

HEAVY ARV EXPOSURE, EXHAUSTED/LIMITED ARV OPTIONS: PREDICTORS AND CLINICAL OUTCOMES

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RESPOND study group, cohort membership and funding :
<https://chip.dk/Research/Studies/RESPOND/Study-group>

Background:

People living with HIV with extensive ARV exposure may have limited/exhausted treatment options (LExTO) due to resistance, drug toxicity or comorbidities but remain poorly characterised.

Aims:

Predictors and outcomes of LExTO were investigated in RESPOND; a European/Australian observational cohort

Methods:

People living with HIV on ART for ≥ 5 years were classified as LExTO at starting one of

- ≥ 2 'core' agents + a third ARV from any class
- exactly 2 'core' agents in a 2-drug regimen*
- ≥ 3 nucleoside reverse transcriptase inhibitors or ENF (\pm other ARVs)

ARVs included were RAL, EVG/c, DTG, BIC, CAB, DRV/b, ATV/b, LPV/r, EFV, ETR, NVP, RPV, DOR, ENF, MVC, ABC, 3TC, TDF, TAF, FTC, ZDV

Baseline was defined as the latest of 1/1/2012, cohort enrolment or 5 years after starting ARVs.

Poisson regression modelled LExTO rates/clinical outcomes

Agents included as 'Core'; *excluding DTG/RPV or CAB/RPV

Results:

Included: 23,288

Developed LExTO: N (%): 2003 (8.6%)

Person-years follow-up: 118,665

Incidence: 1.7/100 PYFU (95% CI 1.6-1.8)

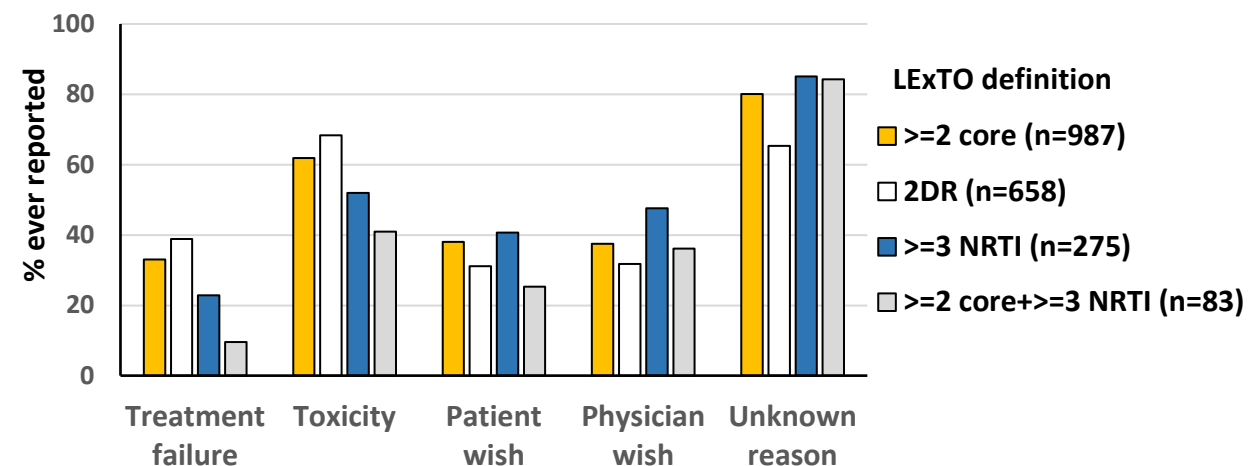
No. ARVs before baseline: median (IQR): 7 (5-9)

Years since starting ART: median (IQR): 14 (9-18)

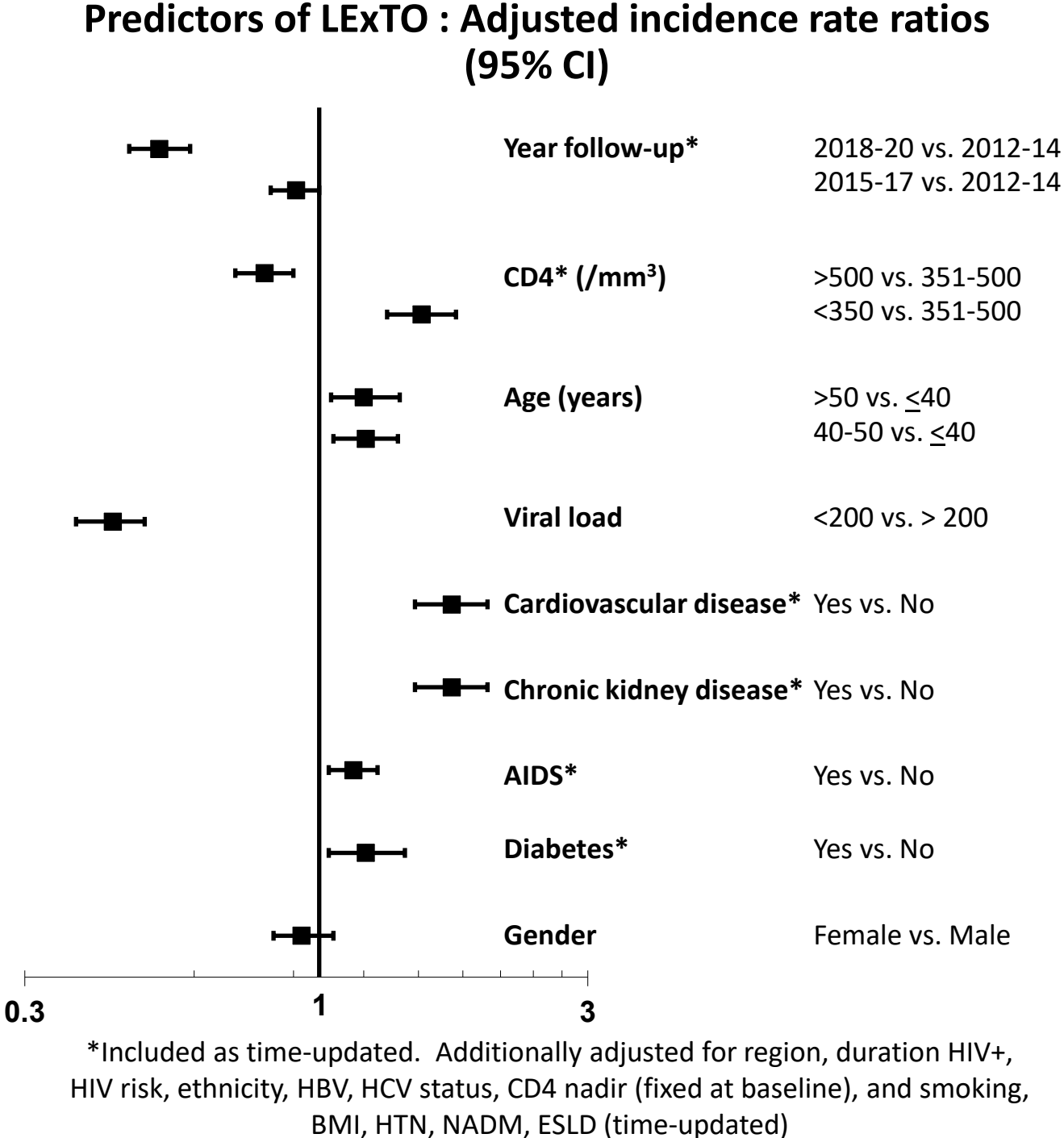
No. individuals on qualifying LExTO regimen: N (%)

- ≥ 2 core ARVs: 987 (49.3%)
- 2 DR (exc. DTG/RPV, CAB/RPV): 658 (32.9%)
- ≥ 3 NRTIs: 275 (13.7%)
- ≥ 2 core ARVs AND ≥ 3 NRTIs: 83 (4.1%)

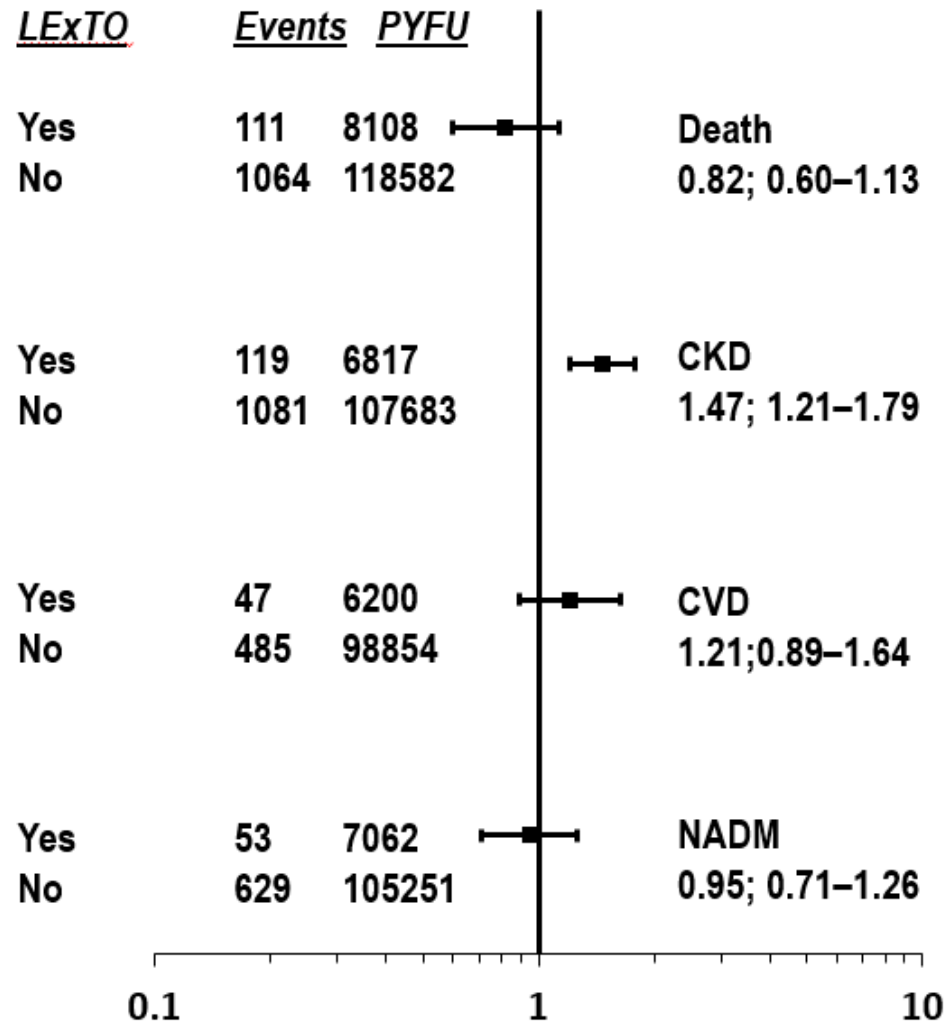
Summary of reported reason for discontinuation of all ARVs used before LExTO in 2003 persons with LExTO; median 7 (IQR 5-9) ARVs used before LExTO



Results: Demographics at baseline (n=23288):		
	No LExTO	LExTO
All; n (%)	21285 (91.4)	2003 (8.6)
Male	15695 (73.7)	1469 (73.3)
Injecting drug user	2782 (13.1)	302 (15.1)
>15 years HIV+	5201 (24.4)	817 (40.8)
Viral load < 200 copies/ml	20249 (95.1)	1770 (88.4)
Region: South Europe/Argentina	4022 (18.9)	372 (18.6)
Central Europe	9890 (46.5)	947 (47.3)
North Europe/Australia	5091 (23.9)	545 (27.2)
East/Central East Europe	2282 (10.7)	139 (6.9)
Diabetes ¹	1047 (4.9)	153 (7.6)
AIDS ¹	4079 (19.2)	571 (28.5)
Non-AIDS defining malignancy ¹	632 (3.0)	96 (4.8)
Cardiovascular disease ¹	522 (2.5)	96 (4.8)
Age (years); median (IQR)	46 (39-52)	48 (42-54)
Baseline CD4 (/mm ³)	614 (450-810)	565 (394-753)
Nadir CD4 (/mm ³)	230 (120-345)	180 (74-280)
¹ Prior to baseline		



Adjusted incidence rate ratio of clinical events following LExTO



Adjusted for sex, age, CD4 nadir, region, HIV VL, ethnicity, HBV/HCV status, years HIV+, smoking*, BMI*, DM*, hypertension*, CKD*, AIDS*¹, NADM*¹, CVD*¹, ESLD*¹, CD4*, calendar year of follow-up*. *time-updated.

¹Variable not adjusted for when variable is the endpoint.

Limitations:

- No resistance, adherence or dosage data available; using an inclusive proxy definition likely over-estimating LExTO
- Including 2DR may misclassify some; sensitivity analyses excluding 2 DR from definition showed similar findings but no regional differences in LExTO
- Regional heterogeneity in ART guidelines

Conclusions:

- The prevalence of LExTO was 9% in RESPOND
- Previous treatment failure and toxicity more commonly reported as reasons for discontinuation in ≥ 2 core agents or 2 DR LExTO regimens
- Incidence of LExTO decreased over time and was associated with region, longer duration of HIV, older age, low CD4, ongoing viremia and comorbidities
- Lack of detailed resistance data makes a definition of LExTO incorporating resistance data challenging
- Impact of more restrictive definition currently being explored