Research Article

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Biomarkers in Medicine

Four-year stability of anthropometric and cardio-metabolic parameters in a prospective cohort of older adults

Aim: To examine the medium-term stability of anthropometric and cardio-metabolic parameters in the general population. **Materials & methods:** Participants were 5160 men and women from the English Longitudinal Study of Ageing (age ≥50 years) assessed in 2004 and 2008. Anthropometric data included height, weight, BMI and waist circumference. Cardio-metabolic parameters included blood pressure, serum lipids (total cholesterol, HDL, LDL, triglycerides), hemoglobin, fasting glucose, fibrinogen and C-reactive protein. **Results:** Stability of anthropometric variables was high (all intraclass correlations >0.92), although mean values changed slightly (-0.01 kg weight, +1.33 cm waist). Cardio-metabolic parameters showed more variation: correlations ranged from 0.43 (glucose) to 0.81 (HDL). The majority of participants (71–97%) remained in the same grouping relative to established clinical cut-offs. **Conclusion:** Over a 4-year period, anthropometric and cardio-metabolic parameters showed good stability. These findings suggest that when no means to obtain more recent data exist, a one-time sample will give a reasonable approximation to average levels over the medium-term, although reliability is reduced.

Keywords: anthropometric • cardio-metabolic • reliability • reproducibility • stability • variability

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Anthropometric variables such as BMI and waist circumference have been established as valuable indicators for risk of chronic diseases (e.g., cardiovascular disease, diabetes, cancer) [1–6]. Cardio-metabolic parameters such as cholesterol, fibrinogen, CRP and fasting glucose are also strongly associated with some of these chronic diseases [7–11].

As the evidence for the clinical importance of anthropometric and cardio-metabolic markers has emerged, many epidemiological studies have incorporated them in their data sets. However, measurements are often taken at only one time due to financial or logistical restrictions. This leaves many data sets with restricted availability of up-to-date measurements when examining links with disease outcomes. The value of the biomarker data in these studies therefore depends on how reliably they capture average 'exposure' over time.

Several cardio-metabolic parameters, including CRP and glycated hemoglobin, have been shown to be relatively stable over short periods (days or weeks) in healthy volunteers [12–17], although diurnal fluctuations may have been overlooked by drawing samples at the same time of day. Other parameters, particularly related to lipids (e.g., triglycerides, LDL cholesterol), appear to fluctuate, at least at levels above a certain threshold [13,18–20]. Less is known about stability in the general population, which would inevitably include people who are not entirely healthy. Studies of stability over longer assessment intervals have typically been in small samples or restricted to analysis of a single cardio-metabolic parameter [21–38], which might be due to the high costs associated with obtaining samples or practical difficulties related to organizing an investigation of this nature. None have explicitly compared healthy indi-

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viduals with those who have existing conditions where variability might be higher.

In this study, we examined the stability of anthropometric and cardio-metabolic parameters in a large cohort of older adults (≥50 years) living in England over a 4-year period. Analyses were run on both the full sample and a healthy subsample.

Materials & methods

Participants & procedures

The data for these analyses are from the English Longitudinal Study of Ageing (ELSA), an ongoing prospective cohort study representative of older men and women living in England. The sampling and methods used in ELSA have been described in detail elsewhere [39]. Briefly, ELSA is a panel study recruited from households responding to the Health Survey for England [40] in 1998, 1999 and 2001. All households with one or more members aged ≥50 years in 2002 were eligible; around 19,924 individuals. Of this group, 2596 individuals had died or were ineligible for follow-up by the onset of ELSA. Of the remainder, 12,099 (70%) became ELSA participants.

ELSA participants take part in biennial assessments. At each wave, participants are visited in their homes by trained interviewers to complete a computer-assisted personal interview, a self-administered questionnaire, and tests of cognitive function and walking speed. On alternate waves (every 4 years), nurses make home visits to collect objective measures of health status, including anthropometric measures, measures of physical function and blood tests from which to assay a range of biomarkers. Waves 2 and 4 (collected 2004–2005 and 2008–2009) form the baseline and follow-up examinations for the present analyses. Wave 2 was completed by 7666 participants, of whom 5745 also completed wave 4. Of these, 5160 participants provided data on at least one cardio-metabolic parameter at both time points, and formed the final analytical sample.

ELSA has received approval from various ethics committees, including the London Multi-Centre Research Ethics Committee. Full informed consent has been obtained from all participants. The consent booklet for nurse visits is available at [41].

Measures

Demographic variables

Interviewers collected demographic information including age, sex, ethnicity and marital status. For the purpose of the present analyses, age was dichotomized at the mean (<65 years vs ≥65 years), ethnicity as white vs non-white, and marital status as married (including living as married) vs unmarried (single/never married, separated, divorced or widowed).

Anthropometric measures

Height was measured to the nearest millimeter using a portable stadiometer and weight to the nearest 0.1 kg using Tanita THD-305 portable electronic scales. Waist circumference, defined as the midpoint between the lowest rib and the upper margin of the iliac crest, was measured to the nearest even millimeter. The nurse recorded any factors that could have compromised the reliability of anthropometric measurements, such as the participant being stooped, not keeping still during the measurements, or being unable or unwilling to remove shoes. Anthropometric data judged by the nurse to be unreliable were excluded from analyses of those variables. Aside from refusal, reasons for height and weight measurements not being taken included factors such as the participant being unsteady, unable to stand upright, chair-bound, confined to bed, or otherwise ill or in pain, and factors related to the equipment, such as the scales not working or the stadiometer not being available. BMI was calculated for all participants with valid weight and height measurements.

Biological measures

We selected ten cardio-metabolic biomarkers that are established as indicators of chronic disease and had been measured at both waves: systolic blood pressure, diastolic blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, fasting glucose, hemoglobin, fibrinogen and CRP.

Blood pressure was measured using the Omron HEM-907 blood pressure monitor, after participants were seated for at least 5 min. Three readings were taken at 1-min intervals. The first was discarded and the mean of the second and third used.

All participants who gave consent were eligible for blood samples to be taken, excluding those who reported clotting or bleeding disorders, history of fits or convulsions, or those on anti-coagulant medication. Viable blood samples were obtained from 4133 participants (80%) at baseline and 3880 participants (75%) at follow-up. Unless participants were over 80 years of age, had diabetes, reported ever having had a fit, were frail, or seemed unwell, where possible blood samples were obtained under fasting conditions, defined as having had no food or drink (except water) for at least 5 h prior to the blood test. Fasting blood samples were obtained from 2595 participants (50%) at baseline and 2261 participants (44%) at follow-up.

The protocol for the collection of the clinical measurements and the blood samples can be found at [42]. Baseline and follow-up samples were analyzed at the Royal Victoria Infirmary laboratory in Newcastle upon Tyne (UK). Detailed information on the analyses and internal and external quality control protocols can be

found in the 2004 Health Survey for England technical report [43], since the Health Survey for England and ELSA employed the same laboratory and the same guidelines and protocols for the blood analysis. Briefly, cholesterol levels were determined using the DAX Oxidase assay. Triglycerides were measured using an enzymatic assay on an Olympus 640 analyzer. Plasma glucose (in fasting samples only) was measured using the Hexokinase method. Hemoglobin was measured using two Abbott Diagnostics CELL-DYN 4000 analyzers. Fibrinogen was analyzed using a modification of the Clauss thrombin clotting method on the Organon Teknika MDA-180 analyzer, with a CV of less than 10%. CRP was analyzed using the N Latex CRP mono-immunoassay on the Behring Nephelometer II analyzer.

Health-related variables

Presence of a long-standing illness was assessed with the question: "*Do you have any long-standing illness, disability or infirmity? By long-standing I mean anything that has troubled you over a period of time or that is likely to affect you over a period of time*." If a positive response was given to the first question, the participant was also asked: "*Does this illness or disability limit your activities in any way?*" Affirmation of any form of limitation classified the participant as having a limiting long-standing illness.

Interviewers also recorded whether participants were currently taking anti-hypertensive medication, injecting insulin for diabetes, or taking action to lower cholesterol. At baseline (wave 2), the latter was assessed using two questions: "*Has any doctor talked to you about how to lower your cholesterol? This would include changing your diet, losing weight, getting more exercise or taking medication*"; if yes: "*Have you done any of these things to lower your cholesterol?*" At follow-up (wave 4), participants were asked whether they were currently taking medication to lower cholesterol.

Statistical analysis

Four health-related variables that were thought likely to influence the cardio-metabolic parameters were used to distinguish a 'healthy' subsample from the full sample: limiting long-standing illness, anti-hypertensive medication, injecting insulin for diabetes, and taking action to reduce cholesterol. We excluded from the healthy subsample all participants who reported a limiting long-standing illness at either wave or had a change in medication use for hypertension or diabetes. We had intended to exclude those with a change in use of cholesterol-lowering medication, but because this was assessed differently at baseline (following doctor-recommended action) and follow-up (medication use) it was not possible to determine whether there had been a change in use of medication. Therefore, all participants reporting action to reduce cholesterol at either wave, not just those with a change in status, were excluded from the healthy subsample. Also excluded were those whose status on any of these four variables was unknown at either baseline or follow-up. All analyses were conducted on both the full sample of eligible participants and the healthy subsample.

All analyses used SPSS version 21. In order to adjust for multiple comparisons, we considered a two-sided p-value < 0.01 statistically significant for each analysis. Repeated-measures analyses of variance (ANOVAs) were used to examine significant mean shifts in each parameter, taking into account age and sex. Non-normally distributed variables (triglycerides, glucose and CRP) were log-transformed for analyses to normalize skewed distributions. Geometric means and 95% CIs are presented for log-transformed variables. The intraclass correlation coefficients (ICC) between baseline and follow-up values were computed for each anthropometric and cardio-metabolic parameter using the formula:

$$\text{ICC} = \frac{\text{Variance (between individuals)}}{\text{Variance (between individuals)} + \text{Variance (within individuals)}}$$

We also calculated the proportion of values remaining consistently above or below the established cut-off for each cardio-metabolic parameter at the two time points. The cut-offs for total, LDL and HDL cholesterol and triglycerides were obtained from the third report of the National Cholesterol Education Program expert panel on detection, evaluation and treatment of high blood cholesterol in adults [44], with cholesterol values converted from mmol/l to mg/dl for these analyses. Cut-offs for blood pressure, fasting glucose and CRP were also obtained from statements by expert panels [45–47], and the cut-off for hemoglobin from two large studies of variability in hemoglobin levels [48,49]. In the absence of an established cut-off for fibrinogen, we used the upper quartile in the full eligible sample at baseline (3.6 g/l) to define high fibrinogen levels, as has been done in previous studies [50].

Finally, we re-estimated the associations between baseline and follow-up measurements controlling for attenuation due to measurement error and short-term intra-individual variability using the method recommended by Nunnally & Bernstein [51], as detailed by Krueger & Schkade [52]. We applied the formula

$$\rho_{xy} = \frac{r_{xy}}{\sqrt{r_{xx} \times r_{yy}}}$$

where x = baseline measurement; y = follow-up measurement; ρ_{xy} = the true correlation between x and y; r_{xy}

= the observed correlation between x and y; r_{xx} = reliability of x; and r_{yy} = reliability of y. Intra-measure reliability (r_{xx} and r_{yy}) for anthropometric variables was based on reliability data from a sample of doctors trained in taking anthropometric measurements [53]. Estimates of reliability for cardio-metabolic parameters were based on findings of a number of different studies [12–13,15,54–57].

Results

Baseline data were collected from 7666 individuals in 2004–2005, of whom 5160 individuals also provided data on at least one outcome at follow-up (2008–2009) and were therefore eligible for inclusion in these analyses. Compared to the 2506 individuals who were ineligible for inclusion, the analyzed sample (n = 5160) included more younger (51% vs 38%, p < 0.001), female (56% vs 53%, p = 0.028), and married participants (67% vs 64%, p = 0.003), but there were no differences in ethnicity (98% vs 98% white). Fewer participants in the analyzed sample reported a limiting long-standing illness (32% vs 42%, p < 0.001), but there were no baseline differences in the proportion taking medication to reduce blood pressure (14% vs 15%), injecting insulin for diabetes (2% vs 2%), or following doctor's advice to control high cholesterol (3% vs 3%). The analyzed sample had a slightly higher mean weight at baseline (76.71 vs 75.18 kg, p < 0.001) but did not differ from the excluded participants on any other anthropometric variable. They had higher diastolic blood pressure (75.42 vs 74.19 mmHg, p < 0.001), total cholesterol (5.96 vs 5.79 mmol/l, p < 0.001), HDL cholesterol (1.53 vs 1.50 mmol/l, p = .002), LDL cholesterol (3.63 vs 3.48 mmol/l, p < 0.001) and hemoglobin (14.40 vs 14.21 g/dl, p < 0.001) than the excluded participants, and lower systolic blood pressure (134.68 vs 136.62 mmHg, p < 0.001), fibrinogen (3.18 vs 3.34 g/l, p < 0.001) and CRP (1.95 vs 2.29 mmol/l, p < 0.001). Levels of triglycerides (1.55 vs 1.58 mmol/l) and fasting glucose (4.90 vs 4.90 mmol/l) did not differ significantly between the included and excluded participants.

The 5160 participants who provided information on at least one cardio-metabolic parameter at baseline and follow-up are henceforth referred to as the 'full eligible sample'. Of these participants, 1862 (36%) were free of limiting long-standing illness, were not taking action to reduce their cholesterol at either wave, and had no change between waves in use of medication for hypertension or diabetes (the 'healthy subsample').

Demographic characteristics of the full eligible sample and the healthy subsample are presented in Table 1. In the full eligible sample, there were roughly equal numbers of 50–64-year-olds and over-65s (51% vs 49%), and slightly more women than men (56% vs 44%). The majority were white (98%) and married (67%). The healthy subsample was similarly distributed by sex and ethnicity, but more were aged 50–64 years (63%) and married (73%).

Table 1 also shows the proportion at baseline, follow-up and both time points, who reported a limiting long-standing illness, were taking action to lower cholesterol levels, or were taking medication for hypertension or diabetes. In the full eligible sample, 45% of participants reported a limiting long-standing illness at baseline or follow-up, 2% stopped taking anti-hypertensive medication between baseline and follow-up, 23% started taking anti-hypertensive medication and 13% were taking medication at both waves. Just two individuals (0.04%) stopped injecting insulin for diabetes, 29 (0.6%) started injecting insulin and 75 (1.5%) were injecting insulin at both baseline and follow-up. A total of 23% of participants were taking action to reduce their cholesterol at one or both waves.

Stability of anthropometric variables

Results of the repeated-measures ANOVAs and intraclass correlations testing the stability of the anthropometric variables are shown in Table 2. There was a small decrease in height over time in both samples (-0.1 cm, SE = 0.01), but no significant change in weight in either sample. BMI therefore increased slightly over time, by 0.08 points (SE = 0.03) in the full eligible sample and by 0.11 points (SE = 0.04) in the healthy subsample. Waist circumference also increased slightly over time (+1.33 cm, SE = 0.07 in the full eligible sample; +1.36 cm, SE = 0.12 in the healthy subsample).

Individuals' positions in the distribution were highly stable between baseline and 4-year follow-up, with high intraclass correlations in both the full eligible sample (ICC > 0.92) and the healthy subsample (ICC > 0.92).

Stability of cardio-metabolic parameters

Results of the repeated-measures ANOVAs and intraclass correlations for the cardio-metabolic parameters are shown in Table 3 (untransformed variables) and Table 4 (log-transformed variables).

Mean changes over time were similar in the full eligible sample and the healthy subsample. Systolic blood pressure decreased slightly in the full eligible sample (-0.88 mmHg, SE = 0.28) and increased slightly in the healthy subsample (+1.10 mmHg, SE = 0.40). Diastolic blood pressure decreased in both samples (-2.09 mmHg, SE = 0.16 in the full eligible sample; -0.61 mmHg, SE = 0.25 in the healthy subsample). There were small decreases in total and LDL cholesterol (-0.4 mmol/l, SE = 0.02 in the full eligible sample;

Table 1. Demographic and health-related characteristics of the full eligible sample (n = 5160) and healthy subsample (n = 1862) of older adults in the English Longitudinal Study of Ageing.

Characteristics	Full eligible sample (n = 5160), n (%)	Healthy subsample[†] (n = 1862), n (%)
Age at baseline (years):		
– 50–64	2631 (51.0)	1166 (62.6)
– ≥65	2529 (49.0)	696 (37.4)
Sex:		
– Male	2278 (44.1)	865 (46.5)
– Female	2882 (55.9)	997 (53.5)
Ethnicity:		
– White	5074 (98.3)	1838 (98.7)
– Non-white	84 (1.6)	24 (1.3)
– Missing	2 (0.04)	–
Marital status:		
– Married	3473 (67.3)	1356 (72.8)
– Unmarried	1687 (32.7)	506 (27.2)
Limiting long-standing illness:		
– Yes at baseline only	485 (9.4)	–
– Yes at follow-up only	652 (12.6)	–
– Yes at baseline and follow-up	1185 (23.0)	–
– No	2836 (55.0)	1862 (100.0)
– Unknown	2 (0.04)	–
Taking medication for hypertension:		
– Yes at baseline only	90 (1.7)	–
– Yes at follow-up only	1192 (23.1)	–
– Yes at baseline and follow-up	648 (12.6)	170 (9.1)
– No	3228 (62.6)	1692 (90.9)
– Unknown	2 (0.04)	–
Taking medication for diabetes:		
– Yes at baseline only	2 (0.04)	–
– Yes at follow-up only	29 (0.6)	–
– Yes at baseline and follow-up	75 (1.5)	4 (0.2)
– No	5008 (97.1)	1858 (99.8)
– Unknown	46 (0.9)	–
Taking action to lower cholesterol[‡]:		
– Yes at baseline only	37 (0.7)	–
– Yes at follow-up only	1135 (22.0)	–
– Yes at baseline and follow-up	101 (2.0)	–
– No	3882 (75.2)	1862 (100.0)
– Unknown	5 (0.1)	–

[†]Excluded are n = 3298 with any limiting long-standing illness, change in use of medication for hypertension or diabetes, or taking action to reduce cholesterol at either baseline or follow-up.
[‡]Baseline = following doctor advice; follow-up = taking medication.

Table 2. Stability of anthropometric variables in the full eligible sample (n = 5160) and healthy subsample (n = 1862) of older adults.

	n	Repeated-measures ANOVA				Intraclass correlation
		Baseline mean (SE)	Follow-up mean (SE)	Change mean (SE)	Change p-value	ICC (95% CI) p-value
Full eligible sample						
Height (cm)	4040	166.50 (0.10)	166.43 (0.10)	-0.07 (0.01)	<0.001	0.999 (0.999–0.999) <0.001
Weight (kg)	4739	77.13 (0.20)	77.12 (0.20)	-0.01 (0.06)	0.863	0.957 (0.954–0.959) <0.001
BMI (kg/m^2)	3863	27.70 (0.07)	27.78 (0.08)	0.08 (0.03)	0.003	0.941 (0.938–0.945) <0.001
Waist (cm)	4698	96.00 (0.17)	97.33 (0.18)	1.33 (0.07)	<0.001	0.926 (0.921–0.930) <0.001
Healthy subsample						
Height (cm)	1569	166.77 (0.17)	166.69 (0.17)	-0.08 (0.01)	<0.001	0.999 (0.999–0.999) <0.001
Weight (kg)	1773	74.87 (0.31)	74.96 (0.32)	0.09 (0.10)	0.342	0.965 (0.961–0.968) <0.001
BMI (kg/m^2)	1522	26.81 (0.11)	26.92 (0.12)	0.11 (0.04)	0.002	0.947 (0.941–0.952) <0.001
Waist (cm)	1749	93.17 (0.27)	94.53 (0.28)	1.36 (0.12)	<0.001	0.928 (0.921–0.934) <0.001

Means at baseline, means at follow-up, and mean changes over time are mutually adjusted for age and sex.
CI: Confidence interval; ICC: Intraclass correlation coefficient; SE: Standard error.

-0.2 mmol/l, SE = 0.02 in the healthy subsample), and small increases in HDL cholesterol (+0.02 mmol/l, SE = 0.004 in the full eligible sample; +0.03 mmol/l, SE = 0.01 in the healthy subsample). Triglyceride levels fell in the full eligible sample (ratio: 0.97, 95% CI: 0.95–0.98) but did not change significantly in the healthy subsample (ratio: 0.99, 95% CI: 0.96–1.01). There were slight reductions in fasting glucose (ratio: 0.99, 95% CI: 0.98–0.99 in the full eligible sample; ratio: 0.98, 95% CI: 0.97–0.99 in the healthy subsample) and hemoglobin (-0.35 g/dl, SE = 0.02 in the full eligible sample; -0.29 g/dl, SE = 0.03 in the healthy subsample) in both samples, and increases in fibrinogen (+0.23 g/l, SE = 0.01 in the full eligible sample; +0.25 g/l, SE = 0.02 in the healthy subsample) and CRP (ratio: 1.03, 95% CI: 1.00–1.07 in the full eligible sample; ratio: 1.13, 95% CI: 1.07–1.19 in the healthy subsample).

Intraclass correlations showed the highest stability for HDL cholesterol in both samples (ICC = 0.81). Other parameters were also moderately to highly stable over time (ICC >0.49), although stability was somewhat lower for glucose (ICC >0.43). Total and LDL cholesterol appeared to be somewhat more stable in the healthy subsample (total cholesterol: ICC = 0.68 vs ICC = 0.59 in the full eligible sample; LDL cholesterol: ICC = 0.65 vs ICC = 0.57 in the full eligible sample), as was systolic blood pressure (ICC = 0.59 vs ICC = 0.50 in the full eligible sample), but no major differences in stability between the samples were observed for any other cardio-metabolic parameters.

In addition to the repeated-measures ANOVAs and ICCs, we also examined the stability of cardio-metabolic values relative to established cut-offs (Table 5). The proportion of participants who were in the same classification at baseline and follow-up (i.e., either above or below the cut-off at both times) ranged from 71% to 95% in the full eligible sample, and from 73% to 97% in the healthy subsample. In both samples, fasting glucose levels showed the most stability within classifications. Systolic blood pressure was the least stable in the full eligible sample and triglycerides were the least stable in the healthy subsample. Stability was slightly higher in the healthy subsample than the full eligible sample for all cardio-metabolic parameters, but differences were small; ranging from 0.4% for HDL cholesterol to 4.4% for triglycerides (mean difference across all variables = 2.4%).

Adjustment of correlations for attenuation

We used the method recommended by Nunnally and Bernstein [51], as detailed by Krueger and Schkade [52],

to estimate attenuation of the true association by measurement error and short-term intra-individual variability. Separate analyses were conducted for the full eligible sample and the healthy subsample (Table 6). While there was little change in the size of correlations for anthropometric variables, adjustment for attenuation resulted in substantial increases in the size of correlations between baseline and follow-up measurements for many cardio-metabolic parameters. For example, fibrinogen correlations rose from 0.53 for the full eligible sample and 0.52 for the healthy subsample to 0.74 and 0.73, respectively. The greatest adjusted correlation was for hemoglobin in the healthy subsample (0.98). The lowest value (0.46) was for fasting glucose in the full eligible sample.

Discussion

This study examined the stability of anthropometric and cardio-metabolic variables in a large cohort of English adults age ≥50 years over 4 years to determine the extent to which older values can be assumed to reflect current status.

We observed very high stability for the anthropometric variables. BMI and waist circumference increased very slightly, and height decreased slightly over the 4-year follow-up period, but mean changes

Table 3. Stability of cardio-metabolic parameters (untransformed variables) in the full eligible sample (n = 5160) and healthy subsample (n = 1862) of older adults.

	n	Repeated-measures ANOVA				Intraclass correlation
		Baseline mean (SE)	Follow-up mean (SE)	Change mean (SE)	Change p-value	ICC (95% CI) p-value
Full eligible sample						
Systolic BP (mmHg)	4217	134.67 (0.28)	133.79 (0.28)	-0.88 (0.28)	0.002	0.496 (0.472–0.518) <0.001
Diastolic BP (mmHg)	4217	75.40 (0.17)	73.31 (0.17)	-2.09 (0.16)	<0.001	0.525 (0.503–0.547) <0.001
Total cholesterol (mmol/l)	3413	5.95 (0.02)	5.52 (0.02)	-0.43 (0.02)	<0.001	0.587 (0.565–0.609) <0.001
HDL cholesterol (mmol/l)	3408	1.53 (0.01)	1.55 (0.01)	0.02 (0.004)	<0.001	0.809 (0.797–0.820) <0.001
LDL cholesterol (mmol/l)	3276	3.62 (0.02)	3.21 (0.02)	-0.41 (0.02)	<0.001	0.574 (0.550–0.596) <0.001
Hemoglobin (g/dl)	3328	14.47 (0.02)	14.12 (0.02)	-0.35 (0.02)	<0.001	0.645 (0.625–0.665) <0.001
Fibrinogen (g/l)	3291	3.16 (0.01)	3.39 (0.01)	0.23 (0.01)	<0.001	0.533 (0.508–0.557) <0.001
Healthy subsample						
Systolic BP (mmHg)	1560	131.84 (0.43)	132.94 (0.45)	1.10 (0.40)	0.006	0.593 (0.560–0.624) <0.001
Diastolic BP (mmHg)	1560	74.83 (0.26)	74.22 (0.27)	-0.61 (0.25)	0.013	0.583 (0.550–0.615) <0.001
Total cholesterol (mmol/l)	1342	6.09 (0.03)	5.90 (0.03)	-0.19 (0.02)	<0.001	0.683 (0.653–0.710) <0.001
HDL cholesterol (mmol/l)	1338	1.57 (0.01)	1.60 (0.01)	0.03 (0.01)	<0.001	0.814 (0.795–0.832) <0.001
LDL cholesterol (mmol/l)	1296	3.77 (0.03)	3.56 (0.03)	-0.21 (0.02)	<0.001	0.653 (0.620–0.683) <0.001
Hemoglobin (g/dl)	1301	14.55 (0.03)	14.26 (0.03)	-0.29 (0.03)	<0.001	0.679 (0.649–0.707) <0.001
Fibrinogen (g/l)	1298	3.09 (0.02)	3.34 (0.02)	0.25 (0.02)	<0.001	0.524 (0.484–0.563) <0.001

BP: Blood pressure; ICC: Intraclass correlation coefficient; SE: Standard error.
Means at baseline, means at follow-up, and mean changes over time are mutually adjusted for age and sex.

Table 4. Stability of cardio-metabolic parameters (log-transformed variables) in the full eligible sample (n = 5160) and healthy subsample (n = 1862) of older adults.

	n	Repeated-measures ANOVA				Intraclass correlation
		Baseline geometric mean (95% CI)	Follow-up geometric mean (95% CI)	Baseline to follow-up ratio (95% CI)	Change p-value	ICC (95% CI) p-value
Full eligible sample						
Triglycerides (mmol/l)	3413	1.55 (1.52–1.58)	1.50 (1.48–1.52)	0.97 (0.95–0.98)	<0.001	0.611 (0.590–0.632) <0.001
Fasting glucose (mmol/l)	1503	4.91 (4.88–4.93)	4.84 (4.81–4.86)	0.99 (0.98–0.99)	<0.001	0.430 (0.388–0.471) <0.001
CRP (mmol/l)	3410	1.89 (1.82–1.96)	1.95 (1.88–2.02)	1.03 (1.00–1.07)	0.041	0.629 (0.608–0.649) <0.001
Healthy subsample						
Triglycerides (mmol/l)	1342	1.45 (1.41–1.49)	1.43 (1.39–1.47)	0.99 (0.96–1.01)	0.328	0.603 (0.568–0.636) <0.001
Fasting glucose (mmol/l)	671	4.88 (4.84–4.92)	4.81 (4.76–4.84)	0.98 (0.97–0.99)	0.001	0.438 (0.375–0.497) <0.001
CRP (mmol/l)	1342	1.54 (1.45–1.63)	1.74 (1.64–1.85)	1.13 (1.07–1.19)	<0.001	0.626 (0.593–0.658) <0.001

Means at baseline, means at follow-up, and the baseline to follow-up ratio are mutually adjusted for age and sex.
Data were log-transformed for analysis. Geometric means and 95% CI (anti-logs) are presented in the table, and ratio of change with 95% CI.
Note: difference between logs = log of ratio, therefore: log (x) - log (y) = log (x/y).
ICC: Intraclass correlation coefficient.

were less than 2% of the baseline value, and baseline and follow-up measurements were highly correlated. The majority of previous research into anthropometric change over time has looked across populations using series of cross-sectional cohorts, which typically show substantial increases in weight, BMI, and waist circumference over time [58–62]. There is less evidence on within-individual change from longitudinal analyses, although what has been published is consistent with the present results. For example, a population study of Finnish adults who were followed over an average of 5.7 years (range: 4–7 years), and one of Australian adults followed over 5 years, both found that individual changes in weight were small, with the majority of participants maintaining their weight within 5 kg of their initial weight [63,64].

Cardio-metabolic parameters were more variable over time than anthropometric measurements. Each of the 10 cardio-metabolic variables we examined changed significantly from baseline to follow-up, with increases in HDL cholesterol, fibrinogen and CRP, and decreases in systolic and diastolic blood pressure, total cholesterol, LDL cholesterol, triglycerides, fasting glucose and hemoglobin. However, despite changes in the means over time, the majority of participants had consistently high or low levels of each parameter at the two times, and the intra-individual correlations were moderate to high. These results confirm the findings of previous studies with smaller samples [21–26,28–33,35–38] or shorter follow-up periods [21,23–25,31,33], and are consistent with two large-scale studies of CRP [27,34].

Inevitably, the observed association between two measurements of a variable is attenuated relative to its 'true' value by errors at each time of measurement, which include errors related to sample collection, processing, storage and laboratory analyses [65]. We therefore used existing data on the extent of error of measurement as a basis for correcting for attenuation. In the present study, the stability of the anthropometric measurements was so high that correcting for attenuation had little effect. However, correcting for attenuation greatly increased the size of the correlations between baseline and follow-up measurements of many of the cardio-metabolic parameters.

In the full eligible sample (available data at both times), the majority (64%) had some health characteristics that could be expected to affect the stability of either anthropometric or cardio-metabolic markers. We therefore repeated the analyses excluding individuals with long-standing limiting illness at either time, taking action to manage raised cholesterol at either time, and change in treatment of hypertension or diabetes between times, to create a 'healthy' subsample. On the whole, the findings in the healthy subsample were very similar to the full eligible sample, except that systolic blood pressure and levels of total and LDL

cholesterol were more stable in the healthy subsample; most likely due to the exclusion of individuals changing their treatment between baseline and follow-up. There were no notable differences between samples in the stability of fasting glucose levels; but very few participants changed their diabetic treatment (n = 31, 0.6% of the full eligible sample). There were also no notable differences in the stability of inflammatory markers such as CRP or fibrinogen, despite 22% of the full eligible sample reporting a change in limiting long-standing illness from baseline to follow-up. However, previous research has indicated that the most common self-reported limiting long-standing illnesses among older adults are respiratory and musculoskeletal diseases, mental health problems and vision problems [66], which might explain why excluding these individuals did not have a marked effect on the stability of most cardio-metabolic parameters.

The present study is subject to several limitations. The findings cannot be assumed to apply to younger adults. Results might differ in specific patient groups, such as those with diabetes or coronary heart disease. The 'healthy' subsample excluded cases with change in medication for hypertension and diabetes, but not changes in other factors that might be expected to affect cardio-metabolic parameters, such as weight, diet, smoking, alcohol, or physical activity [67–71]. It also did not take into account use of hormone replacement therapy in women, which could affect the stability of some of the markers (e.g., CRP) [72], and although it excluded participants with a change in use of insulin for diabetes, it did not consider changes in use of oral hypoglycemic agents which would also have influenced glucose levels. However, applying stricter exclusion criteria would likely have only served to increase the already high estimates of stability. Another important limitation is that follow-up data were not available for all individuals who provided data at baseline. Compared to those who only had data at baseline, the analyzed sample was younger and healthier – consistent with findings on retention in other longitudinal studies [73]; so results may not be population-representative. In addition, there were missing data among the analyzed sample for individual markers, which may have resulted in a bias toward greater stability. For example, reasons for missing height and weight data included the participant being confined to bed or otherwise ill or in pain; factors likely to be associated with energy imbalance and resultant loss or gain of body weight. There were several exclusion criteria for blood samples, such as having a clotting or bleeding disorder, which might have affected the estimates of stability in blood markers. Bias may be even more pronounced for glucose results, because fasting blood samples were not obtained from >80-year-olds, diabetics, or participants who had ever reported a fit, were frail, or seemed unwell. Moreover, assessment of changes in glucose over time is limited by the use of a single fasting plasma glucose measurement; more reliable estimates might have been obtained by using glycated hemoglobin, which is subject to less fluctuation but still changes over time. The use of non-fasting triglyceride measurements is also likely to have affected estimates of stability.

Nonetheless, despite these numerous limitations, the results of this study provide useful benchmark data on typical changes in anthropometric and cardio-metabolic

Table 5. Stability of cardio-metabolic parameters within clinical classifications in the full eligible sample (n = 5160) and healthy subsample (n = 1862) of older adults.

Cardio-metabolic parameters	Cut-off	Full eligible sample (n = 5160)				Healthy subsample (n = 1862)			
		n	% above cut-off at baseline	% above cut-off at follow-up	% stable	n	% above cut-off at baseline	% above cut-off at follow-up	% stable
Systolic BP	≥140 mmHg	4217	35.7	34.0	70.5	1560	26.6	30.3	76.3
Diastolic BP	≥90 mmHg	4217	9.2	6.8	89.1	1560	7.0	7.5	90.8
Total cholesterol	≥240 mg/dl	3413	39.1	28.3	74.2	1342	42.5	37.8	77.6
HDL cholesterol	≥60 mg/dl	3408	44.1	45.7	82.2	1338	48.1	50.9	82.6
LDL cholesterol	≥160 mg/dl	3276	29.4	19.4	76.3	1296	32.6	26.7	76.3
Triglycerides	≥1.7 mmol/l	3413	43.4	40.7	71.9	1342	38.1	36.8	73.1
Fasting glucose	≥6.1 mmol/l	1503	5.6	4.9	95.1	671	2.7	2.4	97.2
Hemoglobin	≥12.5 g/dl	3328	93.5	90.0	90.8	1301	95.4	94.6	93.9
Fibrinogen	≥3.6 g/l	3291	25.0	36.1	72.9	1298	19.6	29.3	76.0
CRP	≥3 mmol/l	3410	34.5	34.7	76.0	1342	25.4	28.4	78.8

Stable = values in the same classification at baseline and follow-up (i.e., low at baseline and low at follow-up or high at baseline and high at follow-up).

Table 6. Correlations between baseline and follow-up measurements of anthropometric variables and cardio-metabolic parameters in the full eligible sample (n = 5160) and healthy subsample (n = 1862) of older adults, adjusted for attenuation by measurement error and short-term intra-individual variability.

	Full eligible sample (n = 5160)				Healthy subsample (n = 1862)			
	r_{xy}	r_{xx}	r_{yy}	ρ_{xy} disattenuated correlation	r_{xy}	r_{xx}	r_{yy}	ρ_{xy} disattenuated correlation
Anthropometric variables								
Height	0.999	0.997	0.997	1.00	0.999	0.997	0.997	1.00
Weight	0.957	0.999	0.999	0.958	0.965	0.999	0.999	0.966
BMI	0.941	0.999	0.999	0.942	0.947	0.999	0.999	0.948
Waist	0.926	0.971	0.971	0.954	0.928	0.971	0.971	0.956
Cardio-metabolic parameters								
Systolic BP	0.496	0.82	0.82	0.605	0.593	0.82	0.82	0.723
Diastolic BP	0.525	0.71	0.71	0.739	0.583	0.71	0.71	0.821
Total cholesterol	0.587	0.90	0.90	0.652	0.683	0.90	0.90	0.759
HDL cholesterol	0.809	0.96	0.96	0.843	0.814	0.96	0.96	0.848
LDL cholesterol	0.574	0.95	0.95	0.604	0.653	0.95	0.95	0.687
Triglycerides	0.611†	0.79	0.79	0.773	0.603†	0.79	0.79	0.763
Fasting glucose	0.430†	0.94	0.94	0.457	0.438†	0.94	0.94	0.466
Hemoglobin	0.645	0.69	0.69	0.935	0.679	0.69	0.69	0.984
Fibrinogen	0.533	0.72	0.72	0.740	0.524	0.72	0.72	0.728
CRP	0.629†	0.955	0.955	0.659	0.626†	0.955	0.955	0.655

†Intraclass correlation based on log-transformed data.
x = baseline measurement; y = follow-up measurement; r_{xy} = observed correlation between x and y; r_{xx} = reliability of x; r_{yy} = reliability of y; ρ_{xy} = true correlation between x and y.

variables over time in the general population. To our knowledge, it is the first study to explicitly compare changes in these markers in healthy individuals to population-wide changes, and the first to address the impact of measurement error, improving the accuracy of stability estimates. The large sample size is also a strength.

Conclusion & future perspective

The present findings showed that changes in most anthropometric and cardio-metabolic variables over a period of 4 years were small, and values were generally highly correlated over time. In studies where it is not possible to obtain recent measures, values from several years before are likely to be a good proxy for analyses of associations with health outcomes. It is important to keep in mind that some variables were more stable than others and the limitations to the reliability such as time of day variation, non-fasting status and lack of control for other medication; although these would likely have increased the correlations over time. The use of older measurements of anthropometric and cardio-metabolic status where more recent data are not available will widen the scope of large-scale epidemiological studies to examine associations with chronic diseases in the future.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Open access

Executive summary

Background

- Many large epidemiological studies include anthropometric and cardio-metabolic measurements, but financial or logistical limitations often restrict measurements to a single time-point. Medium-term stability has only sporadically been assessed.

Method & results

- This study examined change over 4 years in a large cohort of older adults and observed only modest changes in most anthropometric and cardio-metabolic variables, with high intra-individual correlations.
- Subgroup analyses demonstrated that stability was similar in the full sample and a 'healthy' subsample that excluded participants with limiting long-standing illness or taking action to lower cholesterol at either wave, or change in medication for hypertension or diabetes between waves.

Conclusion

- Based on these findings, we conclude that a one-time sample is probably adequate to capture anthropometric and cardio-metabolic parameters over the medium term in general-population samples.

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