CORRECTION

Correction: The association between antihypertensive treatment and serious adverse events by age and frailty: A cohort study

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It has come to the attention of the authors that some outcomes, related to fall events, were not included in the original analysis dataset, due to an error during data management. This has now been corrected, and the analysis re-run resulting in the corrections listed below. Furthermore, the original published manuscript described outcomes as an event associated with hospitalisation or death. However, deaths that were not preceded by a hospitalisation, were not included in the analysis. Finally, Table 1 presents the number (%) of males in the cohort, not females, as described in the original published manuscript.
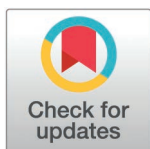
In the Methods and findings subsection of the Abstract, there is an error in the fourth sentence of the paragraph. The correct sentence is: The primary outcome was hospitalisation within 10 years from falls.

In the Methods and findings subsection of the Abstract, there is an error in the 10th sentence. The correct sentence is: Antihypertensives were associated with an increased risk of hospitalisation from falls (adjusted Hazard Ratio [aHR] 1.10, 95% Confidence Interval 1.08–1.12), hypotension (aHR 1.32, 95% CI 1.29–1.35), syncope (aHR 1.20, 95% CI 1.17–1.22), AKI (aHR 1.44, 95% CI 1.41–1.47), electrolyte abnormalities (aHR 1.45, 95% CI 1.43–1.48) and primary care attendance with gout (aHR 1.35, 95% CI 1.32–1.37).

In the Methods and findings subsection of the Abstract, there is an error in the 12th sentence. The correct sentence is: In older patients (80–89 years) and those with severe frailty, this absolute risk was increased, with 38 and 39 fall events per 10,000 patients treated per year (respectively).

In the What Did the Researchers Do and Find subsection of the Author Summary, there is an error in the third and fourth bullet. The correct bullets are:

- In a total of 3,834,056 patients, blood pressure lowering treatment was associated with an increased risk of hospitalisation from falls, hypotension, syncope (but not fracture), acute kidney injury, electrolyte abnormalities and primary care consultations for gout.

- These risks were much higher in older patients and those with frailty. For example, in those aged 40–49 years 913 patients would need to be treated for 5 years to

cause a serious fall. However, for those aged 80–89 years, only 53 patients would need to be treated for 5 years to cause a serious fall.

In the Outcomes subsection of the Methods, there is an error in the first, second and fourth sentences. The correct first sentence is: The primary outcome of this analysis was first hospitalisation with a primary diagnosis of a fall (defined according to ICD9 and ICD10 codes listed in S3 Table). The correct second sentence is: Secondary outcomes were first hospitalisation with a primary diagnosis of hypotension, syncope, fractures, acute kidney injury, electrolyte abnormalities and primary care attendance with gout (S3 Table and our github page for codelists). The correct fourth sentence is: Serious adverse events were defined as first hospitalisation with a primary diagnosis of any of the conditions mentioned above (with the exception of gout which was not included because it is typically less serious and usually only captured in primary care records).

In the Population Characteristics subsection of the Results, there is an error in the first sentence of the second paragraph. The correct sentence is: Patients entered the cohort throughout the period of observation (between 1998 and 2019, S7 Figure) and were followed up for a median of 7.1 years (interquartile range [IQR] 3.0 to 10.0 years).

In the Population Characteristics subsection of the Results, there is an error in the second sentence of the third paragraph. The correct sentence is: A total of 429,787 treated patients were compared to 429,787 similar controls for the matched analysis (S11 Table).

In the Primary outcome subsection of the Results, there is an error in the first, second and fifth sentences. The correct first sentence is: During follow-up, a total of 147,251 patients (3.8%) were hospitalised following a fall, including 31,386 patients (6.5%) in the exposure group and 115,865 (3.5%) in the non-exposed group. The correct second sentence is: In the primary analysis, using propensity score adjustment, antihypertensive treatment exposure was associated with an increased risk of hospitalisation from falls (adjusted Hazard Ratio [aHR] 1.10, 95% CI 1.08 to 1.12). The correct fifth sentence is: The overall absolute risk of falls with antihypertensive treatment was very low, with just six events (95% CI 5–7) per 10,000 patients treated per year, equivalent to a number needed to harm of 371 and 169 over five and 10 years respectively (Table 2).

In the Secondary outcomes subsection of the Results, there is an error in the first sentence. The correct first sentence is: Antihypertensive treatment exposure was also associated with an increased risk of hospitalisation from hypotension, syncope, acute kidney injury, electrolyte abnormalities and primary care consultations for, but not fracture (Fig 1, Table 2).

In the Subgroup and sensitivity analyses subsection of the Results, there is an error in the first and second sentences. The correct sentences are: The relative association between antihypertensive treatment and serious adverse events increased with age for acute kidney injury, electrolyte abnormalities and gout (Fig 2). These trends were less obvious in subgroups by baseline frailty (Fig 3).

In the Subgroup and sensitivity analyses subsection of the Results, there is an error in the fourth to seventh sentences. The correct sentences are: For example, the absolute risk of hospitalisation from a fall with antihypertensive treatment in individuals aged 40−49 years was 2 events (95% CI 1–3) per 10,000 patients treated per year (equivalent to a number needed to harm [NNH] of 913 at 5 years and 457 at 10 years). In those aged 80−89 years, this was increased to 38 events (95% CI 29–46) per 10,000 patients treated per year (equivalent to a NNH of 53 and 26 at 5 and 10 years respectively). Similarly, in fit patients, the absolute risk of a serious fall with antihypertensive treatment was 5 events (95% CI 4–6) per 10,000 patients treated per year (equivalent to a NNH of 414 at 5 years and 207 at 10 years). However, in those with severe frailty, this was increased to 39 events (95% CI −17–83) per 10,000 patients treated per year (equivalent to a NNH of 52 and 26 at 5 and 10 years respectively).

In the Subgroup and sensitivity analyses subsection of the Results, there is an error in the second sentence of the second paragraph. The correct sentence is: Further sensitivity analyses, using a competing risks approach to examine the primary outcome, also found no difference between the sub-hazard ratio for serious falls (adjusted Sub-Hazard Ratio 1.11, 95% CI 1.1.09 to 1.13) and the adjusted hazard ratio from the primary analysis (S13 Table).

In the Summary of main findings subsection of the Discussion, there is an error in the first sentence in the first paragraph. The correct sentence is: In this observational study of 3.8 million patients, previously untreated and with raised systolic blood pressure, antihypertensive treatment was associated with an increased risk over the subsequent decade of hospitalisation from falls, hypotension, syncope (but not fracture), acute kidney injury, electrolyte abnormalities and primary care consultations for gout.

In the Summary of main findings subsection of the Discussion, there is an error in the second sentence of the second paragraph. The correct sentence is: In older patients, the absolute risk of harm from a fall with treatment ($NNH_5 = 53$) was found to be very similar to the likelihood of benefit (number needed to treat [NNT_5] = 38)[21], and in such situations, the decision about whether or not to prescribe treatment is more finely balanced.

In the Strength and limitations subsection of the Discussion, there is an error in the third sentence of the first paragraph. The correct sentence is: Outcomes were based on secondary care data on the primary cause or hospitalisation, and therefore were less likely to be biased by any knowledge that patients were taking antihypertensive therapy.

In the Strength and limitations subsection of the Discussion, there is an error in the third sentence of the third paragraph. The correct sentence is: Similarly, the definition of acute kidney injury used here was based on clinical codes at hospital admission and maybe difference from that used in trials where kidney function is measured much more closely.

In the Implications for clinical practice subsection of the Discussion, there is an error in the third sentence of the second paragraph. The correct sentence is: By contrast, in older patients (80–90+years), the NNH_5 for serious falls was 37–53 (or 52 for those with severe frailty), whilst the NNT_5 for major cardiovascular events is 38[21].

Tables 1 and 2 were uploaded incorrectly. Please see the correct Tables 1 and 2 here.

There is an error in the caption for Figs 1–3. Please see the correct Fig captions here.

Estimates from randomised controlled trials represent risk ratios rather than hazard ratios. For rare events such as the outcomes presented here, these would be expected to be equivalent. The total number of patients included in each analysis varies due exclusion of participants who experienced the outcome of interest on the index date, model convergence and variation in the matching algorithm.

The total number of patients included in each analysis varies due exclusion of participants who experienced the outcome of interest on the index date. Models adjusted for propensity score.

The total number of patients included in each analysis varies due to exclusion of participants who experienced the outcome of interest on the index date. Models adjusted for propensity score.

Reference

1. Sheppard JP, Koshiaris C, Stevens R, Lay-Flurrie S, Banerjee A, Bellows BK, et al. The association between antihypertensive treatment and serious adverse events by age and frailty: A cohort study. PLoS Med. 2023;20(4):e1004223. https://doi.org/10.1371/journal.pmed.1004223 PMID: 37075078

Table 1. Baseline characteristics of the study population.

Characteristic	No antihypertensive prescription during 12 month exposure period (non-exposed)		Antihypertensive prescription during 12 month exposure period (exposed)	
	Mean/number	SD/%	Mean/number	SD/%
Total population	3,349,869		484,187	
Age (years) (SD)	55.9	12.1	61.7	12.9
Sex (%male)	1,666,304	49.7%	245,498	50.7%
White ethnicity (%)*	1,477,232	67.9%	270,144	73.7%
Black ethnicity (%)*	68,806	3.2%	15,209	4.1%
South Asian ethnicity (%)*	59,856	2.8%	12,951	3.5%
Other ethnicity (%)*	569,195	26.2%	68,335	18.6%
High deprivation (IMD score of 5) (%)*†	480,976	15.4%	82,698	18.4%
Current smoking status (%)*	770,592	24.4%	98,215	21.4%
Alcohol consumption (heavy drinker) (%)*	59,238	2.4%	9,122	2.5%
Body mass index (kg/m^2) (SD)	27.0	5.2	28.5	5.7
Systolic blood pressure (mmHg) (SD)	141.4	10.8	150.8	13.7
Diastolic blood pressure (mmHg) (SD)	83.2	9.0	88.2	11.8
QRisk2 risk score (SD)	10.8%	11.0%	22.2%	15.5%
eFrailty index score (SD)	0.04	0.05	0.08	0.06
Co-morbidities				
Stroke (%)	41,229	1.2%	19,973	4.1%
Transient ischemic attack (%)	19,309	0.6%	9,404	1.9%
Myocardial infarction (%)	18,560	0.6%	25,893	5.3%
Heart failure (%)	12,118	0.4%	13,782	2.8%
Peripheral vascular disease (%)	14,657	0.4%	7,744	1.6%
Coronary artery bypass graft (%)	3,404	0.1%	6,170	1.3%
Angina (%)	26,816	0.8%	31,356	6.5%
Atrial fibrillation (%)	34,551	1.0%	24,218	5.0%
Diabetes (%)	150,771	4.5%	70,884	14.6%
Chronic kidney disease (%)	28,219	0.8%	21,309	4.4%
Cancer (%)	116,589	3.5%	24,303	5.0%
Treatment prescriptions				
ACE inhibitors (%)	0	0%	187,209	38.7%
Angiotensin II receptor blockers (%)	0	0%	48,229	10.0%
Calcium channel blockers (%)	0	0%	141,454	29.2%
Thiazides and thiazide-like diuretics (%)	0	0%	148,652	30.7%
Beta-blockers (%)	0	0%	162,211	33.5%
Alpha-blockers (%)	0	0%	20,074	4.1%
Other antihypertensives (%)‡	0	0%	8,143	1.7%
Statins (%)	215,128	6.4%	151,603	31.3%
Antiplatelets/anticoagulants (%)	228,947	6.8%	146,849	30.3%
Anticholinergics (%)	295,101	8.8%	40,000	8.3%
Antidepressants (%)	604,344	18.0%	88,625	18.3%
Hypnotics/anxiolytics (%)	582,895	17.4%	79,284	16.4%
Opioids (%)	930,773	27.8%	140,760	29.1%

*Proportions based on the number of patients with information available (i.e., excluding those with missing values).

†IMD = indices of multiple deprivation; IMD score of 5 indicates patients in the highest quintile of deprivation (most deprived).

‡Other antihypertensives = centrally acting antihypertensives, direct renin inhibitors and vasodilators.

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Table 2. Hazard ratios, absolute risk differences, and numbers needed to harm to cause one outcome at 5 and 10 years.

Outcome	Unadjusted analyses		Adjusted analyses*		Absolute risk difference (additional events per 10,000 patients per year)		Number needed to harm	
	Hazard ratio	95% CI	Adjusted Hazard ratio	95% CI	Events	95% CI	5 years	10 years
Falls (primary outcome)	1.93	1.91 to 1.96	1.10	1.08 to 1.12	6	5–7	371	169
Hypotension	2.43	2.39 to 2.48	1.32	1.29 to 1.35	7	6–7	434	153
Syncope	2.02	1.98 to 2.05	1.20	1.17 to 1.22	5	5–6	429	183
Fracture**	1.45	1.43 to 1.47	0.99	0.97 to 1.01	0	−1–0	–	–
Acute kidney injury	2.92	2.88 to 2.96	1.44	1.41 to 1.47	16	15–17	174	64
Electrolyte abnormalities	2.64	2.60 to 2.68	1.45	1.43 to 1.48	14	14–15	205	72
Gout	1.99	1.97 to 2.02	1.35	1.32 to 1.37	13	12–14	135	79

* Models adjusted for propensity score.

** Absolute risk difference too small to estimate number needed to harm.

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Subgroup and Study design	Total population	Intervention population	Intervention events	Control population	Control events		Adjusted hazard ratio (95% CI)
Falls (primary outcome)							
Propensity score adjustment	3,833,636	484,130	31,366	3,349,506	115,812		1.10 (1.08, 1.12)
Multivariable adjustment	3,833,636	484,130	31,366	3,349,506	115,812		1.10 (1.08, 1.11)
Propensity score matching	859,465	429,737	26,473	429,728	25,721		1.06 (1.03, 1.08)
Propensity score IPTW	3,833,636	484,130	31,366	3,349,506	115,812		1.21 (1.19, 1.24)
Randomised controlled trials	29,481	14,719	913	14,762	877		1.05 (0.89, 1.24)
Hypotension							
Propensity score adjustment	3,833,697	484,144	12,330	3,349,553	36,063		1.32 (1.29, 1.35)
Multivariable adjustment	3,833,697	484,144	12,330	3,349,553	36,063		1.28 (1.25, 1.31)
Propensity score matching	859,496	429,755	10,000	429,741	8,042		1.29 (1.24, 1.34)
Propensity score IPTW	3,833,697	484,144	12,330	3,349,553	36,063		1.37 (1.33, 1.42)
Randomised controlled trials	182,122	88,575	5,390	93,547	3,121		1.97 (1.67, 2.32)
Syncope							
Propensity score adjustment	3,833,676	484,142	15,035	3,349,534	53,059		1.20 (1.17, 1.22)
Multivariable adjustment	3,833,676	484,142	15,035	3,349,534	53,059		1.18 (1.16, 1.21)
Propensity score matching	859,463	429,732	12,521	429,731	11,154		1.15 (1.12, 1.19)
Propensity score IPTW	3,833,676	484,142	15,035	3,349,534	53,059		1.34 (1.30, 1.38)
Randomised controlled trials	102,261	51,072	644	51,189	543		1.28 (1.03, 1.59)
Fracture							
Propensity score adjustment	3,833,656	484,140	23,239	3,349,516	113,703		0.99 (0.97, 1.01)
Multivariable adjustment	3,833,656	484,140	23,239	3,349,516	113,703		1.02 (1.00, 1.03)
Propensity score matching	859,538	429,774	20,277	429,764	21,112		0.98 (0.95, 1.00)
Propensity score IPTW	3,833,656	484,140	23,239	3,349,516	113,703		1.11 (1.08, 1.13)
Randomised controlled trials	12,913	6,447	230	6,466	267		0.93 (0.58, 1.48)
Acute kidney injury							
Propensity score adjustment	3,833,686	484,142	26,283	3,349,544	64,381		1.44 (1.41, 1.47)
Multivariable adjustment	3,833,686	484,142	26,283	3,349,544	64,381		1.36 (1.33, 1.38)
Propensity score matching	859,474	429,739	20,853	429,735	15,662		1.37 (1.33, 1.40)
Propensity score IPTW	3,833,686	484,142	26,283	3,349,544	64,381		1.52 (1.48, 1.55)
Randomised controlled trials	95,600	43,467	909	52,133	785		1.18 (1.01, 1.39)
Electrolyte abnormalities							
Propensity score adjustment	3,833,688	484,144	20,441	3,349,544	55,374		1.45 (1.43, 1.48)
Multivariable adjustment	3,833,688	484,144	20,441	3,349,544	55,374		1.39 (1.37, 1.42)
Propensity score matching	859,515	429,761	16,715	429,754	12,324		1.41 (1.37, 1.45)
Propensity score IPTW	3,833,688	484,144	20,441	3,349,544	55,374		1.52 (1.49, 1.56)
Randomised controlled trials	119,399	19,748	517	19,528	274		1.54 (0.63, 3.75)
Gout							
Propensity score adjustment	3,833,589	484,121	24,955	3,349,468	89,546		1.35 (1.32, 1.37)
Multivariable adjustment	3,833,589	484,121	24,955	3,349,468	89,546		1.34 (1.32, 1.36)
Propensity score matching	859,433	429,717	21,005	429,716	15,447		1.46 (1.42, 1.51)
Propensity score IPTW	3,833,589	484,121	24,955	3,349,468	89,546		1.31 (1.28, 1.34)
Randomised controlled trials	32,661	16,524	249	16,137	26		3.84 (0.95, 15.57)

0.5 1 1.5 2 2.5 3 3.5 4.5

Treatment better   Treatment worse

Fig 1. Association between antihypertensive treatment and serious adverse events leading to hospitalisation, based on analyses of electronic health records and meta-analyses of randomised controlled trials.

https://doi.org/10.1371/journal.pmed.1004885.g001

Subgroup	Total population	Intervention population	Intervention events	Control population	Control events	Adjusted Hazard ratio (95% CI)	Absolute risk difference (additional events per 10,000 patients per year) (95% CI)
Falls (primary outcome)							
40-49 yrs	1,374,232	100,672	1,312	1,273,560	11,846	1.13 (1.06, 1.21)	2 (1, 3)
50-59 yrs	1,092,980	122,159	2,640	970,821	15,157	1.08 (1.03, 1.14)	2 (1, 3)
60-69 yrs	729,547	121,696	5,389	607,851	20,632	1.16 (1.12, 1.21)	9 (7, 11)
70-79 yrs	415,556	90,405	10,486	325,151	32,954	1.11 (1.08, 1.14)	17 (12, 21)
80-89 yrs	180,442	42,034	9,762	138,408	28,272	1.12 (1.10, 1.15)	38 (29, 46)
90+ yrs	40,886	7,168	1,781	33,718	6,954	1.16 (1.10, 1.23)	54 (33, 73)
Hypotension							
40-49 yrs	1,374,237	100,674	669	1,273,563	3,797	1.39 (1.26, 1.54)	2 (1, 3)
50-59 yrs	1,092,990	122,159	1,400	970,831	5,781	1.23 (1.14, 1.32)	2 (1, 3)
60-69 yrs	729,555	121,696	2,750	607,859	8,014	1.39 (1.32, 1.47)	9 (7, 10)
70-79 yrs	415,563	90,408	4,185	325,155	10,469	1.32 (1.27, 1.38)	18 (15, 20)
80-89 yrs	180,457	42,038	2,949	138,419	6,801	1.33 (1.26, 1.39)	36 (30, 43)
90+ yrs	40,895	7,169	377	33,726	1,201	1.28 (1.14, 1.45)	39 (20, 61)
Syncope							
40-49 yrs	1,374,232	100,674	1,205	1,273,558	8,203	1.45 (1.35, 1.56)	5 (4, 6)
50-59 yrs	1,092,989	122,160	2,010	970,809	9,233	1.25 (1.18, 1.33)	4 (3, 5)
60-69 yrs	729,549	121,694	3,327	607,855	10,909	1.27 (1.21, 1.33)	8 (6, 9)
70-79 yrs	415,559	90,406	4,889	325,153	14,044	1.19 (1.15, 1.24)	13 (10, 16)
80-89 yrs	180,452	42,038	3,166	138,414	9,071	1.09 (1.04, 1.14)	12 (6, 18)
90+ yrs	40,895	7,170	438	33,725	1,599	1.17 (1.05, 1.31)	29 (9, 50)
Fracture							
40-49 yrs	1,374,232	100,672	1,764	1,273,560	20,746	1.08 (1.02, 1.14)	2 (1, 4)
50-59 yrs	1,092,976	122,159	2,880	970,817	20,956	1.03 (0.99, 1.08)	1 (-0, 3)
60-69 yrs	729,552	121,696	4,356	607,856	20,816	1.04 (1.01, 1.08)	2 (0, 4)
70-79 yrs	415,556	90,405	7,292	325,151	26,705	1.00 (0.97, 1.03)	0 (-4, 4)
80-89 yrs	180,450	42,038	5,952	138,412	19,897	1.00 (0.97, 1.03)	1 (-6, 9)
90+ yrs	40,890	7,170	995	33,720	4,583	1.02 (0.95, 1.09)	5 (-22, 32)
Acute kidney injury							
40-49 yrs	1,374,235	100,673	1,416	1,273,562	6,869	1.38 (1.29, 1.48)	4 (3, 5)
50-59 yrs	1,092,989	122,158	2,947	970,831	9,480	1.30 (1.24, 1.37)	5 (4, 6)
60-69 yrs	729,553	121,697	5,977	607,856	13,963	1.52 (1.46, 1.57)	20 (18, 22)
70-79 yrs	415,556	90,404	8,629	325,152	18,161	1.48 (1.43, 1.52)	43 (39, 46)
80-89 yrs	180,455	42,039	6,312	138,416	13,187	1.40 (1.35, 1.45)	75 (67, 82)
90+ yrs	40,898	7,171	1,002	33,727	2,721	1.54 (1.42, 1.66)	124 (100, 146)
Electrolyte abnormalities							
40-49 yrs	1,374,236	100,674	1,416	1,273,562	7,481	1.44 (1.35, 1.55)	5 (4, 6)
50-59 yrs	1,092,986	122,158	2,545	970,828	10,007	1.20 (1.14, 1.27)	4 (3, 5)
60-69 yrs	729,552	121,697	4,879	607,855	12,790	1.50 (1.44, 1.56)	17 (15, 19)
70-79 yrs	415,563	90,407	6,506	325,156	14,650	1.45 (1.40, 1.50)	33 (30, 36)
80-89 yrs	180,454	42,037	4,488	138,417	8,882	1.54 (1.48, 1.60)	74 (67, 82)
90+ yrs	40,897	7,171	607	33,726	1,564	1.64 (1.48, 1.81)	103 (80, 128)
Gout							
40-49 yrs	1,374,199	100,670	4,029	1,273,529	29,325	1.32 (1.27, 1.38)	10 (8, 12)
50-59 yrs	1,092,962	122,153	6,147	970,809	27,061	1.22 (1.18, 1.26)	8 (6, 9)
60-69 yrs	729,527	121,690	7,341	607,837	19,188	1.38 (1.33, 1.42)	16 (14, 18)
70-79 yrs	415,550	90,402	5,478	325,148	10,516	1.55 (1.49, 1.61)	25 (23, 27)
80-89 yrs	180,453	42,035	1,777	138,418	3,046	1.47 (1.37, 1.57)	19 (15, 23)
90+ yrs	40,898	7,171	183	33,727	410	1.63 (1.35, 1.96)	21 (12, 31)

0.5   1   1.5   2
Treatment better   Treatment worse

-50   0   50   100   150
Treatment better   Treatment worse

Fig 2. Association between antihypertensive treatment and serious adverse events leading to hospitalisation, by age at the index date.

https://doi.org/10.1371/journal.pmed.1004885.g002

Subgroup	Total population	Intervention population	Intervention events	Control population	Control events	Adjusted Hazard ratio (95% CI)	Absolute risk difference (additional events per 10,000 patients per year) (95% CI)
Falls (primary outcome)							
Fit	3,541,011	391,467	18,060	3,149,544	90,707	1.10 (1.08, 1.12)	5 (4, 6)
Mild frailty	255,795	80,387	10,461	175,408	20,535	0.96 (0.94, 0.99)	-7 (-13, -1)
Moderate frailty	32,550	10,893	2,461	21,657	3,951	1.05 (0.99, 1.11)	14 (-6, 33)
Severe frailty	4,287	1,387	388	2,900	622	1.13 (0.98, 1.30)	39 (-17, 83)
Hypotension							
Fit	3,541,033	391,469	7,353	3,149,564	28,935	1.35 (1.31, 1.39)	6 (5, 6)
Mild frailty	255,812	80,390	4,043	175,422	5,900	1.14 (1.09, 1.20)	10 (6, 15)
Moderate frailty	32,562	10,897	806	21,665	1,052	1.19 (1.07, 1.32)	25 (7, 40)
Severe frailty	4,290	1,388	128	2,902	176	1.08 (0.84, 1.38)	15 (-37, 67)
Syncope							
Fit	3,541,022	391,470	9,794	3,149,552	44,593	1.22 (1.19, 1.26)	5 (5, 6)
Mild frailty	255,805	80,389	4,383	175,416	7,277	1.03 (0.99, 1.08)	3 (-2, 7)
Moderate frailty	32,559	10,895	768	21,664	1,048	1.10 (0.99, 1.22)	14 (-5, 30)
Severe frailty	4,290	1,388	90	2,902	141	0.96 (0.72, 1.28)	-7 (-54, 38)
Fracture							
Fit	3,541,007	391,467	15,377	3,149,540	96,419	1.01 (0.99, 1.03)	1 (0, 2)
Mild frailty	255,800	80,389	6,442	175,411	14,734	0.85 (0.82, 0.88)	-23 (-29, -18)
Moderate frailty	32,560	10,896	1,238	21,664	2,257	0.95 (0.88, 1.03)	-13 (-32, 6)
Severe frailty	4,289	1,388	182	2,901	293	1.09 (0.88, 1.33)	22 (-39, 78)
Acute kidney injury							
Fit	3,541,031	391,471	15,022	3,149,560	51,541	1.43 (1.40, 1.46)	13 (12, 14)
Mild frailty	255,807	80,387	8,965	175,420	10,473	1.33 (1.28, 1.37)	40 (35, 45)
Moderate frailty	32,559	10,896	1,966	21,663	2,054	1.29 (1.20, 1.38)	65 (50, 84)
Severe frailty	4,289	1,388	330	2,901	313	1.51 (1.27, 1.79)	131 (75, 190)
Electrolyte abnormalities							
Fit	3,541,031	391,470	12,147	3,149,561	44,701	1.46 (1.43, 1.50)	12 (11, 13)
Mild frailty	255,807	80,389	6,659	175,418	8,835	1.29 (1.25, 1.34)	31 (26, 36)
Moderate frailty	32,561	10,897	1,416	21,664	1,605	1.32 (1.22, 1.43)	62 (42, 80)
Severe frailty	4,289	1,388	219	2,901	233	1.39 (1.13, 1.70)	86 (36, 138)
Gout							
Fit	3,540,941	391,456	19,667	3,149,485	84,732	1.33 (1.31, 1.36)	12 (11, 13)
Mild frailty	255,801	80,384	4,618	175,417	4,359	1.47 (1.40, 1.54)	22 (19, 25)
Moderate frailty	32,557	10,893	612	21,664	415	1.61 (1.40, 1.86)	33 (22, 43)
Severe frailty	4,290	1,388	58	2,902	40	1.57 (1.00, 2.47)	28 (0, 59)

0.50   1.00   1.50   2.00   -50   0   50   100   150
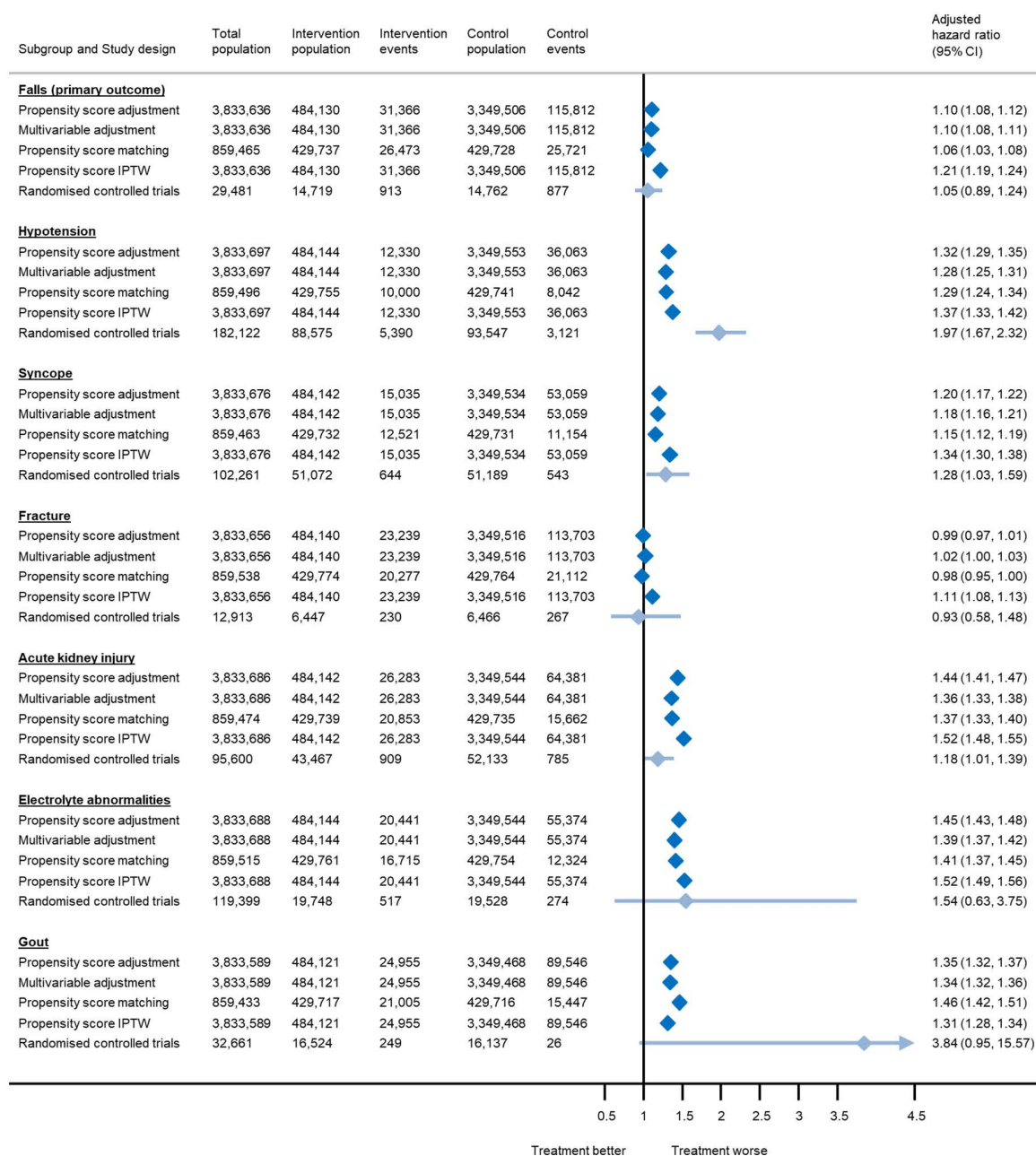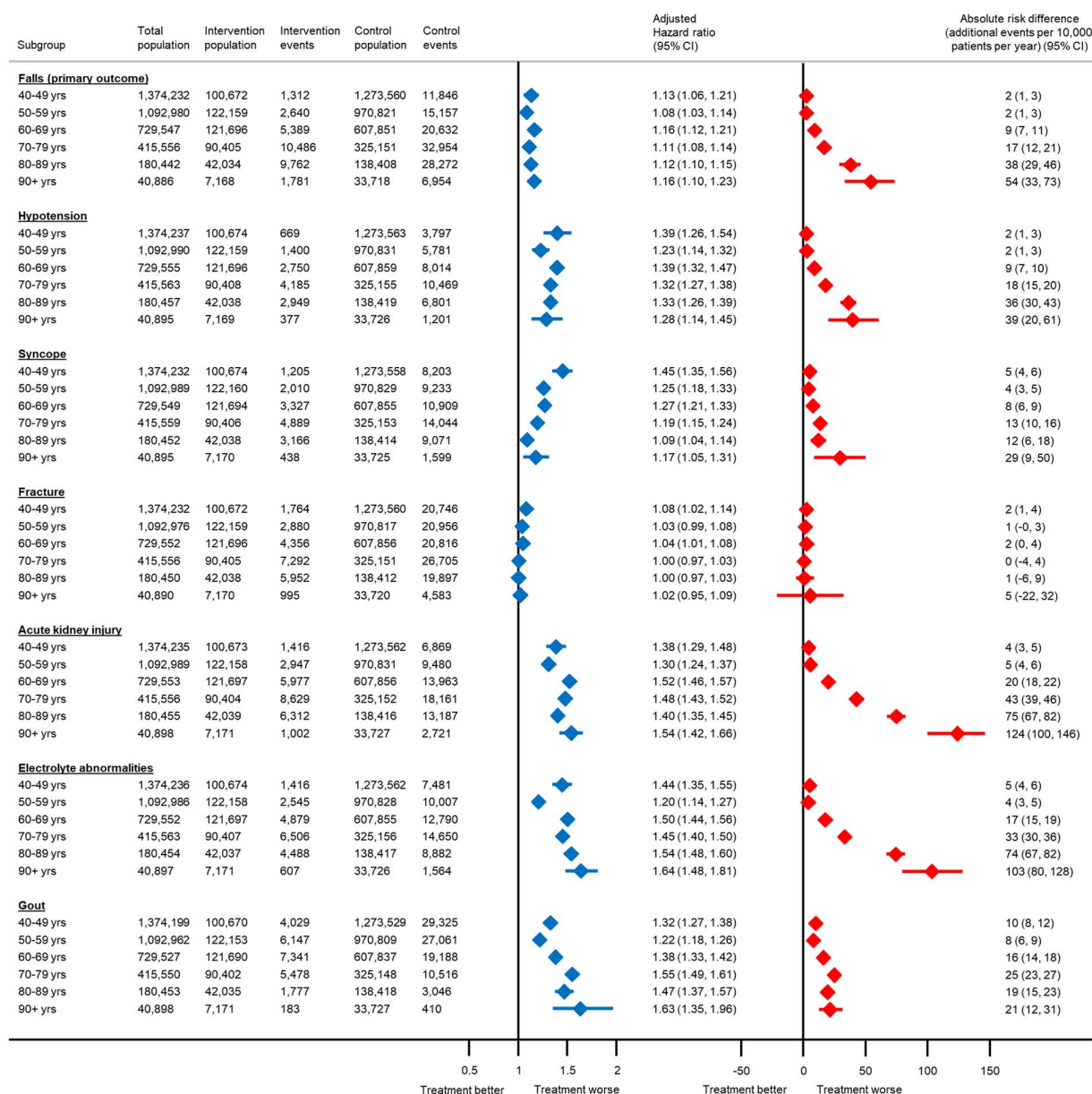
Treatment better   Treatment worse   Treatment better   Treatment worse
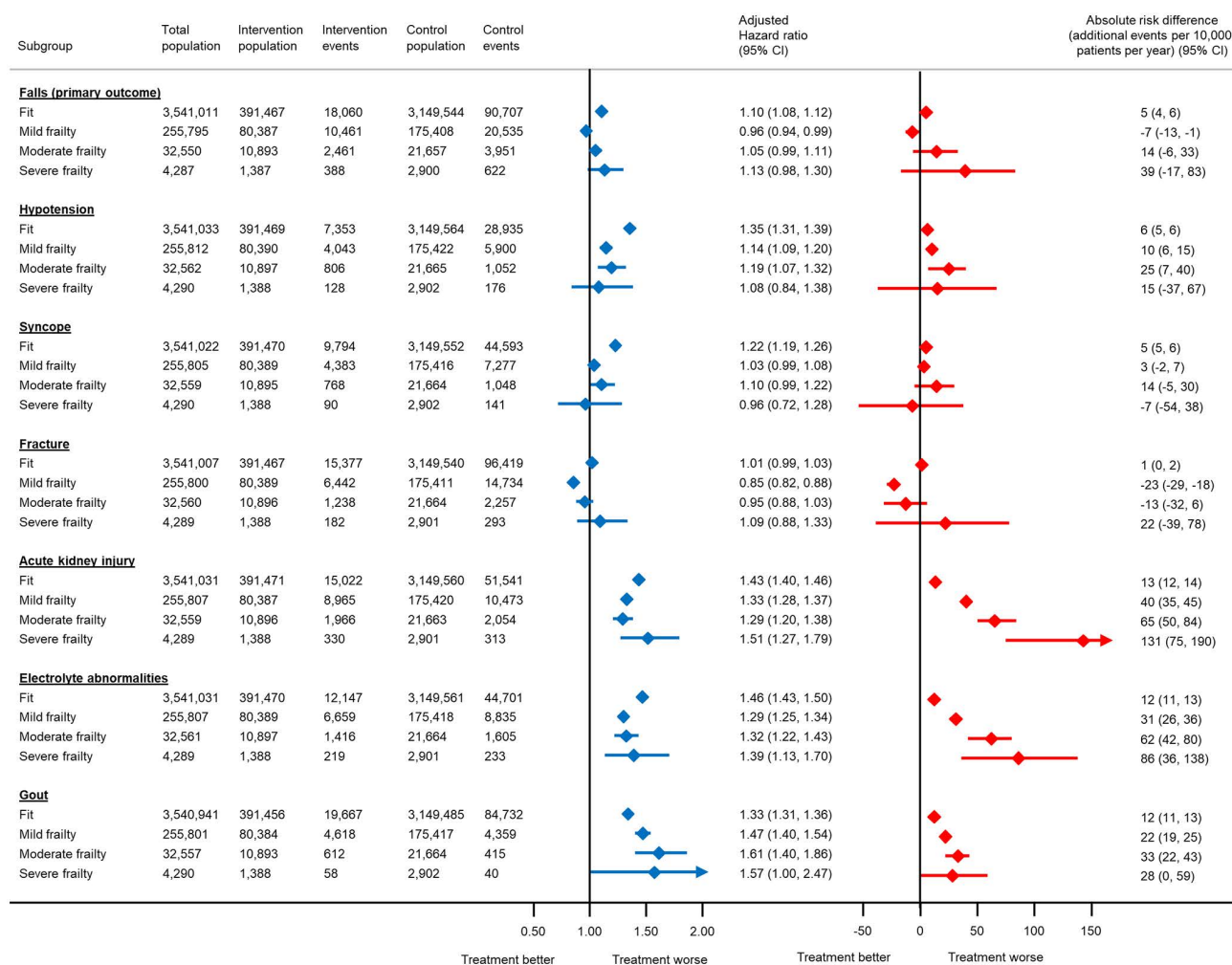
Fig 3. Association between antihypertensive treatment and serious adverse events leading to hospitalisation, by frailty status at the index date.

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