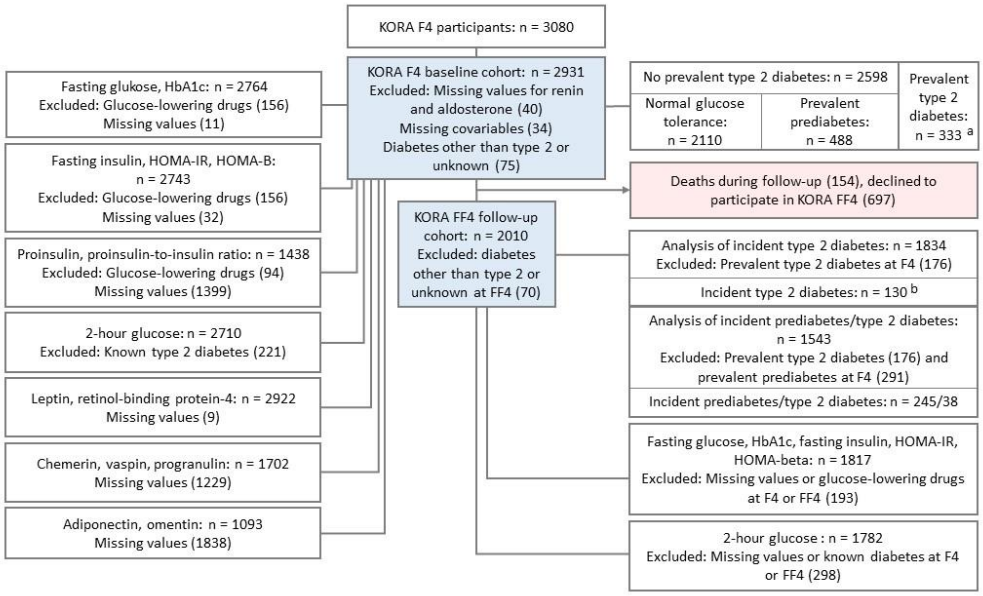
**Supplementary Figure 1** Flow chart showing sample sizes and reasons for exclusions. The median (1st; 3rd quartile) follow-up time was 6.5 (6.3; 6.6) years between KORA F and KORA FF4.




[a] In KORA F4, type 2 diabetes was newly diagnosed by oral glucose tolerance test in 112 participants and was previously known in 221 cases.

[b] In KORA FF4, incident type 2 diabetes was newly diagnosed by oral glucose tolerance test in 70 participants and was diagnosed by the treating physician between F4 and FF4 in 60 participants. N = 92 participants with incident type 2 diabetes in KORA FF4 had progressed from prediabetes in KORA F4, n = 38 participants had progressed from normal glucose tolerance in KORA F4.

**Supplementary Table 1** Odds ratios (95% confidence interval) for prevalent prediabetes (versus normal glucose tolerance) and prevalent type 2 diabetes (versus no type 2 diabetes) per standard deviation increase of active plasma renin concentration, aldosterone and ARR after exclusion of participants taking angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, diuretics or calcium channel blockers.

| | Prevalent prediabetes (yes: n = 253; no: n = 1666) | P value | Prevalent type 2 diabetes (yes: n = 90; no: n = 1919) | P value |
|---|---|---|---|---|
| Renin | **1.26 (1.08,1.46)** | **0.003** | **1.49 (1.18,1.89)** | **< 0.001** |
| Aldosterone | 1.17 (1,1.36) | 0.048 | 1.05 (0.83,1.33) | 0.685 |
| ARR | 0.93 (0.8,1.08) | 0.329 | **0.72 (0.57,0.91)** | **0.005** |

Bold print indicates significance after correction for multiple testing using the Bonferroni method ($p < 0.008$ ($0.05 \div 6$)). Abbreviations: ARR: aldosterone-to-renin-ratio.

The logistic regression models were adjusted for sex, age, BMI, arterial hypertension, eGFR and potassium.

**Supplementary Table 2** Cross-sectional beta estimates ± standard error of the association of active plasma renin concentration, aldosterone and ARR (per standard deviation increase) and continuous measures of glucose metabolism (per standard deviation) after exclusion of participants taking angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, diuretics or calcium channel blockers.

| | n | Renin | Aldosterone | ARR |
|---|---|---|---|---|
| Fasting glucose | 1971 | **0.07 ± 0.02** *** | 0.01 ± 0.02 | **−0.07 ± 0.02** *** |
| 2-hour glucose | 1953 | **0.07 ± 0.02** ** | 0.03 ± 0.02 | −0.04 ± 0.02 |
| HbA1c | 1971 | 0.04 ± 0.02 | −0.01 ± 0.02 | −0.05 ± 0.02 * |
| Insulin | 1954 | **0.10 ± 0.02** *** | **0.07 ± 0.02** *** | −0.04 ± 0.02 |
| Proinsulin | 1001 | 0.08 ± 0.03 * | 0.08 ± 0.03 ** | −0.01 ± 0.03 |
| Proinsulin-to-insulin ratio | 1001 | −0.00 ± 0.03 | 0.05 ± 0.03 | 0.04 ± 0.03 |
| HOMA-B | 1954 | 0.05 ± 0.02 * | 0.06 ± 0.02 ** | 0.01 ± 0.02 |
| HOMA-IR | 1954 | **0.11 ± 0.02** *** | **0.07 ± 0.02** *** | −0.05 ± 0.02 * |

* p < 0.05; ** p < 0.01; *** p < 0.001; bold print indicates significance after correction for multiple testing using the Bonferroni method (p < 0.0021 (0.05 ÷ 24)). Abbreviations: ARR: aldosterone-to-renin-ratio.

The linear regression models were adjusted for sex, age, BMI, arterial hypertension, eGFR and potassium.

**Supplementary Table 3** Cross-sectional beta estimates ± standard error of the association of active plasma renin concentration, aldosterone and ARR (per standard deviation increase) and adipokines (per standard deviation) after exclusion of participants taking angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, diuretics or calcium channel blockers.

| | n | Renin | Aldosterone | ARR |
|---|---|---|---|---|
| Leptin | 2005 | 0.03 ± 0.01 * | **0.04 ± 0.01** *** | 0.01 ± 0.01 |
| Retinol-binding protein-4 | 2005 | 0.01 ± 0.02 | 0.05 ± 0.02 * | 0.03 ± 0.02 |
| Adiponectin | 455 | −0.09 ± 0.04 * | −0.04 ± 0.04 | 0.03 ± 0.04 |
| Omentin-1 | 455 | 0.00 ± 0.05 | −0.06 ± 0.05 | −0.08 ± 0.05 |
| Chemerin | 1047 | 0.05 ± 0.03 | 0.01 ± 0.03 | −0.03 ± 0.03 |
| Progranulin | 1047 | −0.03 ± 0.03 | −0.04 ± 0.03 | 0.00 ± 0.03 |
| Vaspin | 1047 | −0.03 ± 0.03 | 0.05 ± 0.03 | 0.07 ± 0.03 * |

* p < 0.05; ** p < 0.01; *** p < 0.001; bold print indicates significance after correction for multiple testing using the Bonferroni method (p < 0.0024 (0.05 ÷ 21)). Abbreviations: ARR: aldosterone-to-renin-ratio.

The linear regression models were adjusted for sex, age, BMI, arterial hypertension, eGFR and potassium.

**Supplementary Table 4** Odds ratios (95% confidence interval) for incident prediabetes/type 2 diabetes (versus non-progressors to prediabetes/type 2 diabetes from normal glucose tolerance) and incident type 2 diabetes (versus non-progressors to type 2 diabetes from normal glucose tolerance or prediabetes) active plasma renin concentration, aldosterone and ARR (per standard deviation increase) after exclusion of participants taking angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, diuretics or calcium channel blockers.

| | Incident prediabetes/type 2 diabetes (yes: n = 191 [a]; no: n = 1068) | P value | Incident type 2 diabetes (yes: n = 67; no: n = 1362) | P value |
|---|---|---|---|---|
| Renin | 1.23 (1.03-1.46) | 0.023 | 1.15 (0.88-1.51) | 0.316 |
| Aldosterone | 1.03 (0.86-1.24) | 0.718 | 1.05 (0.80-1.39) | 0.725 |
| ARR | 0.86 (0.72-1.03) | 0.101 | 0.90 (0.68-1.17) | 0.429 |

[a] Includes 167 cases of incident prediabetes in KORA FF4 and 24 cases of incident type 2 diabetes in KORA FF4 that had progressed from normal glucose tolerance in KORA F4.

Significance level after correction for multiple testing using the Bonferroni method ($p < 0.008$ ($0.05 \div 6$)). Abbreviations: ARR: aldosterone-to-renin-ratio.

The linear regression models were adjusted for sex, age, BMI, arterial hypertension, eGFR and potassium.

**Supplementary Table 5** Longitudinal beta estimates ± standard error of the association of active plasma renin concentration, aldosterone and ARR (per standard deviation increase) and deltas of continuous measures of glucose metabolism (per standard deviation).

| Delta | n | Renin | Aldosterone | ARR |
|---|---|---|---|---|
| Fasting glucose | 1817 | −0.08 ± 0.03 ** | −0.00 ± 0.02 | 0.07 ± 0.03 ** |
| 2-hour glucose | 1782 | 0.01 ± 0.023 | 0.01 ± 0.02 | 0.00 ± 0.02 |
| HbA1c | 1817 | −0.06 ± 0.03 * | −0.02 ± 0.02 | 0.03 ± 0.03 |
| Insulin | 1817 | **−0.12 ± 0.02** *** | −0.05 ± 0.02 * | **0.07 ± 0.02** *** |
| HOMA-B | 1817 | 0.03 ± 0.03 | 0.01 ± 0.02 | −0.02 ± 0.03 |
| HOMA-IR | 1817 | −0.02 ± 0.03 | 0.01 ± 0.02 | 0.03 ± 0.03 |

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; bold print indicates significance after correction for multiple testing using the Bonferroni method ($p < 0.0028$ ($0.05 \div 18$)).

Abbreviations: ARR: aldosterone-to-renin-ratio.

The linear regression models were adjusted for sex, age, BMI, arterial hypertension, eGFR, potassium, use of angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, diuretics and calcium channel blockers.

**Supplementary Table 6** Longitudinal beta estimates ± standard error of the association of active plasma renin concentration, aldosterone and ARR (per standard deviation increase) and deltas of continuous measures of glucose metabolism (per standard deviation) after exclusion of participants

taking angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, diuretics or calcium channel blockers.

| Delta | n | Renin | Aldosterone | ARR |
|---|---|---|---|---|
| Fasting glucose | 1404 | −0.03 ± 0.03 | 0.01 ± 0.03 | 0.02 ± 0.03 |
| 2-hour glucose | 1387 | −0.03 ± 0.03 | −0.00 ± 0.03 | 0.02 ± 0.03 |
| HbA1c | 1404 | 0.00 ± 0.03 | −0.02 ± 0.03 | −0.03 ± 0.03 |
| Insulin | 1404 | **−0.10 ± 0.02 ***** | −0.06 ± 0.02 * | 0.04 ± 0.02 |
| HOMA-B | 1404 | 0.03 ± 0.03 | 0.00 ± 0.03 | −0.03 ± 0.03 |
| HOMA-IR | 1404 | 0.01 ± 0.03 | 0.01 ± 0.03 | −0.00 ± 0.03 |

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; bold print indicates significance after correction for multiple testing using the Bonferroni method ($p < 0.0028$ ($0.05 \div 18$)). Abbreviations: ARR: aldosterone-to-renin-ratio.

The linear regression models were adjusted for sex, age, BMI, arterial hypertension, eGFR and potassium.