Longer term All-Cause and Cardiovascular Mortality with Intensive Blood Pressure Control

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# ABSTRACT

**Background**. Both the Systolic Blood Pressure Intervention Trial (SPRINT) and the Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients (STEP) trial have shown benefits of intensive blood pressure control on cardiovascular morbidity and mortality. However, as both trials were ended after slightly more than 3 years of follow-up, the legacy effect of intensive treatment on longer term cardiovascular and all-cause mortality is unknown.

**Methods**. We linked participants in SPRINT to the National Death Index (NDI, 2016 to 2020), assessing cardiovascular mortality using the NDI plus system. Cox and competing risk regression models were used to model the effect of intensive treatment through the trial and during post-trial follow-up on all-cause and cardiovascular mortality respectively

**Results**. Over a median follow-up of 8.76 years, there were 248 and 818 cardiovascular and all-cause deaths with intensive treatment respectively, and 273 cardiovascular / 826 all-cause deaths for standard treatment. Intensive treatment was beneficial for both cardiovascular (Hazard Ratio [HR] = 0.69, 95% CI 0.49 to 0.98) and all-cause mortality (HR = 0.83, 95% CI 0.68 to 1.01) through close-out visits for the trial (follow-up through July 2016). However, there was no indication of benefit during post-trial follow-up for either cardiovascular (HR = 1.06, 95% CI 0.84 to 1.35) or all-cause mortality (HR = 1.08, 95% CI 0.94 to 1.23). Results were similar for subgroups based on baseline age, cognitive function, and frailty status.

**Conclusions**. Our results show a clear benefit for cardiovascular and all-cause mortality during the trial which was largely attenuated during post-trial observational follow-up. Given indications of increasing blood pressures in SPRINT participants randomized to intensive treatment following the trial, these results highlight the importance of consistent long-term management of hypertension in line with current guidelines.

# INTRODUCTION

# METHODS

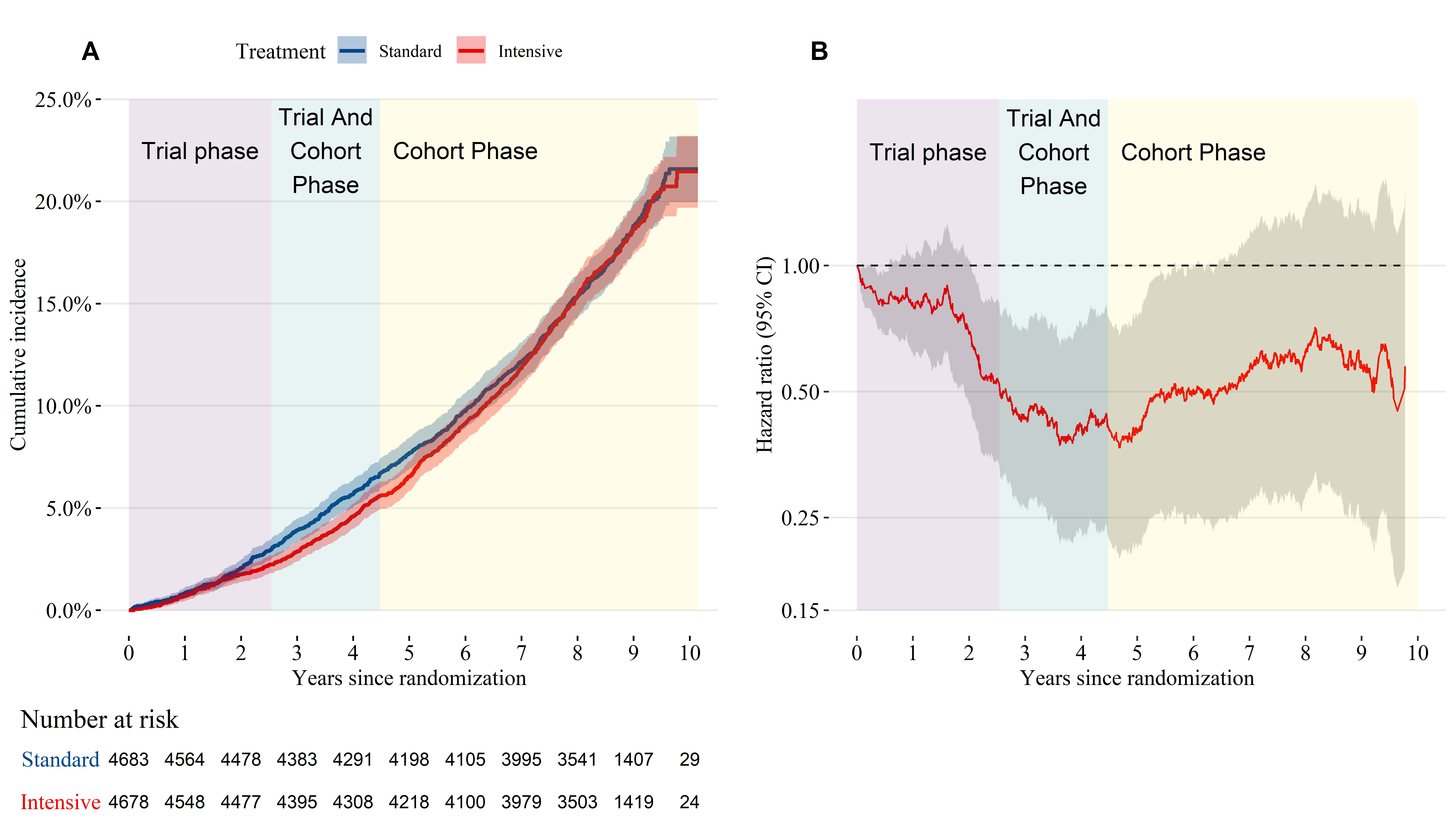
# RESULTS

# DISCUSSION

**Table 1**: All-cause mortality by treatment group and subgroup

|  | **Trial Follow-up Through Close-out Visits** | | | **Post-trial Follow-up** | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Incidence (95% CI)** | | **Hazard Ratio (95% CI)** | **Incidence (95% CI)** | | **Hazard Ratio (95% CI)** |
| **Standard** | **Intensive** | **Standard** | **Intensive** |
| Overall | 15.1 (13.4, 16.9) | 12.5 (11.0, 14.2) | 0.83 (0.68, 1.01) | 29.6 (27.1, 32.1) | 31.9 (29.3, 34.5) | 1.08 (0.94, 1.23) |
| *Age, years* | | | | | | |
| <75 years | 9.73 (8.19, 11.5) | 8.18 (6.78, 9.77) | 0.84 (0.63, 1.11) | 18.9 (16.7, 21.3) | 18.1 (15.9, 20.5) | 0.96 (0.78, 1.17) |
| ≥75 years | 29.8 (25.3, 34.7) | 24.3 (20.3, 28.8) | 0.82 (0.62, 1.07) | 61.6 (54.7, 69.1) | 73.3 (65.7, 81.5) | 1.21 (1.00, 1.46) |
| *Sex* | | | | | | |
| Male | 17.2 (15.0, 19.6) | 13.8 (11.9, 16.0) | 0.80 (0.64, 1.01) | 30.3 (27.3, 33.6) | 34.6 (31.3, 38.1) | 1.14 (0.97, 1.34) |
| Female | 11.4 (9.02, 14.1) | 10.2 (8.01, 12.8) | 0.89 (0.61, 1.28) | 28.2 (24.3, 32.5) | 27.0 (23.2, 31.2) | 0.94 (0.74, 1.20) |
| *Race* | | | | | | |
| Non-Black | 16.0 (13.9, 18.2) | 13.0 (11.2, 15.0) | 0.80 (0.64, 1.01) | 31.4 (28.4, 34.6) | 34.2 (31.1, 37.6) | 1.10 (0.94, 1.28) |
| Black | 13.2 (10.5, 16.3) | 11.5 (8.95, 14.4) | 0.85 (0.59, 1.24) | 25.7 (21.8, 30.0) | 26.7 (22.6, 31.1) | 1.02 (0.78, 1.32) |
| *Chronic Kidney Disease* | | | | | | |
| No | 11.1 (9.49, 13.0) | 8.45 (7.02, 10.1) | 0.76 (0.58, 1.01) | 22.3 (19.8, 24.9) | 24.2 (21.7, 26.9) | 1.07 (0.90, 1.29) |
| Yes | 25.8 (21.6, 30.4) | 23.0 (19.1, 27.4) | 0.87 (0.65, 1.15) | 52.3 (45.9, 59.3) | 55.0 (48.4, 62.1) | 1.03 (0.84, 1.27) |
| *Cognitive Function* | | | | | | |
| >10th percentile | 15.1 (13.1, 17.2) | 10.8 (9.14, 12.6) | 0.70 (0.55, 0.89) | 26.9 (24.2, 29.8) | 30.7 (27.8, 33.8) | 1.13 (0.96, 1.33) |
| ≤10th percentile | 15.3 (12.1, 19.0) | 16.5 (13.2, 20.3) | 1.13 (0.79, 1.62) | 36.8 (31.7, 42.6) | 34.7 (29.6, 40.2) | 0.98 (0.76, 1.26) |
| *Frailty Status* | | | | | | |
| Fit (FI≤0.10) | 6.90 (4.35, 10.3) | 5.68 (3.45, 8.73) | 0.90 (0.43, 1.87) | 11.3 (7.88, 15.5) | 13.4 (9.71, 17.8) | 1.26 (0.72, 2.19) |
| Pre-frail (0.10<FI≤0.21) | 10.7 (8.79, 12.8) | 9.52 (7.71, 11.6) | 0.90 (0.66, 1.24) | 26.1 (23.0, 29.5) | 27.8 (24.5, 31.3) | 1.07 (0.87, 1.30) |
| Frail (FI>0.21) | 26.4 (22.5, 30.7) | 20.4 (17.1, 24.2) | 0.75 (0.57, 0.98) | 46.2 (40.7, 52.2) | 49.9 (44.2, 56.0) | 1.07 (0.87, 1.30) |

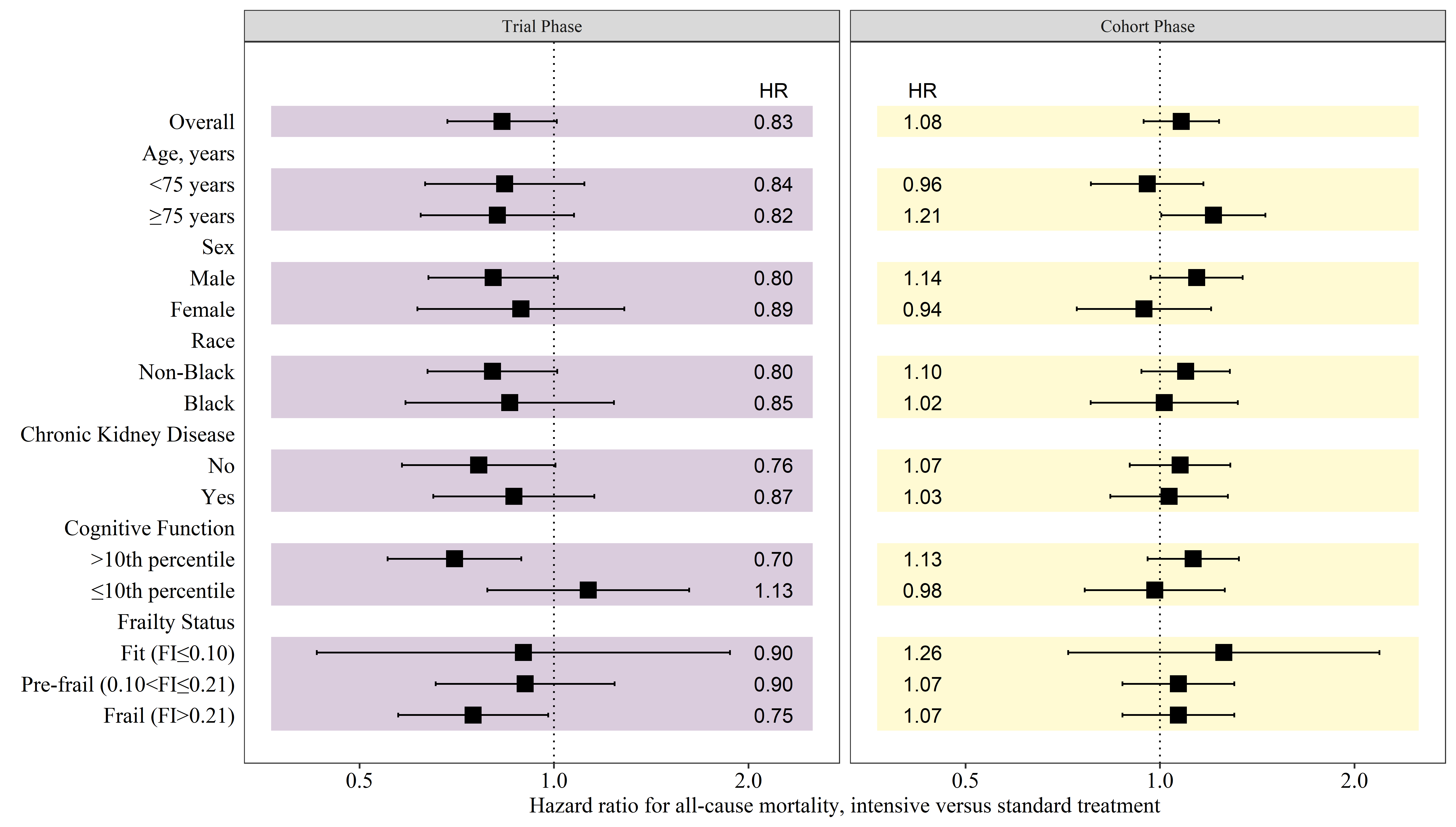
**Figure 1**: (A) Cumulative incidence of all-cause mortality by treatment group. (B) Time-dependent effect of being randomized to intensive treatment on all-cause mortality.



**Figure 2**: (A) Cumulative incidence of cardiovascular and non-cardiovascular mortality by treatment group. (B) Time-dependent effect of being randomized to intensive treatment on cardiovascular mortality.



**Figure 3**: Hazard ratio for all-cause mortality for participants randomized to intensive versus standard treatment, overall and in subgroups.



# SUPPLEMENT

We have a total of 14 plots showing all-cause mortality and mortality split into cardiovascular and non-cardiovascular causes. They are automated enough to dynamically set text and axis values that will look reasonable. To show what I mean, I’ve added the figures for adults 75 years or older, who have a much higher incidence.

**Figure S1**: Cumulative incidence of all-cause mortality among participants 75 years or older.

**Figure S2**: Cumulative incidence of cardiovascular and non-cardiovascular mortality among participants 75 years or older.