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# Use of Preventive Measures for Cardiovascular Disease in People Living with HIV

RESPOND International Cohort Consortium of Infectious Diseases

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## Background

- Prior studies reported suboptimal cardiovascular disease (CVD) risk prevention and management for people living with HIV[1,2]
- Previous investigations focused on overall usage of individual CVD preventive measures without providing a wider overview of multiple preventive measures
- Few analyses considered ART usage as a potential CVD preventive measure as recommended in European AIDS Clinical Society (EACS) Guidelines [3]
- Limited data for key subgroups, e.g., women, older individuals, etc.

## Methods

- RESPOND[4] participants for whom an estimated 10-year D:A:D CVD risk[5] could be calculated were included
- Baseline: date of first 10-year CVD risk calculation after cohort enrolment or 01/01/2012
- Annual prevalence (01/07/2012 – 01/07/2019) of CVD preventive measure use was assessed among very high (>10%) estimated 10-year CVD risk individuals
  - Eligible for each preventive measure
  - With ≥12 months of follow-up
- Binomial regression was used to assess factors associated with uptake of each CVD preventive measure at very high 10-year CVD risk & eligible for the respective measure

## Results

- 22,050 individuals were included
- Compared to those with <10% CVD risk, individuals at very high risk were older, and a larger proportion had classic risk factors for CVD at baseline (**Table 1**)
- Crude proportions of individuals at very high estimated 10-year CVD risk increased from 31.5% (4,144/13,146) in 2012 to 49.0% (7,819/15,964) in 2019 (p<0.0001)

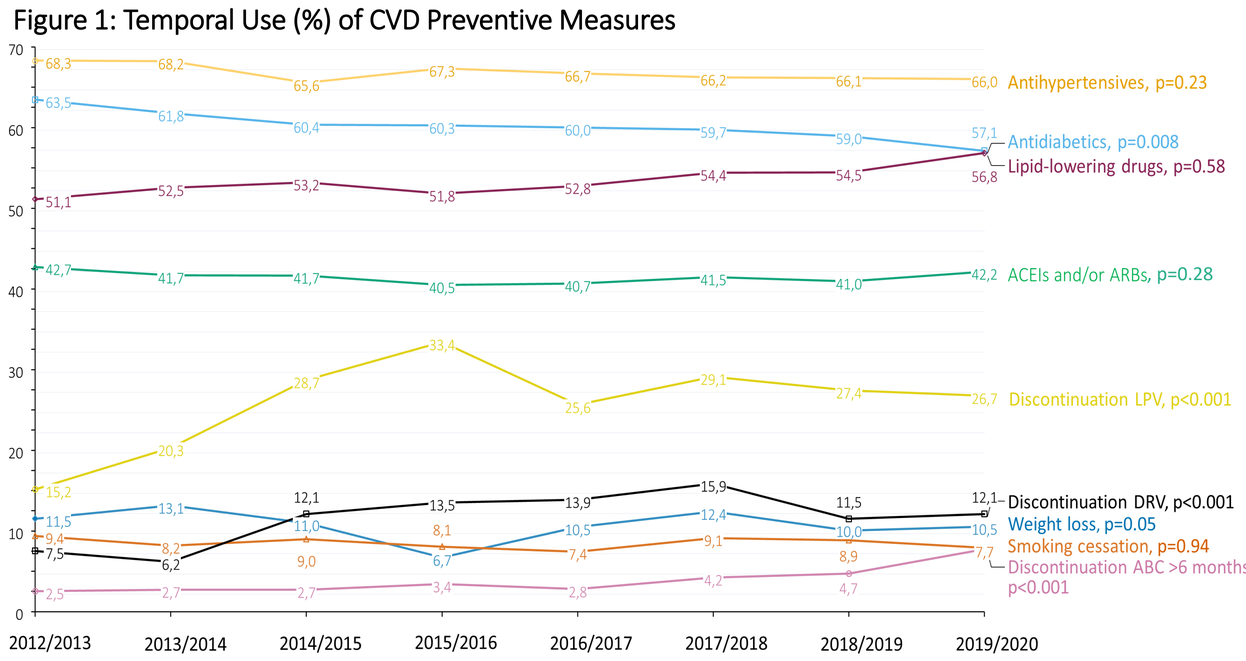
Table 1: Baseline characteristics, stratified by 10-year estimated D:A:D CVD risk

| | | All | | Low CVD risk <1% | | Medium CVD risk 1-5% | | High CVD risk 5-10% | | Very high CVD risk >10% | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % | n | % | n | % |
| All | | 22050 | 100 | 2931 | 13.3 | 8397 | 38.1 | 5002 | 22.7 | 5720 | 25.9 |
| Gender | Male | 16564 | 75.1 | 1748 | 59.6 | 5818 | 69.3 | 3969 | 79.3 | 5029 | 87.9 |
| Risk of HIV acquisition | MSM | 10122 | 45.9 | 1280 | 43.7 | 3799 | 45.2 | 2343 | 46.8 | 2700 | 47.2 |
| | IDU | 3150 | 14.3 | 188 | 6.4 | 1084 | 12.9 | 851 | 17.0 | 1027 | 18.0 |
| Ethnicity | White | 16584 | 75.2 | 1911 | 65.2 | 6004 | 71.5 | 3951 | 79.0 | 4718 | 82.5 |
| Diabetes | | 1184 | 5.4 | 43 | 1.5 | 97 | 1.2 | 170 | 3.4 | 874 | 15.3 |
| Dyslipidemia | | 9448 | 42.8 | 752 | 25.7 | 2704 | 32.2 | 2382 | 47.6 | 3610 | 63.1 |
| Hypertension | | 4267 | 19.4 | 177 | 6.0 | 789 | 9.4 | 1087 | 21.7 | 2214 | 38.7 |
| Smoking status | Current | 9817 | 44.5 | 781 | 26.6 | 3262 | 38.8 | 2460 | 49.2 | 3314 | 57.9 |
| BMI (kg/m²) | 25-30 | 5521 | 25.0 | 568 | 19.4 | 1951 | 23.2 | 1387 | 27.7 | 1615 | 28.2 |
| | >30 | 1863 | 8.4 | 203 | 6.9 | 709 | 8.4 | 419 | 8.4 | 532 | 9.3 |
| Exp. Lopinavir | | 5862 | 26.6 | 530.0 | 18.1 | 1827 | 21.8 | 1412.0 | 28.2 | 2093 | 36.6 |
| Exp. Darunavir | | 3669 | 16.6 | 426 | 14.5 | 1341 | 16.0 | 848 | 17.0 | 1054 | 18.4 |
| Exp. Indinavir | | 3447 | 15.6 | 108 | 3.7 | 535 | 6.4 | 881 | 17.6 | 1923 | 33.6 |
| Exp. Abacavir | | 7369 | 33.4 | 540 | 18.4 | 2017 | 24.0 | 1830 | 36.6 | 2982 | 52.1 |
| Exp. INSTI | | 2713 | 12.3 | 425 | 14.5 | 1193 | 14.2 | 545 | 10.9 | 550 | 9.6 |
| | | Median | IQR | Median | IQR | Median | IQR | Median | IQR | Median | IQR |
| Age | | 45 | (37, 52) | 31 | (26, 36) | 40 | (35, 45) | 48 | (44, 52) | 55 | (50, 62) |
| CD4 cell count | | 552 | (390, 742) | 523 | (385, 710) | 546 | (385, 728) | 569.5 | (396, 760) | 560 | (392, 762) |
| Baseline | | 01/12 | (01/12, 01/15) | 06/12 | (01/12, 05/15) | 01/12 | (01/12, 01/15) | 01/12 | (01/12, 09/14) | 01/12 | (01/12, 03/14) |

Abbreviations: IDU- intravenous drug use, MSM- men having sex with men, BMI- body mass index, INSTI- integrase strand transfer inhibitor, IQR- interquartile range

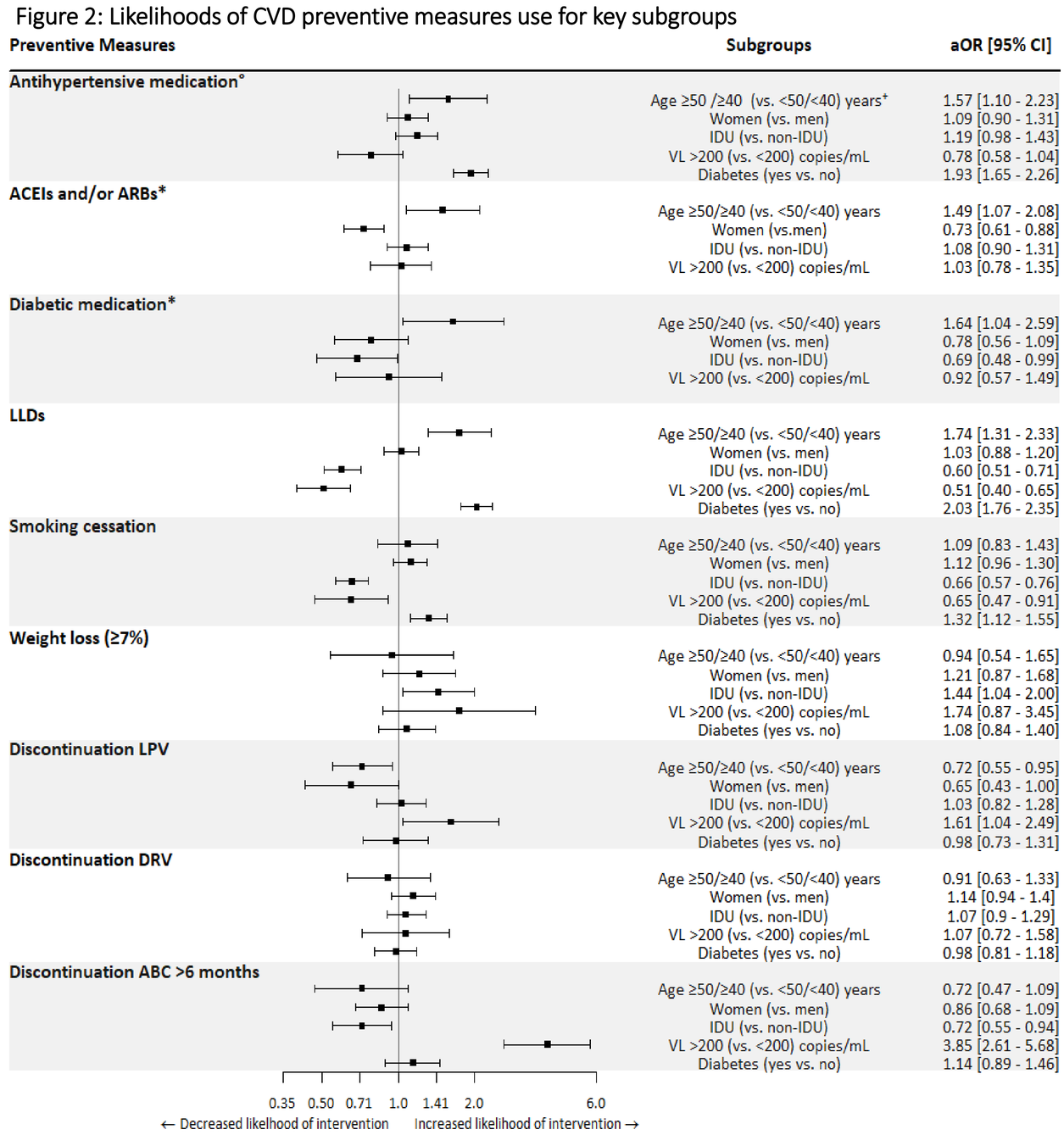
- In 2019/2020, among very high 10-year CVD risk individuals:
  - Antihypertensives were used in 66% (1,562/2,367) of participants with hypertension
  - Lipid-lowering drugs (LLDs) in 56.9% (1,642/2,888) with dyslipidemia
  - Angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) in 42.1% (1,128/2,677) with diabetes and/or hypertension
  - Smoking cessation was observed in 7.9% (182/2,297) of current smokers
  - A loss of ≥7% body weight was seen in 10.5% (53/503) with BMI>30 kg/m²
- No significant changes over time in use of any of these CVD preventive measures (2012–2019, **Figure 1**)
- However, fewer individuals with diabetes received antidiabetics in later years: 63.5% (382/602) in 2012/2013 vs 57.1% (453/793) in 2019/2020; multivariate p=0.008
- Discontinuation of darunavir (7.5% [49/650] in 2012/2013 vs 12.1% [91/752] in 2019/2020), lopinavir (15.2% [90/593] vs 26.7% [23/86]) and abacavir (2.5% [34/1,337] vs 7.7% [124/1,604]) increased among participants receiving the respective drug; all multivariate p<0.001 (**Figure 1**)
- After adjustment (**Figure 2**), older individuals (≥40 years for men, ≥50 for women vs <40/<50) were more likely to use antihypertensives, ACEIs/ARBs, antidiabetics and LLDs
- Individuals with diabetes (vs those without) were also more likely to use antihypertensives, LLDs and cease smoking
- LLD use and smoking cessation were less likely in those with viral load ≥200 copies/mL (vs <200 copies/mL ) and IDU as HIV acquisition risk (vs non-IDU)
- Besides women being less likely to receive ACEIs/ARBs, the use of CVD preventive measures was similar between genders

Figure 1: Temporal Use (%) of CVD Preventive Measures




All p are global, multivariate p-values for each preventive measure with calendar years per 2-year groups.

Figure 2: Likelihoods of CVD preventive measures use for key subgroups




Adjusted for age, gender, ethnicity, CVD risk region, body mass index (*not included for weight loss*), HIV acquisition risk, CD4 cell count, CD4 nadir, hypertension (*not included for antihypertensives and ACEIs/ARBs*), diabetes (*not included for diabetic medication and ACEIs/ARBs*), AIDS, cancer, chronic kidney disease, dyslipidaemia (*not included for LLDs*), calendar year, current smoking (*not included for smoking cessation*), cumulative exposure to LPV, DRV, and IDV, ABC use in the past six months, and INSTIs exposure.

°Antihypertensives also include ACEIs and ARBs

⁺Age subgroup: <40/≥40 years of age for men, <50/≥50 for women

*Not including diabetes as a subgroup since it's part of the eligibility criteria for ACEIs/ARBs and antidiabetics

Abbreviations: LPV- lopinavir, DRV- darunavir, ABC- abacavir, aOR- adjusted odds ratio, CI- confidence interval

## Limitations

- Residual confounding cannot be ruled out (e.g., diet, physical activity, CVD family history)
  - ARVs may not necessarily have been discontinued because of increased CVD risk
- We were unable to capture adherence levels to any CVD preventive measure

## Conclusions

- We observed an increase in the proportion of individuals at very high estimated CVD risk (49% in 2019 vs 31.5% in 2012)
- While CVD preventive measures were generally underused in RESPOND, discontinuation of ARVs previously associated with CVD increased over time among very high CVD risk individuals
- Older individuals and those with diabetes were more likely to receive some preventive measures (e.g., antihypertensives, LLDs), while those with viremia and IDU as HIV acquisition risk were less likely (e.g., LLDs, smoking cessation)
- Our findings call for greater awareness of management guidelines for CVD risk factors in people living with HIV

*References:* **1**: Hatleberg CI et al. Curr Opin Hiv Aids; 2017, **2**: Shahmanesh M et al. AIDS; 2016, **3**: European Aids Clinical Society Guidelines, V 11.0 **4**: Neesgaard et al. Microorganisms, 2020, **5**: Friis-Møller et al. Eur J Prev Cardiol.; 2016

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The RESPOND Study Group https://www.chip.dk/Studies/RESPOND/Study-Group
RESPOND Scientific Interest Groups https://chip.dk/Research/Studies/RESPOND/SIGs

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