Supplemental Material

Serum Sodium and Impaired Cognition in Older Community-Dwelling Men

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Supplemental Table 1. Associations (β-estimates; 95% CI) between tertiles of serum sodium levels and 3MS score at baseline (cross-sectional analysis)

Variable	Tertile 1 (126-140 mmol/L) (n=1814)	Tertile 2 (141-142 mmol/L) (n=1818)	Tertile 3 (143-153 mmol/L) (n=1803)	Continuous (per 5 mmol/L lower serum sodium)
Unadjusted	6.13 [-3.56, 15.84]	Ref	5.47 [-3.59, 15.20]	-0.49 [-8.21, 7.23]
Model 1	5.51 [-3.04, 14.07]	Ref	4.28 [-4.29, 12.85]	0.63 [-6.18, 7.44]
Model 2	5.63 [-2.92, 14.18]	Ref	3.91 [-4.61, 12.43]	1.26 [-5.56, 8.08]
Model 3	5.41 [-3.11, 13.94]	Ref	3.46 [-5.04, 11.96]	1.54 [-5.26, 8.34]
Model 4	4.14 [-4.50, 12.78]	Ref	2.88 [-5.72, 11.48]	0.48 [-6.42, 7.39]

3MS score, modified mini-mental examination score. 3MS score was transformed in analyses as: log(sqrt(110-3MS score)). All values are $x10^{-3}$. Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol, body-mass index, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=141.

Supplemental Table 2. Associations (β-estimates; 95% CI) between tertiles of serum sodium levels and Trails B time at baseline (cross-sectional analysis)

Variable	Tertile 1 (126-140 mmol/L) (n=1814)	Tertile 2 (141-142 mmol/L) (n=1818)	Tertile 3 (143-153 mmol/L) (n=1803)	Continuous (per 5 mmol/L lower serum sodium)
Unadjusted	3.47 [0.82, 6.12]	Ref	1.16 [-1.49, 3.82]	3.13 [1.02, 5.24]
Model 1	3.29 [0.90, 5.68]	Ref	1.14 [-1.25, 3.53]	2.81 [0.91, 4.71]
Model 2	2.93 [0.56, 5.30]	Ref	1.06 [-1.31, 3.43]	2.68 [0.78, 4.57]
Model 3	2.83 [0.47, 5.18]	Ref	0.90 [-1.45, 3.26]	2.75 [0.86, 4.63]
Model 4	2.83 [0.44, 5.23]	Ref	1.05 [-1.33, 3.44]	2.61 [0.69, 4.52]

Trails B time, Trail Making Test part B time. Trails B time was transformed in analyses as log(Trails B time). All values are $x10^{-2}$. Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index category, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=141.

Supplemental Table 3. Associations (β-estimates; 95% CI) between tertiles of serum sodium levels and change in 3MS score at follow-up (longitudinal analysis)

Variable	Tertile 1 (126-140 mmol/L) (n=1175)	Tertile 2 (141-142 mmol/L) (n=1214)	Tertile 3 (143-153 mmol/L) (n=1222)	Continuous (per 5 mmol/L lower serum sodium)
Unadjusted	-0.17 [-0.65, 032]	Ref	0.07 [-0.41, 0.55]	-0.06 [-0.37, 0.25]
Model 1	-0.16 [-0.64, 0.32]	Ref	0.07 [-0.41, 0.54]	-0.02 [-0.32, 0.28]
Model 2	-0.15 [-0.63, 0.33]	Ref	0.06 [-0.41, 0.54]	0.02 [-0.29, 0.32]
Model 3	-0.12 [-0.59, 0.36]	Ref	0.05 [-0.43, 0.52]	0.06 [-0.24, 0.37]
Model 4	-0.16 [-0.64, 0.32]	Ref	-0.02 [-0.50, 0.45]	0.09 [-0.22, 0.40]

3MS score, modified mini-mental examination score. Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index category, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=81.

Supplemental Table 4. Associations (β-estimates; 95% CI) between tertiles of serum sodium levels and change in Trails B time at follow-up (longitudinal analysis)

Variable	Tertile 1 (126-140 mmol/L) (n=1175)	Tertile 2 (141-142 mmol/L) (n=1214)	Tertile 3 (143-153 mmol/L) (n=1222)	Continuous (per 5 mmol/L lower serum sodium)
Unadjusted	-0.93 [-4.52, 2.66]	Ref	-0.72 [-4.52, 2.66]	-0.88 [-3.78, 2.03]
Model 1	-0.91 [-4.48, 2.66]	Ref	-0.75 [-4.29, 2.79]	-0.91 [-3.80, 1.98]
Model 2	-0.77 [-4.35, 2.81]	Ref	-0.64 [-4.18, 2.90]	-0.91 [-3.81, 1.99]
Model 3	-0.97 [-4.56, 2.61]	Ref	-0.60 [-4.14, 2.95]	-1.12 [-4.03, 1.79]
Model 4	-0.88 [-4.51, 2.75]	Ref	-0.17 [-3.76, 3.42]	-1.37 [-4.32, 1.59]

Trails B score, Trail Making Test part B score. Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index cateogry, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=81.

Supplemental Table 5. Associations (odds ratio; 95% CI) between clinical cut-offs of serum sodium levels and prevalent cognitive impairment (cross-sectional analysis)

Model	Hyponatremia (<136 mmol/L) (n=100)	Normonatremia (136-145 mmol/L) (n=5120)	Hypernatremia (>145 mmol/L) (n=215)	Continuous (per 5 unit lower serum sodium)
Unadjusted	1.95 [1.22, 3.13]	Ref	1.40 [0.97, 2.01]	1.19 [1.02, 1.37]
Model 1	2.30 [1.39, 3.82]	Ref	1.35 [0.91, 2.00]	1.24 [1.06, 1.45]
Model 2	2.42 [1.45, 4.03]	Ref	1.37 [0.93, 2.03]	1.25 [1.07, 1.47]
Model 3	2.38 [1.42, 3.98]	Ref	1.39 [0.94, 2.06]	1.24 [1.05, 1.45]
Model 4	2.35 [1.39, 3.97]	Ref	1.40 [0.94, 2.08]	1.24 [1.05, 1.46]

Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index category, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=141.

Supplemental Table 6. Associations (odds ratio; 95% CI) between clinical cut-offs of serum sodium levels and cognitive decline (longitudinal analysis)

Model	Hyponatremia (<136 mmol/L) (n=52)	Normonatremia (136-145 mmol/L) (n=3417)	Hypernatremia (>145 mmol/L) (n=142)	Continuous (per 5 unit lower serum sodium)
Unadjusted	0.77 [0.30, 1.94]	Ref	1.32 [0.83, 2.11]	1.01 [0.83, 1.24]
Model 1	0.73 [0.28, 1.87]	Ref	1.34 [0.83, 2.15]	0.99 [0.81, 1.22]
Model 2	0.73 [0.28, 1.89]	Ref	1.32 [0.82, 2.12]	1.00 [0.82, 1.22]
Model 3	0.74 [0.28, 1.91]	Ref	1.33 [0.82, 2.14]	0.99 [0.81, 1.21]
Model 4	0.74 [0.29, 1.92]	Ref	1.39 [0.86, 2.25]	0.97 [0.79, 1.19]

Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index category, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=81.

Supplemental Table 7. Associations (odds ratio; 95% CI) between quartiles of serum sodium levels and prevalent cognitive impairment (cross-sectional analysis).

Model	Quartile 1 (126-139 mmol/L) (n=1083)	Quartile 2 (140-141 mmol/L) (n=1618)	Quartile 3 (142 mmol/L) (n=931)	Quartile 4 (143-153 mmol/L) (n=1803)	Continuous (per 5 mmol/L lower serum sodium)
Unadjusted	1.39 [1.11, 1.72]	Ref	0.98 [0.77, 1.25]	1.08 [0.88, 1.31]	1.19 [1.02, 1.37]
Model 1	1.43 [1.13, 1.80]	Ref	0.91 [0.70, 1.18]	1.05 [0.85, 1.31]	1.24 [1.06, 1.45]
Model 2	1.47 [1.16, 1.87]	Ref	0.91 [0.70, 1.19]	1.06 [0.86, 1.32]	1.25 [1.07, 1.47]
Model 3	1.44 [1.14, 1.83]	Ref	0.92 [0.71, 1.20]	1.07 [0.86, 1.32]	1.24 [1.05, 1.45]
Model 4	1.47 [1.15, 1.88]	Ref	0.91 [0.70, 1.20]	1.07 [0.86, 1.34]	1.24 [1.05, 1.46]

Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index category, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=141.

Supplemental Table 8. Associations (odds ratio; 95% CI) between quartiles of serum sodium levels and cognitive decline (longitudinal analysis).

Model	**Quartile 1** (126-139 mmol/L) (n=687)	**Quartile 2** (140-141 mmol/L) (n=1076)	**Quartile 3** (142 mmol/L) (n=626)	**Quartile 4** (143-153 mmol/L) (n=1222)	**Continuous** (per 5 mmol/L lower serum sodium)
Unadjusted	1.33 [1.00, 1.76]	Ref	0.94 [0.68, 1.29]	1.19 [0.93, 1.53]	1.01 [0.83, 1.24]
Model 1	1.31 [0.98, 1.75]	Ref	0.92 [0.67, 1.27]	1.20 [0.92, 1.55]	0.99 [0.81, 1.22]
Model 2	1.31 [0.98, 1.76]	Ref	0.92 [0.66, 1.27]	1.20 [0.92, 1.55]	1.00 [0.82, 1.22]
Model 3	1.31 [0.98, 1.76]	Ref	0.92 [0.67, 1.27]	1.20 [0.93, 1.55]	0.99 [0.81, 1.21]
Model 4	1.28 [0.95, 1.73]	Ref	0.89 [0.64, 1.24]	1.22 [0.94, 1.59]	0.97 [0.79, 1.19]

Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index category, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life and serum glucose level. Serum glucose level is missing in n=81.

Supplemental Table 9. Associations (odds ratio; 95% CI) between categories of serum sodium levels (<136, 136-138, 139-140, 141-142, 143-144, and ≥145 mmol/L) and prevalent cognitive impairment (cross-sectional analysis)

Model	Category 1 (<136 mmol/L) (n=100)	Category 2 (136-138 mmol/L) (n=528)	Category 3 (139-140 mmol/L) (n=1186)	Category 4 (141-142 mmol/L) (n=1818)	Category 5 (143-144 mmol/L) (n=1275)	Category 6 (≥145) (n=528)
Unadjusted	2.12 [1.30, 3.44]	1.44 [1.10, 1.88]	1.12 [0.90, 1.39]	Ref	1.05 [0.85, 1.31]	1.21 [0.91, 1.60]
Model 1	2.53 [1.50, 4.25]	1.43 [1.07, 1.90]	1.17 [0.92, 1.43]	Ref	1.06 [0.84, 1.33]	1.23 [0.91, 1.66]
Model 2	2.67 [1.58, 4.51]	1.47 [1.10, 1.96]	1.16 [0.92, 1.47]	Ref	1.06 [0.84, 1.34]	1.23 [0.91, 1.67]
Model 3	2.61 [1.54, 4.43]	1.44 [1.07, 1.92]	1.14 [0.90, 1.45]	Ref	1.06 [0.84, 1.33]	1.23 [0.91, 1.66]
Model 4	2.59 [1.54, 4.44]	1.43 [1.06, 1.93]	1.16 [0.91, 1.48]	Ref	1.06 [0.84, 1.34]	1.24 [0.91, 1.69]

Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index category, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=141.

Supplemental Table 10. Associations (odds ratio; 95% CI) between categories of serum sodium levels (<136, 136-138, 139-140, 141-142, 143-144, and ≥145 mmol/L) and cognitive decline (longitudinal analysis)

Model	Category 1 (<136 mmol/L) (n=52)	Category 2 (136-138 mmol/L) (n=333)	Category 3 (139-140 mmol/L) (n=790)	Category 4 (141-142 mmol/L) (n=1214)	Category 5 (143-144 mmol/L) (n=855)	Category 6 (≥145) (n=367)
Unadjusted	0.93 [0.36, 2.37]	1.99 [1.43, 2.78]	1.15 [0.86, 1.53]	Ref	1.27 [0.97, 1.67]	1.37 [0.97, 1.95]
Model 1	0.88 [0.34, 2.30]	1.95 [1.39, 2.75]	1.17 [0.88, 1.57]	Ref	1.26 [0.96, 1.67]	1.47 [1.02, 2.09]
Model 2	0.90 [0.35, 2.36]	1.97 [1.40, 2.78]	1.18 [0.88, 1.58]	Ref	1.28 [0.97, 1.69]	1.45 [1.01, 2.08]
Model 3	0.90 [0.34, 2.38]	1.95 [1.39, 2.75]	1.17 [0.88, 1.57]	Ref	1.28 [0.97, 1.69]	1.45 [1.01, 2.07]
Model 4	0.94 [0.36, 2.47]	1.93 [1.35, 2.74]	1.25 [0.93, 1.68]	Ref	1.34 [1.01, 1.78]	1.53 [1.06, 2.21]

Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol intake, body-mass index category, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=141.

Supplemental Table 11. Associations (odds ratio; 95% CI) between tertiles of serum sodium levels and prevalent cognitive impairment, excluding individuals with serum sodium level <136 mmol/L (cross-sectional analysis)

Variable	Tertile 1 (136-140 mmol/L) (n=1714)	Tertile 2 (141-142 mmol/L) (n=1818)	Tertile 3 (143-153 mmol/L) (n=1803)	Continuous (per 5 mmol/L lower serum sodium)
Unadjusted	1.22 [1.00, 1.47]	Ref	1.09 [0.90, 1.33]	1.09 [0.92, 1.29]
Model 1	1.25 [1.01, 1.54]	Ref	1.11 [0.90, 1.36]	1.12 [0.93, 1.34]
Model 2	1.26 [1.02, 1.55]	Ref	1.11 [0.90, 1.37]	1.13 [0.94, 1.35]
Model 3	1.23 [1.00, 1.52]	Ref	1.10 [0.90, 1.36]	1.11 [0.93, 1.34]
Model 4	1.25 [1.00, 1.55]	Ref	1.11 [0.90, 1.38]	1.11 [0.92, 1.34]

3MS score, modified mini-mental examination score. Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol, body-mass index, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=102.

Supplemental Table 12. Associations (odds ratio; 95% CI) between tertiles of serum sodium levels and cognitive decline, excluding individuals with serum sodium level <136 mmol/L (longitudinal analysis)

Variable	Tertile 1 (136-140 mmol/L) (n=1123)	Tertile 2 (141-142 mmol/L) (n=1214)	Tertile 3 (143-153 mmol/L) (n=1222)	Continuous (per 5 mmol/L lower serum sodium)
Unadjusted	1.38 [1.08, 1.78]	Ref	1.30 [1.02, 1.67]	1.07 [0.86, 1.32]
Model 1	1.39 [1.08, 1.80]	Ref	1.32 [1.03, 1.70]	1.05 [0.84, 1.34]
Model 2	1.41 [1.09, 1.82]	Ref	1.33 [1.03, 1.71]	1.05 [0.84, 1.31]
Model 3	1.40 [1.08, 1.81]	Ref	1.33 [1.03, 1.71]	1.04 [0.83, 1.30]
Model 4	1.44 [1.11, 1.88]	Ref	1.40 [1.08, 1.81]	1.02 [0.81, 1.28]

3MS score, modified mini-mental examination score. Model 1: adjusted for age, race/ethnicity, and education. Model 2: adjusted for model 1, smoking, alcohol, body-mass index, and physical activity. Model 3: Model 2 + estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration equation), and history of cardiovascular disease, diabetes, hypertension, stroke and chronic obstructive pulmonary disease. Model 4: model 3 + quality of life measures and serum glucose level. Serum glucose level is missing in n=52.