# Renal Cachexia

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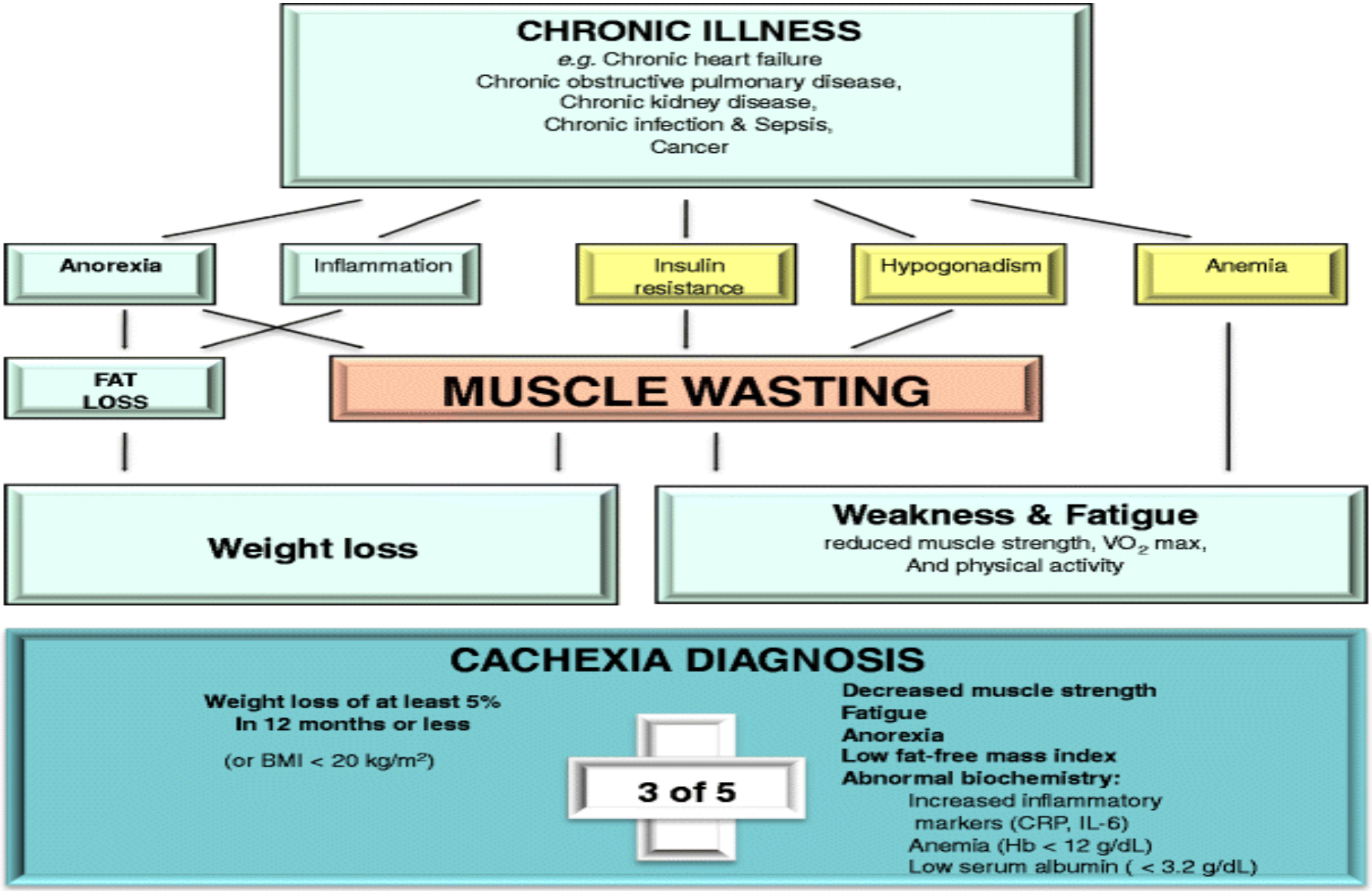
# Cachexia

- Cachexia is ‘a complex metabolic syndrome associated with underlying illness and characterised by muscle loss, with or without loss of fat’

- Definition of cachexia in chronic illness
  - weight loss of at least 5% within ≤12 months or Body Mass Index (BMI) <20 kg/m$^2$
    - plus three of the following five features:
      - decreased muscle strength;
      - fatigue;
      - anorexia;
      - low fat-free mass index;
      - abnormal biochemistry (increased inflammatory markers [CRP, IL-6], anaemia [Hb <120 g/L], low serum albumin [<32g/L] (Evans *et al.* 2008).

**Evans** *et al*. (2008). Cachexia, a new definition. *Clinical Nutrition* 27,793–799.

# Pathogenesis of cachexia



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# Importance of the problem - cachexia

- Cachexia is linked with poor outcomes for the patients
- Cachexia causes great morbidity, limits therapy
- No standardised 'best treatment' for cachexia
- Lack of guidelines / protocols in clinical practice

# Importance of the problem – cachexia in renal disease

- Between 30-60% of advanced CKD patients will have cachexia
  - Among potential candidates to explain the high rate of morbidity and mortality in CKD patients, cachexia continues to top the list

- Limited attention has been devoted to cachexia in renal disease

- For renal cachexia there are no standardised definitions or inclusion criteria to help inform practice or research

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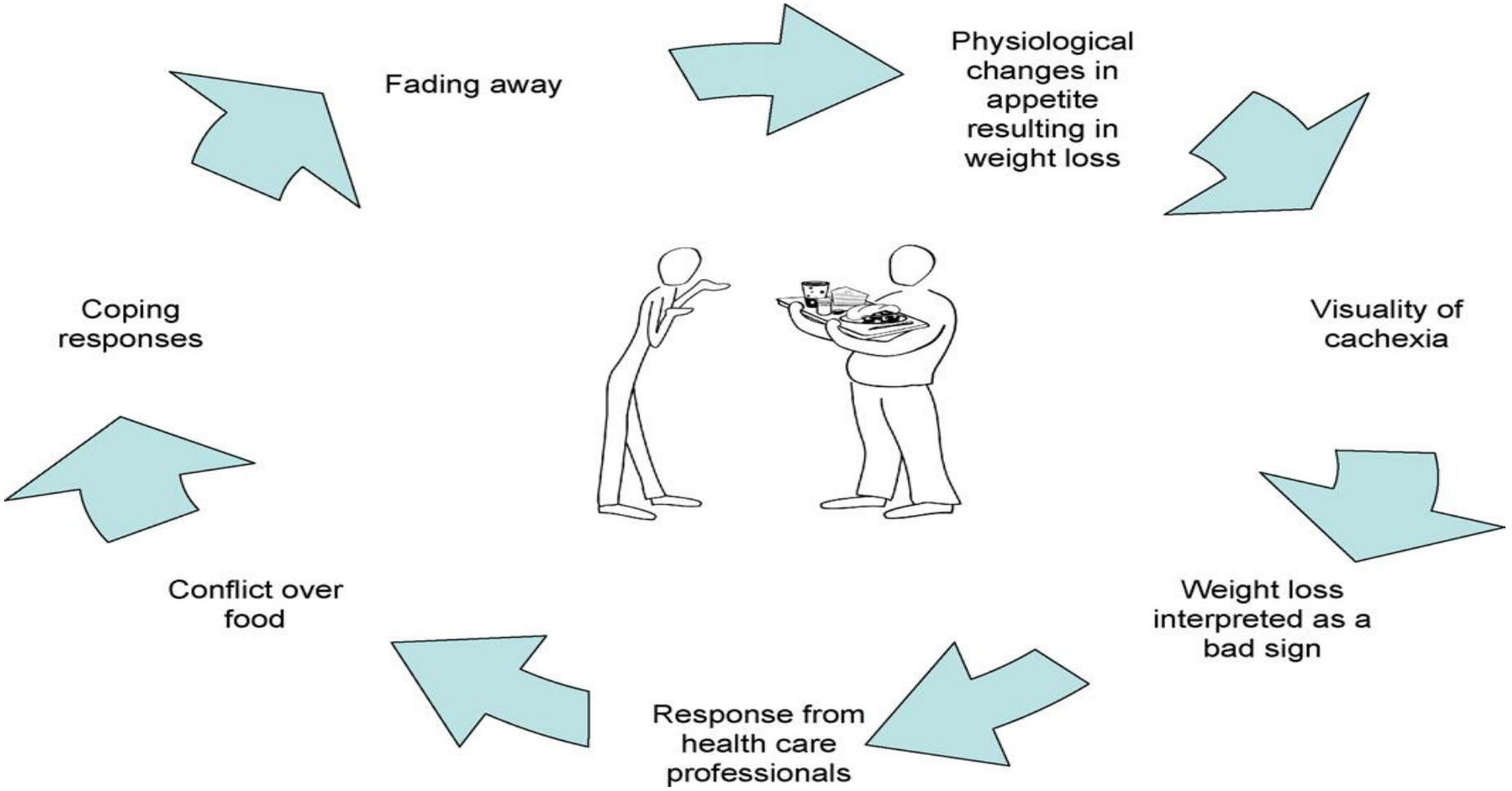
# Management of cachexia in renal disease

- Challenging – definition needs refinement for renal population
- Discriminating cachexia from other causes of malnutrition
- Clinically differentiate between cachexia and Protein energy wasting as each state may require distinct management strategies

# Previous cachexia work: advanced cancer population




Reid et al (2009). The experience of cancer cachexia: A qualitative study of advanced cancer patients and their family members. *International Journal of Nursing Studies*, *46*(5), 606-616.

# Project grant

- Grant award Public Health Agency

- Aims and objectives
  - Identify the prevalence of cachexia in haemodialysis patients
  - Determine the percentage of haemodialysis patients who experience the known characteristics of cachexia (how many and to what degree)
  - Develop a definition of cachexia specific to this ESKD population

# Study population

- Adult chronic haemodialysis patients at BHSCT Nephrology Unit will be recruited into a 2 year longitudinal study
- Patients are monitored for one year (or time of death if < 1 year)
- Recruitment over 7 months
- Expected recruitment rate of 145 patients on maintenance haemodialysis for at least 90 days
- Attrition: Regional Nephrology Unit, Belfast indicates an annual mortality of 16% for patients with stage 5 CKD receiving maintenance haemodialysis
- Inclusion/exclusion criteria:

| **Inclusion criteria** | **Exclusion criteria** |
|---|---|
| Confirmed diagnosis of stage 5 CKD (estimated GFR <15 mL/min/1.73m$^2$) receiving dialysis | Stage 1-4 CKD |
| Able to read and write English | Stage 5 CKD who had declined haemodialysis |
| Over 18 | Lacking capacity to give consent |
| | Under the age of 18 |
| | Non-English speaking patients |

# Data collection

| Time point 0 | Time point 1 | Time point 2 | Time point 3 | Time point 4 | Time point 5 | Time point 6 |
|---|---|---|---|---|---|---|
| 0 months | 2 months | 4 months | 6 months | 8 months | 10 months | 12 months |
| **BASELINE MEASURES** | | | | | | |
| **< BIO-CHEMISTRY, BODY MASS MEASUREMENTS AND STANDARDIZED QUESTIONNAIRES >** | | | | | | |

**Baseline**

- Socio-demographic information
- Charlson Comorbidity Index
- Primary renal disease
- Dialysis vintage

**Baseline & every two months**

**Bio-chemistry**

- Recent hospitalization
- Frequency and dosage of any steroids, immunosuppressant's and erythropoietin stimulants
- Urea clearance
- Residual renal function
- Routine bloods for CRP, albumin, HB

**Body mass measurements**

- Weight
- BIA
- Hand grip strength
- Skin fold thickness
- Mid upper arm circumference

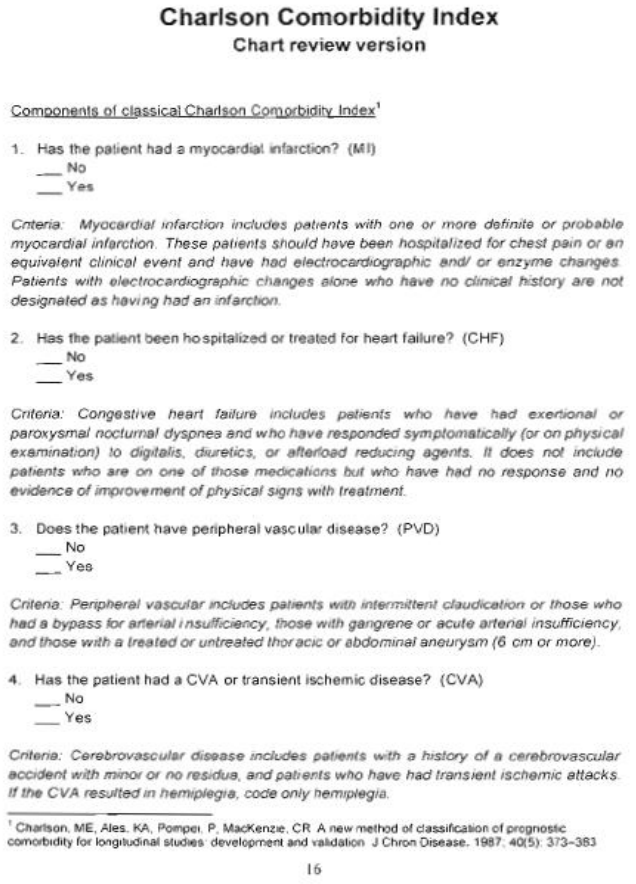
**Standardized questionnaires**

- Quality of life - KDQOL-SF36
- Appetite – FAACT questionnaire
- Fatigue - FACIT fatigue scale

# Baseline measures

- Demographics e.g. sex, age
- Primary renal disease
- Dialysis vintage
- Charlon Comorbidity Index

  (Charlson, 1984)



**Charlson Comorbidity Index**
**Chart review version**

Components of classical Charlson Comorbidity Index[1]

1. Has the patient had a myocardial infarction? (MI)
   ___ No
   ___ Yes

*Criteria: Myocardial infarction includes patients with one or more definite or probable myocardial infarction. These patients should have been hospitalized for chest pain or an equivalent clinical event and have had electrocardiographic and/ or enzyme changes. Patients with electrocardiographic changes alone who have no clinical history are not designated as having had an infarction.*

2. Has the patient been hospitalized or treated for heart failure? (CHF)
   ___ No
   ___ Yes

*Criteria: Congestive heart failure includes patients who have had exertional or paroxysmal nocturnal dyspnea and who have responded symptomatically (or on physical examination) to digitalis, diuretics, or afterload reducing agents. It does not include patients who are on one of those medications but who have had no response and no evidence of improvement of physical signs with treatment.*

3. Does the patient have peripheral vascular disease? (PVD)
   ___ No
   ___ Yes

*Criteria: Peripheral vascular includes patients with intermittent claudication or those who had a bypass for arterial insufficiency, those with gangrene or acute arterial insufficiency, and those with a treated or untreated thoracic or abdominal aneurysm (6 cm or more).*

4. Has the patient had a CVA or transient ischemic disease? (CVA)
   ___ No
   ___ Yes

*Criteria: Cerebrovascular disease includes patients with a history of a cerebrovascular accident with minor or no residua, and patients who have had transient ischemic attacks. If the CVA resulted in hemiplegia, code only hemiplegia.*

[1] Charlson, ME, Ales, KA, Pompei, P, MacKenzie, CR. A new method of classification of prognostic comorbidity for longitudinal studies: development and validation. J Chron Disease. 1987; 40(5): 373–383

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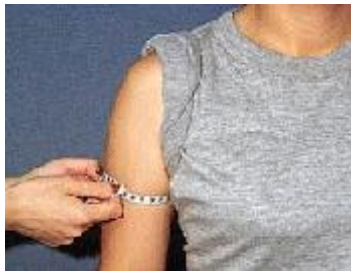
# Bio-chemistry

- Residual renal function & urea clearance levels
- Routine bloods for CRP, albumin, HB
- Drugs
  - –steroids
  - –immunosuppressants
  - –erythropoietin stimulants

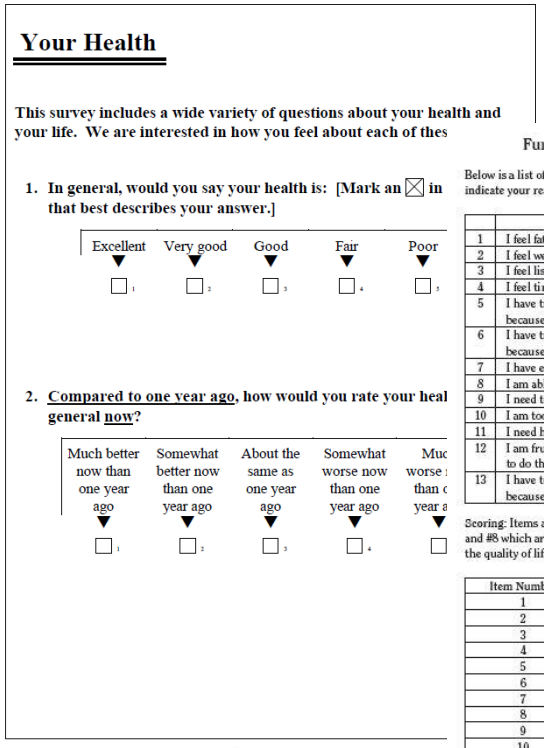
# BODY MASS AND MUSCLE STENGTH

- Weight - scales
- Body mass index – Bioelectrical impedance Analysis (BIA)
- Skin fold thickness - callipers
- Mid upper arm circumference
- Hand grip strength - dynamometry

# Standardised assessments

## Kidney Disease Quality of Life instrument Short Form- KDQOL-SF36



**Your Health**

**This survey includes a wide variety of questions about your health and your life. We are interested in how you feel about each of thes**

1. **In general, would you say your health is: [Mark an ☒ in that best describes your answer.]**

| Excellent | Very good | Good | Fair | Poor |
|---|---|---|---|---|
| ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ 5 |

2. **Compared to one year ago, how would you rate your heal general now?**

| Much better now than one year ago | Somewhat better now than one year ago | About the same as one year ago | Somewhat worse now than one year ago | Muc worse than year a |
|---|---|---|---|---|
| ☐ 1 | ☐ 2 | ☐ 3 | ☐ 4 | ☐ |

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## FACIT -fatigue scale

Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale (Version 4)

Below is a list of statements that other people with your illness have said are important. Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

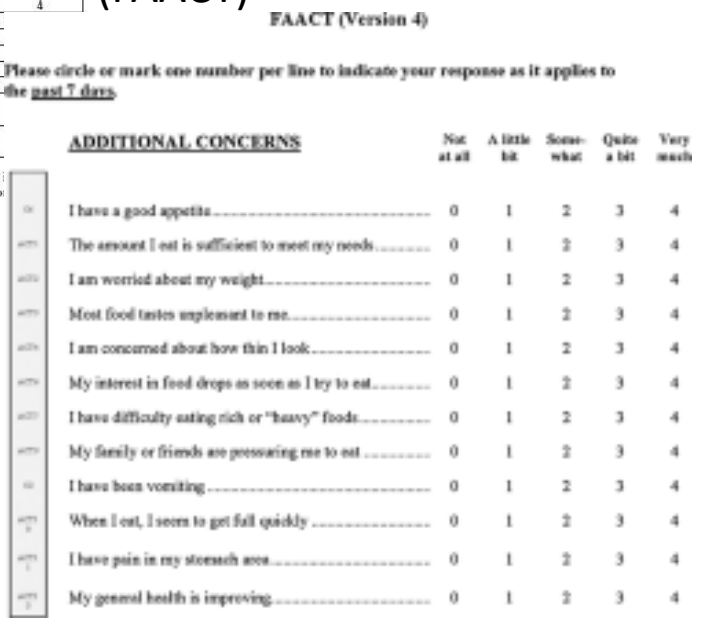
| | | Not At All | A Little Bit | Somewhat | Quite a Bit | Very Much |
|---|---|---|---|---|---|---|
| 1 | I feel fatigued | 0 | 1 | 2 | 3 | 4 |
| 2 | I feel weak all over | 0 | 1 | 2 | 3 | 4 |
| 3 | I feel listless ("washed out") | 0 | 1 | 2 | 3 | 4 |
| 4 | I feel tired | 0 | 1 | 2 | 3 | 4 |
| 5 | I have trouble starting things because I am tired | 0 | 1 | 2 | 3 | 4 |
| 6 | I have trouble finishing things because I am tired | 0 | 1 | 2 | 3 | 4 |
| 7 | I have energy | 0 | 1 | 2 | 3 | |
| 8 | I am able to do my usual activities | 0 | 1 | 2 | 3 | |
| 9 | I need to sleep during the day | 0 | 1 | 2 | 3 | |
| 10 | I am too tired to eat | 0 | 1 | 2 | 3 | |
| 11 | I need help doing my usual activities | 0 | 1 | 2 | 3 | |
| 12 | I am frustrated by being too tired to do the things I want to do | 0 | 1 | 2 | 3 | |
| 13 | I have to limit my social activity because I am tired | 0 | 1 | 2 | 3 | |

Scoring: Items are scored as follows: 4=Not At All; 3=A Little Bit; 2=Somewhat; 1=Quite A Bit; 0=Very Much, EXCEPT and #8 which are reversed scored. Score range 0-52. A score of less than 30 indicates severe fatigue. The higher the sco the quality of life.

| Item Number | Reverse Item? | | Item Response | Item Score |
|---|---|---|---|---|
| 1 | 4 | - | | = |
| 2 | 4 | - | | = |
| 3 | 4 | - | | = |
| 4 | 4 | - | | = |
| 5 | 4 | - | | = |
| 6 | 4 | - | | = |
| 7 | 0 | + | | = |
| 8 | 0 | + | | = |
| 9 | 4 | - | | = |
| 10 | 4 | - | | = |
| 11 | 4 | - | | = |
| 12 | 4 | - | | = |
| 13 | 4 | - | | = |

Sum individual item scores: _____
Multiply by 13: _____
Divide by number of items answered: _____

## Functional Assessment of Anorexia/Cachexia Therapy (FAACT)



**FAACT (Version 4)**

**Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

| ADDITIONAL CONCERNS | Not at all | A little bit | Some-what | Quite a bit | Very much |
|---|---|---|---|---|---|
| I have a good appetite | 0 | 1 | 2 | 3 | 4 |
| The amount I eat is sufficient to meet my needs | 0 | 1 | 2 | 3 | 4 |
| I am worried about my weight | 0 | 1 | 2 | 3 | 4 |
| Most food tastes unpleasant to me | 0 | 1 | 2 | 3 | 4 |
| I am concerned about how thin I look | 0 | 1 | 2 | 3 | 4 |
| My interest in food drops as soon as I try to eat | 0 | 1 | 2 | 3 | 4 |
| I have difficulty eating rich or "heavy" foods | 0 | 1 | 2 | 3 | 4 |
| My family or friends are pressuring me to eat | 0 | 1 | 2 | 3 | 4 |
| I have been vomiting | 0 | 1 | 2 | 3 | 4 |
| When I eat, I seem to get full quickly | 0 | 1 | 2 | 3 | 4 |
| I have pain in my stomach area | 0 | 1 | 2 | 3 | 4 |
| My general health is improving | 0 | 1 | 2 | 3 | 4 |

# Analysis

- Mean inferential statistics across all variables

  - Age
  - Sex
  - Unintentional weight loss ≥5% in 6 months or ≥10% 12 months (in the absence of documented weights, BMI <20 kg/m$^2$) and in the absence of starvation
  - Decreased muscle strength
  - Fatigue
  - Anorexia
  - Lean tissue depletion
  - Abnormal biochemistry: increased inflammatory markers [CRP >5mg/L]; anaemia [haemoglobin <120 g/L]; low serum albumin [<32g/L]
  - Drug use (specifically frequency and dosage of immunosuppressants, steroids and erythropoietin stimulants)
  - Charlson Comorbidity Index score
  - Recent hospitalisation
  - Quality of life score (KDQOL-SF36)

- T-tests: provide information on ESKD participants who do and do not exhibit known characteristics of cachexia

- Latent growth modelling: systematic change and inter-individual variability

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# Future considerations

- Pilot clinical data to inform an application to develop a consensus definition for stage 5 CKD haemodialysis patients who have cachexia and test a treatment modality aimed at improving morbidity and mortality
- Establishing a clinical phenotype and in turn a consensus definition for renal cachexia will allow for early recognition and identification of the syndrome
- Future research can develop and test targeted interventional strategies aimed at improving both quality of life and morbidity in patients on haemodialysis
- Help to standardise holistic care to this client group through the development of patient centred care guidelines and patient care pathways

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- Questions?

- Please contact j.reid@qub.ac.uk