BASHH: HIV papers

Laura Waters
Consultant GU/HIV Medicine
Mortimer Market Centre, CNWL, London

Content

- 5 in 1
- A new dawn
- Weight
- Lungs
- But first….

What do YOU think?

- What has changed most in your discussions with patients?
- PARTNER-2 trial

Literally the best message ever!

Literally the best message ever!

TELL ALL PATIENTS & STAFF, AS MANY TIMES AS NECESSARY

Thank you Professor Alison Rodger

Stigma: a cloud over the HIV cascade

90:90:90:90

DIAGNOSED ON ART VL UD QoL

5 IN 1

5 DRUGS IN 1 SLIDE

Recent/imminent*

*according to your country

An ideal first-line regimen?

Good for defined groups
Weakness is rilpivirine?
Safety & tolerability driven by comparators
No first-line data

Role in NNRTI resistance?
Dual therapy?

GEMINI 96W imminent
FDC in England not imminent?
Caution late presenters
Caution renally adjusted 3TC

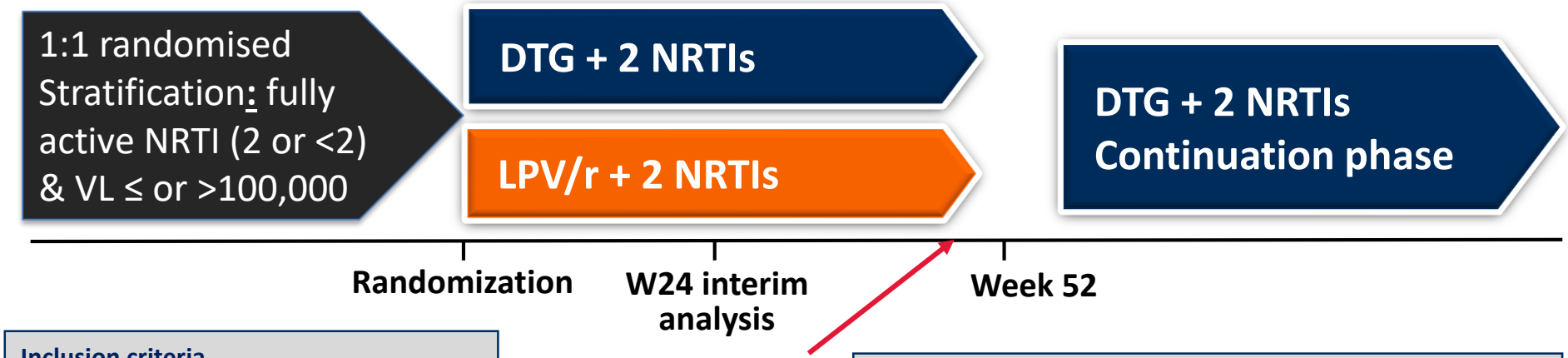
Looks good
Non-TAF indication in England?
Caution resistance data

Presenter's possibly off-licence & arguably not entirely evidence based opinions

A NEW DAWN(ING)

DAWNING: Study Design

Open-label, randomized noninferiority phase IIIb study



Inclusion criteria

- On failing 1st-line 2 NRTIs + NNRTI ≥6M, (VL ≥400 on 2 occasions)
- No primary viral resistance to PIs or INSTIs
- Investigator-selected NRTIs had to include ≥1 fully active NRTI based on viral resistance testing at screening

Primary endpoint at 48 wk: participants with VL <50 c/mL (ITT-E snapshot)[a]

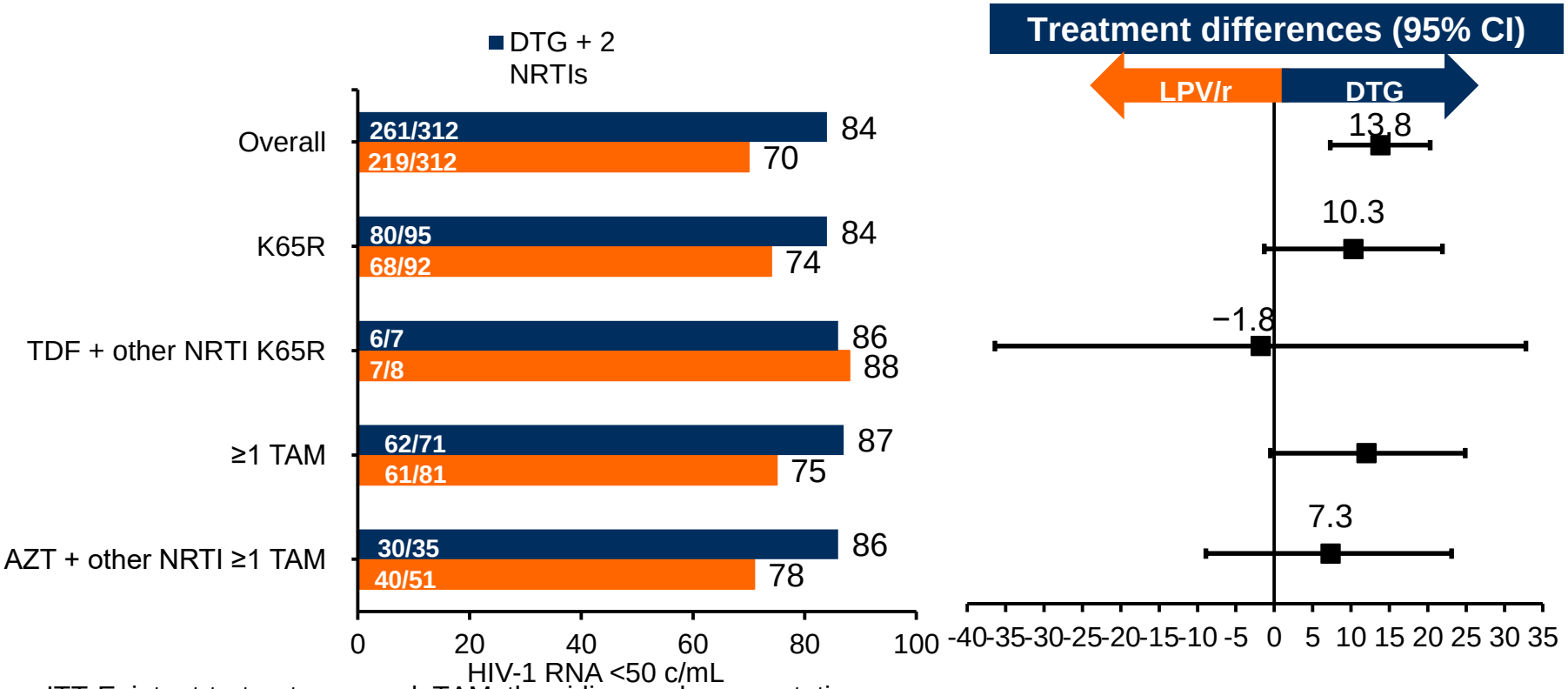
Countries

Argentina
Brazil
Chile
Colombia
Mexico
Peru
Kenya
South Africa
China
Thailand
Romania
Russia
Ukraine

[a]–12% noninferiority margin. BL, baseline; ITT-E, intent-to-treat–exposed; VL, viral load.

Brown et al. CROI 2019; Seattle, WA. Slides 144. Aboud et al. *Lancet Infect Dis*. 2019 [Epub ahead of print].

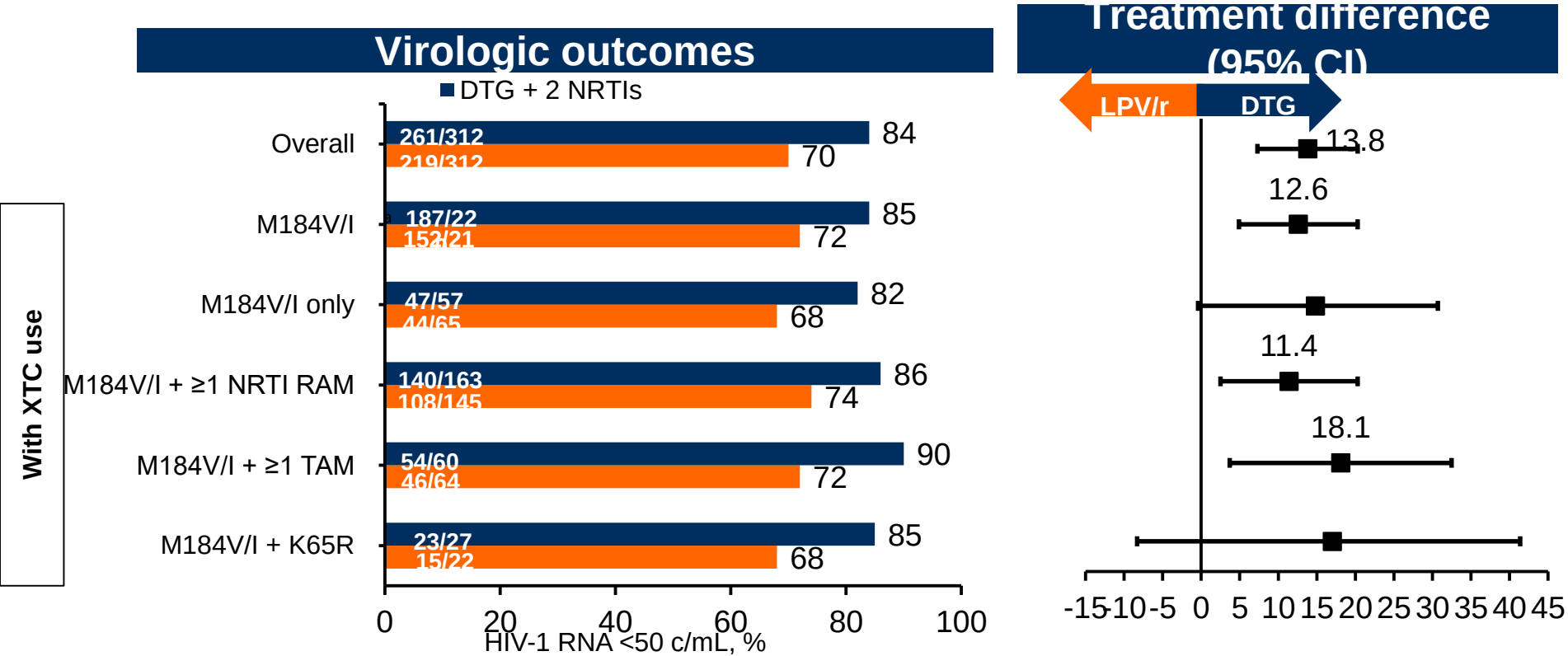
W48 ITT-E by K65R & TAMs



ITT-E, intent-to-treat–exposed; TAM, thymidine analogue mutation.

Brown et al. CROI 2019; Seattle, WA. Slides 144.

W48 ITT-E by M184V/I +/- other NRTI RAMs



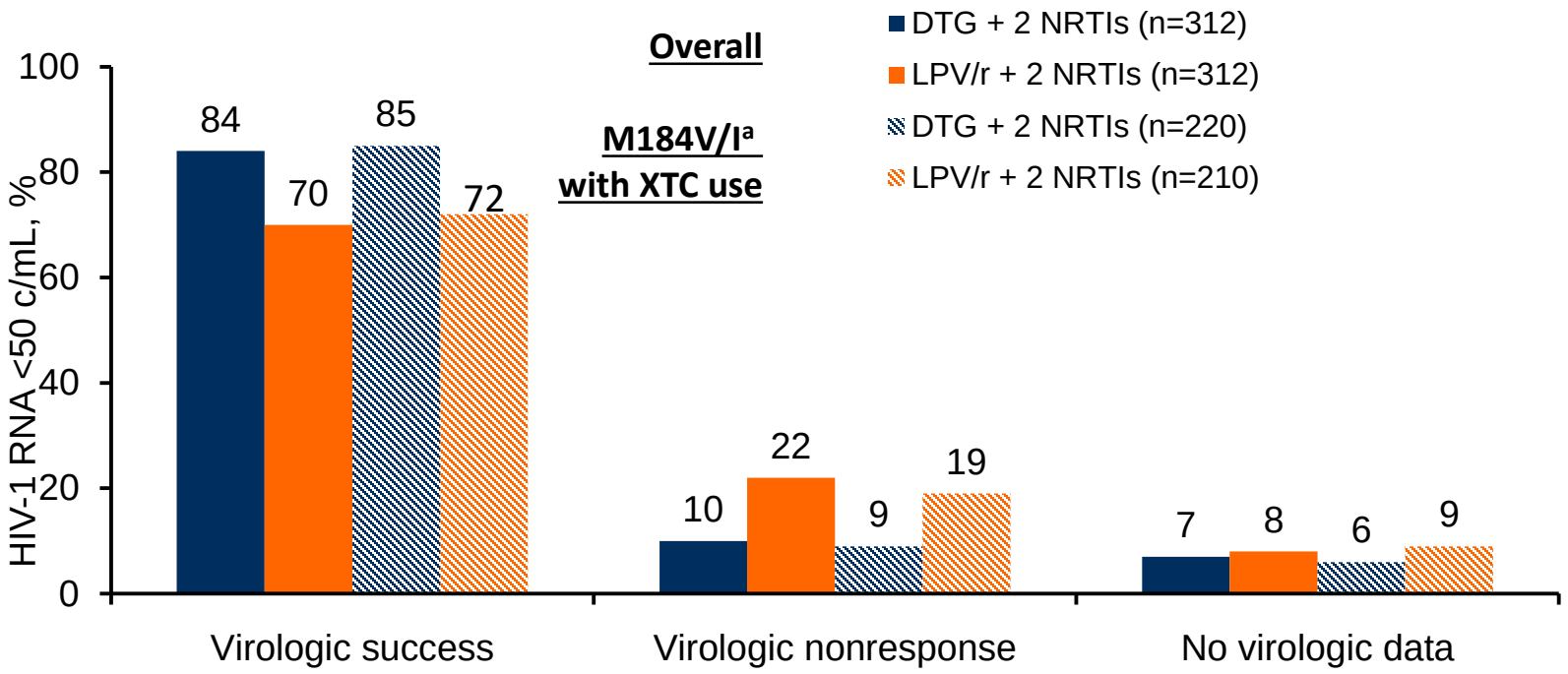
Among the 11 (4%) CVWs in the DTG group, 5/11 (45%) had M184V/I at baseline with use of XTC

Among the 30 (10%) CVWs in the LPV/r group, 15/30 (50%) had M184V/I at baseline with use of XTC

[a]M184V/I alone or plus additional NRTI mutations. TAM, thymidine analogue mutation. XTC, 3TC or FTC.

Brown et al. CROI 2019; Seattle, WA. Slides 144.

Snapshot outcomes overall & M184V/I With XTC population at W48: ITT-E Analysis



[a]M184V/I alone or plus additional NRTI mutations. ITT-E, intent to treat–exposed; XTC, 3TC or FTC use.

Brown et al. CROI 2019; Seattle, WA. Slides 144.

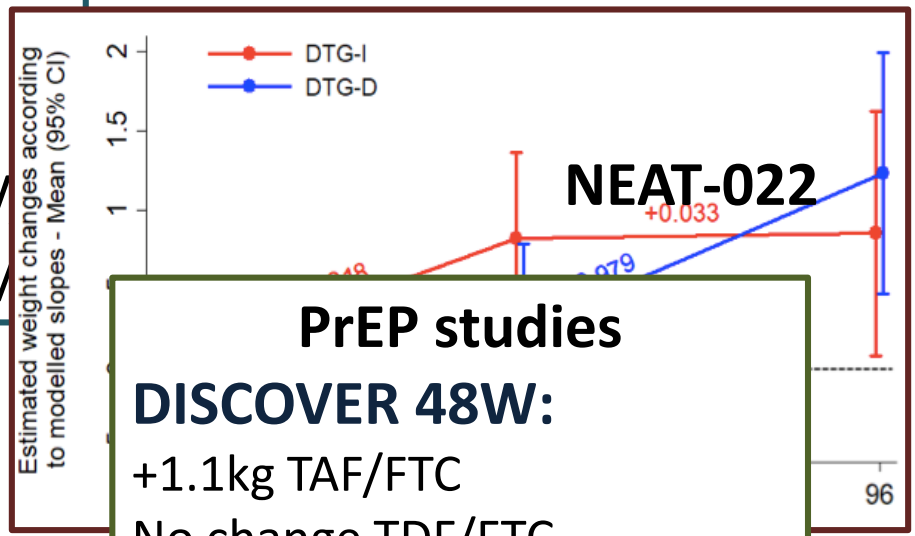
Applying DAWNING to practice

- DTG superior to LPV/r second line
  - Can we extrapolate to DRV/r?
- DTG works well with an impaired NRTI backbone
- EACS guidelines for VF with resistance:
  - Any regimen should use at least 1 fully active boosted plus 1 drug from a new class, or 1 NNRTI assessed by genotypic testing.
  - Alternatively, DTG (when fully active) + 2 NRTIs, of which at least 1 NRTI is fully active

WEIGHT

Weight: randomised studies

NEAT-001
Trunk fat 7.3%
more on RAL/DRV
vs TDF/FTC + DRV/



ACTG 5256s
More severe
Weight gain on
RAL vs ATV/r

PrEP studies

DISCOVER 48W:
+1.1kg TAF/FTC
No change TDF/FTC

HPTN077
No difference CAB vs placebo

Spring-1
Greater weight
rise on all DTG
doses vs EFV

GS-1490 W96
+3.9 kg on DTG
+3.5 kg on BIC

Waters L et al. P102 Glasgow 2018; Hill A et al, J Virus Erad 2019; Landowitz et al., CROI 2019 abstract 34LB; Hare et al., abstract 104

Weight: cohort data

- Several (not all) studies (switch & 1st line) report greater weight on INSTI vs other classes
- DTG > earlier INSTI
- ABC & TAF > TDF
- Risk factors
  - Female, non-white, >50 years

Hill A et al, J Virus Erad 2019

Why?

- Return to health?
- A new lipohypertrophy?
- ‘Obesogenic’ environment?
- Fewer GI side effects?
- Are people happier (or sadder) on integrases?
- Backbone? Is TDF protective?
- Something else? DTG & melanocortin….
- Is it clinically important????

Every cloud….

June 14, 2019 EDITORIAL

Could excess body weight be good for cognitive health in chronic HIV infection?

Lucette A. Cysique, Lambros Messinis, Steven M. Albert

First published June 14, 2019, DOI: https://doi.org/10.1212/WNL.0000000000007769

Article Info & Disclosures

Cognitive health in HIV-infected persons continues to be an important area of investigation, especially as the HIV epidemic is aging. Understanding the factors that may contribute to, or guard against, cognitive decline in the aging HIV population is necessary to develop and evaluate treatments that improve outcomes and reduce elderly dementia risk. In this issue of *Neurology*®, a complex study[1] focusing on men's cognitive health using data from the prospective Multicenter AIDS Cohort Study (MACS) shows established but also unexpected relationships among midlife adiposity, and waist circumference, HIV status, and 10-year trajectory of cognitive performance.

Neurology. 2019 Jun 14.

What can we do?

- Counsel people
- Promote healthy lifestyle (NHS Choices!)
- Record weight & waist circumference
- Collate data

LUNGS

Lung cancer: Kaiser Permanente cohort

Rate ratio (confidence interval) for PLHIV vs HIV-negative PLWHIV = 24,768 (4.9 PYFU); HIV-negative = 257,600 (5.8 PYFU)				***P*-value *trend***
Unadjusted	2.0 (1.7-2.2)			<0.001
Adjusted				
Demographics	1.9 (1.5-2.4)			<0.001
+ risk factors	1.4 (1.1-1.7)			0.014
+ prior pneum	1.1 (0.9-1.5)			0.37
Recent CD4 (36 months prior)				
	<200	*200-499*	*>500*	
Unadjusted	2.4 (1.2-4.9)	2.3 (1.6-3.4)	1.4 (0.8-2.4)	*<0.001*
Adjusted				
Demographics	2.2 (1.1-4.5)	1.9 (1.3-2.8)	1.2 (0.7-2.0)	*0.008*
+ risk factors	1.4 (0.7-2.9)	1.3 (0.9-1.9)	0.9 (0.5-1.5)	*0.58*
+ prior pneum	1.2 (0.6-2.5)	1.2 (0.8-1.8)	0.8 (0.5-1.4)	*0.98*

***Demographics**: age, sex, race/ethnicity, year cohort entry; **Cancer risks**: smoking, drug/alcohol abuse, overweight/obesity*

Marcus JL et al. AIDS. 2017 Apr 24;31(7):989-993.

Lung cancer screening: US

- **USPSTF guidelines:**
  - Annual low-dose CT (LDCT) for current/former* (quit within 15yrs) smokers aged 55-80 yrs with ≥30 PY history
  - Based on NLST trial (n=55,000 PLWH excluded)
- **WIHS/MACS analysis (n=12,339; 7,591 with HIV):**
  - F > M, younger age & shorter smoking history
  - USPSTF guidelines would have screened only 25% of cases

*quit less then 15 years prior

Moyer VA et al. Ann Intern Med. 2014;160(5):330-338; Sellers et al, abstract 0015; CROI 2019, Seattle

Lung cancer screening: UK

- **UKLS**
  - RCT single LDCT vs usual care in high risk (>5% 5-year risk by http://www.MylungRisk.org) 50-75 year olds
  - Lung cancer: 1.7% baseline, 0.4% at 12-month follow-up
  - 86% early stage, 83% resected, £8,466 per QALY gained
- **SUMMIT (started December 2018)**
  - Largest ever UK trial, 50,000 50-77 year olds (half high risk)
  - Blood marker screening for all, LDCT for high-risk

https://thorax.bmj.com/content/71/2/161; https://www.nihr.ac.uk/news/largest-ever-uk-lung-cancer-screening-study-launches-in-london/9808

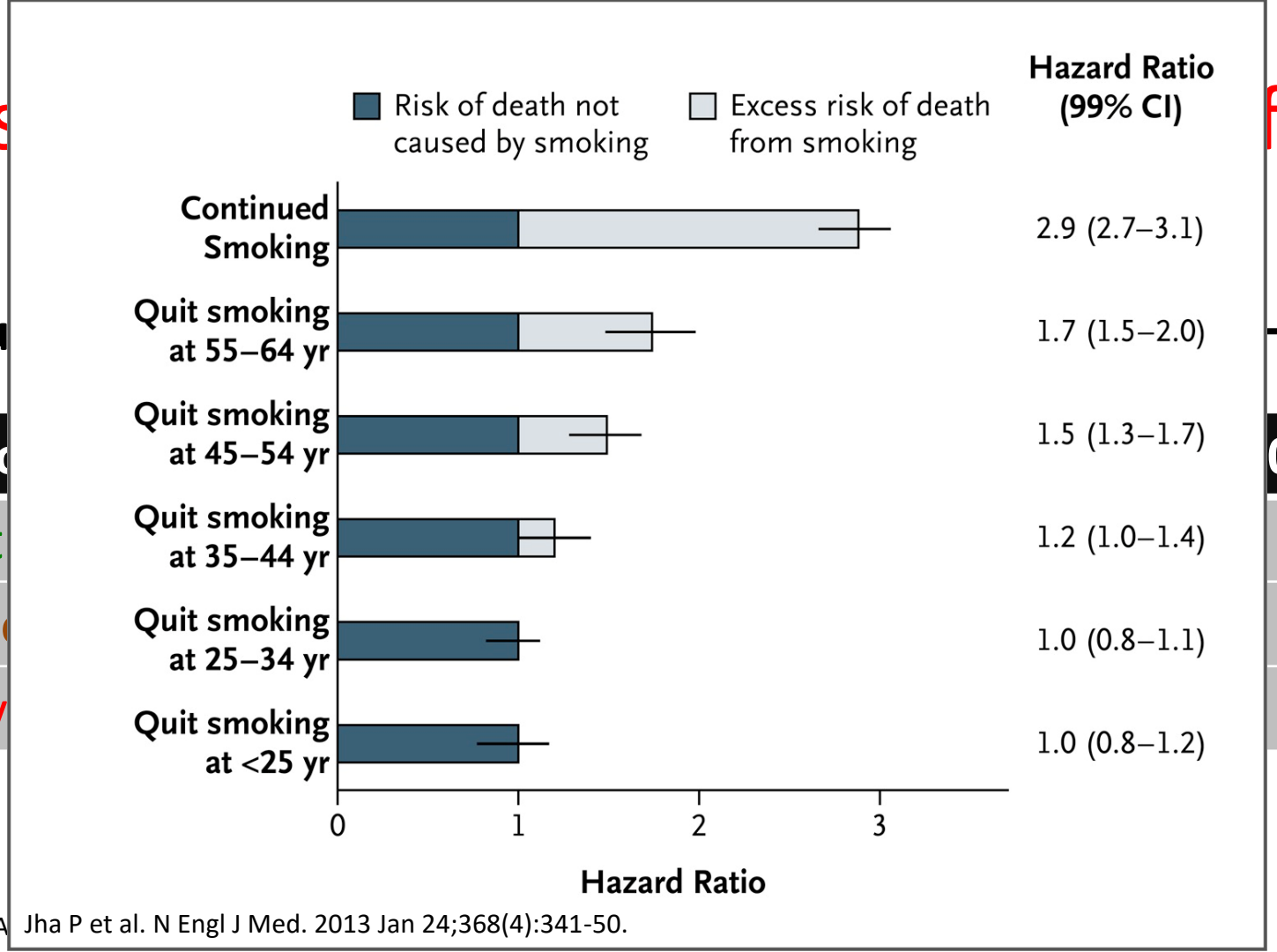
Take home message

- People with HIV are at higher risk of lung cancer
- Screening thresholds may differ
- Ensure appropriate follow-up of lung nodules
- **STOP SMOKING, STOP SMOKING, STOP SMOKING**

Ens fit

Cu HIV

Smo	0
Light	
Mod	
Heav	



Reddy KP et al. JA

Jha P et al. N Engl J Med. 2013 Jan 24;368(4):341-50.

Summary

- We must talk about U=U uniformly & unambiguously
- New drugs-a-coming (use may be limited in England)
- DAWNING supports use of DTG where previously only PIs dared to treat
- Weight is an emerging issue, aetiology uncertain
- We must all be equipped to discuss smoking cessation

Thank you!

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lwaters@nhs.net

@drlaurajwaters