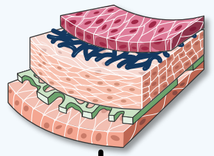
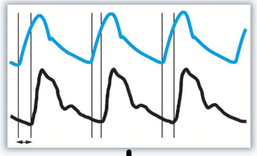
To identify optimal biomarkers for assessing vascular aging

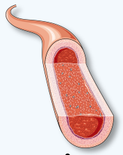
4 structural biomarkers



8 functional biomarkers



4 circulating biomarkers



Validation and Comparison

Effectiveness	Generalizability	Reliability
Two methods for effect synthesis	223 studies 1,325,186 subjects Across diverse populations	Trial sequential analysis
Subgroup analysis		Sensitivity analysis

Evaluation Framework

	cIMT	CP	CACS	Carotid diameter	baPWV	cfPWV	Low ABI	High ABI	CAVI	AIx	FMD	RHI	CEPCs	EMPs	E-selectin	LTL
All death	⊕	⊕	⊕	+	⊕	⊕	⊕	⊕	?	⊖	⊖	−	⊖	+	⊖	⊕
CV death	⊕	⊕	⊕	?	⊕	⊕	⊕	⊕	+	⊖	⊖	−	+	?	⊖	⊕
Stroke	⊕	⊕	⊕	+	⊕	⊖	⊕	⊖	⊕	+	⊖	⊕	?	?	−	−
MI	?	+	⊕	?	⊖	+	⊕	⊕	−	−	⊖	−	?	?	?	+
MACEs	⊕	⊕	⊕	?	?	⊕	⊕	⊕	⊕	⊖	+	+	+	+	+	−

– Notes for main analysis
- ⊕ Significant effect of both pooled HR and crude RR
- ⊕ Significant effect of only one pooled result
- ⊖ Non-significant effect of both pooled results

– Notes for qualitative review
- \+ Consistent positive results
- − Consistent negative results
- ? Not clear

– Notes for TSA result
- ⊕ ⊕ Cross TSMB of TSA
- ⊕ Reach required IS of TSA
- ⊕ Cross TSMB and reach required IS in TSA

Interpretability for Assessment

Accuracy for Prediction

Usefulness for Practice

CACS	Low ABI	LTL

To operationalize the concept of vascular aging