Incidence of and risk factors for tuberculosis among people with HIV on antiretroviral therapy in the UK

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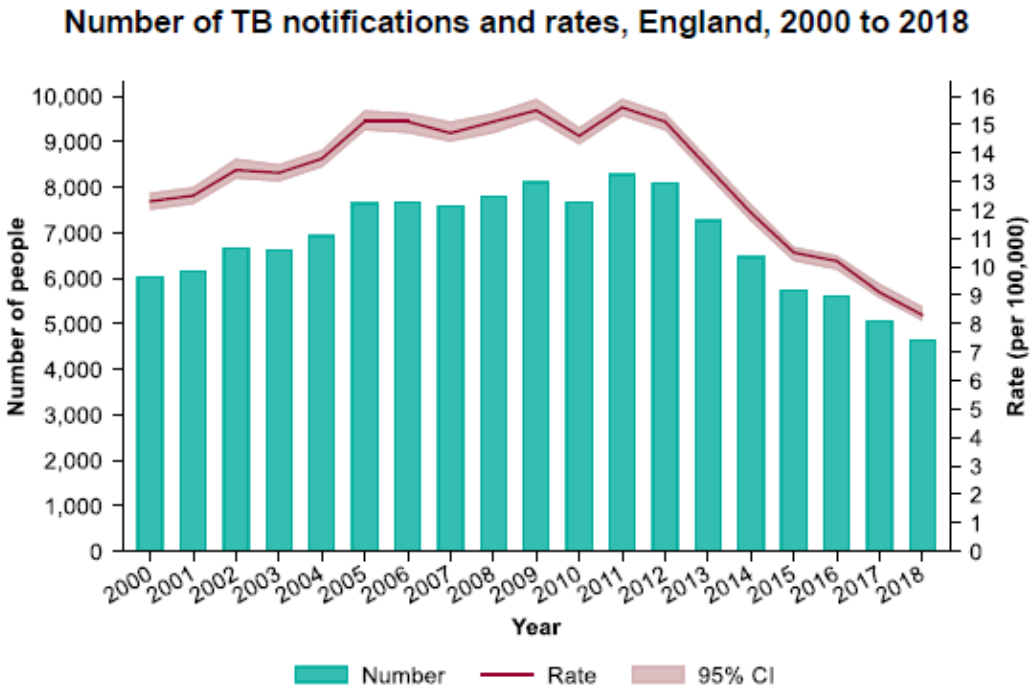
Background

- Tuberculosis (TB) incidence in the UK is low (<10/100,000/year) and falling since 2012[1]
- 72% of notifications are of TB in people born outside of the UK[1]
- In 2018, 2.7% of people starting treatment for TB were living with HIV[1]
- Antiretroviral therapy (ART) is strongly protective against active TB[2]



[1]PHE Tuberculosis in England annual report, 2019; [2]Suthar AB, *et al*, PLoS Med 2012;9:e1001270

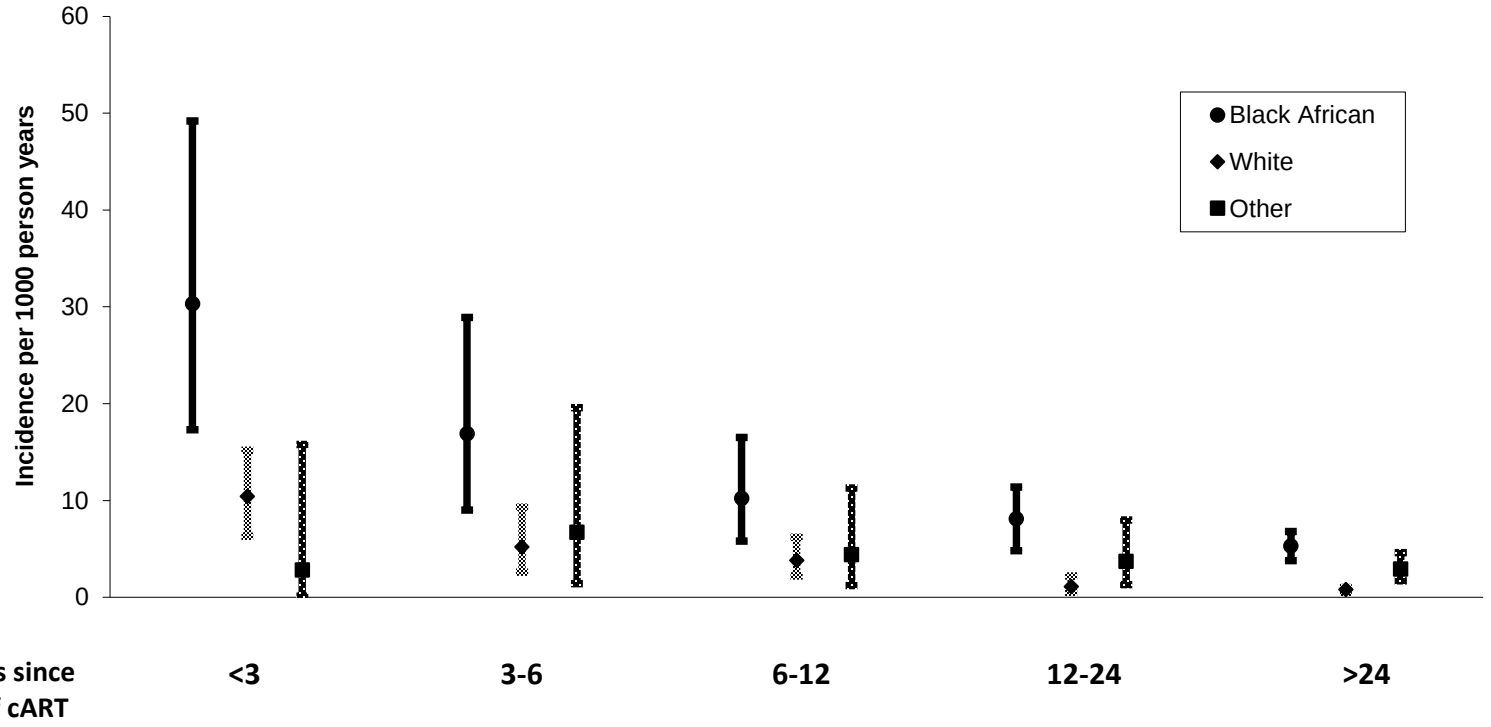
Background

- The UK Collaborative HIV Cohort Study (UK CHIC) collates routine data on people accessing care for HIV at UK centres, since 1996.
- Data are currently collected from 25 centres in England and Scotland and the dataset contained information on 74,269 individuals in 2018
- Data are collected on AIDS diagnoses including TB, classified as pulmonary, extra-pulmonary or other/unknown

[1]UK CHIC; HIV Med 2004;5:115-124; www.ukchic.org.uk

Background

- In 2009, UK CHIC data on tuberculosis were analysed and published
- Despite over 2 years of ART, TB incidence remained disproportionately high among Black African people



[1]Grant AD *et al* for UK CHIC, AIDS 2009;23:2507-2515

ART = antiretroviral therapy; TB = tuberculosis; PY = person-years; bars = 95% confidence interval around point estimate of incidence

Aims

1. To examine the incidence of TB among people with HIV, on ART, in the UK CHIC cohort study

2. To describe trends over time, since 2009

3. To identify risk factors for, or associations with, incident TB

ART = antiretroviral therapy; TB = tuberculosis

Methods

- Included data collected up to 31 December 2017
- Included those age >15 entering UK CHIC between 1996 and 2017, with follow up of at least 3 months and at least one CD4 cell count after entry

Statistical analyses

- TB incidence calculated based on first TB episode recorded after entry to UK CHIC cohort study
- Excluded follow up time equivalent to treatment duration (6 months) if TB diagnosed within 3 months after study entry
- Poisson regression models used to investigate factors independently associated with incident TB after starting ART

3 analyses

1. Whole study population
2. On ART only
3. Ethnicity subgroups, excluding white ethnicity

ART = antiretroviral therapy; TB = tuberculosis

Participant characteristics at UK CHIC entry

Year of study entry	Total (n=58595)	<2004 (n=22515)	2004-2007 (n=11797)	2008-2011 (n=10991)	>2011 (n=13473)
Age at UK CHIC entry (median) years	**34**	33	35	36	37
Female sex (%)	**26.3**	23.7	33.4	29.9	21.2
Ethnicity (%)					
White	**54.5**	60.3	47.9	50.1	54.2
Black	**32.0**	27.6	42.4	36.9	25.9
Other/unknown	**13.5**	12.1	9.7	13.0	19.9
CD4 count (median, cells/µL)	**385**	307	355	403	494
Log_{10} HIV viral load (median, log_{10} copies/mL)	**2.8**	3.7	3.2	2.8	2.0

Total follow-up time: 546617 person-years
Median follow-up time per person: 8.2 years (IQR 3.6 – 13.8)

Incidence of TB in study population

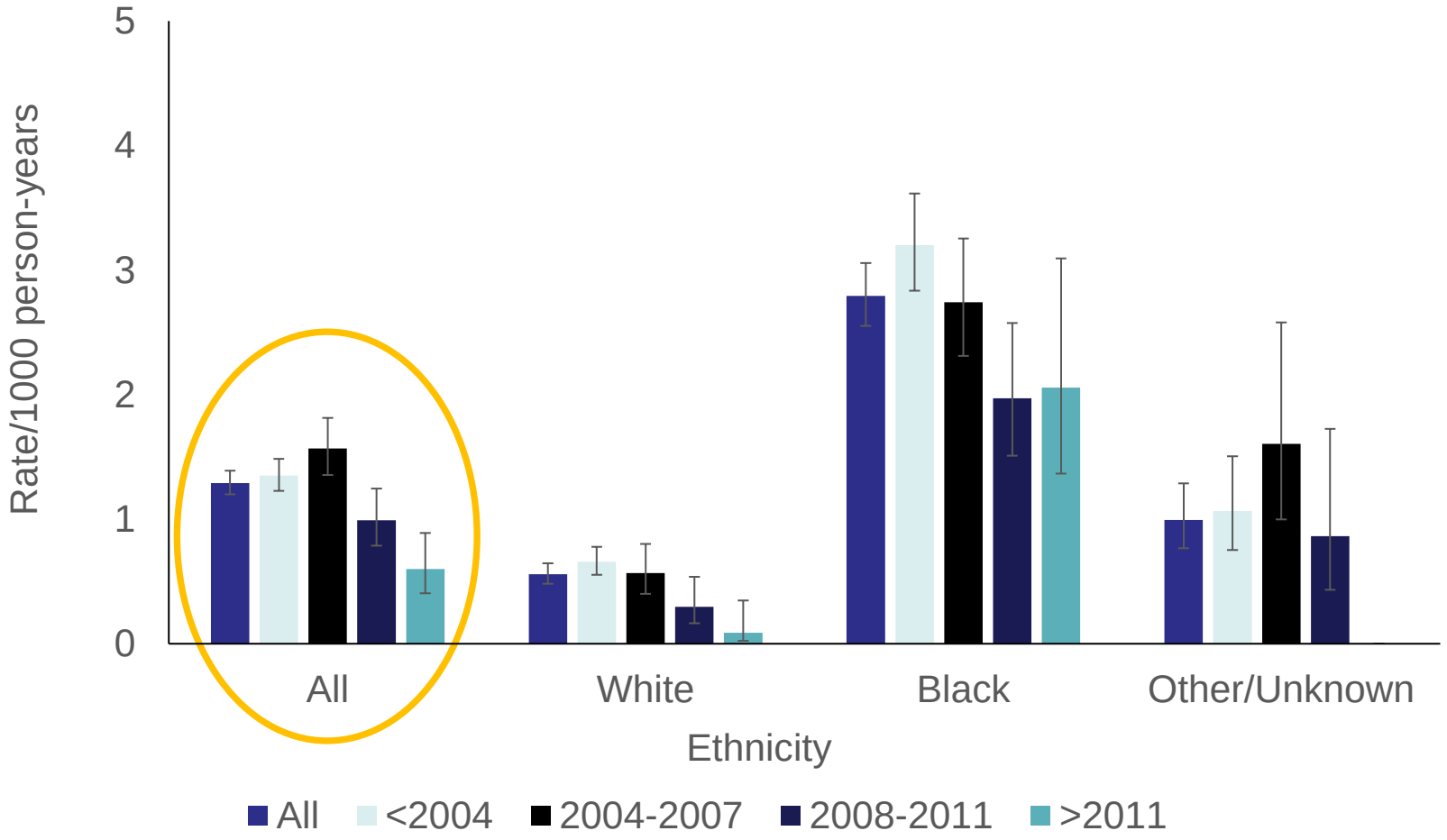
- 704 (of 58595) individuals had TB during follow up time
- Incidence = **1.3/1000 person years** (95% CI 1.2 – 1.4)
- Site of disease was pulmonary in 56.5%; extra-pulmonary in 38.8%

ART status at the time of TB episode
TB episode after starting ART: **409/704** (58.1%)
TB episode after starting ART, with undetectable viral load: **283/409** (69.2%)

CI = confidence interval

Incidence of TB over time

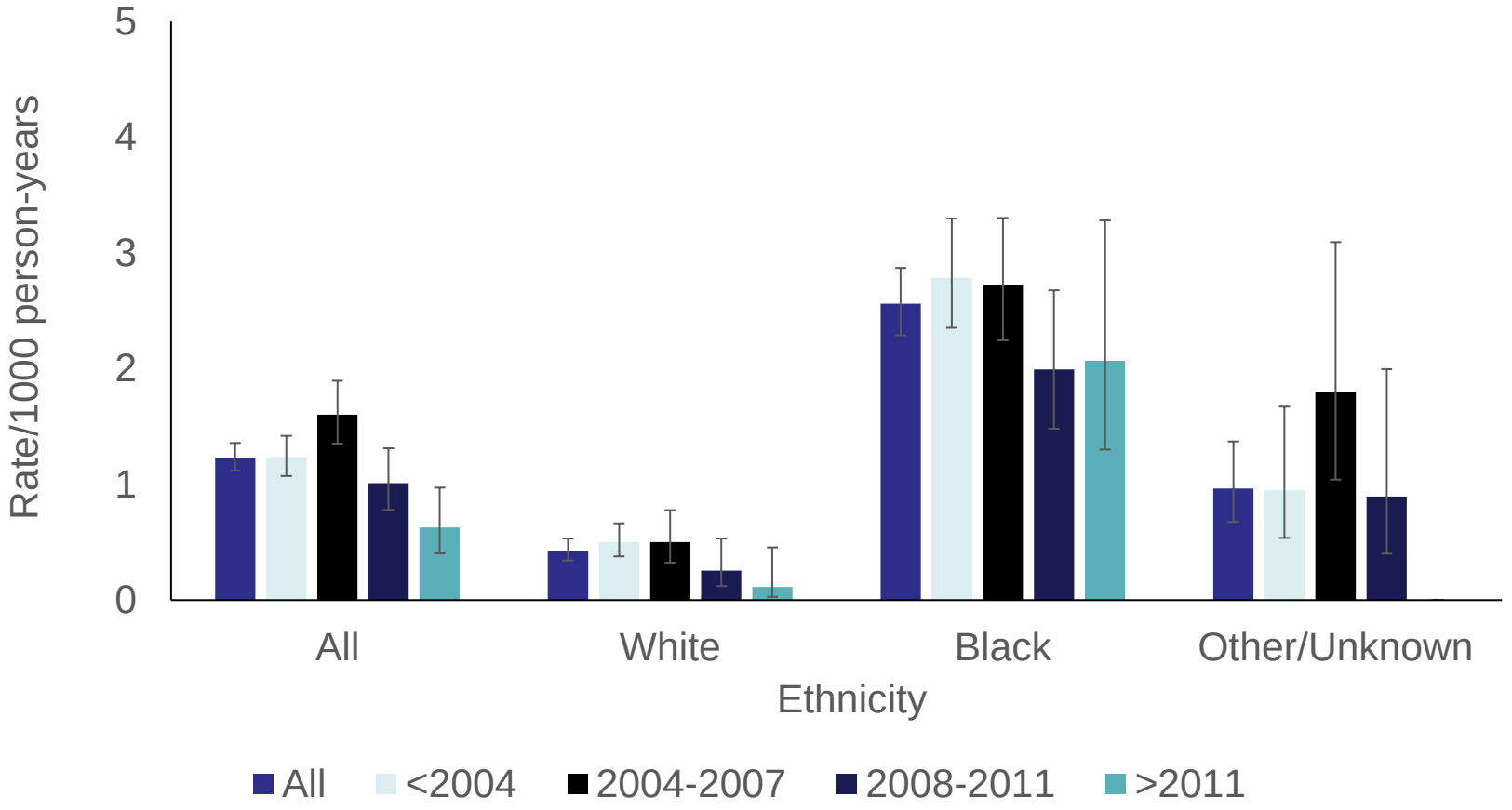
Incidence decreased from **1.3/1000 PY to 0.6/1000 PY** from <2004 to >2011



PY = person-years

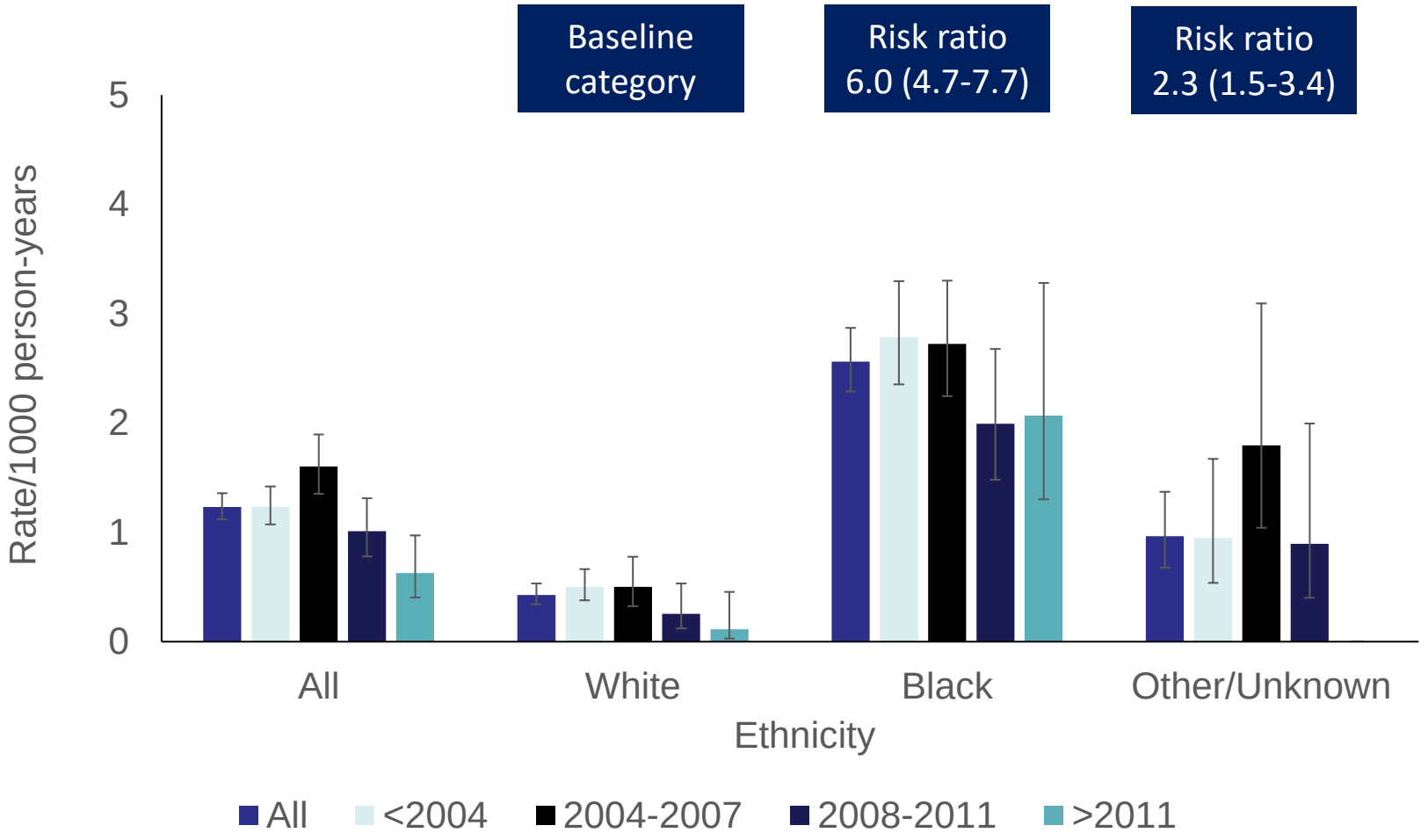
Incidence of TB among people on ART

Similar decrease in incidence overall, compared with analysis including whole group (includes those starting ART; 409 TB events)



Risk ratio: incidence of TB in that group, compared with baseline category, ratio (95% confidence interval)

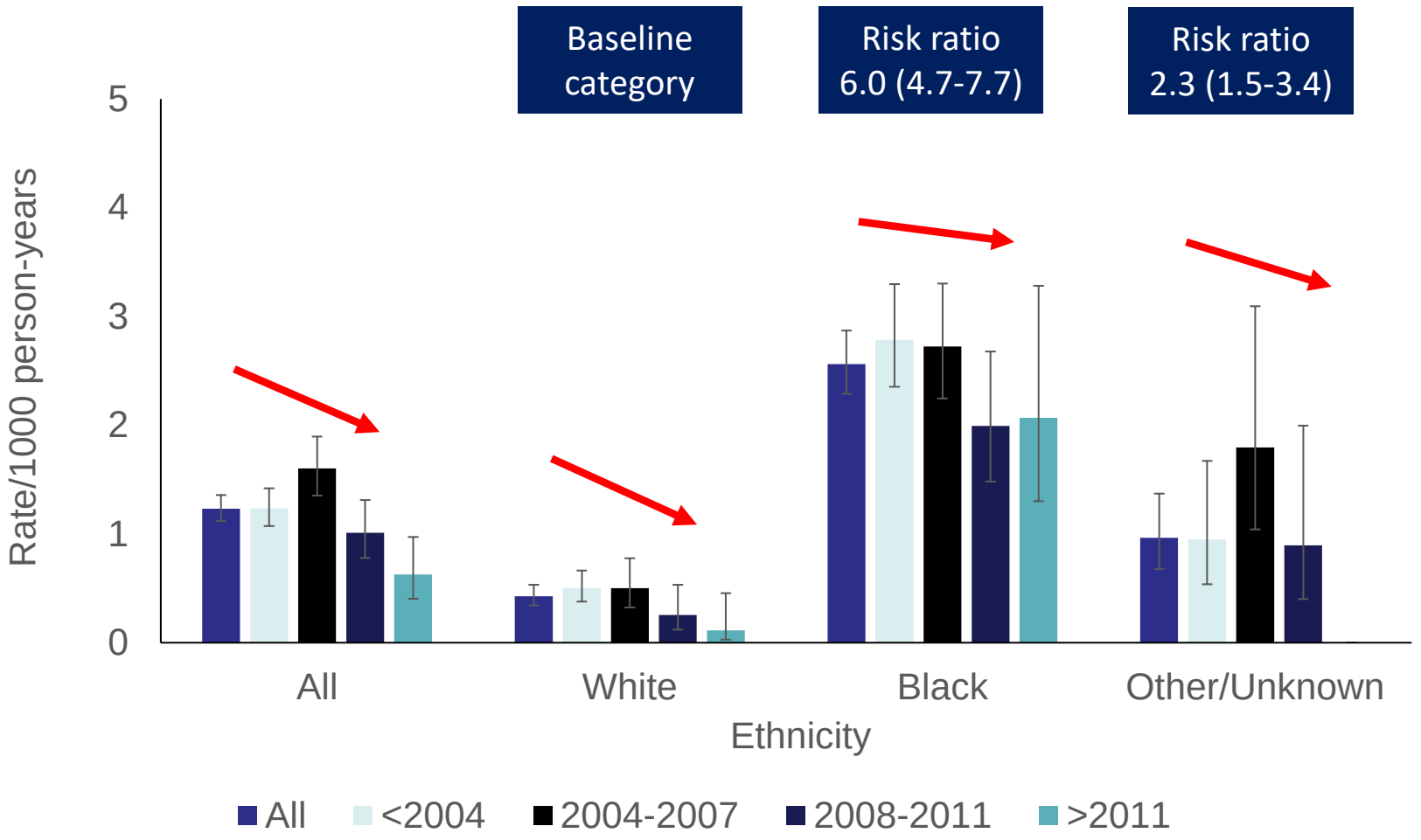
Incidence of TB among people on cART



Risk ratio: incidence of TB in that group, compared with baseline category, ratio (95% confidence interval)

Incidence of TB among people on cART

Interaction between ethnicity and calendar period: p=0.02



Risk ratio: incidence of TB in that group, compared with baseline category, ratio (95% confidence interval)

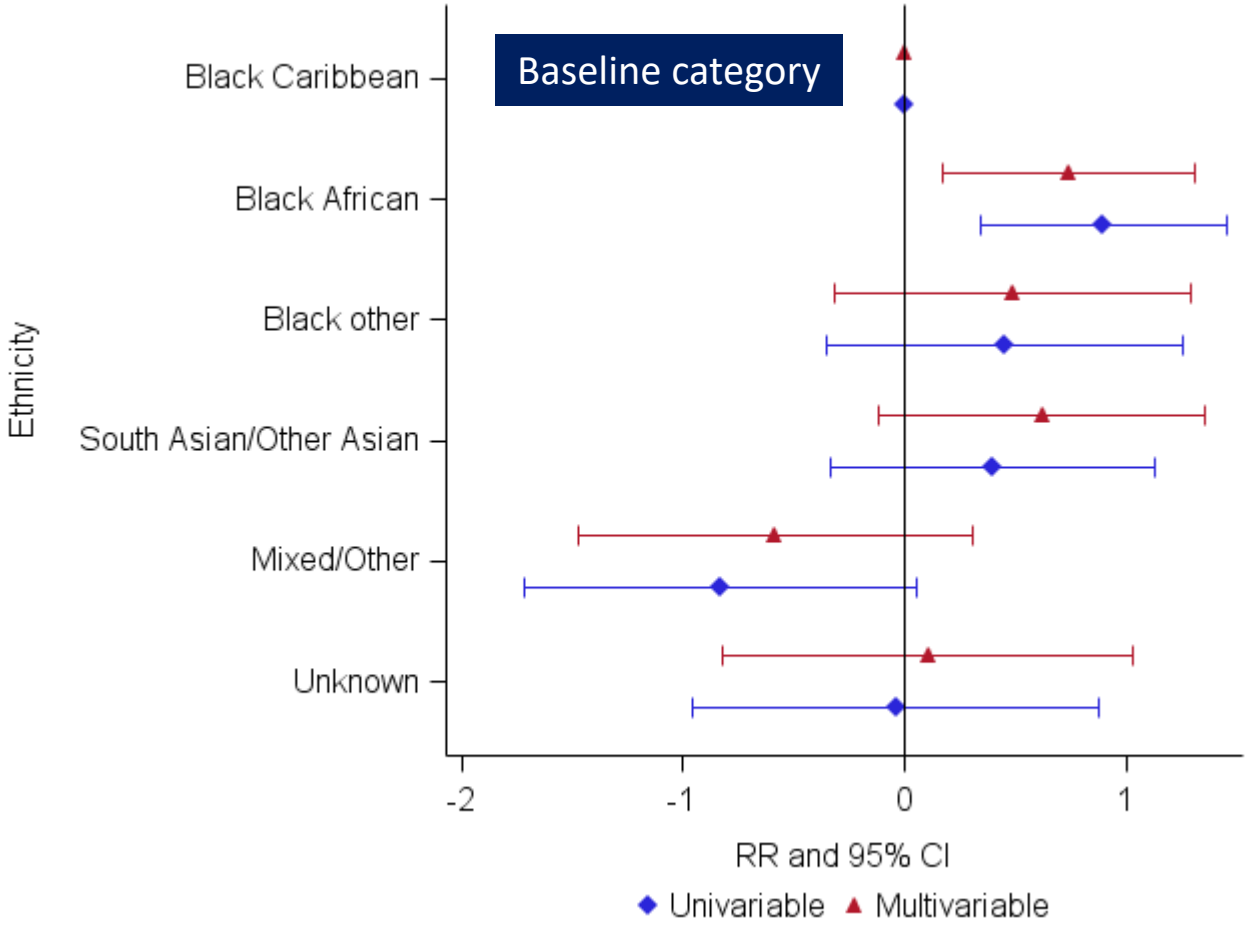
Risk factors for TB among people who started cART

Variable		Risk ratio (95% CI)	p-value
Age	/10 years older	0.96 (0.0.86 – 1.08)	0.52
Ethnicity	Black vs white Other/unknown vs white	3.13 (2.23 – 4.38) 1.85 (1.20 2.85)	0.01
HIV viral load (time updated)	/$\log_{10}$ copies/ml	1.43 (1.32 – 1.55)	0.01
CD4 count (time updated)	/100 cells/µL	0.85 (0.80 – 0.89)	0.01
Years since ART initiation	/additional year	0.95 (0.92 – 0.99)	0.01
Year of ART initiation	/later year	0.93 (0.91 – 0.95)	0.01

Results of multivariable Poisson regression model, adjusted for variables shown, plus reported mode of HIV acquisition

Ethnicity subgroup analysis

Includes 331 TB episodes



aRR 2.10 (1.19 – 3.70)

Adjusted for: age, HIV viral load, CD4 count, years since ART initiation, year of ART initiation. aRR = adjusted risk ratio

Summary

- Tuberculosis still occurs among people with HIV on ART, with an incidence higher than that of the general population
- Despite the protection of ART, a continuing disproportionately high TB incidence is seen among Black African people with HIV compared with other groups.

Limitations

- Ethnicity information is as reported by centre
- No data on birth or long-term residence in country with high TB incidence, the likely confounder for association between ethnicity and TB incidence
- TB site: pulmonary/extra-pulmonary is blunt and limits description
- No data on microbiological confirmation of TB and cannot exclude increase in empirical treatment and clinical/radiological diagnosis in those of Black African ethnicity
- No data on treatment of latent TB; although implementation of guidelines thought to be poor[1,2,3]

[1]White *et al*, Thorax 2017;72:180-182; [2]Fox-Lewis *et al*, Int J STD AIDS 2016;27:901-905; [3]Rickman *et al*; Int J STD AIDS 2018;29:1234-1237

Conclusions

- TB is an ongoing problem disproportionately affecting Black African people with HIV in the UK
- Prevention, through testing for and treating latent TB infection, may reduce this incidence

Update

OPEN

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Steering Committee:

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