

Appendix 1: Frailty phenotype criteria

Criterion	Definition
Unintentional weight loss	Self-report of unintentional loss of ≥ 4.5 kg in prior year or ≥ 2.3 kg in prior 6 months.
Weakness	Maximum grip strength ^a : average value of 3 measurements, using writing hand. Criterion considered present in lowest 20% per stratum of combined cohort. Strata ^b : Male BMI ≤ 24 Female BMI ≤ 23 Male BMI 24.1-26.0 Female BMI 23.1-26.0 Male BMI 26.1-28.0 Female BMI 26.1-29.0 Male BMI ≥ 28.1 Female BMI ≥ 29.1
Exhaustion	Subjects answering “occasionally” or “most of the time” to either one of two statements ^c : During the last week, how often have you felt that: (a) Everything you did was an effort or (b) I could not ‘get going’ Answer options: “rarely (<1 day)”, “some of the time (1-2 days)”, “occasionally (3-4 days)” or “most of the time (5-7 days)”

Slowness

Walking time/4.57 m (15 feet) at usual walking pace^d.

Criterion was considered present in lowest 20% per stratum of combined cohort. Strata^b:

Male height ≤173

Female height ≤159

Male height >173

Female height >159

Low physical activity

Subjects answering “yes, limited a lot” when asked whether their health limits vigorous activities such as running, lifting heavy objects, participating in strenuous sports.

Answer options: “not at all”, “yes, limited a little” or “yes, limited a lot”

^ausing a Jamar handheld dynamometer (Jamar Plus+ Digital Hand Dynamometer, Jamar,

US); subjects with pain in the dominant hand were excluded; ^bstrata as previously

described by Fried [1]; ^cderived from the Center of Epidemiologic Studies Depression

(CES-D) scale; ^dindividuals were excluded if walking was painful or impossible without

assistance

Appendix 2: definitions of comorbidities and metabolic syndrome

AANCC:

Diabetes mellitus was defined as an HbA1c (IFCC) ≥ 48 mmol/mol and/or blood glucose (non-fasting) ≥ 11.1 mmol/L and/or blood glucose (fasting) ≥ 7.0 mmol/L, and/or in those taking antidiabetic medication. Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min using the Chronic Kidney Disease Epidemiology Collaboration formula (CKD-EPI).

Hypertension was defined as having a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg in 3 consecutive measurements with a one minute interval (Omron 705IT), and/or the use of antihypertensive drugs.

Chronic obstructive pulmonary disease was defined as a forced expiratory volume in one second to forced vital capacity ratio < 0.7 in all three forced expiratory spirometric measurements (MicroDirect SpiroUSB) without bronchodilation, and/or in those currently taking bronchodilators. Osteoporosis was defined as a dual-energy X-ray absorptiometry T-score ≤ -2.5 standard deviations (postmenopausal women and men aged ≥ 50) or Z-score ≤ -2 standard deviations (premenopausal women and men aged < 50), or in those reporting atraumatic fracture by questionnaire.

The following conditions were self-reported by questionnaire: myocardial infarction, angina pectoris, peripheral arterial disease, ischemic cerebrovascular disease and non-AIDS/AIDS associated cancer. 100% of diagnoses reported by HIV-infected participants were medically validated using hospital records. 88.4% of diagnoses reported by HIV-uninfected participants were validated by using general practitioners' medical files.

The diagnosis of the metabolic syndrome was based on the consensus definition proposed by the International Diabetes Federation Task Force on Epidemiology and Prevention, National Heart, Lung, and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity [22].

Metabolic syndrome was diagnosed if an individual satisfied any three of the following conditions:

- Waist-circumference ≥ 94 cm in men or ≥ 80 cm in women.
- Triglycerides ≥ 1.7 mmol/L and/or taking triglyceride lowering drugs (i.e. fibrates or nicotinic acid analogues).
- HDL-cholesterol < 1.0 mmol/L in men and < 1.3 mmol/L in women and/or taking HDL-increasing drugs (i.e. fibrates or nicotinic acid analogues).
- Blood pressure: systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥ 85 mmHg and/or taking antihypertensive drugs.
- Fasting glucose ≥ 5.5 mmol/L and/or non-fasting glucose ≥ 11.1 mmol/L* and/or HbA1c (IFCC) ≥ 48 mmol/mol* and/or taking antidiabetic drugs.

**adaptations compared to the consensus definition*