## SUPPLEMENTAL MAETRIAL

## Supplemental tables

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Table S1: Conversion of NT-proBNP from pmol/L to pg/mL					
NT-proBNP [pmol/L]	9	15	28	76	
NT-proBNP [pg/mL]	75	125	233	633	
The conversion factor for NT-proBNP expressed as $pg/mL$ is 1 $pg/mL = 0.12 \text{ pmol/L}$ .					
Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide.					

**<u>Table S2</u>**: Akaike Information Criterion score for different models of the relationships between continuous NT-proBNP levels and screening effects on primary and secondary outcomes

	Linear relationship with NT-proBNP on the original scale	Linear relationship with log-transformed NT-proBNP	Restricted cubic spline model
Stroke or SE	5233.03	5219.72	5226.21
Stroke, SE or cardiovascular death	7863.97	7815.90	7821.99
All-cause death	11,166.36	11,069.53	11,076.62

The restricted cubic spline model assessed NT-proBNP as a continuous variable, with knots located at the 5<sup>th</sup>. 35<sup>th</sup>, 65<sup>th</sup>, and 95<sup>th</sup> percentiles.

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; SE, systemic embolism.

Table S3: Crude event rates and hazard ratios of primary and secondary outcomes in the entire cohort	
according to NT-proBNP subgroups	

Endpoints	NT-proBNP	Events	Participants	Event rates	Hazard ratios	
Strake or SF	$\leq$ 15 pmol/L	135	2940	0.89 [0.74- 1.05]	Reference	
SHOK OF BE	>15 pmol/L	175	2879	1.21[1.04- 1.40]	1.21 [0.96- 1.54]	
Stroke, SE, or cardiovascular death	$\leq$ 15 pmol/L	172	2940	1.13[0.97- 1.31]	Reference	
	>15 pmol/L	298	2879	2.06 [1.83- 2.31]	1.60 [1.32- 1.95]	
All-cause death	≤15 pmol/L	214	2940	1.38 [1.20- 1.58]	Reference	
	>15 pmol/L	455	2879	3.07 [2.80- 3.37]	1.91 [1.61- 2.26]	

Crude event rates are presented as event number per 100 person-years. Hazard ratios are presented with 95% confidence intervals and were estimated in cause-specific Cox regression models adjusted for sex, age, body mass index, weekly alcohol consumption, smoking pack years, estimated glomerular filtration rate, total cholesterol concentration, hypertension, diabetes, prior stroke, heart failure, valvular heart disease, ischemic heart disease, and peripheral artery disease.

The conversion factor for NT-proBNP expressed as pg/mL is 1 pg/mL = 0.12 pmol/L. Hence, 15 pmol/L corresponds to 125 pg/mL.

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; SE, systemic embolism.

<u>Table S4</u>: Crude event rates and hazard ratios of AF diagnosis for ILR versus Control according to NTproBNP subgroups

NT-	NT- Control group		ILR group		Hazard ratios	Pinteraction
Groups	Event / participant	Event rates	Event / participant	Event rates		
≤15 pmol/L	152 / 2188	1.35 [1.15-1.59]	181 / 752	5.60 [4.82-6.48]	4.06 [3.27-5.04]	0.012
>15 pmol/L	392 / 2168	3.83 [3.46-4.23]	289 / 711	11.42 [10.14-12.82]	2.89 [2.49-3.37]	

Crude event rates are presented as event number per 100 person-years. Hazard ratios and p-value for interaction were estimated in cause-specific Cox regression models.

The conversion factor for NT-proBNP expressed as pg/mL is 1 pg/mL = 0.12 pmol/L. Hence, 15 pmol/L corresponds to 125 pg/mL.

**Abbreviations**: AF, atrial fibrillation; ILR, implantable loop recorder; NT-proBNP, N-terminal pro-B-type natriuretic peptide.





The figure shows the risks of stroke/SE, stroke/SE/cardiovascular death, and all-cause death in the entire study cohort according to NT-proBNP as a continuous variable. Hazard ratios were estimates with the median NT-proBNP value (15 pmol/L) as reference, in cause-specific Cox models adjusted for sex, age, body mass index, weekly alcohol consumption, smoking pack years, estimated glomerular filtration rate, total cholesterol concentration, hypertension, diabetes, prior stroke, heart failure, valvular heart disease, ischemic heart disease, and peripheral artery disease. The colored areas represent 95% confidence intervals.

The conversion factor for NT-proBNP expressed as pg/mL is 1 pg/mL = 0.12 pmol/L. Hence, 15 pmol/L corresponds to 125 pg/mL.

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; SE, systemic embolism.



The figure shows the absolute risks of stroke/SE, stroke/SE/cardiovascular death, and all-cause death according to randomization assignment among participants with baseline NT-proBNP  $\leq$ 15 pmol/L (**panel A**) and >15 pmol/L (**panel B**). Cumulative incidences were plotted using the Kaplan-Meier estimator for all-cause death and the Aalen-Johansen estimator for other outcomes with death as competing risk. HRs and p-values were estimated in cause-specific Cox regression models.

The conversion factor for NT-proBNP expressed as pg/mL is 1 pg/mL = 0.12 pmol/L. Hence, 15 pmol/L corresponds to 125 pg/mL.

**Abbreviations**: CI, confidence interval; HR, hazard ratio; ILR, implantable loop recorder; NT-proBNP, N-terminal pro-B-type natriuretic peptide; SE, systemic embolism.



The figure shows the absolute risk of ILR-detected AF episodes  $\geq$ 24 hours in the ILR group, according to NTproBNP subgroups. The curves are truncated after four years, which was the maximum duration of ILR monitoring in the LOOP Study. Cumulative incidences were plotted using the Aalen-Johansen estimator with death as competing risk. HRs and p-values were determined in cause-specific Cox models adjusted for sex, age, body mass index, weekly alcohol consumption, smoking pack years, estimated glomerular filtration rate, total cholesterol concentration, hypertension, diabetes, prior stroke, heart failure, valvular heart disease, ischemic heart disease, and peripheral artery disease.

The conversion factor for NT-proBNP expressed as pg/mL is 1 pg/mL = 0.12 pmol/L. Hence, 15 pmol/L corresponds to 125 pg/mL.

**Abbreviations**: AF, atrial fibrillation; Cl, confidence interval; HR, hazard ratio; ILR, implantable loop recorder; NT-proBNP, N-terminal pro-B-type natriuretic peptide.



assignment (**upper panel**) and mean changes in systolic blood pressure in participants with baseline NT-proBNP levels  $\leq 15$  and  $\geq 15$  pmol/L (**lower panel**). Error bars represent 95% confidence intervals of mean blood pressure changes.

The conversion factor for NT-proBNP expressed as pg/mL is 1 pg/mL = 0.12 pmol/L. Hence, 15 pmol/L corresponds to 125 pg/mL.

Abbreviations: ILR, implantable loop recorder; NT-proBNP, N-terminal pro-B-type natriuretic peptide.