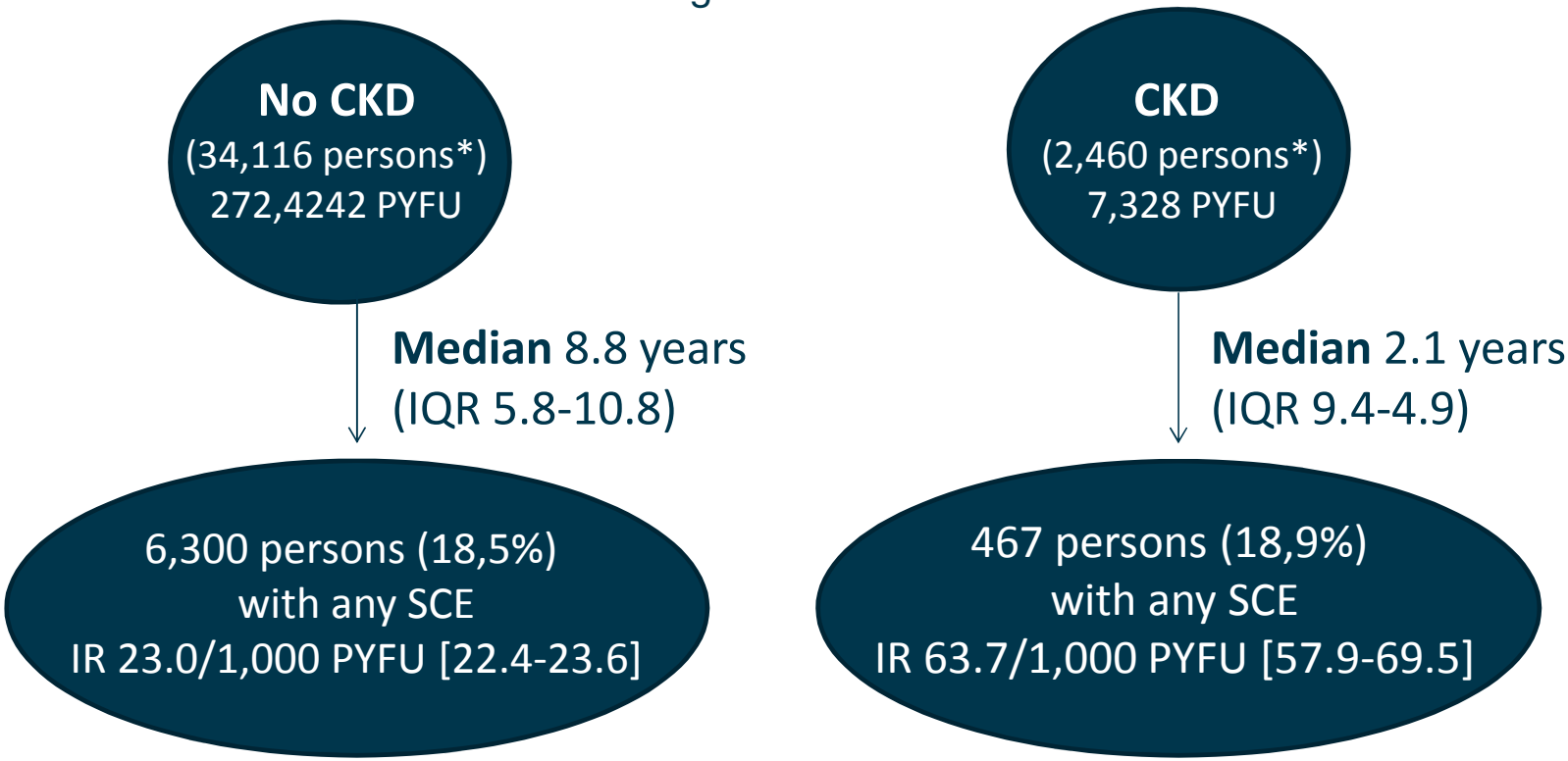
Results in Perspective (I)
SCE in Persons With & Without CKD

Participants followed from first eGFR in D:A:D to SCE and follow-up and events stratified according to with/without CKD*



*NOT the same population as previously; analysis has different inclusion and exclusion criterion for descriptive purposes only

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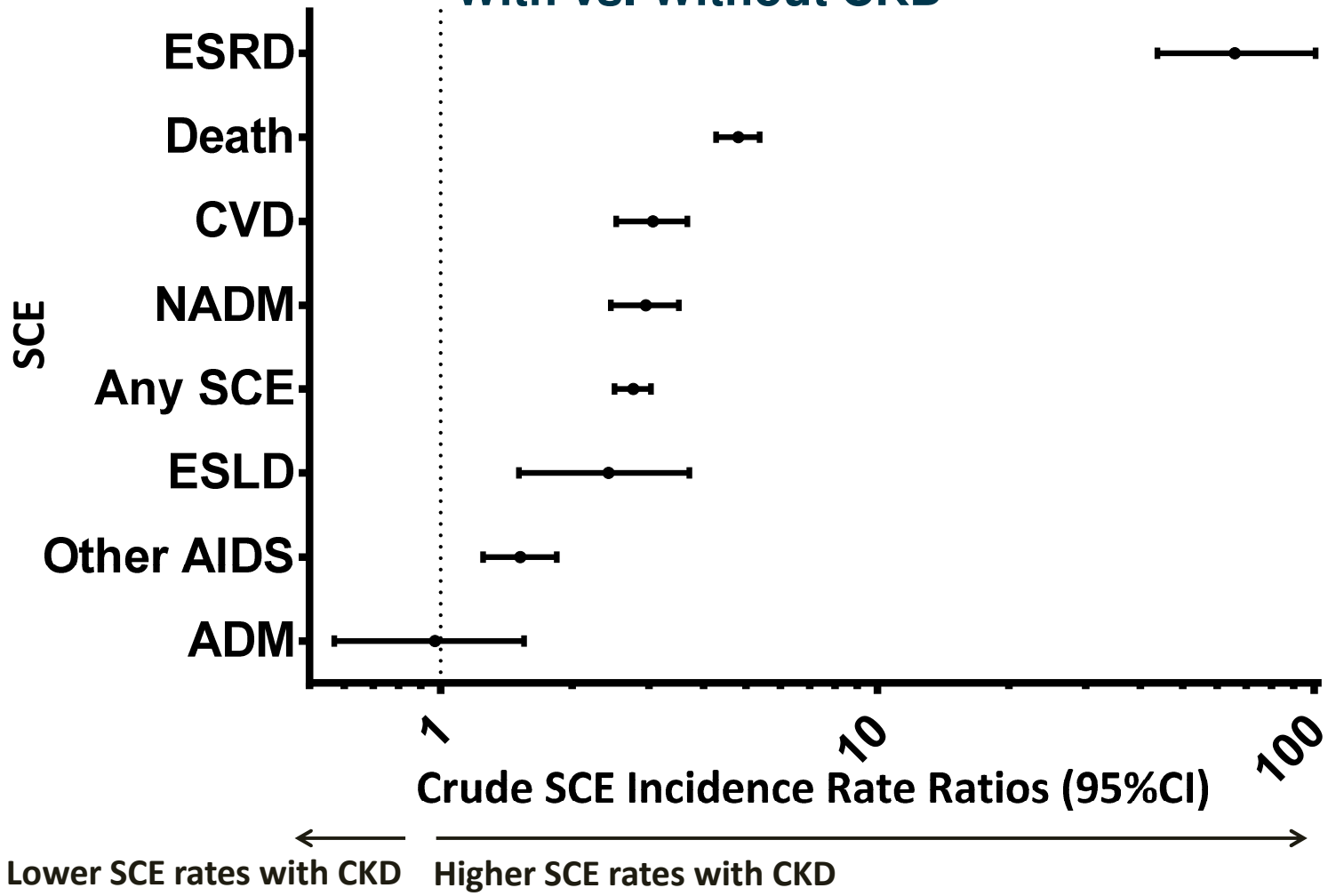
Results in Perspective (II)
Crude SCE Incidence Rate Ratios in those With vs. Without CKD



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Limitations

- Follow-up time after CKD was limited to median 2.7 years
- Possible effect modification by proteinuria could not be assessed as proteinuria data not collected systematically in D:A:D
- Risk of unmeasured confounding (e.g. use of NSAID)
- High proportion of participants with unknown ancestry due to national regulations

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Conclusions I

- In an era where many HIV-positive persons require less monitoring due to effective antiretroviral treatment, those living with CKD have a high SCE burden with almost 1/5 developing SCE within 3 years, which require closer monitoring

- Compared to persons without CKD, those living with CKD have substantially higher rates of organ dysfunction, NADM and non-malignant AIDS events

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Conclusions

- Our data further suggest modifiable risk factors including

  - *Smoking for Death, CVD, Other AIDS & NADM*
  - *Dyslipidemia for Death & CVD*
  - *Poor HIV-control for Death & Other AIDS*
  - *Diabetes for Death & CVD*
  - *Low BMI and low eGFR for Death*

  play a central role for post-CKD morbidity and mortality and highlight the need of increased awareness, effective treatment and preventive measures for those living with CKD

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Steering Committee: Members indicated w/ *; ¢ chair;
Cohort PIs: W El-Sadr* (CPCRA), G Calvo* (BASS), F Bonnet/F Dabis* (Aquitaine), O Kirk*/ A Mocroft* (EuroSIDA), M Law* (AHOD), A d'Arminio Monforte* (ICONA), L Morfeldt* (HivBIVUS), C Pradier* (Nice), P Reiss* (ATHENA), R Weber* (SHCS), S De Wit* (Brussels)
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Cancer: CA Sabin*, L Ryom, CI Hatleberg, M Law*, A d'Arminio Monforte*, F Dabis*, F Bonnet, P Reiss*, FWNM Wit, CJ Smith, DA Kamara, J Bohlius, M Bower, G Fätkenheuer, A Grulich, JD Lundgren*¢ **External endpoint reviewer**: A Sjøl (CVD), P Meidahl (oncology), JS Iversen (nephrology)
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