

## Appendices

### Appendix 1: Fried Frailty Index derived from Cardiovascular Health Study

Criterion	Frailty Status
<b>Shrinking</b>	<b>Frailty cut point:</b> <b>Baseline:</b> Self reported unintentional weight loss $\geq 10$ lb in previous year <b>Follow-up:</b> Unintentional weight loss $\geq 5\%$ of previous year's body weight <u>OR</u> BMI $< 18.5$ kg/m <sup>2</sup>
<b>Physical endurance/energy</b>	<i>Geriatric Depression Scale:</i> 1. Do you feel full of energy? 2. During the last 4 weeks how often you rested in bed during day?  Response options: Every day, every week, once, not at all.  <b>Frailty cut point:</b> No to 1 and every day or every week to 2.
<b>Low physical activity</b>	<i>Frequency of mildly energetic, moderately energetic and very energetic physical activity.</i>  Response options: $\geq 3$ times per week, 1-2 times per week, 1-3 times per month, hardly ever/never  <b>Frailty cut point:</b> Hardly ever/never for very energetic physical activity AND for moderately energetic physical activity.
<b>Weakness</b>	Hand grip strength in Kg: GRIP-D hand held dynamometer, dominant hand, average of 3 measures.  <b>Frailty cut point:</b> <b>Grip strength:</b> lowest 20% (by gender, body mass index) <i>Men</i> BMI $\leq 24$ $\leq 29$ BMI 24.1–26 $\leq 30$ BMI 26.1–28 $\leq 30$ BMI $> 28$ $\leq 32$ <i>Women</i> BMI $\leq 23$ $\leq 17$ BMI 23.1–26 $\leq 17.3$ BMI 26.1–29 $\leq 18$ BMI $> 29$ $\leq 21$
<b>Slow walking speed</b>	Walking time in seconds (usual pace) over 15 feet  <b>Frailty cut point:</b> Slowest 20%, stratified by gender and median standing height. <i>Men</i> Height $\leq 173$ cm $\geq 7$ seconds Height $> 173$ cm $\geq 6$ seconds <i>Women</i> Height $\leq 159$ cm $\geq 7$ seconds Height $> 159$ cm $\geq 6$ seconds  <u>OR</u> Time to complete "timed up and go test" (TUG)  <b>Frailty cut point:</b> TUG time $\geq 19$ seconds

**Frail:**  $\geq 3$  criteria present; **Intermediate or Pre-Frail:** 1 or 2 criteria present; **Robust :** 0 criteria present

Adapted from Fried et al, Cardiovascular Health Study Collaborative Research G. Frailty in older adults: Evidence for a phenotype. *The Journals of Gerontology. Series A, Biological sciences and medical sciences.* 2001;56:M146-156.

## Appendix 2: Rockwood Frailty Index derived from Canadian Study of Health and Aging

1	Very fit – robust, active, energetic, well motivated and fit; these people commonly exercise regularly and are in the most fit group for their age
2	Well – without active disease, but less fit than people in category 1.
3	Well, with treated co-morbid disease – disease symptoms are well controlled compared with those in category 4
4	Apparently vulnerable – although not frankly dependent, these people commonly complain of being “slowed up” or have disease symptoms.
5	Mildly frail – with limited dependence on others for instrumental activities of daily living
6	Moderately frail – help is needed with both instrumental and non-instrumental activities of daily living
7	Severely frail – completely dependent on others for the activities of daily living, or terminally ill.

*Adapted from Rockwood et al, A global clinical measure of fitness and frailty in elderly people. Canadian Medical Association Journal 2005;173:489-495*

### Appendix 3: Definitions of outcome measures

Outcome	Definition
Death	Death from any cause Classified as cardiovascular or non-cardiovascular
Myocardial Infarction*	Defined as below
Type 1	Spontaneous myocardial infarction related to ischaemia due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection
Type 2	Myocardial infarction secondary to ischaemia due to either increased oxygen demand or decreased supply, e.g. coronary artery spasm, coronary embolism, anaemia, arrhythmias, hypertension, or hypotension
Type 3	Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischaemia, accompanied by presumably new ST elevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood
Type 4a	Myocardial infarction associated with PCI
Type 4b	Myocardial infarction associated with stent thrombosis as documented by angiography or at autopsy
Type 5	Myocardial infarction associated with CABG
Revascularisation	PCI to lesions not identified previously. CABG for new symptoms or complications of PCI Target lesion or target vessel revascularisation
Target Lesion Revascularisation	Re-interventions inside the implanted stent or within 5 mm proximally or distally
Target Vessel Revascularisation	Re-interventions in the same vessel by PCI or by CABG
Stroke	Stroke is defined as the presence of a new focal neurologic deficit thought to be vascular in origin, with signs or symptoms lasting more than 24 hours. It is strongly recommended (but not required) that an imaging procedure such as CT scan or MRI be performed. Stroke will be further classified as ischaemic, haemorrhagic or type uncertain.
Heart Failure	Heart failure will be defined as a hospital admission with any of the following symptoms and signs: worsening breathlessness, fatigue, fluid overload, pulmonary oedema, elevated venous pressure and elevated NT-prohormone Brain Natriuretic Peptide. Confirmation of heart failure according to local expert judgement and evidence of impaired left ventricular function will be required for the event to be classified as heart failure.
Rehospitalisation	Repeat hospitalisation for any reason during follow up period
Adverse Event	Any untoward medical occurrence
Serious Adverse Event	Any untoward medical occurrence that: Results in death and is life-threatening. The term "life-threatening" in the definition of "serious adverse event" refers to an event that 1. Requires hospitalisation or prolongation of existing inpatient's hospitalisation; 2. Results in persistent or significant disability or incapacity.

*PCI-Percutaneous Coronary Intervention, CABG-Coronary Artery Bypass Graft, CT-Computerised Tomography, MRI-Magnetic Resonance Imaging*

*\* Adapted from Thygesan et al, Universal definition of myocardial infarction, European Heart Journal (2007) 28, 2525–2538*

## Appendix 4: Bleeding Academic Research Consortium (BARC) definition for bleeding

Type 0	No bleeding
Type 1	Bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a healthcare professional. May include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional.
Type 2	Any overt, actionable sign of haemorrhage (e.g. more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for Type 3, 4 or 5 but does meet at least one of the following criteria: (1) requiring non-surgical, medical intervention by a healthcare professional, (2) leading to hospitalization or increased level of care, or (3) prompting evaluation.
Type 3a	Overt bleeding plus haemoglobin drop of 3 to <5g/dl* (provided haemoglobin drop is due to bleed) Any transfusion with overt bleeding
Type 3b	Overt bleeding plus haemoglobin drop $\geq 5\text{g/dl}^*$ (provided haemoglobin drop is due to bleed) Cardiac tamponade Bleeding requiring surgical intervention for control (excluding dental/nasal/ skin/ haemorrhoid) Bleeding requiring intravenous vasoactive agents
Type 3c	Intracranial haemorrhage (does not include micro-bleeds or haemorrhagic transformation, does include intraspinal) Subcategories confirmed by autopsy or imaging or lumbar puncture Intraocular bleed compromising vision
Type 4:	CABG-related bleeding Perioperative intracranial bleeding within 48 hours Reoperation following closure of sternotomy for the purpose of controlling bleeding Transfusion of $\geq 5$ units of whole blood or packed red blood cells within a 48-hour period† Chest tube output $\geq 2$ litres within a 24-hour period If a CABG-related bleed is not adjudicated as at least a Type 3 severity event, it will be classified as 'not a bleeding event'.
Type 5a	Probable fatal bleeding; no autopsy or imaging confirmation, but clinically suspicious
Type 5b	Definite fatal bleeding; overt bleeding or autopsy or imaging confirmation

\*Corrected for transfusion (1 U packed red blood cells or 1 U whole blood 1 g/dL haemoglobin).

†Cell saver products are not counted.

Adapted from Mehran et al, Standardized bleeding definitions for cardiovascular clinical trials: A consensus report from the bleeding academic research consortium. *Circulation*. 2011;123:2736-2747