Oral Abstract Session-10

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179 - Frailty Is Associated With Higher MACE Incidence but Does Not Appear to Modify Pitavastatin Effects

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BACKGROUND

- People with HIV (PWH) are at increased risk for ASCVD and geriatric syndromes (such as frailty)
- Frail older adults in the general population appear to have a higher risk of MACE, and may be under-prescribed statins due to perceived risks
- REPRIEVE demonstrated a 36% reduction in MACE with pitavastatin, however:
  1) More events than anticipated per PCE 10 year ASCVD risk score in some groups
  2) Nearly 5 events/1000 person-years occurred among those on pitavastatin

PCE, pooled cohort equation; ASCVD, atherosclerotic cardiovascular disease; MACE, major adverse cardiovascular event

GOALS OF THE CURRENT STUDY

REPRIEVE represents a unique opportunity to test the hypotheses that:

1) Frailty is associated with MACE among people with HIV, even after accounting for ASCVD risk

2) Pitavastatin prevents MACE across the spectrum of frailty

ASCVD, atherosclerotic cardiovascular disease; MACE, major adverse cardiovascular event

METHODS

- REPRIEVE was a prospective, double-blind, placebo-controlled trial comparing pitavastatin 4mg daily to placebo for prevention of MACE among people with HIV

- Primary MACE outcome was a composite of:
  - Cardiovascular death or death from an undetermined cause; myocardial infarction or hospitalization for unstable angina; stroke or transient ischemic attack (TIA); peripheral arterial ischemia; revascularization of a coronary, carotid, or peripheral artery

  - Evaluated in time-to-event analysis

MACE, major adverse cardiovascular event

METHODS

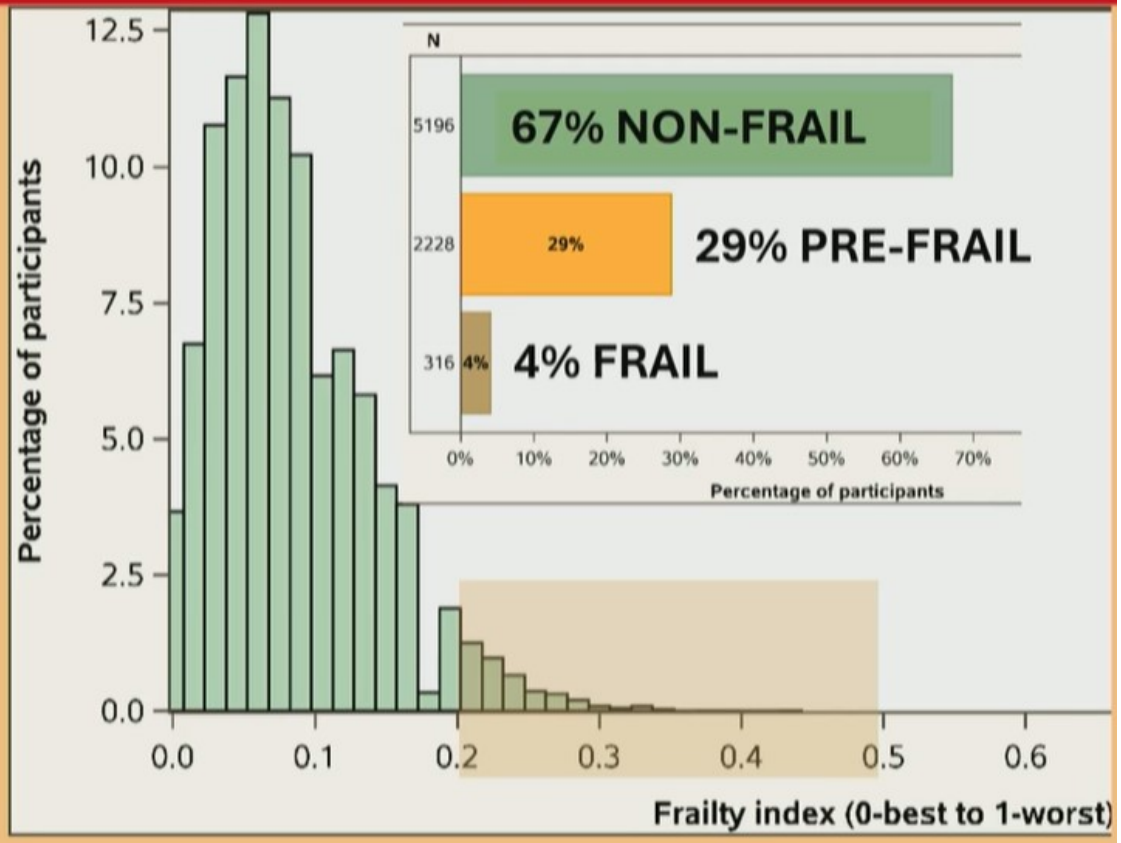
- We developed a 32-item **frailty index (FI)** according to the standard procedure for accumulation of deficits approach*
  - Incorporated REPRIEVE baseline data on comorbidities, medications, laboratory values, vital signs, symptoms, and components of self-reported activity limitations
  - Components primarily coded as 0 if absent and 1 if present
  - Sum scores/number of non-missing items (required 25)
  - <0.1 = non-frail, 0.1-0.2 = pre-frail, >0.2 = frail

- We validated the constructed FI with all-cause mortality

* Searle et al (BMC Geriatr, 2008)

RESULTS: Overall Population & Frailty Distribution

- >99% of REPRIEVE participants had data for at least 25 frailty index components (n=7740 of 7769, 50% pitavastatin and 50% placebo)
  - Median age 50
  - ASCVD risk 4.5%
  - 31% female
  - 65% non-White



ASCVD, atherosclerotic cardiovascular disease

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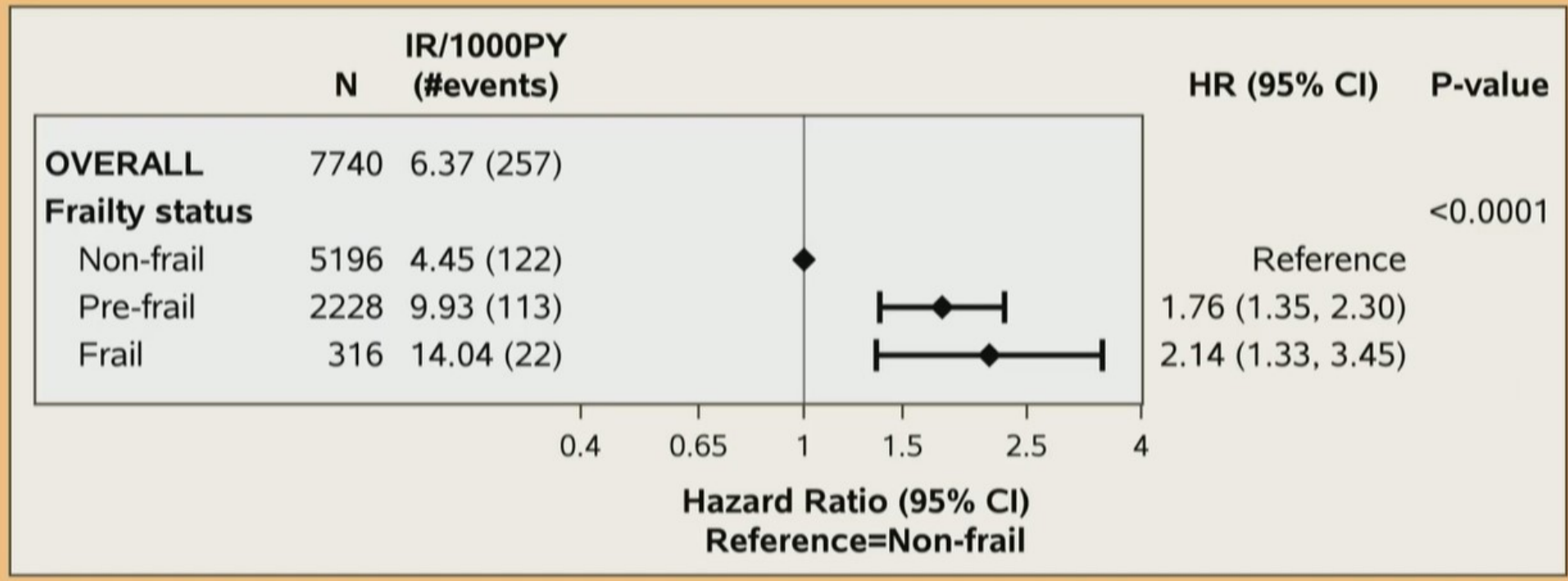
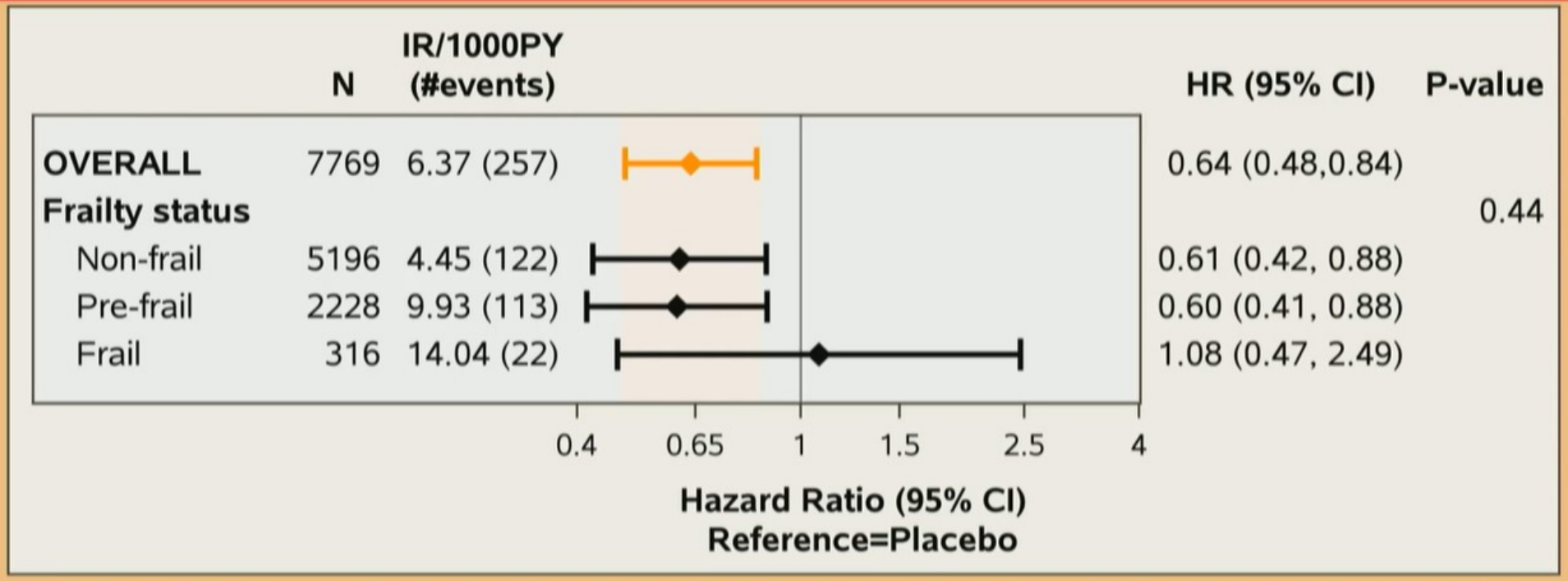
RESULTS: Frailty as Prognostic Factor of MACE



HR, hazard ratio; IR, incidence rate; MACE, major adverse cardiovascular event; PY person-years
Estimated HRs from cause-specific hazards model for time-to-first MACE adjusted for treatment group, and for age, sex, atherosclerotic cardiovascular risk score at baseline

RESULTS: Frailty as a Statin Effect Modifier



- No difference in pitavastatin effect on MACE events among frailty groups, though data in frail group non-conclusive due to small event number (n=22)

MACE, major adverse cardiovascular event
P-value is for the interaction between frailty status and treatment group

KEY STRENGTHS & LIMITATIONS

- Multi-national, double-blind, randomized controlled trial
- 1/3 female, > 50% non-White

- Relatively healthy & young cohort
- Limited sample size and event number in the frail group

CONCLUSIONS

- Increasing frailty was associated with higher MACE hazard, even after accounting for ASCVD risk factors
- Frailty status did not modify protective effects of pitavastatin seen in the primary trial
- Incorporating frailty assessment into routine care may help identify PWH for whom the greatest benefit might be seen from statin therapy for ASCVD prevention

ASCVD, atherosclerotic cardiovascular disease; MACE, major adverse cardiovascular event

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REPRIEVE

ACTG

NIH National Heart, Lung, and Blood Institute

NIH National Institute on Aging

NIH National Institute of Allergy and Infectious Diseases

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