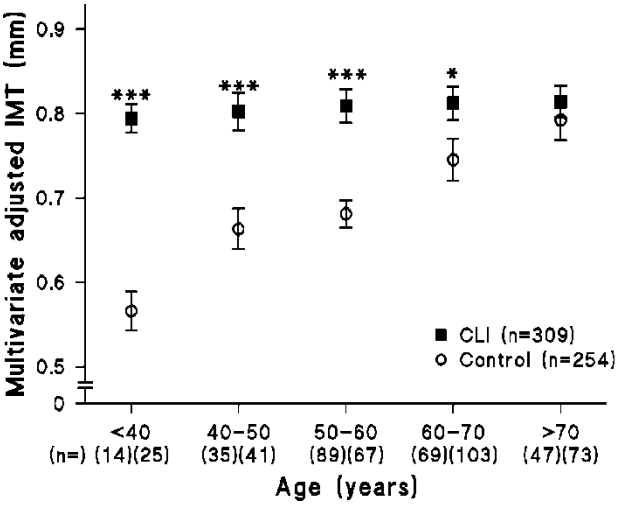
Figure S1. Multivariate-adjusted carotid intima-media thickness (IMT) across the adult lifespan in cases with non-cardiac arterial vascular events (stroke and critical limb ischemia [CLI]) and age, sex-and ethnicity-matched randomly selected controls from a community sample in Africa. Data shown are multivariate adjusted means and SEM. Adjustments are for sex, hypertension, diabetes mellitus, and smoking. *p<0.05, **p<0.005, ***p<0.0001 *vs* controls.

Figure S2. Prevalence of an increased carotid intima-media thickness (IMT) across the adult lifespan in cases with non-cardiac arterial vascular events (stroke and critical limb ischemia [CLI]) and age, sex-and ethnicity-matched randomly selected controls from a community sample in Africa. Upper panels show prevalence rates for thresholds >95% confidence intervals for age and lower panels for thresholds >0.80 mm at any age. *p<0.05, **p<0.001, ***p<0.0001 *vs* controls.

Figure S3. Multivariate adjusted odds (Odds ratio [OR] and 95% confidence interval [CI]) of a non-cardiac arterial vascular event (stroke or critical limb ischemia) across the adult lifespan with the presence of carotid plaque (open circles) or an increased carotid intima-media thickness (IMT) (closed circles) in Africa. Adjustments are for hypertension, diabetes mellitus, and smoking. An increased IMT was defined as values above 0.80 mm.

Figure S4. Impact of the addition of an increased carotid intima-media thickness (IMT) and carotid plaque to receiver operator characteristic (ROC) curves for the detection of critical limb ischemia or stroke at an age less than (upper panel) or more than (lower panel) 50 years of age . An increased IMT was defined as values above the 95th percentile for age in the community. Curves are for the presence of plaque or an increased IMT considered separately or for either the presence of plaque or an increased IMT considered together. *p<0.005; **p<0.0001 *vs* the presence of plaque or an increases IMT considered together.

Figure S1.


Multivariate adjusted IMT (mm)
0.9
0.8
0.7
0.6
0.5
0
***
***
***
*
CLI (n=309)
Control (n=254)
<40
40–50
50–60
60–70
>70
(n=) (14)(25)
(35)(41)
(89)(67)
(69)(103)
(47)(73)
Age (years)

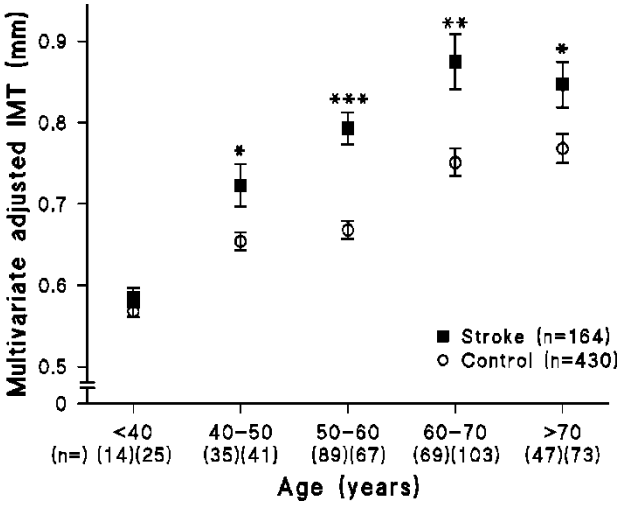
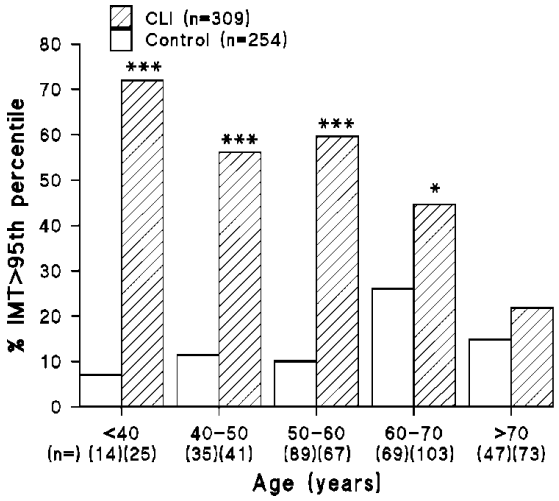
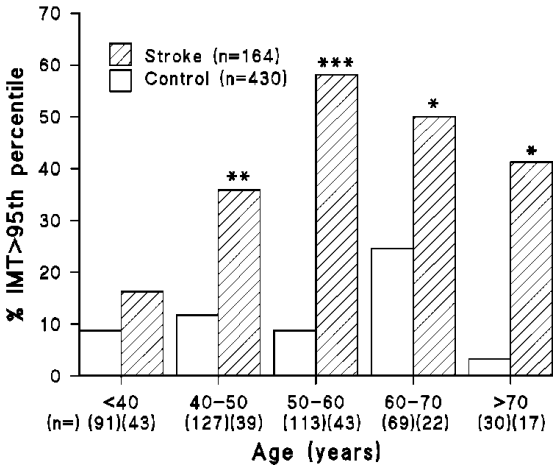
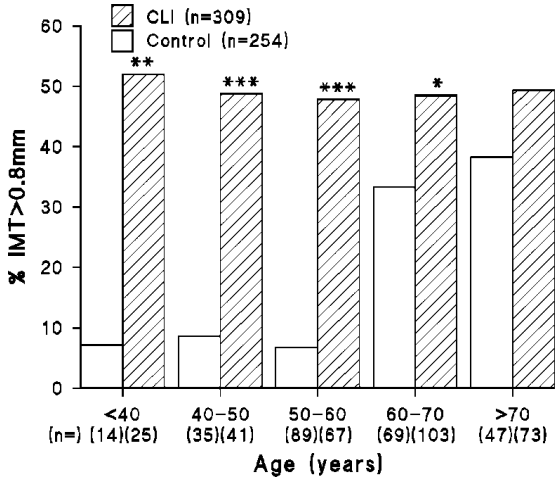

Multivariate adjusted IMT (mm)
0.9
0.8
0.7
0.6
0.5
0
*
***
**
*
Stroke (n=164)
Control (n=430)
<40
40–50
50–60
60–70
>70
(n=) (14)(25)
(35)(41)
(89)(67)
(69)(103)
(47)(73)
Age (years)

Figure S2.


CLI (n=309)
Control (n=254)
% IMT>95th percentile
***
***
***
*
<40 40-50 50-60 60-70 >70
(n=) (14)(25) (35)(41) (89)(67) (69)(103) (47)(73)
Age (years)


Stroke (n=164)
Control (n=430)
% IMT>95th percentile
**
***
*
*
<40 40-50 50-60 60-70 >70
(n=) (91)(43) (127)(39) (113)(43) (69)(22) (30)(17)
Age (years)


CLI (n=309)
Control (n=254)
% IMT>0.8mm
**
***
***
*
<40 40-50 50-60 60-70 >70
(n=) (14)(25) (35)(41) (89)(67) (69)(103) (47)(73)
Age (years)

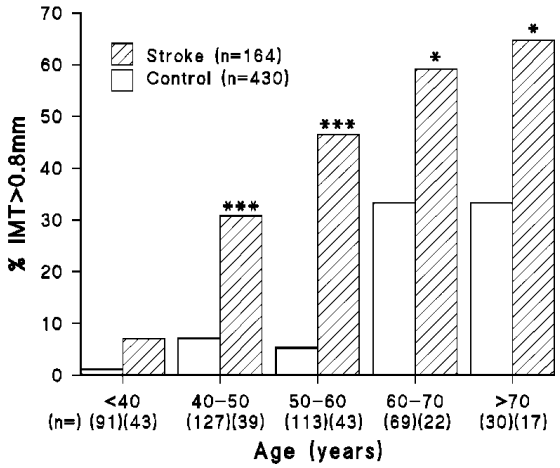
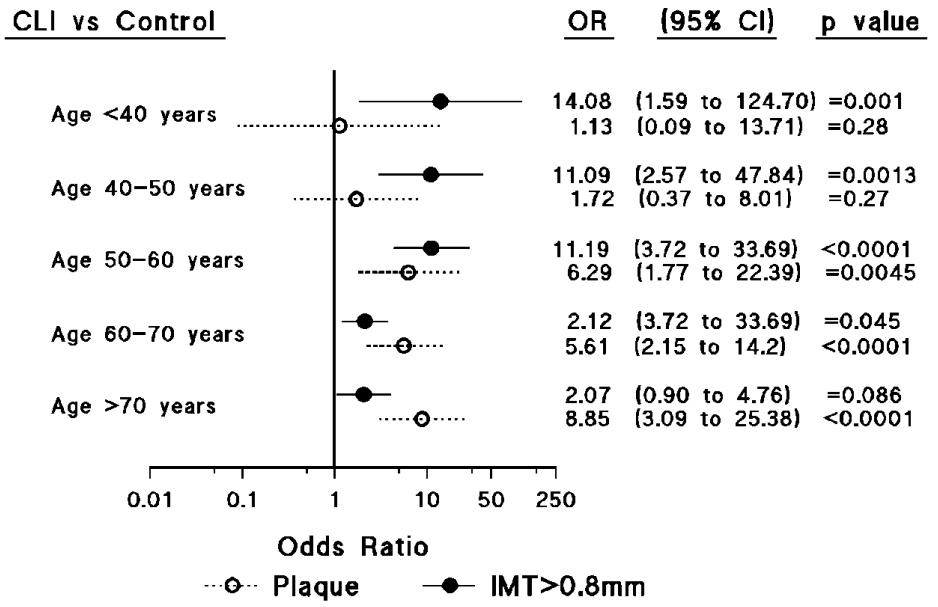

Stroke (n=164)
Control (n=430)
% IMT>0.8mm
***
***
*
*
<40 40-50 50-60 60-70 >70
(n=) (91)(43) (127)(39) (113)(43) (69)(22) (30)(17)
Age (years)

Figure S3.


CLI vs Control
OR
(95% CI)
p value
Age <40 years
14.08 (1.59 to 124.70) =0.001
1.13 (0.09 to 13.71) =0.28
Age 40–50 years
11.09 (2.57 to 47.84) =0.0013
1.72 (0.37 to 8.01) =0.27
Age 50–60 years
11.19 (3.72 to 33.69) <0.0001
6.29 (1.77 to 22.39) =0.0045
Age 60–70 years
2.12 (3.72 to 33.69) =0.045
5.61 (2.15 to 14.2) <0.0001
Age >70 years
2.07 (0.90 to 4.76) =0.086
8.85 (3.09 to 25.38) <0.0001
0.01
0.1
1
10
50
250
Odds Ratio
Plaque
IMT>0.8mm

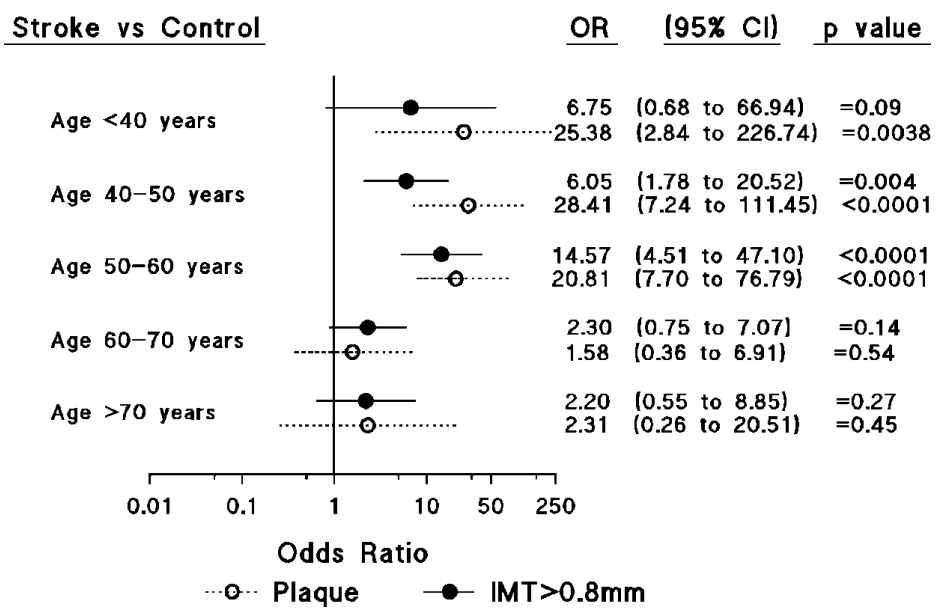

Stroke vs Control
OR
(95% CI)
p value
Age <40 years
6.75 (0.68 to 66.94) =0.09
25.38 (2.84 to 226.74) =0.0038
Age 40–50 years
6.05 (1.78 to 20.52) =0.004
28.41 (7.24 to 111.45) <0.0001
Age 50–60 years
14.57 (4.51 to 47.10) <0.0001
20.81 (7.70 to 76.79) <0.0001
Age 60–70 years
2.30 (0.75 to 7.07) =0.14
1.58 (0.36 to 6.91) =0.54
Age >70 years
2.20 (0.55 to 8.85) =0.27
2.31 (0.26 to 20.51) =0.45
0.01
0.1
1
10
50
250
Odds Ratio
Plaque
IMT>0.8mm

Figure S4.

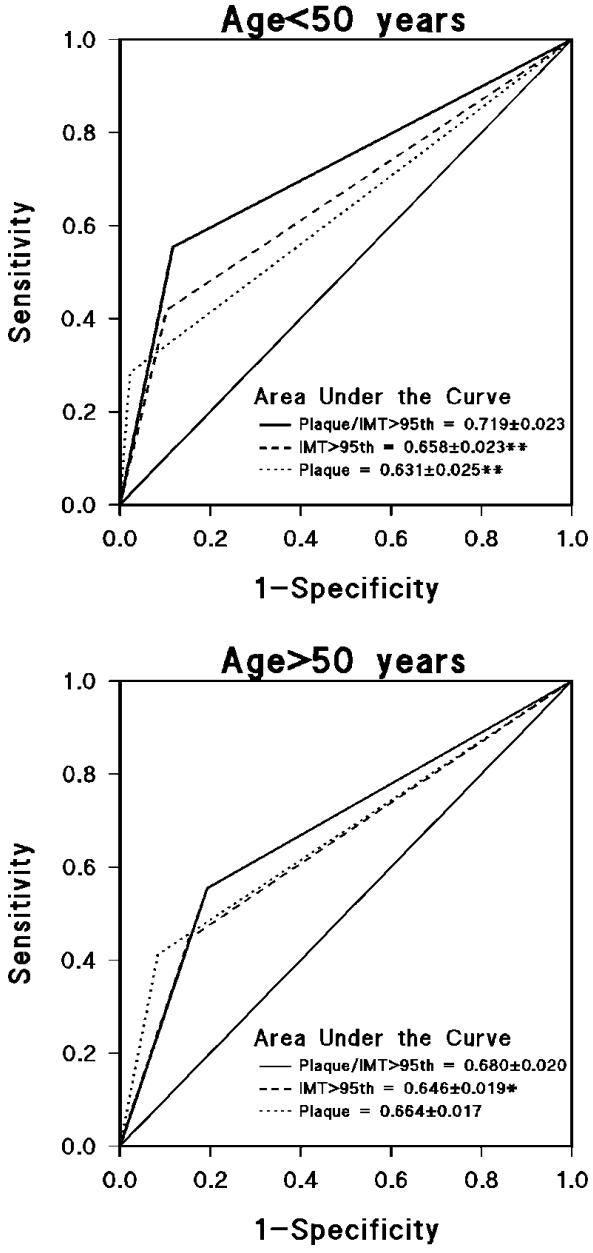

Age<50 years
Sensitivity
1−Specificity
0.0
0.2
0.4
0.6
0.8
1.0
Area Under the Curve
Plaque/IMT>95th = 0.719±0.023
IMT>95th = 0.658±0.023**
Plaque = 0.631±0.025**
Age>50 years
Sensitivity
1−Specificity
Area Under the Curve
Plaque/IMT>95th = 0.680±0.020
IMT>95th = 0.646±0.019*
Plaque = 0.664±0.017

Table S1. Characteristics of participants with critical limb ischemia with histological assessment of arterial tree of amputated limbs (n=54).

Age (years)	62.0±14.6
Sex (% male)	74.1
Body mass index (kg/m^2)	24.4±4.7*
% Hypertensive	57.4
% Diabetes mellitus	25.9
% Regular smoking	35.2
SBP/DBP (mm Hg)	127±21/77**±12*
Total cholesterol (mmol/l)	3.67±1.35
LDL cholesterol (mmol/l)	1.90±0.88
HDL cholesterol (mmol/l)	0.83±0.42**
Glycated hemoglobin (%)	7.26±2.69

Data shown are proportions, mean±SD. CLI, critical limb ischemia; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low density lipoprotein; HDL, high density lipoprotein. *p<0.05; **p<0.005 *vs* all CLI.

Table S2. Age adjusted carotid intima-media thickness (IMT) and plaque in different stroke subtypes based on the TOAST classification.

	IMT (mm)	Plaque (%)
Hemorrhagic (n=18)	0.796±0.034	44.4
Atherosclerotic (n=9)	0.750±0.048	33.3
Small vessel (n=29)	0.773±0.027	55.2
Cardio-embolic (n=31)	0.750±0.026	48.4
Other determinants (n=13)	0.717±0.043	23.1
Indeterminate (n=64)	0.772±0.018	37.5