



# Recent Abacavir Use and Incident Cardiovascular Disease in Contemporary Treated PLWH within the RESPOND Cohort Consortium

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Disclosed no conflict of interest

## Background:

- An increased risk of myocardial infarction (MI) with recent abacavir (ABC) use was first reported by the D:A:D study in 2008 <sup>[1]</sup>
  - The association persisted in the period from 2008-2013 <sup>[2]</sup>
- Somewhat inconsistent findings across other studies <sup>[3-5]</sup>
- Increased platelet reactivity suggested as a possible causal mechanism <sup>[6]</sup>

## Purpose:

- To assess whether the association between ABC and cardiovascular disease (CVD) remained amongst contemporarily treated PLWH within RESPOND
- To investigate whether the association depends on the estimated 5-year CVD or chronic kidney disease (CKD) risk score strata

## Inclusion:

- RESPOND<sup>[1]</sup> participants aged  $\geq 18$  years were followed from latest of cohort enrolment or 1<sup>st</sup> of January 2012 (baseline)

## Outcomes:

- Cardiovascular disease (CVD) - rigorously defined composite endpoints: MIs, strokes, invasive cardiovascular procedures (ICP)

## Statistical analysis:

- Individuals followed to the first CVD event, last follow-up or 31<sup>st</sup> of December 2019, whichever occurred first
- Recent ABC use: current use or use within six months<sup>[2]</sup>

## Statistical analyses:

- Logistic regression to assess the odds of initiating ABC by the estimated D:A:D 5-year CVD and 5-year CKD risk score strata
- Negative binomial regression to assess the association between recent ABC use and risk of CVD, adjusted for:
  - Age, sex, ethnicity, region, BMI, HIV transmission risk group, CD4 count, hypertension, diabetes, AIDS, CVD, CKD and dyslipidemia – all fixed at baseline
  - Calendar year, smoking status, exposure to INSTI, cumulative exposure to boosted lopinavir and darunavir, indinavir, didanosine and stavudine – all time updated
- Interaction analyses between relative CVD risk with recent ABC use and 5-year CVD and 5-year CKD risk score

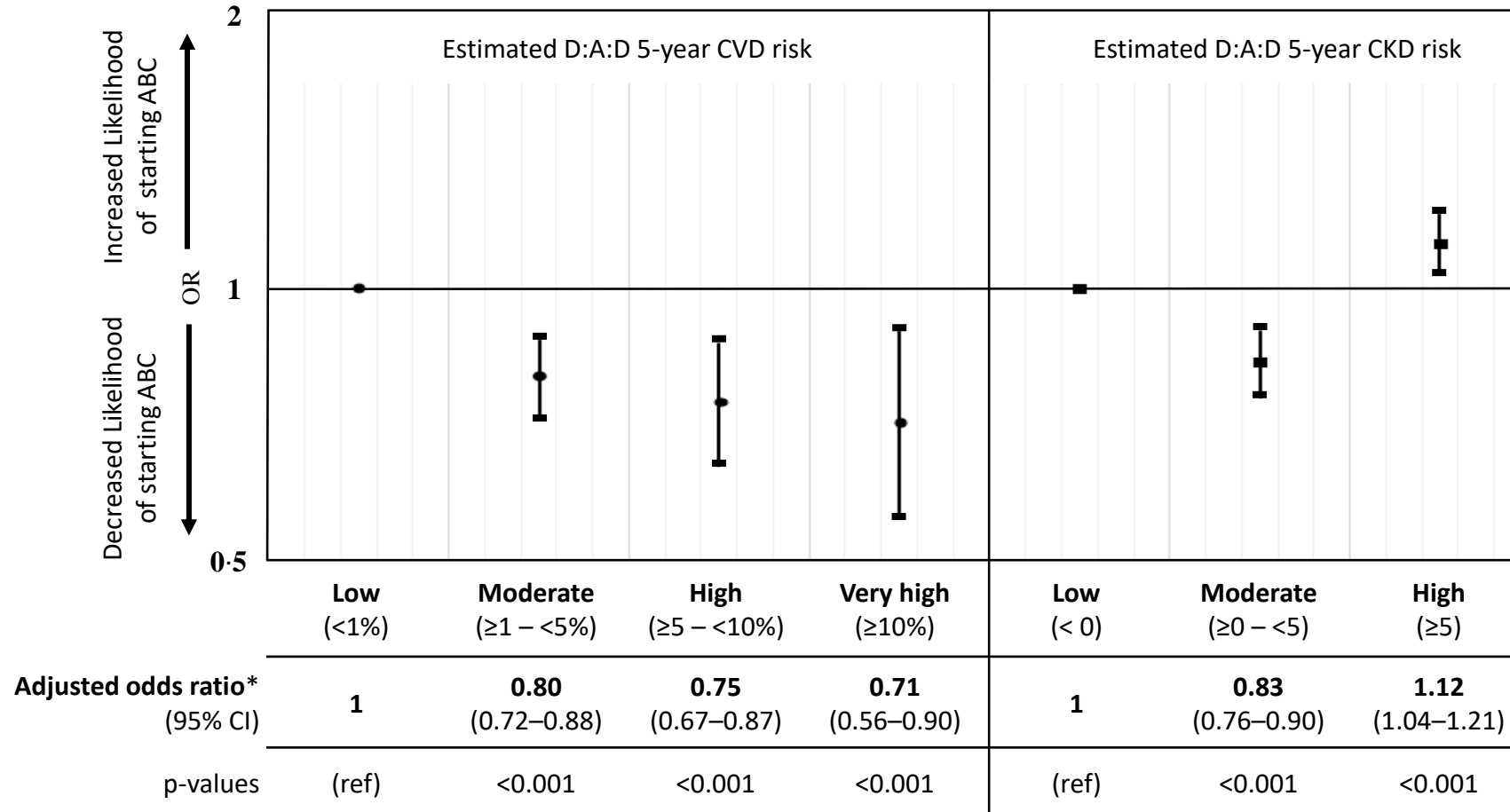
## Demographics:

- A total of **29,340** individuals included: median age **44 years** (IQR 36 – 51) and median CD4 count **524 cells/ $\mu$ L** (IQR 357-715)
- Predominantly male (**74%**), White (**70%**) with MSM as primary mode of transmission (**45%**)
- Baseline CVD risk factors: Diabetes (**4%**), hypertension(**19%**), current smoking (**28%**), any dyslipidemia (**61%**)
- Overall, **34%** were recently using ABC; of those, **32%** were on boosted protease inhibitors

## CVD events:

- During **6.16 years** median follow-up (IQR 3.87-7.52; 160,252 person-years of follow-up, PYFU), **748 CVD events: 299 MIs, 228 strokes and 221 ICPs**
  - Incidence rate **4.7/1000 PYFU** (95% CI 4.3-5.0)

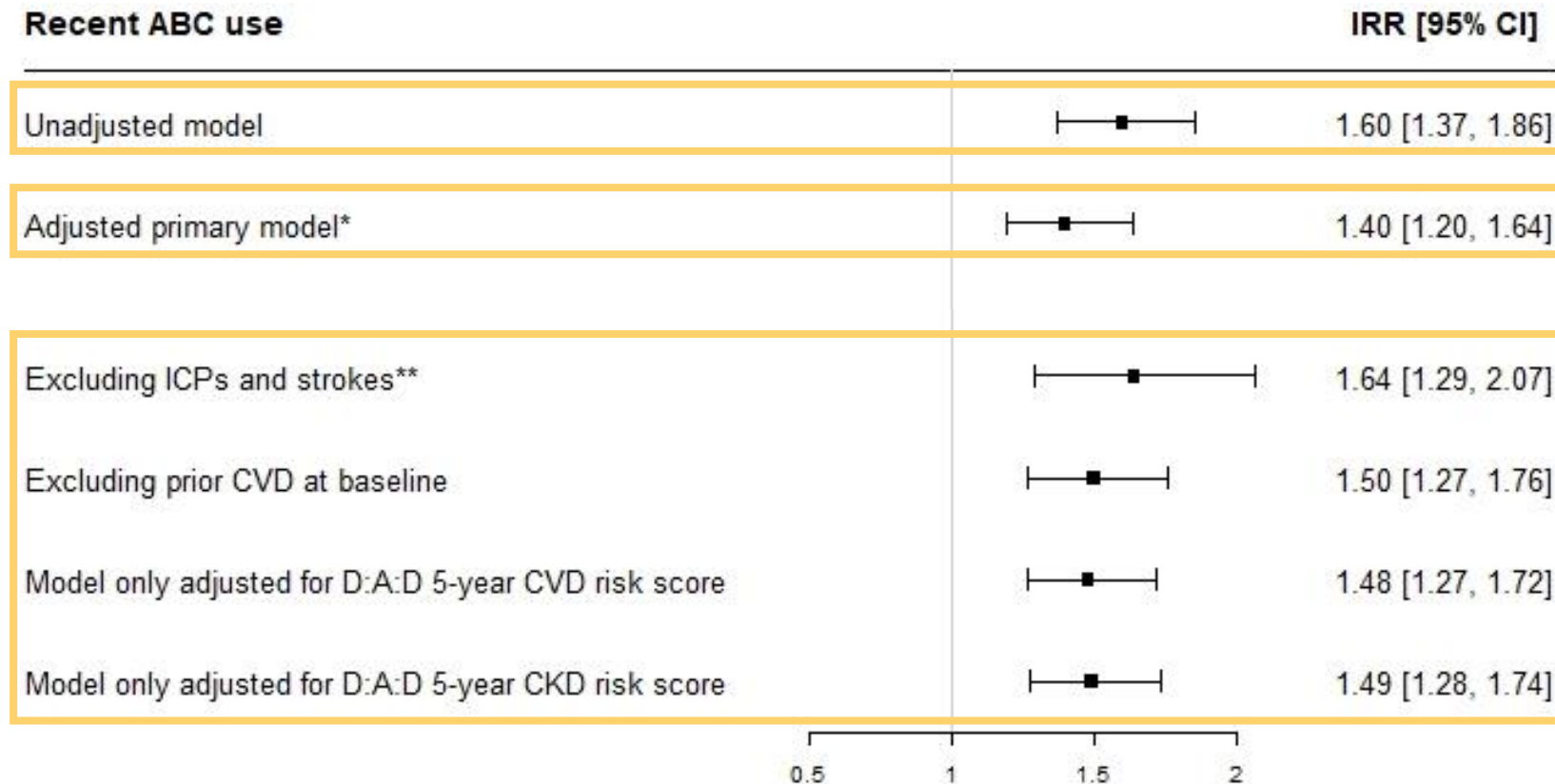
## Odds of initiating ABC by 5-year CVD and CKD risk score:



\*adjusted for baseline year

# Results

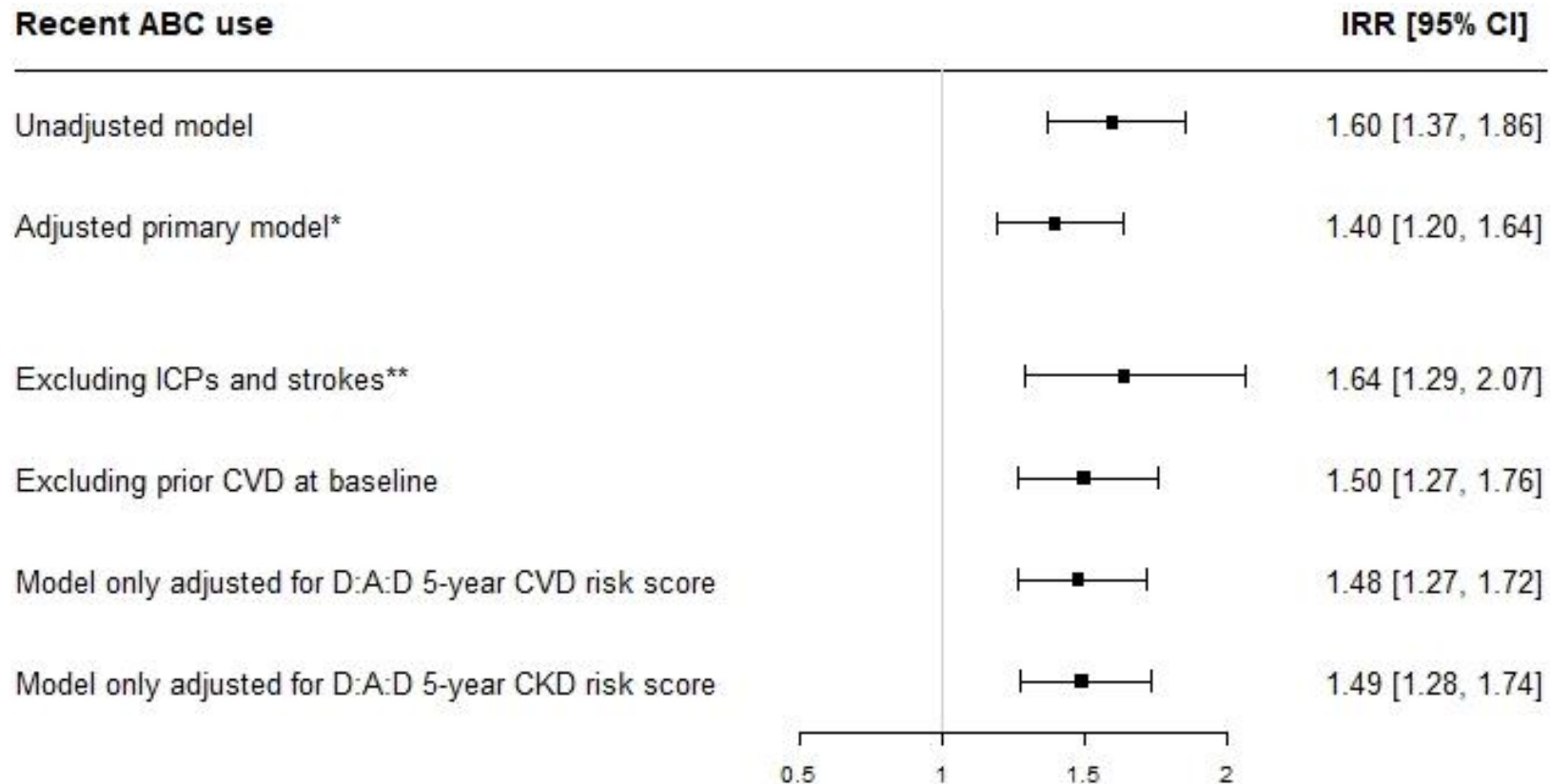
## Incidence rate ratios (IRR) of CVD: recent ABC use compared to no recent ABC use



\*Adjusted for age, sex, ethnicity, region, BMI, HIV risk, CD4 count, hypertension, diabetes, AIDS, CVD, CKD, dyslipidemia (all fixed at baseline), calendar year, smoking status, exposure to INSTI, cumulative exposure to boosted lopinavir and darunavir, indinavir, didanosine and stavudine (all time updated)

\*\*Only adjusted for age, CD4 nadir, smoking status and prior CVD

## Incidence rate ratios (IRR) of CVD: recent ABC use compared to no recent ABC use



No evidence suggesting relative CVD risk with recent ABC use differed according to CVD or CKD risk score strata; p-value for interaction: CVD: 0.56, CKD: 0.98

# Limitations and Conclusions

## Limitations:

- Potential confounding by indication and residual confounding

## Conclusions:

- Within RESPOND, after adjustment for potential confounders, recent ABC use was associated with a 40% increased CVD rate, compared to no recent ABC use
  - Robust results when only including MIs
- Despite individuals with increased estimated CKD risk had higher odds of starting ABC compared to those with low risk, the association between CVD and ABC was unchanged after adjustment for renal function and did not differ according to estimated CVD or CKD risk

# ACKNOWLEDGEMENTS

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## Members of the scientific interest group:

The Outcomes with antiretroviral treatment scientific interest group; details at:  
<https://chip.dk/Research/Studies/RESPOND/SIGs/Outcomes-with-ARVs>

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