Supplemental Material

Supplemental Table 1. Improvement in prediction statistics for CVD risk by adding each additional subclinical measure to conventional predictors in CKD stage 1-2 vs. 3-5

| Predictors | CKD stage 1-2† | | | | | |
|---|---|---|---|---|---|---|
| | ΔC-statistics‡ | Categorical NRI | | Continuous NRI | | IDI |
| | | Event | Non-Event | Event | Non-Event | |
| CAC | 0.027 (-0.022, 0.076) | 0.045 (-0.100, 0.206) | 0.077 (0.015, 0.133) | 0.274 (0.023, 0.503) | 0.222 (0.127, 0.323) | 0.036 (0.019, 0.053) |
| IMT | 0.010 (-0.012, 0.032) | -0.001 (-0.095, 0.075) | 0.005 (-0.037, 0.045) | 0.076 (-0.165, 0.356) | 0.215 (0.118, 0.305) | 0.004 (-0.003, 0.011) |
| ABI | 0.010 (-0.016, 0.036) | 0.001 (-0.092, 0.112) | 0.032 (-0.033, 0.068) | -0.087 (-0.344, 0.175) | 0.028 (-0.087, 0.121) | 0.009 (-0.001, 0.023) |
| Predictors | CKD stage 3-5 | | | | | |
| | ΔC-statistics‡ | Categorical NRI | | Continuous NRI | | IDI |
| | | Event | Non-Event | Event | Non-Event | |
| CAC | 0.028 (-0.000, 0.055) | 0.062 (-0.066, 0.182) | -0.007 (-0.044, 0.033) | 0.318 (0.123, 0.486) | 0.125 (0.050, 0.200) | 0.029 (0.011, 0.045) |
| IMT | -0.000 (-0.007, 0.006) | 0.011 (-0.033, 0.066) | -0.009 (-0.032, 0.015) | -0.041 (-0.244, 0.140) | 0.174 (0.101, 0.248) | 0.004 (-0.000, 0.009) |
| ABI | 0.008 (-0.002, 0.018) | -0.054 (-0.117, 0.010) | 0.011 (-0.010, 0.048) | -0.166 (-0.346, 0.015) | -0.009 (-0.080, 0.067) | 0.001 (-0.006, 0.010) |

NRI: net reclassification improvement, IDI: integrated discrimination improvement, CAC: coronary artery calcium, IMT: intima-media thickness, ABI: ankle brachial index

†CKD stage 1-2 and 3-5 were defined as eGFR ≥60 ml/min/1.73m$^2$ +ACR ≥30 mg/g and eGFR <60 ml/min/1.73m$^2$, respectively.

‡C-statistic with conventional predictors, eGFR and ACR was 0.706 in CKD stage 1-2 and 0.742 in CKD stage 3-5.

Supplemental Table 2. Improvement in prediction statistics for CVD risk by adding each additional subclinical measure to conventional predictors in CKD aged < vs. ≥65 years old

| Predictors | CKD† & age<65 | | | | | |
|---|---|---|---|---|---|---|
| | ΔC-statistics‡ | Categorical NRI | | Continuous NRI | | IDI |
| | | Event | Non-Event | Event | Non-Event | |
| CAC | 0.027 (-0.030, 0.083) | 0.184 (-0.072, 0.381) | 0.032 (-0.028, 0.085) | 0.416 (0.035, 0.710) | 0.469 (0.382, 0.567) | 0.107 (0.053, 0.182) |
| IMT | 0.014 (-0.023, 0.051) | 0.192 (0.000, 0.389) | 0.012 (-0.064, 0.052) | 0.236 (-0.144, 0.581) | 0.406 (0.305, 0.494) | 0.041 (0.005, 0.088) |
| ABI | -0.001 (-0.025, 0.024) | -0.094 (-0.234, 0.030) | -0.006 (-0.043, 0.034) | -0.284 (-0.617, 0.074) | 0.043 (-0.060, 0.151) | 0.034 (0.005, 0.072) |
| Predictors | CKD† & age 65+ | | | | | |
| | ΔC-statistics‡ | Categorical NRI | | Continuous NRI | | IDI |
| | | Event | Non-Event | Event | Non-Event | |
| CAC | 0.030 (0.001, 0.059) | 0.092 (-0.019, 0.179) | 0.051 (0.011, 0.092) | 0.343 (0.176, 0.492) | 0.041 (-0.031, 0.111) | 0.020 (0.011, 0.029) |
| IMT | 0.002 (-0.005, 0.009) | 0.023 (-0.017, 0.070) | 0.006 (-0.021, 0.024) | -0.016 (-0.178, 0.163) | 0.154 (0.082, 0.226) | 0.002 (-0.000, 0.004) |
| ABI | 0.010 (-0.008, 0.028) | -0.005 (-0.061, 0.054) | 0.021 (-0.006, 0.043) | -0.159 (-0.315, 0.021) | 0.101 (0.032, 0.168) | 0.008 (0.000, 0.017) |

NRI: net reclassification improvement, IDI: integrated discrimination improvement, CAC: coronary artery calcium, IMT: intima-media thickness, ABI: ankle brachial index

†CKD was defined as eGFR using the CKD-EPI equation <60 ml/min/1.73m$^2$ or ACR ≥30 mg/g.

‡C-statistic with conventional predictors, eGFR and ACR was 0.813 in CKD and age <65 and 0.686 in CKD and age 65+.

Supplemental Table 3. Improvement in prediction statistics for CVD risk by adding each additional subclinical measure to conventional predictors in CKD eGFR <45 and/or ACR 30+

| Predictors | eGFR <45 and/or ACR 30+ | | | | | |
|---|---|---|---|---|---|---|
| | ΔC-statistics‡ | Categorical NRI | | Continuous NRI | | IDI |
| | | Event | Non-Event | Event | Non-Event | |
| CAC | 0.026 (-0.006, 0.057) | 0.009 (-0.107, 0.118) | 0.076 (0.032, 0.121) | 0.296 (0.115, 0.469) | 0.147 (0.064, 0.223) | 0.027 (0.017, 0.038) |
| IMT | 0.012 (-0.003, 0.027) | -0.005 (-0.070, 0.057) | 0.023 (-0.003, 0.050) | 0.091 (-0.097, 0.292) | 0.229 (0.148, 0.308) | 0.008 (0.002, 0.016) |
| ABI | 0.012 (-0.010, 0.035) | -0.027 (-0.106, 0.056) | 0.029 (-0.004, 0.064) | -0.110 (-0.285, 0.075) | 0.067 (-0.017, 0.160) | 0.021 (0.008, 0.036) |

NRI: net reclassification improvement, IDI: integrated discrimination improvement, CAC: coronary artery calcium, IMT: intima-media thickness, ABI: ankle brachial index

‡C-statistic with conventional predictors, eGFR and ACR was 0.684 in CKD and 0.748 in non-CKD.

Supplemental Table 4. Improvement in prediction statistics for CHD risk by adding each additional subclinical measure to conventional predictors

| Predictors | ΔC-statistics* | Categorical NRI | | Continuous NRI | | IDI |
|---|---|---|---|---|---|---|
| | | Event | Non-event | Event | Non-event | |
| | | | CKD† | | | |
| CAC‡ | 0.074 (0.029, 0.119) | 0.166 (0.025, 0.294) | 0.078 (0.040, 0.114) | 0.312 (0.122, 0.513) | 0.240 (0.182, 0.297) | 0.045 (0.034, 0.059) |
| IMT§ | 0.006 (-0.008, 0.021) | -0.022 (-0.112, 0.071) | 0.025 (0.004, 0.047) | -0.031 (-0.257, 0.161) | 0.201 (0.145, 0.259) | 0.006 (0.001, 0.012) |
| ABI | 0.003 (-0.010, 0.017) | -0.022 (-0.096, 0.054) | 0.019 (0.000, 0.042) | -0.145 (-0.360, 0.059) | 0.094 (0.037, 0.150) | 0.004 (0.000, 0.009) |
| | | | Non-CKD | | | |
| CAC‡ | 0.060 (0.032, 0.088) | 0.219 (0.114, 0.309) | -0.035 (-0.047, -0.024) | 0.340 (0.177, 0.469) | 0.287 (0.259, 0.311) | 0.022 (0.019, 0.027) |
| IMT§ | 0.011 (0.0001, 0.022) | -0.037 (-0.100, 0.025) | 0.009 (0.001, 0.016) | -0.056 (-0.204, 0.087) | 0.158 (0.131, 0.188) | 0.005 (0.003, 0.007) |
| ABI | 0.011 (-0.002, 0.024) | 0.031 (-0.040, 0.101) | 0.012 (0.005, 0.019) | 0.067 (-0.092, 0.231) | 0.103 (0.077, 0.129) | 0.009 (0.006, 0.013) |

NRI: net reclassification improvement, IDI: integrated discrimination improvement, CAC: coronary artery calcium, IMT: carotid intima-media thickness, ABI: ankle-brachial index.

*C-statistic with only conventional predictors was 0.704 in CKD and 0.737 in non-CKD.

†CKD was defined as eGFR using the CKD-EPI equation <60 ml/min/1.73m$^2$ or ACR ≥30 mg/g.

‡ln(CAC score + 1), §Z score for overall maximal internal common carotid IMT

Supplemental Table 5. Improvement in prediction statistics for stroke risk by adding each additional subclinical measure to conventional predictors

| Predictors | ΔC-statistics* | Categorical NRI | Continuous NRI | IDI |
|---|---|---|---|---|
| | | CKD† | | |
| CAC‡ | -0.0006 (-0.002, 0.001) | NA | 0.020 (-0.291, 0.359) | 0.000 (-0.000, 0.000) |
| IMT§ | -0.003 (-0.009, 0.003) | NA | 0.188 (-0.126, 0.517) | 0.000 (-0.000, 0.001) |
| ABI | 0.006 (-0.005, 0.017) | NA | -0.065 (-0.403, 0.280) | 0.001 (-0.000, 0.004) |
| | | Non-CKD | | |
| CAC‡ | 0.002 (-0.019, 0.022) | NA | 0.284 (-0.009, 0.606) | 0.002 (0.001, 0.003) |
| IMT§ | 0.0002 (-0.0004, 0.0007) | NA | -0.022 (-0.284, 0.322) | 0.000 (-0.000, 0.000) |
| ABI | 0.004 (-0.003, 0.011) | 0.023 (0.015, 0.057) | -0.103 (-0.390, 0.219) | 0.000 (-0.000, 0.001) |

NRI: net reclassification improvement, IDI: integrated discrimination improvement, CAC: coronary artery calcium, IMT: carotid intima-media thickness, ABI: ankle-brachial index, NA: NRI was not available due to no reclassification to higher or lower risk categories in some bootstrap samples.

*C-statistic with only conventional predictors was 0.745 in CKD and 0.778 in non-CKD.

†CKD was defined as eGFR using the CKD-EPI equation <60 ml/min/1.73m$^2$ or ACR ≥30 mg/g.

‡ln(CAC score + 1), §Z score for overall maximal internal common carotid IMT

Supplemental Table 6. Improvement in prediction statistics for HF risk by adding each additional subclinical measure to conventional predictors

| Predictors | ΔC-statistics* | Categorical NRI | Continuous NRI | IDI |
|---|---|---|---|---|
| | | | CKD† | |
| CAC‡ | 0.020 (-0.020, 0.059) | 0.086 (-0.067, 0.238) | 0.431 (0.131, 0.670) | 0.008 (0.004, 0.013) |
| IMT§ | 0.006 (-0.002m 0.013) | 0.004 (-0.068, 0.110) | 0.208 (-0.108, 0.499) | 0.000 (-0.001, 0.001) |
| ABI | 0.0004 (-0.002m 0.003) | NA | -0.340 (-0.607, -0.046) | 0.000 (-0.000, 0.000) |
| | | | Non-CKD | |
| CAC‡ | -0.001 (-0.024, 0.022) | 0.098 (0.020, 0.215) | 0.299 (0.051, 0.565) | 0.003 (0.002, 0.005) |
| IMT§ | 0.0004 (-0.002, 0.003) | NA | -0.095 (-0.324, 0.150) | 0.000 (-0.000, 0.000) |
| ABI | 0.0006 (-0.0003, 0.0015) | NA | 0.374 (0.138, 0.603) | -0.000 (-0.000, 0.000) |

NRI: net reclassification improvement, IDI: integrated discrimination improvement, CAC: coronary artery calcium, IMT: carotid intima-media thickness, ABI: ankle-brachial index, NA: NRI was not available due to no reclassification to higher or lower risk categories in some bootstrap samples.

*C-statistic with only conventional predictors was 0.741 in CKD and 0.785 in non-CKD.

†CKD was defined as eGFR using the CKD-EPI equation <60 ml/min/1.73m$^2$ or ACR ≥30 mg/g.

‡ln(CAC score + 1), §Z score for overall maximal internal common carotid IMT

Supplemental Table 7. Improvement in prediction statistics for PAD risk by adding each additional subclinical measure to conventional predictors

| Predictors | ΔC-statistics* | Categorical NRI | Continuous NRI | IDI |
|---|---|---|---|---|
| | | CKD† | | |
| CAC‡ | 0.016 (-0.025, 0.057) | 0.259 (0.094, 0.481) | 0.498 (0.101, 0.832) | 0.019 (0.002, 0.042) |
| IMT§ | 0.027 (-0.011, 0.066) | NA | 0.300 (-0.126, 0.685) | 0.001 (-0.009, 0.011) |
| ABI | 0.092 (0.009, 0.176) | 0.301 (-0.034, 0.604) | 0.787 (0.357, 1.147) | 0.155 (0.074, 0.271) |
| | | Non-CKD | | |
| CAC‡ | 0.055 (0.010, 0.100) | NA | 1.045 (0.665, 1.250) | 0.008 (0.005, 0.015) |
| IMT§ | 0.024 (-0.004, 0.052) | NA | 0.551 (0.133, 0.910) | 0.003 (0.001, 0.008) |
| ABI | 0.071 (0.016, 0.126) | 0.279 (0.020, 0.552) | 0.370 (-0.049, 0.770) | 0.037 (0.018, 0.076) |

NRI: net reclassification improvement, IDI: integrated discrimination improvement, CAC: coronary artery calcium, IMT: carotid intima-media thickness, ABI: ankle-brachial index, NA: NRI was not available due to no reclassification to higher or lower risk categories in some bootstrap samples.

*C-statistic with only conventional predictors was 0.806 in CKD and 0.852 in non-CKD.

†CKD was defined as eGFR using the CKD-EPI equation <60 ml/min/1.73m$^2$ or ACR ≥30 mg/g.

‡ln(CAC score + 1), §Z score for overall maximal internal common carotid IMT