Certainty assessment							Summary of findings				
No. of participants (studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall certainty of evidence**	**Study event rates (%)**		**Relative effect (95% CI)**	**Anticipated absolute effects**	
							With low dose ACEI	**With high dose ACEI**		**Risk with low dose ACEI**	**Risk difference with high dose ACEI**
All cause mortality											
5 828 (8 RCTs)	not serious	not serious	not serious	serious [a]	none	⊕⊕⊕◯ MODERATE	800/3257 (24.6%)	726/2571 (28.2%)	**RR 0.95** (0.88 to 1.02)	246 per 1.000	**12 fewer per 1.000** (29 fewer to 5 more)
Cardiovascular mortality											
4 048 (6 RCTs)	not serious	not serious	not serious	serious [b]	none	⊕⊕⊕◯ MODERATE	662/2119 (31.2%)	601/1929 (31.2%)	**RR 0.93** (0.85 to 1.01)	312 per 1.000	**22 fewer per 1.000** (47 fewer to 3 more)
All cause hospitalization											
5 394 (5 RCTs)	not serious	not serious	not serious [c]	serious [d]	none	⊕⊕⊕◯ MODERATE	863/2981 (29.0%)	731/2413 (30.3%)	**RR 0.95** (0.82 to 1.10)	290 per 1.000	**14 fewer per 1.000** (52 fewer to 29 more)
Cardiovascular hospitalization											
5 242 (4 RCTs)	serious [e]	not serious	not serious [f]	serious [g]	none	⊕⊕◯◯ LOW	633/2880 (22.0%)	590/2362 (25.0%)	**RR 0.98** (0.83 to 1.17)	220 per 1.000	**4 fewer per 1.000** (37 fewer to 37 more)
Functional capacity											
555 (4 RCTs)	serious [h]	not serious	not serious	serious [i]	none	⊕⊕◯◯ LOW	-	-	-	-	SMD **0.38 higher** (0.20 higher to 0.55 higher)
Side effects – Hypotension											
3 783 (4 RCTs)	serious [h,j]	not serious	not serious	not serious	none	⊕⊕⊕◯ MODERATE	111/1955 (5.7%)	178/1828 (9.7%)	**RR 1.64** (1.30 to 2.05)	57 per 1.000	**36 more per 1.000** (17 more to 60 more)
Side effects – Dizziness											

4 994 (3 RCTs)	serious [h,j]	not serious	not serious	serious [k]	none	⊕⊕◯◯ LOW	391/2758 (14.2%)	414/2236 (18.5%)	**RR 1.37** (0.97 to 1.93)	142 per 1.000	**52 more per 1.000** (4 fewer to 32 more)
Side effects – Cough											
5 146 (4 RCTs)	serious [h,j]	not serious	not serious	not serious	none	⊕⊕⊕◯ MODERATE	380/2859 (13.3%)	253/2287 (11.1%)	**RR 0.85** (0.73 to 0.98)	133 per 1.000	**20 fewer per 1.000** (6 fewer to 3 fewer)
Quality of life											
144 (1 RCT)	serious [h]	not serious	not serious	not serious	none	⊕⊕⊕◯ MODERATE	The baseline mean score for all patients was 44 points. After 3 months, the mean change for the high dose ACEI group was -6 points and for the low dose ACEI group was -10 points. Mean difference between groups was -4 points.				

CI, Confidence interval; RR, Risk ratio; MD, Mean difference

Explanations:

a. For clinically important reduction (considered as a 10% relative risk reduction), optimum information size was not reached (DARIS = 9097).

b. For clinically important reduction (considered as a 10% relative risk reduction), optimum information size was not reached (DARIS = 7109).

c. In one study (The Network, 1998), it is not clear if the number of hospitalizations reported accounts only for first hospitalization or also cases of re-hospitalization. However, the quality of the outcome was not downgraded because this study showed results similar to those of the other studies included in this analysis.

d. For clinically important reduction (considered as 10% relative risk reduction), optimum information size was not reached (DARIS = 23717).

e. Clement, 2000 and Nanas, 2000 present high risk of bias for this outcome on the outcome measurement domain.

f. One study (The Network, 1998) reported only heart failure related hospitalizations, and not hospitalizations for all cardiovascular causes. However, because heart failure is the main cause of cardiovascular hospitalization in other included studies, we included this data in our analysis without downgrading the quality of evidence for indirectness.

g. For clinically important reduction (considered as 10% relative risk reduction), optimum information size was not reached (DARIS = 42372).

h. No protocol was found for any of the included studies; therefore, they were classified as having some concerns regarding selection of reported results for these outcomes.

i. Imprecise confidence interval: in the worst scenario, can increase exercise time by 0.20 SMD, which is considered a small effect; in the best scenario, can increase exercise time by 0.55 SMD, which is considered a moderate effect.

j. Clement, 2000 presents high risk of bias for the outcome measurement domain due to lack of blinding of outcome assessors.

k. Imprecise confidence interval: in the best scenario, high dose ACEIs can decrease the risk of dizziness by 3%; in the worst scenario, they can increase the risk by 93%.