University of Southampton

Faculty of Medicine

Human Development and Health

Exploring Influences on Appetite in Ageing

by

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Abstract

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Appetite loss is common in older people and when due to the ageing process is termed anorexia of ageing. There is little guidance for management of anorexia of ageing despite its associations with negative health outcomes. This research involved a series of studies, using a range of methods, to explore potentially-modifiable influences on appetite in older people, with a view to informing future interventions for anorexia of ageing.

First, current evidence for influences on appetite was appraised and organised into categories relating to - physiology (maintaining energy balance), hedonism (pleasure and reward in eating) and external cues (social and environmental contexts of eating). Next, a systematic review highlighted multiple approaches to appetite assessment in older people, with the Simplified Nutritional Appetite Questionnaire (SNAQ) a candidate for standardisation. In addition, there was a paucity of interventions for anorexia of ageing with only small single studies signalling benefit of a range of interventions, which were not replicated.

Influences on appetite in older people were then examined in different cohorts of older individuals. Continuous analysis of hospital inpatients (n=474, mean age 84 years) identified that low mood (measured by Geriatric Depression Scale 15) and low level of habitual physical activity (measured by Physical Activity Scale for the Elderly) were associated with poorer appetite during admission (measured by SNAQ). In the community setting, experiences of 13 individuals were analysed using qualitative reflexive thematic analysis. Perceptions of appetite and appetite loss involved use of two narratives- as an emotional experience or a reflection of physical need. Influences on appetite related to these narratives- hedonic factors and external cues to emotional experience and physical factors to physical need. In a second community study, continuous analysis (n=86, mean age 78 years) identified higher social network score (measured by Lubben Social Network Score 6) associated with better appetite (SNAQ). Whereas watching TV more often while eating main meals and greater comorbidities linked with poorer appetite (SNAQ).

This research has identified complex and wide-ranging influences on appetite in older people, organised into the categories- physiological, hedonic and relating to external cues. These categories were represented in hospital and community settings and may also impact individuals differently depending on their perception of appetite and the role it serves. Influences on appetite need to be assessed together and over time to determine their relationships with appetite and one another. There may be a role for multi-component interventions to manage the anorexia of ageing, which will likely be most effective when based on the older individual's perceptions of their appetite loss and their needs and priorities.

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Research Thesis: Declaration of Authorship

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I declare that this thesis and the work presented in it are my own and has been generated by me as the result of my own original research.

I confirm that:

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3. Where I have consulted the published work of others, this is always clearly attributed;

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- Cox NJ, Morrison L, Ibrahim K, Robinson SM, Sayer AA, Roberts HC. New Horizons in appetite and the anorexia of ageing. *Age and Ageing*. 2020 Feb; afaa014.
- Cox NJ, Lim SER, Howson F, Moyses H, Ibrahim K, Sayer AA, Roberts HC, Robinson S. Poor appetite is associated with six month mortality in hospitalised older men and women. *Journal Nutrition Health and Aging* 2020 Jul; 24, 1107–1110.
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Acknowledgements

Abbreviations

AgRP ....Agouti-Related Peptide

AHPSQ...................................Appetite, Hunger and Sensory Perception Questionnaire

ACC..Anterior Cingulate Cortices

ARC..Hypothalamic Arcuate Nucleus

BMR.......................................Basal Metabolic Rate

BMI..Body Mass Index

CaSIO.....................................Cachexia: Skeletal loss and Inflammation in Older Women Study

CGA ....Comprehensive Geriatric Assessment

CSF...Cerebrospinal Fluid

CCK ....Cholecystokinin

COPD ....Chronic Obstructive Pulmonary Disease

CNAQ......................................Council on Nutrition Appetite Questionnaire

DMH ....Dorsomedial Nucleus

DRAQ......................................Disease Related Appetite Questionnaire

FCs..Fermentable Carbohydrates

FFAR ....Free Fatty Acid Receptors

fMRI..Functional Magnetic Resonance Imaging

GDS-15 ....Geriatric Depression Scale Short Form 15

GLP-1......................................Glucagon Like Peptide 1

IPAQ ....International Physical Activity Questionnaire

LiLL ....Lifestyle in Later Life study

LH ....Lateral Hypothalamic Area

LSNS-6 ....Lubben Social Network Scale 6

MA..Megestrol Acetate

MET ....Metabolic Equivalent

MUST......................................Malnutrition Universal Screening Tool

Abbreviations

MCS................................... Melanocortin System

ME...................................... Median Eminence

MMSE................................. Mini-Mental State Examination

MNA................................... Mini-Nutritional Assessment

MSG .... Monosodium Glutamate

NICE .... National Institute for Health and Care Excellence

NPY.................................... Neuropeptide Y

NTS.................................... Nucleus of the Solitary Tract

ONS .... Oral Nutritional Supplements

OFC.................................... Orbitofrontal Cortex

OXM .... Oxyntomodulin

PASE .... Physical Activity Scale for the Elderly

PFA..................................... Perifornical Area

POMC................................. Pro-opiomelanocortin

PP .... Pancreatic Polypeptide

PVN .... Periventricular Nucleus

PYY .... Peptide YY

RCT.................................... Randomised Controlled Trial

SNAQ................................. Simplified Nutritional Appetite Questionnaire

SCFAs .... Short Chain Fatty Acids

SMART .... Southampton Mealtime Assistance Roll-out Trial

SoMoVe .... Southampton Mobility Volunteer Study

SGA .... Subjective Global Assessment

VAS.................................... Visual Analogue Scale

VMH .... Ventromedial Nucleus

αMSH .... Alpha Melanocyte Stimulating Hormone

5-HT .... Serotonin

Chapter 1   Introduction

1.1   The context- appetite, nutrition and an ageing population.

Over the last century life expectancy has greatly increased and the UK population is ageing, with 12.4 million people aged 65 years and over in 2019, 1.6 million of whom were in the rapidly-expanding age bracket of 85 years and over [1]. Ageing populations is a global phenomenon and the United Nations world estimates in 2019 included 703 million people aged 65 years and over, a figure expected to increase to 1.5 billion by 2050 [2]. However, extended life expectancy does not infer years gained in good health. Rather, many older people are living with complex multi-morbidity and a number of ageing syndromes, such as frailty (a reduced ability to recover bodily homeostasis following an insult, resulting in disproportionate change to health [3]), sarcopenia (a generalised skeletal muscle disorder characterised by loss of strength, mass and function [4]) and cognitive impairment. These reduce independence and quality of life and increase health and social care utilisation. Many of these health conditions have an underlying nutritional basis, as malnutrition, particularly weight loss, is a major contributor to sarcopenia through loss of muscle mass and is an important component of the frailty phenotype. The annual cost of malnutrition in the United Kingdom (with undernutrition particularly prevalent amongst older people) has been previously estimated at £19.6 billion [5]. This can only be expected to rise in the context of an ageing society, so novel approaches to prevent or delay onset of undernutrition in the older population is important.

Appetite loss is common, affecting over 20% of community dwelling older people, and over 40% of those admitted into acute care [6-11]. An increasing body of scientific work has established the importance of appetite loss in malnutrition and other health burdens in the older population, including frailty and sarcopenia. Despite this, there is currently no clear clinical guidance on management of appetite loss in older people.

This thesis explores appetite in the context of ageing. Firstly, the current evidence for appetite regulation and changes implicated for appetite amongst older people, will be reported. Then, the clinical context of appetite assessment and management of appetite loss in older people. A series of exploratory studies considering influences on appetite in later life, which may result in its change, are then described. A particular interest is given to modifiable factors amenable to intervention, which may provide avenues of interest in managing appetite loss in older people, as a novel way of preventing undernutrition.

1.2   Appetite and its regulation

The term appetite derives from the Latin appetitus meaning 'desire for' and can be defined as a natural desire to satisfy a bodily need, especially for food [12]. It is a collection of sensations often broken down into three components; that of hunger, satiation and satiety [13]. Hunger is the sensation driving a person to eat, satiation is the fullness governing the extent and end of a meal, and satiety directs the length of time after eating until hunger dominates again [13].

The concept of how appetite is regulated has developed over more than a century. The initial basis for appetite control comes from the theory of homeostasis, first described by Cannon in 1932 who built upon Bernard's 1859 work "*Le milieu intérieur*" [14]. Homeostasis maintains that the body upholds an existence of equilibrium via multiple complex physiological processes in order to function properly. This theory was broadened into the context of behaviour by Richter in the 1940s [15], who through a series of studies showed that animals will alter their behaviour, such as eating, following changes in their underlying physiology. Thus, he proposed that the drive to maintain homeostasis creates a powerful influence on behaviour [15].

The theory of appetite regulation was taken a step further in the 1980s by Weingarten [16]. He suggested homoeostasis did not explain eating behaviour in certain situations, particularly with reference to an increasing prevalence of obesity. So he incorporated the idea of external stimuli or cues that a person associates with food playing a role in learned behaviours around eating [16]. He termed this behaviour 'incentive-induced hunger' and proposed that it was quick to dominate over satiety after exposure to certain cues, driving a person to eat [16]. The concept of incentive-induced hunger has been built upon further to incorporate the role of the reward system and sensory appreciation of food, now often referred to as the hedonic dimension of appetite [17]. The role of behavioural responses to external cues is also acknowledged to expand beyond their relationship with hedonism, particularly when placing appetite within a societal and cultural context, such as social norms around eating [18]. All of these regulatory mechanisms are thought to interact to control feelings of hunger, satiation and satiety in a psychobiological process [17, 19].

1.2.1   The key central nervous system components in appetite

1.2.1.1   The hypothalamus (appetite control centre)

The psychobiological regulation of appetite has a fundamental neuro-endocrine basis. These complex signalling pathways are predominantly coordinated by an appetite control centre located within the hypothalamic arcuate nucleus (ARC) (Figure 1) [17, 20]. The ARC is closely related to two important structures, the third ventricle and a circumventricular organ called the median eminence (ME) [21]. Both of these structures have increased permeability compared to other areas of the brain (the ME to the circulation and the third ventricle to cerebrospinal fluid (CSF)), making the ARC very receptive to signalling molecules in both the CSF and circulation [22].

Within the ARC, the melanocortin system (MCS) signals appetite. This is made up of two circuits: a stimulatory circuit using the antagonist agouti-related peptide (AgRP) and an inhibitory circuit with the agonist alpha melanocyte stimulating hormone (αMSH) (derived from pro-opiomelanocortin (POMC)) [21, 22]. The stimulatory circuit also expresses neuropeptide Y (NPY) and GABA; these signalling molecules are important in appetite but are also widespread throughout the nervous system [22]. Built-in redundancy within the system has been proposed, to ensure starvation does not occur, if disrupted [21, 22].

The MCS system responds directly to upstream neurotransmitters and circulating hormones, acting as a signal transducer to fine-tune appetite in response to physiology and learning (Figure 2). The MCS system then transmits appetite information to other areas of the brain (including other areas of the hypothalamus (Figure 1), the brainstem and limbic system) and the periphery [22]. Targets of these downstream signalling pathways include areas within the brain implicated in arousal, attention and feeding, the sympathetic and autonomic nervous systems, the thyroid axis, the gastrointestinal tract (both via the vagus nerve and endocrine cells in the gastric and intestinal mucosa) as well as the pancreas [21]. Downstream signalling also interacts with peripheral and central nervous signals to feedback to the ARC [21]. This leads to hypothalamic ability to register low energy states and release hunger signals, then, following consumption of food upregulate satiety signalling molecules to terminate a meal [17].
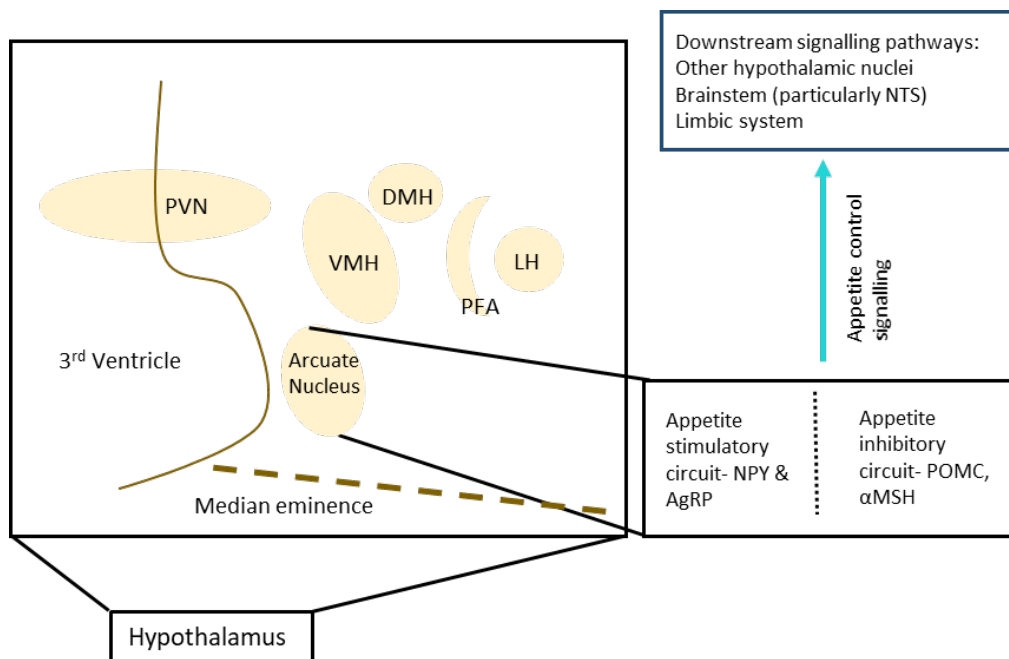
Figure 1   The hypothalamus and appetite.

The arcuate nucleus is the central appetite control centre and is closely related to the third ventricle and median eminence, with downstream signalling pathways to other hypothalamic nuclei and other areas of the brain.

PVN-periventricular nucleus, VMH- ventromedial nucleus , DMH- dorsomedial nucleus , PFA- perifornical area , LH- lateral hypothalamic area , NTS- nucleus of the solitary tract , NPY- neuropeptide-Y, AgRP- agouti-related peptide, αMSH- alpha melanocyte stimulating hormone, POMC- pro-opiomelanocortin.

1.2.1.2   The flavour centres

During a meal the brain's primary taste centre is activated by oral temperature to identify a food's taste; the brain's olfactory centre identifies its smell. Oro-sensory signals from the gut when receiving food are transmitted by the vagus nerve to the nucleus of the solitary tract (NTS) in the brainstem [23, 24]. The NTS processes these inputs, which are then linked to the olfactory, taste and visual information. These all project to the secondary taste centres in the orbitofrontal cortex (OFC) and anterior cingulate cortices (ACC) [23, 24], with different areas activated by pleasant and unpleasant odours. These secondary taste centres form flavour, interacting with learned associations and inputs from the visual cortex [24]. The amygdala also receives olfactory and taste inputs as well as inputs from the OFC; both then project onto the hypothalamus which transduces these signals alongside energy signalling (Figure 2).
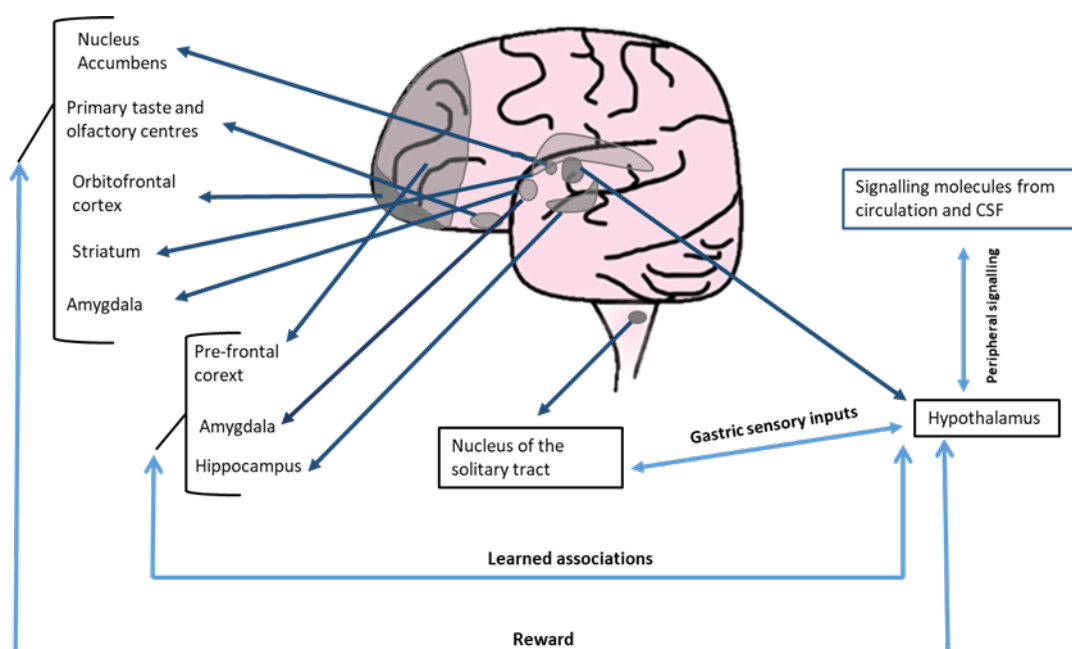
Figure 2   The hypothalamus as a signal transducer.

Central centres of reward and learning feedback to the hypothalamus, particularly the lateral hypothalamic nucleus alongside gastric sensory inputs and peripheral signalling molecules to regulate appetite.

1.2.1.3   The reward centres

The activation of the OFC, ACC and amygdala correlate with a person's ratings of pleasantness. It is therefore proposed that these areas of the brain represent where flavour pleasantness and a 'reward value' is placed on a food [24]. The OFC (via the ACC) and amygdala also project into the striatum (a principle component of the reward system) [24]. The reward system is integral to the hedonic aspect of appetite, and the nucleus accumbens (NA) in the ventral striatum is an essential component [21]. Known signalling molecules for reward-associated eating include dopamine, opioids, endocannabinoids and serotonin [25]. These transmit signals relating to palatability and the reinforcing effect pleasant foods have on eating. The NA and downstream signalling pathways of the ARC, particularly the lateral hypothalamus, all interact, modulating one another to balance the hedonism with the other appetite drivers (such as gut neuro-endocrine signalling, which will be discussed later in this chapter) (Figure 2) [17, 21, 23].

1.2.1.4   The learning centres

Learned responses to external cues can be separated in some instances from reward. The forebrain networks of the amygdala, prefrontal cortex and hippocampus all produce these learned responses by associative learning, memory and decision making with undetermined signalling molecules [26]. The amygdala, in particular, appears to play a crucial role in responses to cues that reduce hunger, alongside its role in producing a reward value for food [26]. These centres of learning also interact with the lateral hypothalamus to integrate into appetite regulation (Figure 2).

1.2.2   Hunger

The sensations of hunger build up as inhibitory effects of the previous meal dissipate, leading to the urge to eat. Physiological drivers for hunger exist but this component of appetite appears particularly responsive to hedonism and learned behaviour from cues.

The only identified hunger hormone is ghrelin, which is released predominantly from the gut but also the brain [20, 21]. It is found in two forms, acetylated and de-acetylated, the former being important in appetite regulation [27]. Circulating levels of ghrelin are raised during fasting; it also varies diurnally, being higher in the morning, and in response to levels of adiposity [17, 21]. The orexigenic effect of ghrelin has been demonstrated in humans following intravenous administration, which increases reported hunger and food intake [21]. Meal initiation also correlates with rising levels of endogenous ghrelin, however it appears it is not indispensable, as null animal models (animals where the gene for ghrelin is disrupted to stop its function) continue

to have a normal food intake [21, 27]. Ghrelin exerts its orexigenic effects via interactions with the appetite stimulatory circuit in the ARC as well as via the vagus nerve and brainstem [21, 26, 27].

It has been proposed that another physiological driver for hunger is derived from resting basal metabolic rate (BMR), in particular the contribution fat free mass makes to this. Resting BMR accounts for 60-70% of daily energy expenditure, of which energy expenditure from fat free mass is the main contributor. A higher resting BMR is independently associated with greater feelings of hunger and food intake [20, 28-30]. Therefore it is thought to be one of the mechanisms that relay information on energy balance, alongside signalling from adipose tissue and the gut, to the appetite centre to achieve energy homeostasis [17, 29].

It has been suggested that physiological drivers for hunger, such as ghrelin and resting BMR, have prominence when people experience extreme energy states- an uncommon prospect in many modern western societies where food is generally abundant. Therefore most people exist in between these extremes, where the physiological mechanisms are 'indifferent' and so appetite and eating behaviour is governed more on the basis of external cues and their learned associations, alongside hedonism [31, 32].Herman and Polivy termed this the boundary model for eating behaviour (Figure 3) [32]. An example in support of the boundary model is the ability for people to display some conscious control over appetite, such as in the context of dieting [19]. This would only really be possible if the person was sitting in a zone of 'physiological indifference'.
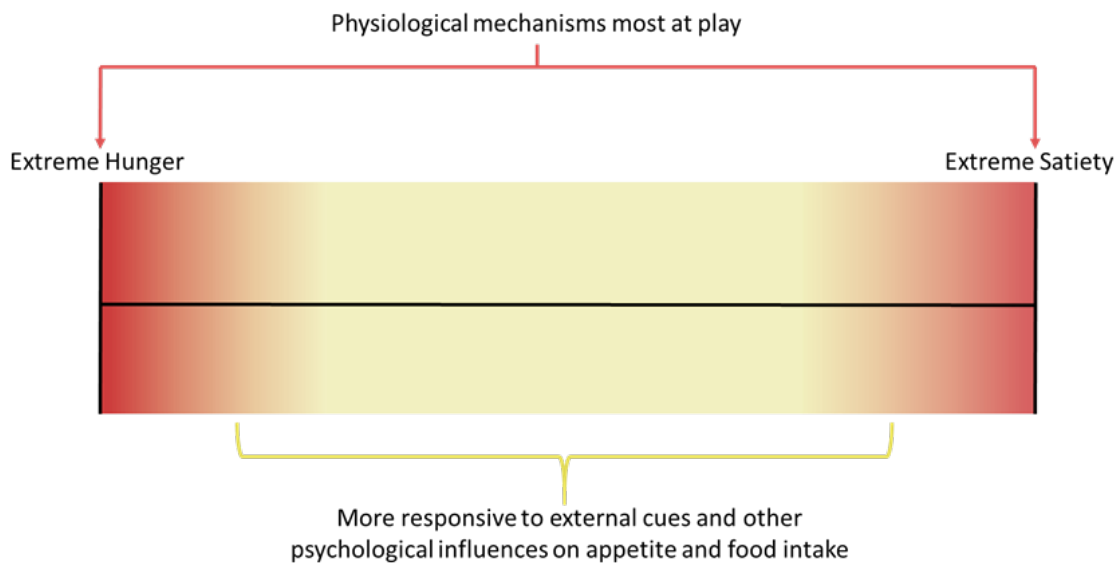
Figure 3   The Boundary model

        Proposed by Herman and Polivy [32], they state that in the context of appetite, a
        person is most responsive to physiology when in states of extreme hunger or
        fullness. Otherwise they are most influenced by external cues and their associations.

The motivation to obtain food, or 'wanting', is a learned response to food which is related to
hunger and responses of the reward system [25]. 'Wanting' is closely linked to another concept in
food reward- 'liking' (pleasurable taste of food), which occurs during eating and also relates to
satiation. 'Liking', along with sight and smell, stimulate the flavour centres [24, 33]. The flavour
centres and other brain centres for palatability (how pleasant the eating experience is), hunger
and satiety, all interact with the reward system to give food items a 'reward value' [24, 33].
Higher reward values feedback to the appetite control centre to promote hunger, so that an initial
taste can drive further eating [24]. It is proposed that the learning centres of the brain turn a
food's high reward value into desire to eat it, with feelings of hunger when the person is re-
exposed to associated cues; whether sight, smell, or the location in which the food was consumed
[25, 33]. The reward signalling molecule dopamine is implicated in linking 'liking' to 'wanting' over
time, with rising levels observed following the smell of a palatable food [25, 31].

Studies assessing the influence of external cues have demonstrated that triggers in the external environment can increase feelings of hunger and induce someone who is otherwise satiated to eat, in a Pavlovian type response [19, 31]. These environmental cues are often food specific and include meal settings such as restaurants, and preparation of food including the packaging or plate used [31]. Contextual cues also influence hunger and meal initiation, such as the time of the day and routines in preparation and consumption of a meal [16, 19].

Mood states are reported to impact upon both the motivational state of 'wanting' and responses to external cues. However this relationship appears complex, for example negative emotions or stress appear to have inhibitory or stimulatory effects on eating, depending on the individual [34, 35]. It has been proposed that if a person relies on their emotions to cope, negative mood may be more likely to stimulate eating- so called 'emotional eating' in an attempt to reduce these negative emotions [34]. An increase in food consumption has also been observed in response to negative emotion for individuals who are usually 'restrained' in their eating [35]. A person can be considered restrained in their eating if they make a deliberate effort to resist the urge to eat (to lose or maintain weight). They may then be more susceptible to external cues and emotions affecting their eating as they become distracted from this effortful restraint [35, 36]. When a person is not usually a restrained or emotional eater, it is thought that stress and negative emotions suppress appetite, as the sensations mimic those of satiety [34]. However this relationship is not fully clear and is under-researched [35]. Importantly, other emotions such as fear can have an inhibitory effect on appetite [26]. This may be related to the intensity of emotion felt and level of arousal produced, with some evidence that emotions with higher intensity and arousal lead to appetite suppression, regardless of the individual's usual eating habits [35].

External or contextual cues, sensory inputs, mood and motivational states, all drive the 'thought of food' [37]. This in turn enacts a change in underlying physiology, including salivary release and gastric acid secretion, in a process termed the cephalic phase of digestion [37]. These cephalic phase responses enable physical preparation for nutrient digestion and absorption but also directly affect sensations of hunger by mediating gastric motility and reducing gastric distention, and by aiding ghrelin release [37].

When exploring hunger and cephalic phase responses, the role of being a restrained eater has been evaluated. Studies on participants with extreme dietary restraint (anorexia nervosa), have identified reduced cephalic phase responses and reported hunger when exposed to food odours. This may reflect the long term effects of their restrained eating, when exposure to external cues did not lead to consumption of food [19]. This behaviour, although extreme, highlights a potential

role that restrained eating such as dieting and perceptions of healthy eating could have on future feelings of hunger [19].

Kristensen [18], has proposed that appetite can be thought of as a point where biology, social norms and cultural meanings are all negotiated by the individual. It appears that the sensations of appetite are experienced differently depending on social contexts, who we are with, and how comfortable we feel [18]. One way appetite and eating are experienced in different social contexts has been described in 'social facilitation of eating' [38]. This concept describes increases in food consumption observed when people eat together, versus eating alone. This works within the 'co-action' paradigm of effect i.e. a person behaves in a similar way to others engaged in that same behaviour [38]. Therefore, this effect is not seen when a person is expected to eat in front of a passive audience- where in studies adults tended to eat less [38]. Social facilitation is more apparent when eating with friends and family, which reflects how comfortable a person feels within a meal setting. Eating with friends and family in a social setting upgrades a meal to an 'event'; along with this are potential learned expectations that the person will eat more and so will prepare more food [38]. Conversely, the effect of strangers can be inhibitory, as a person may become concerned with making a good impression and feel their normal eating behaviour could be construed as excessive or unhealthy [38].

Alongside social contexts, culture is another determinant of attitudes towards eating, particularly to certain food types and meal practices [19]. Culture is one way of communicating 'social eating norms', these are perceived standards for eating whether amount or type of food. These eating norms can be observed at national, family and friendship level [39]. Following social eating norms is linked to acceptance and strengthening of relationships within social groups and also ensuring correct things are eaten (for example avoiding poisonous substances) [31, 39]. Social norms around eating are thought to affect a person's feelings of self-perception and identity (i.e. I am someone who eats in this way) and also their self-efficacy (i.e. they are like me, so I am capable of eating in this way) and also affects feelings of reward in a positive way [39].

1.2.3 Satiation

Satiation increases during eating to dominate over hunger and eventually lead to termination of a meal. This component of appetite may be considered to be influenced by both physiology and hedonism.

A number of different neuronal and hormonal signalling pathways feedback from the gut following food intake, alongside the mechanical effects of the food bolus itself. The physiology of satiation is strongly linked to distension of the stomach and also entrance of food into the small

intestine [19]. Food entry into the stomach and duodenum causes release of the hormone cholecystokinin (CCK) which is thought to enhance the satiating effect of gastric distention [37]. CCK also appears to potentiate its effects via the vagus nerve to receptors on the brainstem and hypothalamus [40].

The role of hedonism in satiation is linked to activity in the flavour centres of the brain, which determine the reward value of a food. The neurons in these centres become saturated and reduce in activity the longer a meal progresses, which leads to sensory specific satiety [23, 24]. This can be demonstrated with oral administration of nutrients compared to a gastric infusion, where feelings of satiation are reported to be higher [37]. Sensory specific satiety is particular to foods in the meal and those with similar stimuli [16]. This can be observed when more variety is present, or other flavours such as condiments are added to a partly consumed meal and food intake increases [41, 42]. Sensory specific satiety thus causes individuals to switch food types in a meal leading to increased variety, and if variety is present, an increase in overall intake.

In contrast to sensory specific satiety, hedonic responses to sensory signals can also cause 'stimulation of eating by eating' for liked foods [43]. This is mediated by flavour centre activity projecting onto the reward system [24]. The reward system upregulates opioids and endocannabinoids when liking occurs. This can be demonstrated by administration of cannabinoid agonists, which enhance the reward value of food. Their administration stimulates reward neurotransmitters to interact with the hypothalamus, to increase activity of the appetite stimulatory circuit and blunt satiety signals [25]. This means that on activation of the reward circuit, satiation may be overridden and appetite is maintained by reward rather than need [17, 43].

The motivation to eat due to learned associations with food has been discussed in the context of hunger and 'wanting' earlier in this chapter (section 1.2.2). However, learning can also occur following negative outcomes from consuming certain foods, such as diarrhoea and vomiting, which act to increase satiation and reduce hunger [19]. Learned associations can also control the size of meal an individual consumes, such that a person has an expected effect from a particular portion size or from sensory aspects of a food affecting feelings of satiation. These learned responses can be affected by the way a meal is presented; in particular an empty plate is a strong cue for satiation [19, 31].

1.2.4   Satiety

Satiety determines the length of time in between periods of eating. It appears to be predominantly governed by physiological signalling but with some overlap with the hedonic effects on satiation, which have been discussed.

The physiological signalling mechanisms of satiety are triggered by both the presence of food in the gut lumen and nutrients in the circulation [44]. The gut has characteristics similar to a sensory organ in that it responds to many different signals whether chemical or mechanical [44]. It then creates both hormonal and neural responses, as well as local mucosal changes. The main signalling cell is the enteroendocrine cell, which lies within the mucosal epithelium and responds to peptides, fat, bitter, sweet and salt tastes [45].

The anorectic hormone glucagon-like peptide 1 (GLP-1) is secreted from enteroendocrine L cells in the distal gut, in response to nutrients in the lumen [46]. There are two peaks of GLP-1, the first, within 15 minutes of starting a meal, appears to be initiated by the stomach or proximal intestine, acting via the vagus and enteric nervous system to stimulate the L cells. The second larger peak occurs later from nutrient sensing by the L cells themselves [46]. GLP-1 is also released centrally by the NTS in the brainstem acting on many parts of the brain including the hypothalamus, reward and learning centres [46]. Alongside its central actions, GLP-1 mediates local changes in the gut, decreasing gastric emptying and intestinal motility via muscular contraction, and increasing colonic transit to optimise digestion and absorption [46]. The effects of GLP-1 appear to influence meal size (giving some overlap with satiation) and the period between meals. Oxyntomodulin (OXM) is another anorectic hormone released from L cells in response to luminal nutrients. It has been shown to reduce energy intake and expenditure but with an unclear mechanism of action [40].

The satiety signalling hormones peptide YY (PYY) and pancreatic polypeptide (PP) are from the same family of peptides as the central neurotransmitter NPY [40]. PYY is also secreted by L cells and exogenous administration reduces food intake in humans. It acts on the ARC directly and indirectly via the brainstem and vagus nerve, and also the flavour and reward centres [20] [40]. PYY may also play a role in regulating energy expenditure, delaying gastric emptying and reducing gastric acid secretion [40]. PP is secreted from PP cells in the pancreas, it appears to act on the brainstem and hypothalamus but may also involve the vagus nerve. Endogenous levels of PP rise in proportion to the amount of calories within food [40]. Another pancreatic hormone, amylin, is released following food intake. Its effects are to reduce appetite via the serotonin, histamine and dopamine pathways and also by reducing the release of the stimulatory neurotransmitter NPY [47].

Serotonin (5-HT) is an additional molecule in satiety signalling, with higher circulating levels associated with satiation and satiety [48]. It acts centrally on the ARC to increase POMC and reduce AgRP expression [49]. The activation of 5-HT is unclear but has been linked to peripheral signalling molecules such as CCK [48]. Downstream signalling components from the ARC also appear susceptible to 5-HT, reducing NPY signalling [48]. 5-HT may also play a role in peripheral energy signalling in the gut and adipose tissue [49].

Key components to feelings of satiety and achieving energy homeostasis over longer timespans are the signalling pathways identifying nutrient and energy abundance in the body. These hormonal pathways work in conjunction with the intermittent signals from the gut. The first of these hormones, leptin, is secreted directly from adipocytes in relation to the amount of adipose tissue, the second, insulin, is secreted from the pancreas. Both are proportionate to body fat content and can cross the blood brain barrier to act centrally in the ARC, brainstem and also the reward and learning centres to inhibit appetite [20]. In terms of these central effects, leptin is thought to be more powerful but there is cross talk between the two, and insulin appears to potentiate leptin's actions [23, 50]. Levels of leptin and insulin reflect the body's nutrient reserves and their potency is greater in energy depleted states; this is reflected in their resistance states in obesity [20].

An additional link in the physiological signalling pathways of appetite, particularly for satiety, is the role of the gut microbiome. The gut microbiome is comprised of the microbiota (bacteria, archaea and eukaryotic microbes), their microbial structural elements, metabolites and signal molecules, and the surrounding environmental conditions, all within the gut [51]. This varies between individuals but overall shifts in diversity and composition are most significant at the extremes of age, and long term dietary habits are considered the dominant influence [52-54]. Changes within the gut microbiome have been linked to a number of disease states [52], and also normal physiological activity, producing the concept of the 'microbiome-gut-brain axis' where the microbiome, endocrine, immune and nervous system all communicate using the gut as a scaffold [54]. Communication occurs bi-directionally, with the microbiome affecting central nervous system function, which then reciprocally effects the microbiome via actions on the gut [54]. Appetite regulation is one example of the 'microbiome-gut-brain axis', and utilises short chain fatty acids (SCFAs) (Figure 4). In the colon, the microbiota ferment undigested dietary fibre to produce SCFAs (butyrate, propionate and acetate), heat and gases [53, 55]. The SCFAs create an energy source for the colonic epithelium (via butyrate) and also act as signalling molecules, with levels detected in the circulation [56-58].

SCFAs act on free fatty acid receptors (FFAR) in the gut epithelium, adipose tissue, skeletal muscle and peripheral nervous system [55]. In animal models acetate and propionate can activate FFA receptors on enteroendocrine L cells, stimulating the satiety signalling hormones PYY and GLP-1 (Figure 4) [55]. An association has also been observed in human studies, where higher levels of fermentable fibre are associated with increased post-prandial GLP-1 [55, 58]. The SCFAs may also have a role in reducing gut transit time, a known effect of GLP-1 and PYY [55]. There is also evidence in animal models that acetate can cross the blood brain barrier to act upon the ARC, increasing appetite inhibitory POMC expression and reducing appetite stimulatory AgRP expression [55, 59].
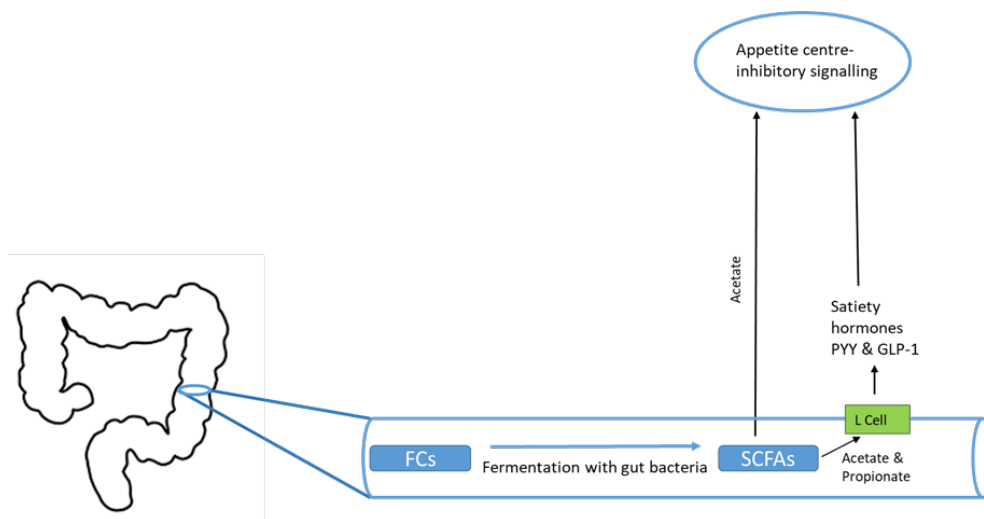
Figure 4   Short chain fatty acid production and appetite signalling.

> Adapted from information in Byrne et al [58]. Short chain fatty acids (SCFAs) are produced from fermentable carbohydrates (FCs) by the gut microbiota in the colon. The SCFAs acetate and propionate act on free fatty acid receptors on L cells to release satiety hormones which interact with the appetite centre. Acetate has also been shown to cross the blood brain barrier to act centrally.

Exercise, particularly rigorous acute bouts, have been demonstrated to have effects on feelings of satiety in a phenomenon termed 'exercise-induce anorexia'; where a person's appetite ratings are transiently reduced [60]. This is echoed by acute exercise (in moderate to vigorous amounts) having small but significant effects on lowering levels of ghrelin and increasing the satiety hormones PYY, PP and GLP-1; effects which appear more substantial following aerobic exercise rather than resistance training [61]. There is more conflicting evidence on the effect of longer-term exercise, with results along the spectrum of increased to decreased appetite [60]. Certain hormones have been shown to change following long term exercise, for example leptin levels appear to reduce, but the effect on other satiety hormones is less clear [60]. Exercise is a subset of physical activity and requires planning, structure and often repetition with the objective of improving physical fitness whether health or skill related [62]. Whereas physical activity is a broader concept defined as "any bodily movement produced by skeletal muscle which results in energy expenditure", and can be categorised into household, occupational, sports, conditioning and other activities [62]. This distinction is particularly important as exercise and physical activity appear to have a different relationships with appetite

When assessing levels of physical activity rather than exercise in healthy adults, a non-linear relationship in the form of a J shaped curve with energy intake has been observed [63] (Figure 5). Untangling energy intake from appetite in studies addressing physical activity is difficult, as the terms are often used interchangeably, and those studies which have assessed appetite ratings specifically are inconclusive [64]. When interrogating the J shaped relationship between physical activity and energy intake, higher levels of physical activity correlate with increased energy intake, which then drops with moderate levels of physical activity [64]. However, energy intake rises again in those with low or very low physical activity [64] (Figure 5).
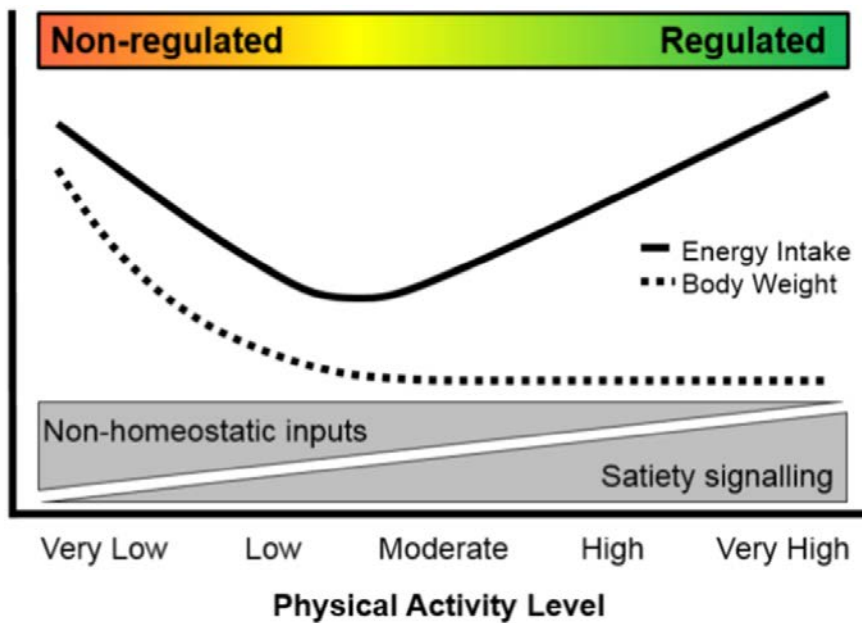
Figure 5   J shaped curve relationship between energy intake and physical activity level

Taken from Beaulieu et al [63]. Higher levels of physical activity correlate with increased energy intake, which drops with moderate levels of physical activity and then rises again in those with low or very low physical activity.

(Reprinted from Physiology & Behavior, Vol 192, Beaulieu K, Hopkins M, Blundell J, Finlayson G, Homeostatic and non-homeostatic appetite control along the spectrum of physical activity levels: An updated perspective, Pg 23-29, Copyright (2018), with permission from Elsevier.)

This J shaped relationship has been postulated to be due to inactive individuals sitting in a 'non-regulated zone', where they are longer sensitised to the physiological regulators of appetite, particularly satiety hormones [65]. This may lead to overconsumption in obese people, driven by hedonism [65, 66]. This theory, proposed by Blundell et al, suggests that increasing levels of physical activity may improve a person's responsiveness to physiological signalling, pushing them back into a regulated zone where food consumption is appropriate to energy balance [65]. This has been shown in a study where increased underlying feelings of hunger alongside an increase in the satiating effect of food was reported by subjects whose activity levels were increased in a 12 week exercise programme [67]. Another effect that physical activity may have to influence appetite is gastric emptying, which is faster in individuals who have higher levels of habitual physical activity [68]. There is also some evidence that levels of physical activity can influence the way a person processes the reward value of food and types of food choices they make but this needs further exploration [69].

1.2.5   Summary of appetite and its regulation

Appetite is a collective of sensations driving the desire to eat and is often broken down into the components of hunger, satiation and satiety. Hunger has a physiological basis but importantly, is driven in the main by hedonism and external cues, which are affected by mood states and wider social and cultural constructs in modern western society. Satiation and satiety are also impacted upon by physiological mechanisms, hedonism and cues but perhaps in a more balanced manner, nevertheless they are still influenced by external factors such as physical activity.

1.3   Approaching influences on appetite

As has been described in this chapter, the concept of appetite is often broken down into the components of hunger, satiation and satiety. Whilst this is useful for laboratory based studies to understand the mechanisms of appetite control, it is perhaps less so for clinical practice, as it does not illustrate the complexity of influences impacting upon regulatory mechanisms. This is important, as a focus on understanding these influences is most likely to yield appropriate preventative or management strategies for those older individuals who lose their appetite.

An alternative approach could be to focus on the influences on appetite and to group these in a coherent way. To achieve this, I re-framed the psychobiological term for appetite to encompass the wider role of environment and social cues. Using this structure, broad categories of influence on appetite can be defined as those relating to physiology, hedonism and external cues, in which specific examples can then be grouped (Figure 6) [70].

Structuring appetite in this way, I suggest, enables a rounded and logical approach for clinicians and clinical researchers to this complex subject [70].

Physiology

Neural signaling pathways- central and peripheral

Hormonal signaling- stimulatory and inhibitory, from organs and adipose tissue

Resting basal metabolic rate

Gut-microbiome-brain-axis

Lifestyle effects e.g. physical activity

Hedonism

Sensory perception- 'liking'

Palatability and and reward value

Learning- 'wanting'

Mood

External Cues

Cephalic phase responses

Environment

Social facilitation

Culture and social eating norms

Figure 6   My approach to ordering multi-factorial influences on appetite

As outlined in Cox et al [70]

1.3.1   Applying this new approach to the context of appetite and ageing

Alterations in appetite (seen predominantly as a reduction) associated with ageing are well recognised, with potentially the earliest documented account by the Roman philosopher Cicero in 44BC as part of his essay 'Cato Maior de Senectute' (Cato the Elder on Old Age):

> *"I am thankful to old age, which has increased my avidity for conversation, while it has removed that for eating and drinking."*

Appetite loss in ageing is often caused by chronic disease states such as heart or renal failure, which have a higher prevalence in older populations [71-73]. It is also associated with the syndrome of cachexia (a complex metabolic syndrome characterised by loss of muscle with or without loss of fat mass, associated with underlying illness) [74]. However a primary loss of appetite, due to ageing, is also recognised and often referred to as the anorexia of ageing- a term first used by Morley and Silver in the 1980s [75]. This primary appetite loss has been explored in a

recent meta-analysis looking at both fasted and post-prandial states in healthy older individuals (age ~70 years), which highlighted a reduction in hunger with greater and longer lived satiety, alongside a reduction in energy intake when compared to younger individuals (age ~26 years) [76].

As has been described in this chapter, the maintenance of an individual's appetite is complex with multiple pathways. This has been inherent to our evolutionary survival and so loss of appetite in ageing is likely to be due to a failure of multiple mechanisms before it becomes evident [77]. Using my approach to influences on appetite (Figure 6), the next sections will discuss current understanding of the mechanisms underlying appetite loss in ageing, with a focus on changes in the major areas of influence on appetite- physiology, hedonism and external cues.

1.3.1.1   Ageing and physiology

The reduction in hunger observed in older people [76], is in part attributable to ghrelin. Initially controlled studies assessing the effects of ghrelin produced mixed results [78]. However, with better understanding of the presence of an active (acetylated) form, lower levels in fasting and post-prandial states have been observed in older people [79]. Although studies on total ghrelin provided mixed results, there is some signal of reduced sensitivity to the total hormone in older compared to younger people [80]. The other main physiological driver of hunger is resting basal metabolic rate (BMR) [29]. A decline in resting BMR in ageing is well documented, and is mostly attributed to loss of fat free mass [77]. A recent randomised trial in healthy older individuals has explored the relationship between fat free mass and appetite [81]. Individuals with increases in fat free mass due to an intervention of protein supplementation and resistance training displayed increased post-prandial appetite ratings, compared to controls who saw no change. However, there were no changes in fasted appetite ratings or in resting metabolic rate [81]. Thus the relationship between appetite, BMR and fat-free mass in older people remains unclear.

The increased feelings of satiety observed in older people [76], also have a multifactorial physiological basis. The ageing gut shows a trend towards reduced gastric emptying [82-85], and changes in compliance of the stomach have also been noted; these are postulated to be via autonomic nervous dysfunction or aberrant nitric oxide production [86]. This may reduce food intake due to earlier food delivery to the small intestine and subsequent release of satiety hormones [77, 80]. Therefore a combination of the stomach's altered ability to handle a food bolus and also changes in transit time may increase satiation and satiety.

Satiety signalling hormones also have alterations with ageing. Raised circulating levels of CCK are present, both post-prandially (independent of the amount of food still present) and during fasting

[76, 78-82]. Raised levels of CCK have also been noted in older people who do not have increased clinical nutritional risk, leading to the suggestion that CCK may have an early role in the pathogenesis of appetite loss [80]. Levels of the satiety hormone PYY also change in the context of ageing, with observed higher post-prandial levels [78, 84, 87]. A recent study has linked this rise to changes in reported appetite of older women [88]. The role of GLP-1 is less clear, as concentrations in previous studies have been similar between age groups, however in one study sensitivity to it appears reduced in older people compared to younger [78]. In other more recent studies, GLP-1 was higher in fasted states with greater increases in older people following a high fat meal compared to younger individuals [89, 90]. Importantly however, older people also display impaired behavioural responses to satiety. This is described in studies looking at the effects of protein, fat and carbohydrate supplements on appetite in older people, where their energy intake was not tempered by a rise in their satiety hormones and reported feelings of fullness [85, 91]. Therefore the wider context of the relationship of satiety and ageing with eating behaviour should be considered complex and is not fully understood.

Higher basal circulating levels and post-prandial increases of insulin are also associated with ageing [92]. This may directly cause anorexia in its role as a satiety hormone but also indirectly via effects on leptin and ghrelin. Higher fasting levels of leptin have also been noted [92].

The effects of ageing on the central appetite centres are currently unclear. Animal models with aged rats show decreased production of the appetite stimulatory neurotransmitter NPY but this is not reflected in human studies on anorexic older people, who conversely have high levels of NPY [80]. The stimulatory peptide AgRP is also reduced in older rats, but this has not been assessed in humans [93].

As discussed in this chapter, other influences have been shown to play a role in the physiological regulation of appetite. These include interactions with the gut microbiome and also an individual's level of physical activity. The composition of the gut microbiome in older people differs to younger adults, with more between-person variation and lower levels of diversity in older individuals [94]. There are also differences in gut microbiota composition across settings, with those in residential care having different phyla (classes of bacteria) compared to those living in their own home, including SCFA producers [94]. We have recently explored differences in gut microbiome composition in the context of appetite in older populations, in community dwelling adults over the age of 65 [95]. When comparing cases with poor appetite and controls with good appetite matched on factors known to affect the microbiome (such as antibiotic use and frailty status), cases have lower diversity of their microbiome and reductions in certain phyla and species of bacteria. This indicates a role for alterations in the gut microbiome in changes in appetite

observed in older individuals but the sequence of this, and how it may link to functioning of the microbiome-host relationship, including hormone signalling, requires further investigation.

The association between levels of physical activity and appetite in older people has recently been explored in a systematic review by Clegg et al [96]. The eight included studies were comprised of participants with mean age of 71 years and a mixture of methodologies, from cross sectional observational studies to randomised control intervention trials. They found insufficient evidence for an association of increasing appetite with higher levels of physical activity. The review was limited by the methodology of the included studies, which often did not have a robust assessment of appetite (for example using oral intake as a proxy) [96]. The authors also included studies with interventions which would be classified as exercise, as well as those based on habitual physical activity – an important distinction when the two have differing relationships with appetite. In general, the older population are less physically active and have longer sedentary periods, often not meeting recommended levels [97] (the current UK Chief Medical Officers' guidelines for each week is at least 150 minutes moderate intensity activity, 75 minutes' vigorous activity, or a mixture of both, strengthening activities on two of the days and to reduce extended periods of sitting). This sedentary behaviour occurs in the community but particularly in hospital settings [98, 99]. The benefits of increased physical activity are well documented, including to physical health, mental health, functional ability and the ageing syndromes of cognitive decline and frailty [100-105]. So, whilst increasing levels of physical activity are known to have a beneficial effect on ageing syndromes, currently any role it may play in appetite is unclear; including whether increasing levels of physical activity could improve poor appetite.

1.3.1.2   Ageing and hedonism

A diminished chemosensory ability related to ageing is well recognised. Older people have reduced ability to identify different odours and also perceive them less intensely, which may be related to changes within the olfactory centres of the brain [93]. They also have reduced capacity for taste with reduced sensitivity and higher thresholds for the five main taste modalities- sweet, salt, bitter, sour and umami to varying degrees [106]; this has been attributed to reductions in taste bud number and structure [77]. Differences in taste perception have also been noted between community-dwelling versus hospitalised older people [107]. Sensory specific satiety, an important element to satiation and increasing variety within a meal, is also impaired in older people, which may lead to monotonous diets and reductions in nutrient variety [108].

Alongside differences in taste perception, older people compared to younger may place a different reward value on food [109]. This change is reflected in altered signalling in the taste perception and reward centres of the brain in functional magnetic resonance imaging (fMRI)

studies [110, 111]. The changes in reward signalling include age dependent loss of dopamine signalling [93]. Opioid levels are also altered but the effect of this is less clear, as one study has demonstrated that acute opioid antagonism did not affect appetite, however this was underpowered and did not include people aged over 85 years [112]. Serotonin has reduced signalling efficiency in ageing but the impact of this on appetite is also uncertain [93]. Therefore, further research is needed on specific signalling pathways to better explain the role of reward in the context of appetite and ageing.

The relationship between mood and appetite also appears to be altered in older people compared to younger. A survey on community dwelling older people (both own home and care home) in the United States found that low emotional well-being and low sense of involvement in life were strongly associated with low appetite, and low mood was also a correlate [113]. This has been investigated further in the context of motivation to eat, using fMRI in a study of older people with depression, which demonstrated changes in the anterior cingulate cortex (part of the flavour and reward centres) [114]. Another finding, consistent with a change in the relationship between mood and appetite with ageing, is that older adults with depression are more likely to lose weight, when the opposite is true for younger people [115]. This observed difference may be related to emotional eating (increased food consumption in response to negative emotion (see section 1.2.2), which appears to reduce with ageing [116]. Instead, older individuals displayed higher levels of expressive suppression, a regulation strategy to reduce or hide an emotion as a way to control it [116]

A qualitative study by Wikby et al [117], in care home dwelling older people with a median age of 89 years, explored descriptions of mood in relation to appetite using grounded theory and constant comparative analysis. The authors created the term the 'willingness to eat' to describe appetite as being an act of will, sometimes forcing and sometimes restraining, with mood impacting upon this. Feeling peaceful and secure was a positive, and anxiety and grief was a negative. Participants described that feelings of independence and integrity, which gave their life meaning and substance, improved their appetite. This was opposed to feelings of dependency and loss of personal values, which negatively impacted appetite. A second qualitative study by Holst et al [118], used a phenomenological hermeneutic approach and constant comparison to understand the experiences of 12 hospitalised older people of being undernourished. They described some themes which related to appetite, linking a lack of physical and psychological wellbeing to inability to eat and general feelings of indifference, lack of concentration and hope. These studies reflect that mood is a combination of different states of affect. These different components of mood state have not been explored further in older people in the context of

appetite but it would be of value to better understand their relationship for potential strategies to manage appetite loss.

1.3.1.3 Ageing and external cues

Changes to their external environment is a common prospect for many older people when transitioning into residential care or requiring care at home. These changes have been identified in predominantly qualitative research to impact upon appetite. Particularly of importance is the way food is prepared and presented, with a preference for 'traditional' foods which meets older adults' eating norms and expectations [117, 119]. The eating environment has also been discussed, particularly in care settings where unclean, noisy eating environments with poor access to facilities, such as the toilet, were considered anorectic [117, 120]. Social facilitation of eating has also been demonstrated in qualitative research on older people, demonstrating that loneliness and monotony can be counteracted by the presence of friends and care staff as companions, particularly if they followed established mealtime routines [117, 121]. This is reflected in observational studies where widowhood and living and eating alone have all been shown to correlate with poor appetite [122-124]. Mealtime routine and its disruption on movement into care facilities has also been described by older people as adversely impacting appetite. This is particularly the case in hospital, where clinical activities interrupt mealtimes and a sense that individuals need to 'accommodate inconvenience' from equipment and procedures, which are prioritised [120].

Discussion of external cues both environmental (such as mealtime settings, food preparation, health and clinical care impacts) and social (such as companionship and mealtime routine) are major components of the research findings both in care home and clinical settings [117, 119-121] . However, the effects of external cues in these studies were largely described in physical terminology which related to amounts eaten and mealtime frequency. Only one study described themes relating to perceptions of cues in relation to appetite, such as feelings of independence, integrity and motivation, linked to health and wholesomeness in a form of self-discipline [117]. However, these may be specific to the study's residential care setting. So whilst some understanding that changes in external cues appear to impact on appetite is present within the literature, the way this may relate to an older individual's perception is not fully understood. This is important, as an individual's perception of their appetite and how it relates to cues and events, may render them more or less able to adapt to potential changes in these cues in later life. This may play a crucial role in the pathway of appetite loss, and so may be part of potential behavioural interventions to manage eating behaviour with poor appetite.

1.3.2   A possible narrative for appetite and ageing using this approach

On reflection, the definition of appetite as *'a natural desire to satisfy a bodily need, especially for food'*, could be considered more complex in modern Western society. Eating behaviour has developed to encompass more than sustaining an energy need, with hedonism and the influence of external cues potentially dominating through the life course. Does this then in part explain why older people lose their appetite?

Whilst living in a modern Western society, where appetite is more than fulfilling an energy need, an individual may have built up a large and complex range of hedonics and external cues with learned associations to appetite. They are also likely to have existed for the majority of their lifetime in the zone of physiological indifference (Figure 3), and so have become dependent on these associations to influence their appetite. Changes in circumstance and environment in later life, as well as sensory change and alterations in reward, may mean those influences are no longer present to increase or drive appetite. Compounding this are changes in physiological appetite regulation, giving aberrant sensations of increased satiety and reduced hunger. The effects of all of these factors then ultimately lead to overall loss of appetite, and the anorexia of ageing [75].

1.4   The anorexia of ageing

The anorexia of ageing is the term often used to describe appetite loss in older people attributable to ageing itself, rather than as a product of chronic illness or medical intervention [75]. The prevalence of individuals with poor appetite in a population varies across settings with 11-28% reported in the community, 12-22% in care homes and 30-60% reported in hospital [6-9, 125]. Cross sectional studies in older populations across these settings have demonstrated that the anorexia of ageing is associated with a number of major health burdens affecting the older population. These include undernutrition, sarcopenia, frailty and higher rates of mortality [10, 126, 127].

Longitudinal studies, including those following hospitalised cohorts after discharge, have also demonstrated an association between poor appetite and adverse outcomes including reduced muscle strength [128], incident undernutrition [129], frailty [130], and mortality [10, 131, 132]. Although a predictive association has been demonstrated, the causal relationship between appetite loss and these health outcomes is not fully understood. However, studies in older people reporting low appetite but with a normal body mass index (BMI) observed dietary change, including reductions in overall food intake, particularly whole grains, fibre, vegetables and protein, which may signal some explanation [124, 132]. A further recent European study has

demonstrated that in adults reporting poor appetite, changes in protein intake are more common in older individuals particularly for those living in the UK [133]. These dietary changes and reduced intake may then proceed to the subsequent weight loss [134] and incident undernutrition [129] observed in those with poor appetite. However changes in dietary pattern may also lead to negative health outcomes beyond loss of body mass, in the form of qualitative malnutrition (inadequate intake of micronutrients including vitamins and minerals). Qualitative malnutrition may be particularly important in the development of sarcopenia, where associations with poor appetite have been seen in individuals without the presence of weight loss [8].

Findings from these observational studies suggest that anorexia of ageing is a preceding agent of some of the important health burdens in the older population. Therefore a focus on appetite loss, before these sequelae have occurred, could potentially provide an opportunity for their prevention. Currently there is little established clinical guidance for the management of the anorexia of ageing. To enable the development of appropriate management strategies, firstly a greater understanding of potentially modifiable influences on appetite is needed, which may provide avenues of interest as targets for intervention (Table 1). However, initially an understanding of how appetite can be assessed in older people is needed, to enable accurate measurement of effect of influences and thus potential interventions.

Table 1   Potential intervention targets to address anorexia of ageing

Structured using my approach to categories of influence on appetite.

Category of influence on appetite	Potential targets for intervention
Physiology	Level of physical activity The gut microbiome
Hedonism	Low mood and anxiety Sensory aspects of food
External Cues	Environmental and social circumstance Eating norms

1.5   Chapter summary and conclusions

Appetite is a collective of sensations commonly broken down into the elements of hunger, satiation and satiety. The mechanisms underlying the regulation of appetite include interactions between areas of the brain for flavour, reward and learning, alongside complex neuroendocrine signalling from the gut and other organs, maintaining bodily energy balance. All of these signalling networks are co-ordinated in the hypothalamus.

Whilst useful for laboratory research elucidating the mechanisms of appetite control, the construct of appetite in terms of the components of hunger, satiation and satiety may be limiting for a clinical context, where the multi-dimensional nature of appetite needs to be considered. I have taken an alternative approach by focussing on mechanisms in terms of influences on appetite, grouped into physiology, hedonism and external cues to give a broader view of personal characteristics. Loss of appetite is common in older people and outside of medical causes this can be explained by recognised changes in the main areas of influence on appetite- physiology, hedonism and external cues. However there are still important gaps in knowledge around aspects of each of these influential factors.

1.6   Aims of the research

The aims of the research outlined in this thesis were to identify how best to assess appetite in clinical and research settings and then to explore potentially modifiable factors on anorexia of ageing, to identify potential routes of intervention. These aims were addressed in a series of studies with the following specific objectives:

1. To assess the current evidence for assessment and management of anorexia of ageing through a systematic review of the literature.
2. To assess the association between appetite and potential influential factors through a secondary analysis of cross-sectional data from a cohort of hospitalised older people aged over 70 years.
3. To explore perceptions of appetite, its loss and influences on the experience in a group of community dwelling older people aged over 65 years through qualitative methods.
4. To assess the association between appetite and potential influential factors through a secondary analysis of cross-sectional data from a cohort of community dwelling older people aged over 60 years.

Chapter 2   Overview of methodology

2.1   Introduction to chapter

This thesis describes a series of research studies with different methodological approaches designed to increase understanding of influences on appetite in older people. This chapter will discuss the reasons for choosing these methodological approaches. This chapter will first explore the philosophical foundations to research within the setting of medicine, giving thought to the development of the most commonly discussed and opposing research paradigms, and how different methodologies relate them. It will then outline the overall methodological design of this thesis taking a pragmatic approach. In-depth descriptions of the methods for each individual study are described at the beginning of the corresponding chapter.

2.2   Philosophical viewpoints, paradigms and methodological approaches

This thesis addresses questions regarding influences on appetite and its loss in older people, with a focus on modifiable factors amenable to potential intervention. As discussed in the introductory chapter, appetite has a wide range of influences which can be widely categorised to the spheres of physiology, hedonism and external cues (see section 1.3). Exploration of these influences means this thesis includes research questions which sit within different philosophical viewpoints pertaining to research and evidence, and utilise different methodologies. It is important to understand these different viewpoints to ensure they are correctly actioned and coherent with the research question and method which is being employed to answer it, as well as to ensure appropriate interpretation of results.

The philosophical foundations to research are concerned with the development of knowledge and the nature of that knowledge, often discussed through the concepts of ontology and epistemology [135]. Ontology refers to the study of being [12], posed often as the question 'what is reality?' For example it might be considered as something material that can be identified and measured, or it could be something that is constructed by and between those experiencing it [136]. Epistemology is then concerned with the study of knowledge [12], asking 'how can I know reality?' Knowledge about a phenomenon might be gained by objective observation and analysis (often quantitative), alternatively, knowledge might be considered subjective and based upon assumptions relating to

culture, values and tradition [136]. In addition, axiology is the study of value or valuation [12], so understanding the role of values held by the researcher within the process of research. There are broadly two commonly discussed opposing positions relating to the questions of ontology and epistemology. Firstly, the realist position (where positivism sits), which sees reality as purely material and present and so always measurable. Thus, knowledge can be generated through observations and experiments to test hypotheses and generate theory, which might be revised only on emergence of new evidence [137]. Then there is the relativist position, where constructionism is most extreme, which views reality as socially constructed by and from communication between person(s) who experience it. This reality results from the context in which it sits, but also the cultural, historical, political and social norms of that context and so can be different for each individual, depending on their understanding and experience of the world. Therefore knowledge is constructed by each individual embedded in their standpoint or tradition of understanding or sense-making [136].

Within the philosophical foundations of research are a number of recognised research paradigms. These are "the set of common beliefs and agreements shared between scientists about how problems should be understood and addressed" (Thomas Kuhn, 1962) [135]. Thus, research paradigms are an arrangement of ontological, epistemological and so methodological assumptions [135]. Largely research paradigms are positivist or constructivist orientated, sitting at either end of the ontological and epistemological positions. The modernist paradigm dominates research within medicine, both historically and current. The modernist approach is underpinned by the positivist viewpoint (the terms often interchange) and is considered to be associated with the phase of 'enlightenment' and the scientific revolution. This encompasses the movement away from religion towards scientific methods of enquiry by the individual based on rational analysis of facts. The founding of which is often attributed to, amongst others, the scholars Bacon, Galileo and also Descartes with his famous statement "*I think therefore I am*" [137, 138]. Modernism sees attainment of knowledge by the researcher as independent and objective, with hypothesis generation based on determinism (that there are causal links between phenomena). It is therefore associated with quantitative methods, which are controlled and precise to ensure knowledge can be considered generalisable, factually trustworthy and transmittable to others [136, 137]. Modernism in medicine has seen great successes in the advancement of understanding physical processes and treatments. The approach has also advanced knowledge in the field of behaviour, as described in the introduction of this thesis with work by Cannon and Richter (see Introduction section 1.2). However, a major critique of the positivist viewpoint and modernist approach is that it can disregard a person's interpretation or sense-making of their world. Thus, there may alternative accounts of a

phenomenon shaped by different pre-existing assumptions and values, which may affect understanding, but those differences cannot be objectively observed [137]. In addition, scientific methods of enquiry may risk overly controlling situations which do not reflect the non-experimental environment [136, 137]. These critiques led to the post-modern movement, which affected social and political spheres, as well as those relating to medicine and science.

The post-modern movement encompassed concerns firstly around ideology, stating that there are no real value-free or objective statements of fact by a person but rather implicit values are ever present in accounts, often supporting a dominant tradition (such as modernism) [136]. Secondly, the movement incorporated concerns that language in itself has inherent rules of use, such as grammar or vocabulary. This can affect the meaning of words and so limit the sense a person may make of any description of a phenomenon. Thirdly, post-modernism challenged scientific knowledge by arguing that often people have no opinion on a statement as it is mystified by scientific language, and an inherent trust in scientific knowledge means facts are often just accepted. Post-modernists go further to suggest that critical analysis of something displayed as a universal fact is further hindered by scientists also believing in 'scientific truth' where a phenomenon is material or measurable; they themselves are thus unable to critique from alternate standpoints [136]. On writing from a postmodern perspective, Gergen instead argues that scientific claims should be seen as 'social constructions' within cultures and traditions, rather than 'nature revealing itself' [136]. This would enable all people the chance to critique the truth, according to their traditions and values, and to make sense of reality. This is one basis for the constructivist approach within science and medicine [136]. This approach is more common in social science where concepts are often seen as requiring examination and interpretation to determine meaning (often through qualitative methods). These utilise the researcher's interpretation of events, taking account of wider contexts, values and traditions in which a phenomenon of interest sits, with an understanding that it is impossible to achieve objective 'knowledge', as it is mediated by subjective and socio-cultural experiences. However, a main concern regarding use of a constructivist approach to inform methodology is the potential to advocate for a particular subjective or idiosyncratic viewpoint of a phenomenon, which then lacks credibility and may not be relevant to others [137].

2.2.1   My personal view

As a clinician by background, training in the medical speciality of Geriatric Medicine I have developed an active interest in the health of older people but admittedly defining evidence for healthcare in terms that would fit in the positivist paradigm, due to my medical training. However, when reflecting upon the main polar viewpoints of positivism and constructivism in the philosophical approaches to

research, I can see the benefit and usefulness of both. I also think that sole use of one or the other cannot fully explain the diversity of phenomena that exist in reality. I believe that there are physical and material realities but also those that have been constructed and are embedded in values, cultures and tradition. In some cases I believe that a material reality can be identified and then further explored in the context of how people experience it. Therefore, for me, the phenomenon of interest is most important (in the case of the research in this thesis- appetite in ageing), alongside the best approach to go about researching it, with a view to generating knowledge. My views therefore fit more with a pragmatic approach to research, which accepts the validity of both positivist and constructivist viewpoints (and those on the spectrum in between) in informing methods to answer diverse research questions around a phenomenon (such as appetite which is complex), utilising a common theoretical framework in the form of pragmatic theory [137].

2.3   A pragmatic approach

The pragmatic approach promotes a movement away from concerns about the metaphysics of epistemology and ontology, with an emphasis instead on the human experience [139]. In pragmatism knowledge results from investigation into some parts of reality, in the interest of improvement and then experiencing the outcome-referred to as pragmatic inquiry [137, 139]. Pragmatic inquiry involves intention and values, so any knowledge gained derives meaning from its evaluation in relation to these, however, it still needs to be grounded in empirical experience [137]. In the context of science, the intention of pragmatic inquiry is often to improve or build upon the best working model of a phenomenon, accepting that there is no absolute truth [137].

This approach enables us to accept that both of the opposing viewpoints of positivism and constructivism can structure approaches to inquiry and so can make equally important claims about the nature of a phenomenon [139]. So, within research this means that the research question is fundamentally the most important issue in determining the method [137]. It has been suggested that using a pragmatic approach can also open up the ability to perform composite analysis when mixed-methods have been used, where the strengths of different methodological approaches can be exploited and their results integrated, to give insights into a phenomenon where "the whole is greater than the sum of its parts" [137]. This is likely to be particularly useful in complex phenomena, such as appetite in later life, and reason why I utilised a range of research methods for the studies in this thesis.

2.4 Outline of the methods used for the research

The studies within this thesis utilise different methodologies, with findings from each study informing the focus of the objectives of subsequent studies (Figure 7). The first two studies described in the thesis sit within the positivist paradigm with attainment of objective knowledge through the systematic review with narrative analysis and quantitative statistical analysis, to address objective research questions on appetite screening and treatment and its measurable associations, in a deterministic approach. The research aim of the third project was to explore individual accounts of appetite in later life, so this study utilised qualitative methods which have greater alignment with the constructivist perspective. The final study in the thesis used quantitative methods to test hypotheses generated from the initial studies, using the positivist approach. Finally the discussion takes learning from all of the studies within the thesis in a composite narrative, integrating the results with the aim of providing an account of appetite in ageing and its influences where "the whole is greater than the sum of its parts" [137].

2.4.1 Reflection on the impact of the COVID-19 pandemic to study design

The outbreak of the global COVID-19 pandemic occurred whilst undertaking the research projects described in this thesis. Due to the nature of the population to which this thesis relates, an adjustment had to be made to the final study as the intended primary data collection and field assessments were not feasible. The original plan for the final study involved prospective data collection to characterise a cohort of community dwelling older people regarding correlates of appetite. The data collection period was planned for May 2020 to May 2021 through face-to-face interviews in the participant's own home. This was amended to a second statistical analysis of existing datasets, however this continued to be informed by the results of the previous studies, with the aim of evaluating influences on appetite in community dwelling older people.

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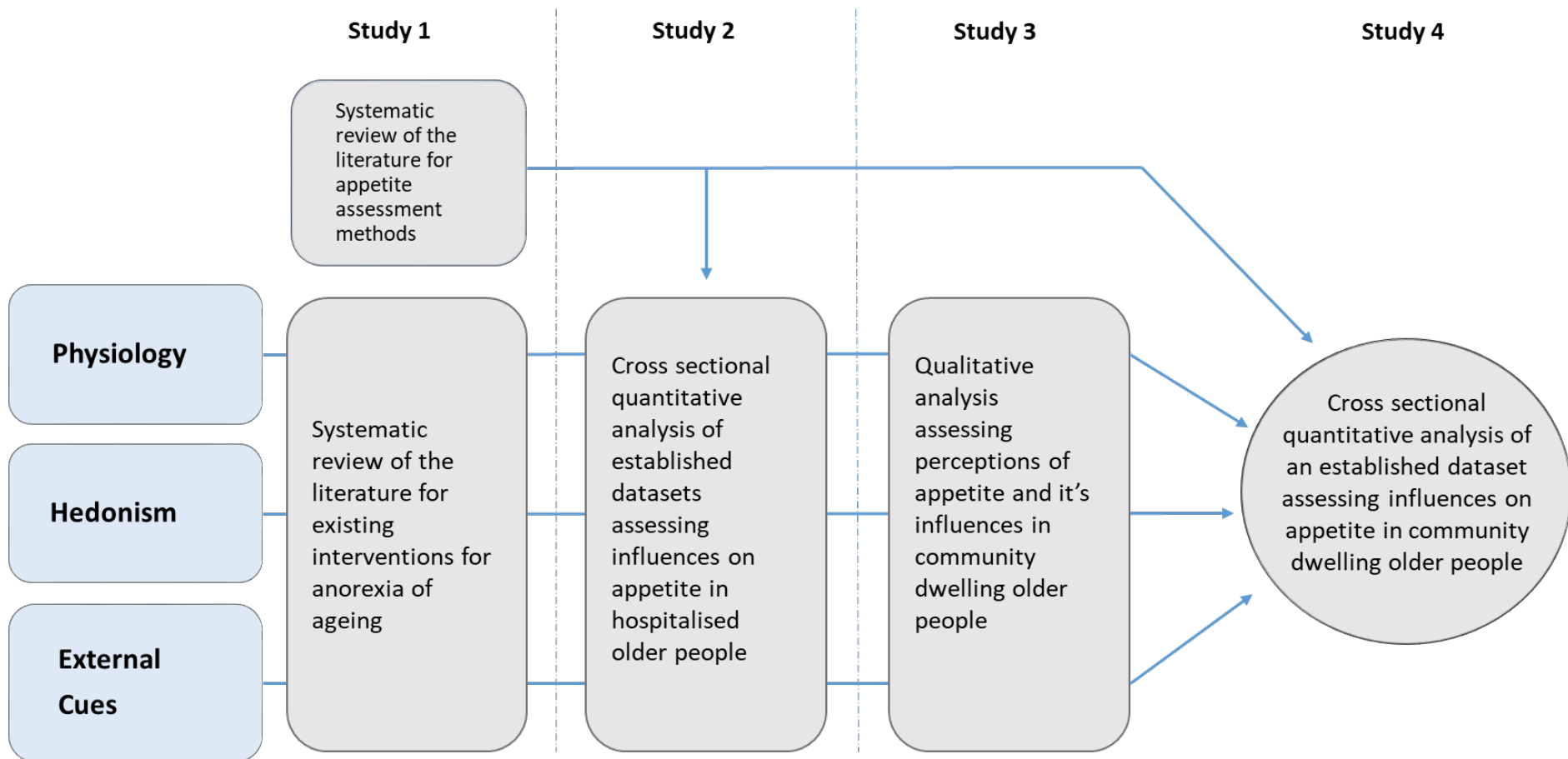
Figure 7   Overview of study design and objectives within the thesis.

The research within this thesis utilises a range of methods, with results informing the direction of the subsequent studies and is guided by the framework of physiology, hedonism and external cues to categorise influences.

Chapter 3 Appetite loss in older people. The current evidence for assessment and management

3.1 Introduction to chapter

This chapter will describe a systematic review of the literature conducted to determine the current evidence for appetite assessment in older people and management for appetite loss, which is most often referred to as the anorexia of ageing. The systematic search has been recently updated and a further 3 articles included in the analysis are presented here, the findings from the initial search were published in 2020 [140].

There is currently no clinical guidance on the management for anorexia of ageing. If this is to be produced then an assessment method for appetite in older people, appropriate for use in clinical practice, is of importance to identify those with anorexia of ageing and to determine potential intervention efficacy. Establishing the current evidence for potential management options will also be of use as this could guide future research and clinical recommendations.

3.2 Assessment of appetite in older people

I undertook a systematic review of the literature to determine the measures of appetite assessment that used in older people. The search was conducted for intervention studies, as I considered appetite assessment methods in the context of an intervention for appetite loss to be of value. This is because they were utilised to assess intervention efficacy and so may be more detailed and have greater clinical relevance than screening questions in epidemiological studies, for example.

3.2.1 Methods

I carried out the systematic review was using the methods recommended by the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [141]. The review was registered on the international prospective register of systematic reviews (PROSPERO) ID number: CRD42018096302 [142].

3.2.1.1   Defining the outcome measure

The outcome measure of interest for the systematic review was a measurement of appetite. This could be by any method but with measurement focus on appetite rather than proxy measures such as oral intake or related to body composition (such as body mass index) or weight. This decision was made due to the difficulties of using proxy measures for appetite, as these can be affected by a number of other factors in older populations including eating problems such as dexterity to consume food, dysphagia and poor oral health for oral intake, as well as conditions likely to affect body composition and weight, including comorbidities and medication. It was also clear from prior scoping reviews for the systematic review and from the initial literature review that the concept of anorexia of ageing was often considered interchangeably or as a component of undernutrition, rather than a separate contributory factor. Therefore I focussed on appetite as the outcome marker of interest to aid clarity between the two concepts.

3.2.1.2   Inclusion and exclusion criteria

Articles for inclusion (Figure 8) related to studies with any design or setting which measured appetite (even if it was not the primary outcome), in people with a mean age of 65 years or over and described a treatment for anorexia of ageing. Initial scoping reviews demonstrated a large amount of interchangeability between the terminology of undernutrition and anorexia of ageing, therefore studies reporting an intervention for undernutrition (also termed malnutrition) that assessed appetite were also included. Articles in any language were considered.

Population	Older people (mean age ≥65 years) in any setting, not defined by a specific health condition
Intervention	Treatment for anorexia of ageing or undernutrition via any method
Comparator	Any, or no, comparator considered
Outcome	Appetite assessment via any method

Figure 8   PICO statement for study inclusion for the systematic review

Studies focusing on a cohort with a specific physical or mental health condition known to impact upon appetite (including cancer, chronic obstructive pulmonary disease (COPD), heart failure, renal failure, depression, anorexia nervosa, and dementia) were excluded to retain a focus on anorexia of ageing. Studies addressing the physiological mechanisms of anorexia of ageing were also excluded, as these did not have a clinical focus.

3.2.1.3   Article screening

I ran a search in four online databases: EMBASE and MEDLINE via the OVID SP platform, the Web of Science and CINAHL via the EBSCO platform. The searches were run from database conception until 30 April 2021 with no limits on the publication type. An example search strategy for the MEDLINE search is included (Appendix A).

Screening of titles and then abstracts against the inclusion criteria was performed independently by myself and one of my supervisors using the Rayyan electronic platform [143]. Following each stage, we conferred and any disputed texts were taken forward to the next stage of screening. Full texts of potentially relevant abstracts were reviewed against the inclusion and exclusion criteria. Hand searching of the reference list and citing works of included texts and relevant reviews was also completed by myself. For multiple articles arising from a single dataset, I selected the most comprehensive article related to appetite assessment for data extraction.

3.2.1.4   Data extraction and quality assessment

Data from the included studies were abstracted into a pre-defined template designed by myself. I contacted authors of the included studies to obtain further information if this was not available from the article. The quality of the publication was assessed using the standardized Joanna Briggs Institute checklists for each study type giving a total score of 13 for randomized controlled trials (RCTs), nine for quasi-experimental studies, and 10 for qualitative studies [144].

3.2.1   Results

3.2.1.1   Study inclusion

The initial search identified 11,454 articles following removal of duplicates. All titles were screened for relevance and 419 abstracts were reviewed. 51 full text articles were reviewed with 21 studies meeting inclusion criteria [145-165]. A summary of screening and eligibility is included in Figure 9.

The reporting format consisted of 20 journal articles and one conference abstract [151]. Quality scores ranged from 5/13 to 13/13 for RCTs (the conference abstract scored poorly due to insufficient data), 8/9 for one within-subject design [165], 9/9 for all others and 8/10 for the qualitative study; no studies were excluded following quality assessment.

Records identified through database searches (n = 14829)

(MEDLINE= 2250, EMBASE= 6535, CINAHL= 698, WoS= 1968)

Records after duplicates removed (n = 11454)

Records title screened (n = 11454)

Records excluded as not relevant
(n = 11035)

Records abstract screened (n = 419)

Records excluded as not relevant
(n = 379)

Further Full text articles identified from reference lists on full text review
(n = 11)

Full-text articles assessed for eligibility (n = 40)

Full-text articles excluded, with reasons (n = 22)

1. Mean age <65 (n=4)
2. No assessment of appetite (n= 10)
3. No intervention to treat anorexia of ageing in study population (n= 4)
4. Duplicate study population (n=3)
5. Unable to obtain full text (n=1)

Full-text articles excluded, with reasons (n = 8)

1 No assessment of appetite (n=7)
2 No intervention to treat anorexia of ageing in study population (n= 1)

Articles included in review
(n = 21)

Figure 9   Flow diagram for screening and eligibility of studies for inclusion.

Due to the heterogeneity of study methodology and interventions, a meta-analysis was unachievable. Therefore, the results are presented as a narrative synthesis of study characteristics and methods used to assess appetite. A summary of the included studies is provided (Table 2).

3.2.1.2 Study characteristics

The included studies comprised twelve RCTs, eight within subject design studies (participants receiving both intervention and control), and one qualitative study [145-165]. A number of countries were represented including the United States, United Kingdom, France, The Netherlands, Sweden, Norway, Australia and Japan. The sample populations were drawn from own home (n=8), care home (n=7), acute hospital (n=5) and rehabilitation (n=3) settings (some studies drew their sample from multiple settings: see Table 2). Two studies followed participants across settings: one from rehabilitation to own home [145], and one during hospital stay and into the community [148].

The studies totalled 1221 participants; with individual sample sizes ranging from 12 to 185 and a mean age range of 74-87 years [145-165]. Seventeen studies reported the mean body mass index (BMI) of participants, which ranged from 19.3 to 30 kg/m^2 but was mostly below 25 kg/m^2 [145-156, 158, 159, 161-164]. Eighteen of the study samples were defined as being either undernourished (using nutritional assessment tools, BMI or weight loss) or having self-reported poor appetite at baseline [145-160, 162, 164]. Samples were predominantly female with only three studies recruiting mostly men [152, 158, 160]; two studies did not report the participant gender [147, 151].

3.2.1.3 Appetite assessment methods

There was a range of methods utilised to assess appetite amongst the studies, these could be categorised into Likert scales, visual analogue scales (VAS), and qualitative method. All of the studies assessed the participant's appetite at baseline. Subsequent assessments ranged from immediately post intervention (e.g. immediately post meal consumption) to 14 months for the longest intervention. There was no association between settings, timing of assessment or type of intervention and the appetite assessment method used [145-160, 164]. The appetite assessment methods are described then with reference to reliability and validity as reported by the study authors.

Table 2   Summary of included studies grouped by intervention categories of physiology, hedonism and external cues.

* Reported as mean (Standard deviation), # Percentage of participants female; BMI = body mass index, DRAQ = Disease Related Appetite Questionnaire, U/K = unknown, AHSPQ = Appetite, Hunger, Sensory Perception Questionnaire, VAS = Visual analogue scale, ONS = oral nutritional supplement.

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
Physiology							
Boudville et al. [146] **2004** **Australia**	Within-subject design (2 sessions)	Rehabilitation N = 14, F # = 100% BMI * = 22.6(3.4)	79 (7.5)	Likert scale 0–5: Hunger, thirst, fullness, prospective consumption, nausea (Pre and post drink and pre and post meal)	Supplementation: ONS -250 mL liquid 90 or 30 min pre-meal (250 Kcal/24 h)	250 mL water -pre-meal	No change (p not reported)
Carlsson et al. [148] **2005** **Sweden**	Open RCT (6 months)	In hospital + discharge out to community N = 45, F # = 100% BMI * = 20.4(2)	83 (5)	Likert scale 0–4: overall appetite (Recruitment, 6 months)	Combination-supplementation +/- medication: -ONS liquid protein rich (200 Kcal/24 h), -nandrolone decanoate 25 mg/3 weekly	Usual care	No change for ONS and ONS + medication versus control (p not reported) Increase from baseline for ONS + medication (p = 0.02)

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
de Jong et al. [149] **1999** **Netherlands**	Open RCT (17 weeks)	Own home N = 165, F # = 68% BMI * = 23.6(2.7)	79 (3.6)	AHSPQ 29 item Likert 1–5 (Recruitment, 17 weeks)	Combination-supplementation +/or exercise: -Micronutrient dense ONS (114 Kcal/24 h). -Muscle strength, coordination, flexibility, endurance 45 min twice a week	Regular ONS (same energy) and social program -90 min every two weeks	No significant change for Exercise (p = 0.61), ONS (p = 0.17) or Combination (p not reported)
Faxen-Irving et al. [150] **2011** **Sweden**	Open RCT (8 days)	Hospital N = 51, F # = 53% BMI * = 21.3(3.7)	84(7)	VAS 10 point: hunger, fullness, desire to eat, prospective consumption, preoccupation with food (Recruitment, 8 days)	Supplementation: ONS -3 × 30 mL fat emulsion based liquid with medications (419.4 Kcal/24 h)	Usual care	Increase vs. control in desire to eat (p = 0.021)

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
Hebuterne et al. [164] **2020** **France**	Within-subject design (4 weeks)	Own home N = 24, F # = 83% BMI * = 20.5 (2.7)	84 (7.2)	VAS 10 point: Overall appetite (Recruitment, 30 days)	Supplementation: ONS -2 × 200 mL liquid with medications (960 Kcal/24 h, 58g protein/24hr))	Usual care	No change
Hubbard et al. [151] **2008** **United Kingdom**	RCT (4 weeks)	Community (Undefined) N = 42, F # = U/K BMI * = 20.9(3.5)	84 (7)	VAS 10 point: hunger, fullness, and desire to eat (Recruitment, 4 weeks)	Supplementation: ONS -3 × 30 mL liquid (400 Kcal/24 h)	Standardized dietary advice sheet	No change (p not reported)
Irvine et al. [152] **2004** **France**	Within-Subject design (3 days)	Hospital N = 12, F # = 33% BMI * = 21.3(2.4)	87 (7.8)	VAS 100 point: Hunger, fullness, desire to eat, preoccupation with food, thirst, cold. (Every 30 min (t = 0 h) to lunch (t = 4.5 h), then hourly to dinner (t = 10.5 h))	Supplementation: ONS -250 mL liquid post-breakfast, High protein (HP) or low protein (LP) content (250 Kcal/24 h)	Usual care	Decrease in hunger pre-lunch, not pre-dinner for HP (p = 0.01) Non-significant for LP (p = 0.1)

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
Ryan et al. [158] **2004** **France**	Within-Subject design (3 days)	Hospital N = 16, F [#] = 38% BMI * = 20(3)	77 (8)	VAS 100 point: Hunger, satiety, desire to eat, preoccupation with food, thirst, stress, cold. (Every 30 min (t = 0 h) to lunch (t = 4.5 h), then hourly to dinner (t = 10.5 h))	Supplementation: ONS -250 mL liquid post-breakfast, High fat (HF) or high carbohydrate (HC) content (250 Kcal/24 h)	Usual care	Decrease in hunger pre-lunch, not pre-dinner for HF (p = 0.04) Non-significant for HC (p = 0.13)
Tylner et al. [162] **2016** **Sweden**	Open RCT with crossover (12 weeks)	Care home N = 39, F [#] = 60% BMI * = 23(3.7)	84 (7)	VAS 10 point: hunger, fullness, desire to eat, prospective consumption, preoccupation with food (Recruitment, 6, 12 weeks)	Supplementation: ONS -3 × 30 mL fat emulsion based liquid with medications (360 Kcal/24 h)	Usual care	Increase vs. control in hunger (p = 0.026)

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
Brocker et al. [147] 1994 France	Double blind placebo RCT (4 months)	Own home N = 185, F $^\#$ = U/K BMI * = calculated Approx. 19	74 (7.4)	VAS 100 point: appetite to meat, overall appetite (Recruitment, 30 and 60 days)	Supplementation: Amino acid pre-cursor -Ornithin Oxoglutarate 10 g in morning	Placebo: Maltodextrine (same energy content)	Increase vs. control 30 days appetite for meat (p = 0.001) & overall appetite (p = 0.001) 60 days appetite for meat (p <0.001) & overall appetite (p <0.001)
Reuben et al. [156] 2005 United States of America	Double blind placebo RCT (63 days)	Care home + rehabilitation (Recent hospital discharge) N = 45, F $^\#$ = 66% BMI * = 22.6(U/K)	82 (U/K)	Likert scale 0–5 or 0–4: Appetite, appetite at start of last meal, hunger at start of last meal (Recruitment 20, 42, and 63 days)	Medication: -Megestrol Acetate, 200 or 400 or 800 mg/24/h	Placebo (undefined)	No change vs. control. (p = 0.07) Increase from baseline in overall appetite at 20 days (p = 0.04), appetite at start of least meal at 42 days (p = 0.02)

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
Yeh at al. [160] **2000** **United States of America**	Double blind placebo RCT (12 weeks)	Care home N = 51, F # = 5% Weight loss of >5%, or weight 20% below IBW	76 (1.3)	Likert scale 1–5: Overall appetite (Recruitment, 12 weeks)	Medication: -Megestrol Acetate, 800 mg/24 h	Placebo (undefined)	Increase vs. control in overall appetite (p = 0.004)
External Cues							
Andersson et al. [145] **2017** **Norway**	Open RCT (3 months)	Rehabilitation + Own home N = 100, F # = 62% BMI * = 20.2 (3.3)	75 (8.7)	DRAQ 10 item Likert 1–5 (Recruitment, 3 months)	Education: -Nutrition plan pre-discharge and counselling post discharge	Usual care	No change (p >0.05)
Robison et al. [157] **2014** **United Kingdom**	Qualitative study (1 year)	Hospital N = 25, F # = 100% BMI * = U/K	U/K	Individual semi-structured interviews (Purposive sample pre-intervention, 1 year)	Meal adjustment: -Mealtime volunteer assistance during a meal	Usual care	No change (Qualitative method)

Divert et al [165] 2015 France	Within-subject design	Care home N = 42, F # = 69% BMI * = U/K	87 (U/K)	7-point scale ranging from "I am not at all hungry" to "I am extremely hungry" (Pre-meal)	Meal adjustments: 1. Portion- a. Size - participants chose quantity they wished to eat b. Variety- meat and green beans and courgette	Control meal- 100 g of meat and 150 g of green beans	Increase in pre-lunch hunger for both size and variety n= 30; P= 0.05
					2. Condiments- a. Additional 4 condiments b. Additional 8 condiments	Usual condiments supplied by the nursing homes (salt, pepper, mustard)	Increase in pre-meal hunger with additional condiments (no significant difference between 4 and 8 condiments) n=27; P= 0.05.
					3. Surroundings- a. Additional décor- participants chose two objects of decor b. Music- participants	Usual setting	No effect compared to control setting n=32, P=0.40

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
					chose music they wished to hear		
					4. Menu wording-	Usual menu wording	No effect compared to control menu wording
					a. Wording suggesting better quality meat		N=33, P=0.45
					b. wording as in a gastronomic restaurant		
Hedonism							
Best et al. [161] **2011** **United Kingdom**	Within subject design (3 sessions)	Own home (Visited research centre for intervention + testing) $N = 18$, F $^{\#}$ = 77% BMI * = 30 (U/K)	77 (U/K)	Likert scale 1–5: Hunger, desire to eat (Pre-test and post-test meal)	Meal adjustment: -Seasoning (2 spoonful's of choice of branded recipe) -Sauce (100 g of choice of branded recipe)	Control meal: -Same basic meal constituents	No change pre or post meal Hunger ($p = 0.28$, $p = 0.65$) Desire to eat ($p = 0.36$, $p = 0.15$)

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
Mathey et al. [154] **2001** **Netherlands**	Open RCT (17 weeks)	Care home N = 42, F$^{\#}$ = 76% BMI * = 28.3 (7.2)	79 (5.6)	AHSPQ 29 item Likert 1–5 (Recruitment, 17 weeks)	Meal adjustment: -Flavour enhancement with four flavours containing MSG	Usual care	Increase vs. control and from baseline in daily feelings of hunger (p <0.05)
Dermiki et al [163] **2015** **United Kingdom**	Within subject design	Own home (Visited research centre for intervention testing) N = 40, F$^{\#}$ = 75% BMI * = 23.7 (U/K)	74 (5.5)	VAS 100 point hunger, desire to eat (Pre-lunch comparing pre and post conditioning)	Meal adjustment: Repeated exposure to 1 can of MSG containing soup at lunchtime over 1 week on alternate days	Repeated exposure to 1 can on non-MSG containing soup over 1 week on the alternative days	No significant difference in hunger or desire to eat comparing pre-lunch ratings in sessions pre and post conditioning. (P=0.35, P= 0.53)
Wijnhoven et al. [159] **2015** **Netherlands**	Within-subject design (2 sessions)	Own home + care home (Visited research centre for intervention + testing) N = 19, F$^{\#}$ = 100% BMI * = 24.8 (4.9)	84 (8)	Likert scale 1–9: Appetite, satiation (Pre and post test-meal)	Meal adjustment: -Increased variety with three different varieties of meat/fish, vegetable & starch on one plate	Control meal -One variety of components on one plate	No change (p not reported)

Author, Reference, Year, Country	Study Design & Intervention Length	Setting & Participants	Age *	Appetite Assessment (Time Points Measured)	Intervention	Control	Effect on Appetite
Pouyssegur et al. [155] **2015** **France**	Open RCT (6 weeks)	Care home N = 154, F [#] = 80% BMI * = 19.2(2.9)	86 (7.1)	VAS 10 point: overall appetite (Recruitment, 18 weeks)	Supplementation: Fortified food -8 cookies (244 Kcal/24 h)	Usual care	Increase from baseline ($p = 0.009$)
Combination physiology and external cues							
Kimura et al. [153] **2013** **Japan**	Cluster RCT With crossover (14 months)	Own home N = 92, F [#] = 80% BMI * = 24.3 (2.9)	74 (5.6)	Questionnaire "yes/no" (Recruitment, 14 months)	Combination-education + exercise: -Dietary Advice -Muscle strengthening 1 h every 2 weeks + self-directed at home	Usual care	No change ($p = 1.0$)

Likert Scales

Ten of the included studies used the Likert scale method to assess appetite. Andersson et al. [145] used the Disease Related Appetite Questionnaire (DRAQ). This questionnaire, based on the Council on Nutrition Appetite Questionnaire (CNAQ), was created for COPD patients [134, 145, 166]. The DRAQ contains 10 domains each using a five point Likert scale. Domains included semi-quantification of appetite, day-to-day variations in appetite, food tastes, frequency of eating, presence of nausea, and impact of mood or co-existing disease on food intake with a maximum score of 50 corresponding to a good appetite.

The studies by Mathey et al [154] and de Jong et al [149] both assessed appetite with the Appetite, Hunger and Sensory Perception Questionnaire (AHSPQ). This is a twenty nine domain questionnaire which utilises a five point Likert scale with domains grouped into present taste perception, present smell perception, present smell perception compared with the past, appetite and daily feelings of hunger. A maximum score of 145 corresponds to positive feelings [167].

Seven studies used unnamed Likert scales to assess appetite [146, 148, 156, 159-161, 165]. The scales had differing domains; these included 'overall appetite', 'appetite at start of last meal', 'hunger', 'hunger at the start of last meal', 'thirst', 'fullness/satiation', 'prospective consumption' and 'desire to eat'. The domain of 'overall appetite' was used widely but no domain was common to all seven of these Likert scales. The Likert scales also varied in the number of rating points, ranging from five to nine.

Visual Analogue Scales (VAS)

Nine studies assessed appetite by VAS [147, 150-152, 155, 158, 162-164]. These numerical scales were reported in different ways as either 10 point or 100 point lengths. Multiple different domains were measured including 'overall appetite', 'hunger', 'fullness', 'desire to eat', 'prospective consumption', 'preoccupation with food', 'thirst', 'stress' and 'cold'. The domains of 'hunger', 'fullness', 'desire to eat' and 'preoccupation with food' predominated but no domain was used across all eight studies. Two studies screened participants on their ability to complete a VAS before inclusion but did not report how many were then excluded due to this [152, 158].

Qualitative Approach

The study by Robison et al [157] assessed subjective appetite perceptions by semi-structured interviews. The interviews broadly covered the topics of appetite, choosing what to eat, managing at mealtimes and food and fluid intake during hospital stay [157]. The authors used prompts to

explore interviewee's experiences pre and post intervention. Framework thematic analysis was used to capture the range of perspectives [157].

Undefined Method

Kimura et al [153] assessed appetite using an undefined method which reported a nominal outcome of 'yes/no'.

3.2.1.4   Reliability and validity of the appetite assessment tools

The accuracy of questionnaires used to collect data is dependent on an assessment of their reliability and validity. Reliability is a statistical measure of how reproducible the data created from the questionnaire is and so indicates the degree of inherent measurement error. Reliability can be assessed by three attributes- homogeneity or internal consistency, stability (using test-retest or alternate form) and equivalence (inter-observer) [168]. Homogeneity or internal consistency assesses the extent to which the scale reliably measures the construct of interest- in this case appetite. The most commonly used method to assess internal consistency is using Cronbach's alpha, which is considered the standard for Likert scales, with a co-efficient of ≥ 0.7 indicating acceptable reliability [169]. Stability refers to how consistent the results of the scale are on repeat testing. This is measured by test-retest, where the same participants are asked to respond to the questionnaire at two time points and their responses compared, with the resultant correlation coefficient often referred to as 'instrument test-retest reliability' (an r of ≥0.70 is considered good) [169]. Stability can also be measured by alternate form (also called parallel form) where the subsequent questionnaire given to the same participants differs in its form, such as the wording. The final attribute of reliability is equivalence, assessed by inter-observer or inter-rater reliability, which determines the level of agreement between observers or raters of the scale with a higher level of consistency indicating higher reliability [168]. Two most common methods to assess the inter-observer reliability is percent agreement and Cohen's kappa statistic. Percent agreement is the number of times the observers agree, divided by the total number of observations, multiplied by 100. The kappa statistic takes into account the potential for chance agreement (values of ≥0.8 indicate a strong level of agreement; <0.6 indicate inadequate agreement) [170].

Reliability of the AHSPQ, used by Mathey and de Jong et al, was assessed by internal consistency and use of Cronbach's alpha. The internal consistency of this questionnaire was moderate to high; Cronbach's alpha was between 0.70 (present smell perception compared to the past) and 0.88 (appetite domains) for the five different variables [167]. There was no reference to reliability for any of the other appetite assessment methods used.

Validity describes how well a measure collects data which are truly representative of the construct of interest (i.e. appetite). It has different elements including face, content, construct (convergent or divergent/discriminate) and criterion (concurrent or predicitive) validity [169]. Face validity refers to the subjective judgement as to whether the concept (appetite) has been operationalised successfully in the measure i.e. that it looks relevant. This encompasses the feasibility and readibility of the measure. Face validity can be assessed using inter-rater agreement. Content validity considers how well the measure reflects the concept in a generalised setting, ensuring all essential elements are present. This can be undertaken via literature reviews and advice from expert panels (which can be referred to as the judgemental approach). Construct validity refers to how well the concept has been transferred into the constructs making up the measure, and has two elements- disciminate (or divergent) and covergent construct validity. Discriminate or divergent construct validity ensures that each of the constructs within the measure discriminate appropriately from one another i.e. that constucts that are not supposed to relate to each other, do not. Whereas in convergent construct validity, an assessment is made to the degree in which constucts that should relate do so. One way to measure construct validity is using principle component analysis. Lastly, criterion validity assesses the extent to which the measure is actually related to the concept of interest- appetite. This can be assessed in a predictive fashion, where the measure accurately predicts what it is supposed to, or concurrently, where it's results correspond to an established measure of the concept (this can be an established measure at a previous time point- then termed postdictive). Predictive criterion validity often requires a long time length and large numbers of participants, therefore concurrent criterion validity is often utilised.

The validity of the AHSPQ used by Mathey et al and de Jong et al, was assessed using the criterion method. Concurrent validity was established by correlations with weight change in community dwelling older people [167]; and in addition de Jong et al assessed correlation with self-reported energy intake by participants (P<.0002) [149]. For the VAS appetite assessment methods, four studies made reference to criterion validity, in ability to predict oral intake, however this had been undertaken in a population of healthy young people [150, 158, 162, 171], and a cohort of patients with cancer [155, 172]. No reference to validity was made in the other four studies utilising VAS, although the domain questions were similar to those that had done so [147, 151, 152, 163, 164].

The DRAQ used by Andersson et al was based on another appetite questionnaire but alterations had been made to the included questions [166]. The initial study using the DRAQ (in patients with COPD) referred to cognitive interviews to determine question interpretation, which may be considered face validity but there were no further measures [166]. The six unnamed Likert scales

had no references to validity; only two referenced previous use but in different populations-healthy older men [146], and another a cancer cohort [160]. Kimura et al made no reference to validity of their appetite assessment method [153].

3.2.2   Discussion

Appetite was assessed in different ways amongst the included studies, predominantly using Likert or VAS methods. Whilst VAS were a commonly used method of appetite assessment in this review, the authors utilising them made no reference to their validity in older populations. However, there are VAS domains which demonstrate predictive criterion validity for subsequent eating behaviour in older people including hunger, prospective consumption and fullness [173, 174]. VAS have originated from the laboratory environment, where they are used to assess physiological mechanisms of appetite control [76, 174]. However, the studies included in this review, have shown that VAS may be transferrable to the clinical environment [150, 152, 155, 158]. Despite this, screening of ability to complete VAS in two of the included studies suggests a potential limitation of its feasibility of use for older people in the clinical environment [152, 158]. This is reflected by use of VAS for the assessment of pain in older populations, where high numbers of completion errors have been reported [175]. In addition, in a research context, the wide variety and lack of standardisation of VAS question domains and lengths limits the ability of their use in statistical pooling of study results, to aid in determining intervention efficacy.

Likert scale methods with a range of different domains and scoring systems were also commonly used amongst the studies in the review. Few have been validated in older people as generally they were created for use in different populations. The Appetite, Hunger and Sensory Perception (AHSPQ) questionnaire was the only appetite assessment method to have a rigorous assessment of both reliability and validity. It had a Cronbach's alpha between 0.70 (present smell perception compared to the past) and 0.88 (appetite domains) for the five different variables [167]. Concurrent criterion validity was established by correlations with weight change and self-reported intake [149, 167]. However, subsequently the AHSPQ proved difficult to adapt to undernourished older populations in clinical settings, where individuals living with greater levels of dependence and cognitive impairment were unable to complete the questionnaire [176]. Thus, the Council on Nutrition Appetite Questionnaire (CNAQ) and its shortened derivative, the Simplified Nutritional Appetite Questionnaire (SNAQ) were developed from the AHSPQ [134]. A judgemental approach was taken to ensure content validity, with the formation of a multi-disciplinary working group including academics and clinical staff applying the Delphi technique to determine consensus as to the content of the questionnaire from the AHSPQ [134].

The SNAQ consists of four domains- appetite, fullness, taste of food, and meal frequency, each of which include a 5 point Likert scale. Predictive criterion validity was demonstrated for subsequent weight loss, with a score of <14 indicating a risk of 5% weight loss within six months in those aged >60 years in the initial study with a sensitivity of 81.6% and specificity of 84.6% [134]. Concurrent criterion validity has also been established against the nutritional assessment tools Subjective Global Assessment (SGA) and Mini-Nutritional Assessment (MNA) but when compared to these it was felt to 'over predict' undernutrition [177, 178]. This perhaps reflects the nature of the SNAQ as an appetite assessment tool, where a proportion of those with anorexia of ageing may not yet have experienced significant weight change, and so are not at immediate nutritional risk but who nevertheless may proceed to be at risk. The SNAQ was developed in a community setting but has shown reliability, validity and ability to predict inadequate intake in the hospital setting [134, 179, 180]. The DRAQ [145], is based on the CNAQ but adds disease-related questions as it was created for COPD patients, making it more relevant for measuring appetite loss due to chronic disease rather than anorexia of ageing.

The systematic review focussed on appetite assessment methods for older people in the context of an intervention. When searching the literature for non-intervention studies there is a large range of methods used; commonly utilised are semi-structured interviews [117, 120, 181, 182] and Likert scales with differing domains and rating points [6, 8, 122, 124, 129, 132, 183-185]. Appetite can also be assessed within nutritional assessment tools such as the Short Nutritional Assessment Questionnaire 65+ (SNAQ 65+) [185] or MNA, which both include a question about loss of or poor appetite, however this may perpetuate lack of clarity between anorexia of ageing and undernutrition. Interestingly, the CNAQ or SNAQ (including different language derivatives) are increasingly being used and are now one of the most common tools highlighting associations between appetite and health conditions in observational studies on older people across settings [10, 113, 180, 186-192]. For example, associations identified with recent use of the SNAQ include presence of dysphagia [193] and use of texture-modified diet [194] with poorer appetite, as well as associations between poor appetite and important health outcomes such as reduced muscle strength, increased nutritional risk and mortality [128, 131, 195]. To date, the SNAQ had been predominantly utilised in the observational setting rather than in intervention studies; reflected in its absence from the studies included in this systematic review. A Japanese version of the CNAQ has recently been used in a study looking assessing the efficacy of an oral health intervention on cognitive function [196] and the SNAQ is beginning to be included in interventional studies yet to report [197]. This all reflects the utility of its use, which continues to increase, in the evidence base for the anorexia of ageing.

3.2.3   Conclusions

There is currently no standardised measure for appetite assessment for older people. The most common appetite assessment methods within this systematic review were Likert and VAS. The VAS were of varying domains with no standardisation and minimal validation, they may also be challenging to administer in the clinical context. Of the Likert scale methods many were also of varying domains and lacked standardisation. The AHSPQ, which utilises Likert responses was the most robustly validated appetite assessment tool included in the review. However, it has lacked translatability into clinical settings amongst older people and so a simpler questionnaire in the form of the SNAQ was developed. The SNAQ has wide use amongst observational studies in older people across settings, highlighting associations between appetite and important health conditions and outcomes in older people. Therefore it could be considered the most appropriate candidate appetite assessment tool to take forward for a unified approach in future research studies.

3.3   Management for the anorexia of ageing

The systematic review of the literature for assessment of appetite in the older population also aimed to determine the current evidence for interventions for anorexia of ageing; trialled in the older population.

3.3.1   Methods

The methodology followed is described in 3.2.1

3.3.2   Results

The included studies are as described in sections 3.2.2.1 and 3.2.2.2 (Table 2). From the 21 included studies, 16 different types of intervention for anorexia of ageing were identified. I categorised these on a basis of theoretical effects to the categories of physiology, hedonism and external cues. Some of the interventions were used in combination. When reported individually for a study arm the effects on appetite are described individually. Otherwise, they are described for the combination (Table 3).

Table 3   Interventions for the anorexia of ageing with included studies

Intervention Category (Number of interventions)	Intervention Type with Included Studies

Physiology (*n= 15*)	Exercise program
	    De Jong et al. (arm 1) [149]
	Oral nutritional supplement
	  Boudville et al. [146]
	  Carlsson et al. (arm 1) [148]
	  De Jong et al. (arm 2) [149]
	  Faxen-Irving et al. [150]
	  Hebuterne et al. [164]
	  Hubbard et al. [151]
	  Irvine et al. [152]
	  Ryan et al. [158]
	  Tylner et al. [162]
	Exercise & oral nutritional supplement
	    De Jong et al. (arm 3) [149]
	Amino acid pre-cursor
	    Brocker et al. [147]
	Medication (megestrol acetate)
	    Reuben et al. [156]
	    Yeh et al. [160]
	Oral nutritional supplement & medication (nandrolone decanoate)
	    Carlsson et al. (arm 2) [148]

External cues (*n =6*)	Nutritional counseling
	    Andersson et al. [145]
	Mealtime volunteer assistance
	    Robison et al. [157]
	Autonomy to select portion size
	    Divert et al. (arm 1a) [165]
	Altered décor in mealtime setting
	    Divert et al (arm 3a) [165]
	Music in mealtime setting
	        Divert et al (arm 3b) [165]
	Altered menu wording
	        Divert et al (arm 4) [165]

Hedonism (*n = 7*)	Flavor enhancement
	    Best et al. [161]
	    Mathey et al. [154]
	    Dermiki et al. [163]
	Availability of and autonomy over condiments
	    Divert et al (arm 2) [165]
	Increased meal variety
	    Wijnhoven et al. [159]
	    Divert et al (arm 1b) [165]
	Fortified Food
	    Pouyssegur et al. [155]

Combination Physiology and External Cues (*n = 1*)	Education & exercise Kimura et al. [153]

3.3.2.1 Interventions relating to physiology

de Jong et al [149] conducted an open RCT with three arms, the first arm trialled a 17 week community based exercise programme. This entailed 45 minute group sessions twice a week focussing on muscle strength, coordination, flexibility, and endurance [149]. Compliance with and physical activity levels during the intervention were not assessed. The authors reported no effect on appetite compared to the controls in the arm attending a class with creative activities (P=0.61) [149].

Oral nutritional supplements (ONS) were assessed in 9 studies (as an individual arm within two studies) [146, 148-152, 158, 162, 164]. The ONS used differed in constituents when specified and included fatty emulsion, high protein, low protein, high fat, high carbohydrate and calorie or micronutrient dense formulas. The total energy content available daily from the ONS ranged from 200-916 Kcal in 30, 200 or 250 ml portions. None of the ONS were directly comparable in terms of ingredients, energy content and volume; they showed mixed effects on appetite. No effect was seen for the ONS with unspecified constituents used by Hubbard et al and Boudville et al (P values not reported) [146, 149, 151] or for those dense in micronutrients (P=0.17) used in the second arm of de Jong et al. These were compared to controls receiving usual care or standardised dietary advice sheets [146, 149, 151]. Carlsson et al's study [148] consisted of two arms, the first used a high protein ONS and reported no effect on appetite at 6 months compared with controls receiving usual care (P value not reported) [148]. An increase in the appetite domains 'desire to eat' and 'hunger' was reported in two different studies by Faxen-Irving et al and Tylner et al respectively, when using fat emulsion ONS, compared to controls receiving usual care (desire to eat P=0.021 [150], 'hunger' P= 0.026. [162]). The fatty acids used in these trials were oleic acid [150] and a mixture of oleic and linoleic acid [162]. A transient decrease in the domain of 'hunger' following a high fat and a high protein ONS after 4.5 hours when compared to participant's baseline was reported by Ryan et al (P=0.04) [158] and Irvine et al (P=0.01) [152] respectively. This did not persist in measurements at later time points [152, 158]. Another high protein and also calorie dense ONS tested by Hebuterne et al over a period of 4 weeks had no effect on appetite measured at 30 days [164]. Three of the studies using ONS reported a loss to follow up of participants due to product intolerance (numbers not specified) [150, 152, 158].

The third arm of the de Jong et al study evaluated 17 weeks of the micronutrient dense ONS in combination with the described exercise programme [149]. There was no change in appetite compared to controls in this arm receiving regular products and classes with creative activities (P value not reported) [149].

An amino acid pre-cursor, ornithine oxoglutarate, was evaluated by Brocker et al [147]. Own home dwellers recently discharged from hospital were given 10 g once a day with placebo controls [147]. An increase in the appetite domains 'overall appetite' and 'appetite for meat' were observed when compared to controls at 60 days (P=<0.001, P=<0.001) [147].

The effect on appetite of the progestogen medication megestrol acetate (MA) was evaluated in two double blind placebo RCTs [156, 160]. MA was prescribed in either 200, 400 or 800 mg doses over 24 hours with mixed results. At a dose of 800 mg, when compared to controls, Yeh et al described an increase in appetite at 12 weeks in care home residents (P=0.004) [160]. Reuben et al observed no difference compared to controls at 3 or 6 weeks for the range 200-800 mg in community dwellers following recent hospital discharge (P=0.07)[156]. Reuben et al did however report an increase from participant's baseline in the domains of 'appetite' and 'appetite at start of last meal' with 800 mg and 400 mg doses respectively (P=0.04, P=0.02) [156]. The authors discussed adverse outcomes; Reuben et al reported significantly lower cortisol levels compared to controls at 20 days (400mg P=0.003, 800mg P=0.02) but no clinical symptoms of adrenal insufficiency [156]. They also observed venous thromboembolism (n=2) and diarrhoea (n=3) [156]. Yeh et al reported no significant differences compared to controls for events related to drug therapy, and no significant difference on mortality (P values not reported) [160].

The effect of a protein rich ONS (244 Kcal in 24 hours) in combination with the anabolic steroid nandrolone decanoate (25 mg every 3 weeks) was assessed in the second arm of Carlsson et al's study [148]. They observed no difference in appetite compared to controls receiving usual care (P not reported) but an increase from baseline appetite for 6 of the 15 participants having the combination (P=0.02) [148]. Adverse incidents relating to nandrolone decanoate were not reported in the article [148]. An article on the same study cohort did note a transient rise of serum calcium, which reverted without therapy change, and increased incidence of urinary tract infections; a diagnosis also present in the control group with no measurement of difference made [198].

3.3.2.2   Interventions relating to external cues

In the study by Andersson et al in Norway a three month education programme was assessed [145]. This entailed individualised nutritional plans to achieve dietary and intake requirements pre-discharge from hospital and then post-discharge counselling [145]. Counselling addressed eating environment, motivation and support to increase intake, food preparation, food choices, and also undefined social and psychological factors [145]. Thirteen percent of participants were lost to follow up and the authors did not state the assessment of compliance with the

intervention. There was no significant effect on appetite when compared to controls receiving usual care (P=>0.05) [145].

The qualitative study by Robison et al [157] explored the effect of one year of trained mealtime volunteer assistants, helping older hospital patients in the UK to eat, on appetite and food intake. The impact of mealtime assistants on appetite was not reported but themes of poor appetite were prevalent in interviews from both the pre and post intervention samples with no apparent difference following volunteer help [157].

A number of interventions relating to external cues were trialled by Divert et al in a nursing home setting in France [165]. Two changes were made to the eating environment, firstly the addition of two items of décor, chosen by the residents in the prior week from two types of table cloth, two types of bread basket, four bouquets of flowers and four water carafes. Secondly, the addition of music throughout the mealtime chosen from a list of 70 songs given at the start of the meal. Neither intervention was associated with an increase in pre-meal hunger (n=32 P=0.40). The authors also made alterations to the wording of the menu, with wording suggesting higher quality meat and wording similar to that of a gastronomic restaurant; when compared to normal menu wording there was no effect on pre-meal hunger (n=33 P=0.45). Finally they also gave residents autonomy in selecting meal portion size. When compared to control portions there was an increase in pre-meal hunger for participants (n=30, P=0.05).

3.3.2.3 Interventions relating to hedonism

Six studies intervened by adjusting the participant's meal or mealtime [154, 157, 159, 161, 163, 165]. Mathey et al [154] used flavour enhancement with different flavours (chicken, beef bouillon, turkey, and lemon butter for fish) depending on the meal constituents, all of which contained monosodium glutamate (MSG). This was added over the whole main meal for 17 weeks for care home residents in the Netherlands. The authors reported increased daily feelings of hunger among participants, compared to both controls having a usual meal and with the participant's baseline appetite (P<0.05)[154]. Dermiki et al also assessed the effects of additional MSG to food, in this instance using two different flavours of potato-based soup (lemongrass and cumin) [163]. Participants were exposed to both soup flavours three times over 6 days, with one flavour also containing MSG; they attended a research centre in the UK for appetite measurements before and after the repeated exposures. There was no significant difference when comparing pre-lunch hunger and desire to eat ratings before and after the repeat exposures (hunger t (74) = 0.93, p = 0.35; desire to eat t (74) = 0.63, p = 0.53). Altering meal flavour was studied by Best et al on UK community dwelling older people who also attended a research centre [161]. They used seasoning on one occasion (two spoonsful of a choice of branded recipe) or sauce on another (100

g of a choice of branded recipe) on a meal of chicken, vegetables and mashed potato. In comparison to a control meal of the same ingredients there was no difference in pre or post meal appetite domains of 'hunger' or 'desire to eat' (hunger P=0.28, P=0.65; desire to eat P=0.36, P=0.15) [161].

In the Divert et al [165] series of interventions for older adults in a French nursing home setting, one arm involved flavour enhancement by use of additional condiments. However, rather than being applied to the meal by researchers, they were presented in bowls in the middle of the table and the participants had autonomy to help themselves (participants with functional disorders asked the researcher for help). Use of an additional four (butter, vinaigrette, mayonnaise, tomato sauce) or eight (the first four plus garlic, shallot, parsley, lemon) condiments to the usual salt and pepper saw an increase in pre-meal hunger ratings (n=27, P=0.05).

Wijnhoven et al [159] changed the constituents of single meals to increase their variety for community dwellers attending a research centre in the Netherlands. Meals with greater variety had three different selections of vegetables of three different colours, three different types of meat (or fish), and three different types of starch all-together on one plate. They reported no change in appetite compared with a control meal of only one variety of vegetable, meat and starch (P not reported) [159]. One arm of the multiple interventions trialled by Divert et al [165] included increasing the variety of constituents of a single meal for participants within their nursing home. The meal with greater variety had an additional 75 g of courgette to meat and green beans and saw an increase in pre-meal hunger ratings compared to control meal (n=30, P=0.05).

Pouyssegur et al [155] assessed fortified food for care home residents in France in the form of cookies between meals delivering 244 Kcal energy in 24 hours. The authors reported an increase in the 'appetite' domain after 18 weeks when compared to participant's baseline (P=0.009) [155].

3.3.2.4 Combination of physiology and external cues

Kimura et al [153], evaluated the combination of exercise and education for older Japanese people in their own home over a fourteen month period. This comprised of one hour exercise classes every two weeks focussing on muscle strengthening, and at-home exercise recommendations with daily records and feedback. Alongside these were five 30 minute lectures on dietary habits with participants recording daily intake, which was reviewed with motivational comments [153]. The authors found no change in appetite in the intervention group, compared to controls receiving usual care (P=1.0) [153].

3.3.3   Discussion

The sixteen different types of intervention for anorexia of ageing identified in the systematic review were categorised according to theoretical effects on physiology, hedonism and external cues. Physiological interventions included exercise, ONS, an amino acid precursor and medications. Interventions with an effect on hedonism including meal adjustments and increased variety, condiment availability and fortification in the form of cookies. External cues were adjusted through counselling and mealtime volunteer assistance, as well as alterations to the environment and autonomy in portion size selection. Of the sixteen different types of intervention, nine exhibited some favourable effects on appetite (ONS, amino acid precursor and megestrol acetate in the physiology category; flavour enhancement, increased variety, condiments and fortified food in the hedonism category; autonomy on portion size in external cues) when compared to controls or from baseline. However these findings were either in single datasets or not replicated across studies.

Amongst physiological interventions for anorexia of ageing, the studies assessing an exercise programme did not suggest any effect on appetite. However, the studies had limitations, in particular related to a lack of reporting on compliance and levels of physical activity achieved by the programs. The impact of medications was also considered, with evidence that megestrol acetate (MA) had a stimulatory effect on appetite- likely by influencing signalling pathways [156, 160]. However MA has been associated with safety concerns in older people including adrenal suppression, venous thromboembolism, hyper- and hypoglycaemia, changes in mental state, diarrhoea, insomnia and osteoporosis [156, 199-201]. The side effect profile of anabolic agents such as nandrolone decanoate is also considerable, including fluid retention, liver injury and prostatic hypertrophy [200]. These findings caution against the use of these medications for anorexia of ageing. Amongst ONS, only the fat emulsion forms demonstrated a positive effect on appetite [150, 162], these contained oleic acid and a mixture of oleic and linoleic acid. Whether the effects on appetite are related to peripheral signalling pathways augmented by the fatty acids is unclear. It is important to note however, that certain ONS may also impact on hedonism if well-liked by participants. However, losses to follow up due to product aversion occurred in ONS studies (numbers not reported) [150, 152, 158], indicating a hedonic mechanism of action is less likely. The fact that ONS were the largest intervention type may reflect current clinical guidance on their use for undernutrition, rather than a hypothesis on appetite stimulatory effects. There was variation in the authors' treatment intentions, whether anorexia of ageing or undernutrition, when measuring appetite as an outcome. Overall for ONS, the effects on appetite were mixed but there seems to be consensus that additional ONS only transiently reduce appetite, if at all [146, 150-152, 158, 164]. The amino acid precursor ornithine oxoglutarate showed stimulatory effects

on appetite [147]. Ornithine is integral to the urea cycle and has been used in liver cirrhosis where it was noted to have anabolic effects, but whether it is this mechanism of action that stimulates appetite is unclear.

Addressing the hedonic influences on appetite through adjustments to participant's meals gave mixed results, which may in part be due to the environment in which appetite was assessed. Those studies altering meals and then assessing appetite at a research centre setting saw no effect [159, 161, 163], whereas the studies in the participant's usual environment saw beneficial effects on appetite [154, 165]. When adjusting a meal, the environment in which it is eaten and where appetite is assessed may well have important impacts when thinking about relationships with wider external cues. In the case of Divert et al there was also additional design in the flavour enhancement intervention, with participants having autonomy in selection and use of the condiments [165]. This may have driven some of the effects on appetite, for example it may have promoted longer or earlier consideration of the meal. Introduction of flavour enhancers may have a beneficial effect in counteracting diminished taste function attributable to ageing [106], with evidence that enhancement increases food palatability and so 'liking' for older individuals, particularly for salt taste [202]. However, in the study by Mathey et al [154], the observed positive effects of MSG on appetite may also be linked to effects outside of palatability. As the repeated exposure to MSG in Dermiki et al's study demonstrated an increase consumption while reported 'liking' was unchanged [163].

The fortified food study by Pouyssegur et al reported an increase in appetite [155]; in this study the food provided was in the form of cookies. Therefore, the hedonic aspect of appetite may have been at play (as generally cookies are well-liked) but be unrelated to the fortification process itself, as this has been shown in other studies to have little impact on the hedonic value of foods for older individuals [203, 204]. So the mechanism of the association between the fortification and appetite observed is unclear. Fortified food is better tolerated by patients compared to ONS [205]; so any potential associated increase in appetite using food items it warrants further exploration.

The interventions based on cues likely to affect a person's appetite, such as their mealtime environment, saw no improvement. This may reflect how individualised a person's relationship with external cues relating to their appetite is. Thus, further information on how people experience and perceive these cues could guide interventions for poor appetite which have greater meaning, efficacy and engagement by older individuals. However, these are likely to be very contextual to countries, settings and potentially the individual. Autonomy in choice of portion size [165], did see an improvement in pre-meal hunger, which again indicates an

individualised relationship and so interventional approaches led by the older person may be fruitful.

3.3.4   Conclusions

There is a paucity of evidence for management strategies for the anorexia of ageing. Different methods have been trialled with some signal of positive results but these were either in single study sets or were not replicated. Amongst physiological interventions a few medications showed beneficial effects but with an intolerable side effect profile. The amino acid precursor ornithine oxoglutarate also showed beneficial effects and may warrant further exploration. A full understanding of lifestyle interventions such as physical activity was limited by study methodology, such as measures of compliance. Potential interventions addressing the hedonic aspect to appetite- such as flavour enhancement, or use of fortified snacks such as cookies - may signal some benefit but again need further investigation. Interventions based on external cues were not shown to be effective in this review, aside from choice of portion size. This is likely to reflect the individualised relationship a person has with specific cues, and that a greater understanding of how they experience these cues is needed. Due to the number and diversity of influences on appetite a multi-component intervention may prove most effective.

3.4   Study strengths and limitations

This systematic review was conducted according to the recommendations of the PRISMA statement [141]. Two researchers worked independently to assess studies for inclusion and quality, plus hand searched reference lists and citing works to ensure appropriate acquisition of studies. No limits on publishing language were set. The authors of two included studies were also contacted with one response providing further information. However, the search did not include the grey literature where sources such as service improvement projects may have been identified.

Articles included in the review were of variable quality but overall were representative of the older population across settings. Despite this, the interventions were variable and many were only represented in single samples. Likewise, the appetite assessment tools used also varied and often had not been validated in older populations.

As reflected in the scoping searches, the terms undernutrition and anorexia of ageing were often used interchangeably by authors, rather than undernutrition being recognised as a potential consequence of anorexia of ageing. Lack of clarity on this is important as some people with poor appetite may not yet be undernourished but rather be at risk of developing it (as seen with

Mathey et al's study sample, with poor appetite but a BMI >25 kg/m^2) and so may be missed if undernutrition is the sole focus [134, 154].

The systematic review had two aims- to identify appetite assessment methods for older people and to identify the current evidence for management strategies for the anorexia of ageing. Combining these aims may have limited the appraisal of assessment methods for appetite in older people, as this did not systematically include observational studies (highlighted in section 3.2.2). I considered it important to appraise appetite assessment methods in the context of an intervention, as this might indicate their utility in determining efficacy. However, this may mean that other appetite assessment methods have not been identified, nevertheless my later appraisal of observational studies will have mitigated this.

3.5 Chapter summary and conclusions

I undertook a systematic review of the literature to understand the current evidence for methods to assess appetite in older people and for interventions for the management of anorexia of ageing.

A number of different appetite assessment methods were used, with Likert and VAS the most common methods. However these varied in scale length and by question domain. The review has highlighted that there is currently no standardised measure for appetite assessment for older people. A candidate for a unified assessment method is the Simplified Nutritional Appetite Questionnaire (SNAQ). This 4 item questionnaire utilising Likert scales is an evolution of the most rigorously tested questionnaire included in this review- the AHSPQ and is being increasingly used in clinical studies to assess appetite in older people across settings.

There is a paucity of evidence for treatments for the anorexia of ageing. Different methods have been trialled with some signal of positive results but these were either in single study sets or not replicated. The amino acid precursor ornithine oxoglutarate, as well as potential interventions addressing the hedonic aspect to appetite- such as flavour enhancement, or use of fortified snacks such as cookies - may signal some benefit but require further investigation. Full understanding of interventions for external cues and other lifestyle factors such as physical activity were limited by study methodology.

Due to the number and diversity of influences on appetite, a multi-component intervention may prove most effective and further research into influences is needed. The following chapters will further evaluate the major influences in hospital and community based datasets.

Chapter 4   Analysis of data from a hospitalised older population- exploring potential influences on appetite

4.1   Introduction to chapter

This chapter will describe the secondary data analysis I undertook of three existing datasets from a population of hospitalised older people, which I combined into a single dataset. Findings from this chapter have been published in [11] and [206]. The previous chapter discussed the paucity of evidence for interventions for the anorexia of ageing. A potential reason for this is a lack of understanding of potential influences on appetite, which are amenable to modification. Analysis of these datasets gives a unique opportunity to explore possible variables which may be influential on appetite.

In a recent review, Roy and colleagues in 2016 assessed the evidence from observational studies on correlates of the anorexia of ageing [207]. The review highlighted correlates of interest, found from both primary research and reviews, with a focus on public health. Correlates were categorised to food-related (consistency, temperature and palatability), psychological factors (anxiety, depression, recent bereavement, alcoholism, sociopathy, anorexia nervosa, body weight dissatisfaction), sociocultural (isolation, inability to cook, ethnicity, poverty, food preference) and environmental (physical environment during meal, social environment, meal-timing, food availability, housing type, public health message misinterpretation) [207]. This review had a public health focus but other correlates of clinical interest identified included changes in smell and taste, pain, reduced mobility, dysphagia, poor oral health, chewing problems, frailty, functional impairment, cognitive decline and polypharmacy. The authors noted that much of the narrative for associations with the anorexia of ageing originates from commentaries and reviews, with a scarcity of primary research, most of which is cross-sectional in design [207].

My further appraisal of the literature on quantitative observational studies assessing appetite in older people, identified additional studies reporting on primary research [6-10, 113, 122-124, 128, 130-133, 183, 187, 189, 191-194, 208-212]. These studies identified additional variables including female gender, medical conditions such as constipation, lower educational level, living alone, lower levels of physical activity, BMI, weight loss and increased nutritional risk. In agreement with Roy and colleagues [207], my assessment of the additional observational studies identified

predominantly cross-sectional designs. Therefore, although association can be determined in these studies, the sequence is unclear. The few observational studies with longitudinal methodology focussed on well-established outcome variables and appetite as the exposure rather than outcome, with most reporting on mortality [9, 10, 131], but also hospital associated infection [10], falls [212], disability [130], and sarcopenia related outcomes [128].

To illustrate how certain variables identified in the cross-sectional observational studies may act as influences on, rather than consequences of, appetite, I developed a theoretical model (Figure 10). This model utilises understanding from my review of the literature and the concept of changes in the categories of physiology, hedonism and external cues as influences on appetite. This study then aimed to identify potential associations between appetite measured in hospitalised older people and factors which are theoretical influences on appetite. To undertake this I used the combined data of three hospital-based studies as an opportunity to explore associations. I employed my theoretical model (Figure 10) to identify the potential influential factors present within the dataset to be included within the analysis. My hypothesis was that all of the identified potential influential factors within the model would be associated with SNAQ due to effects on physiology, hedonism or external cues with no pre-determined level of importance.
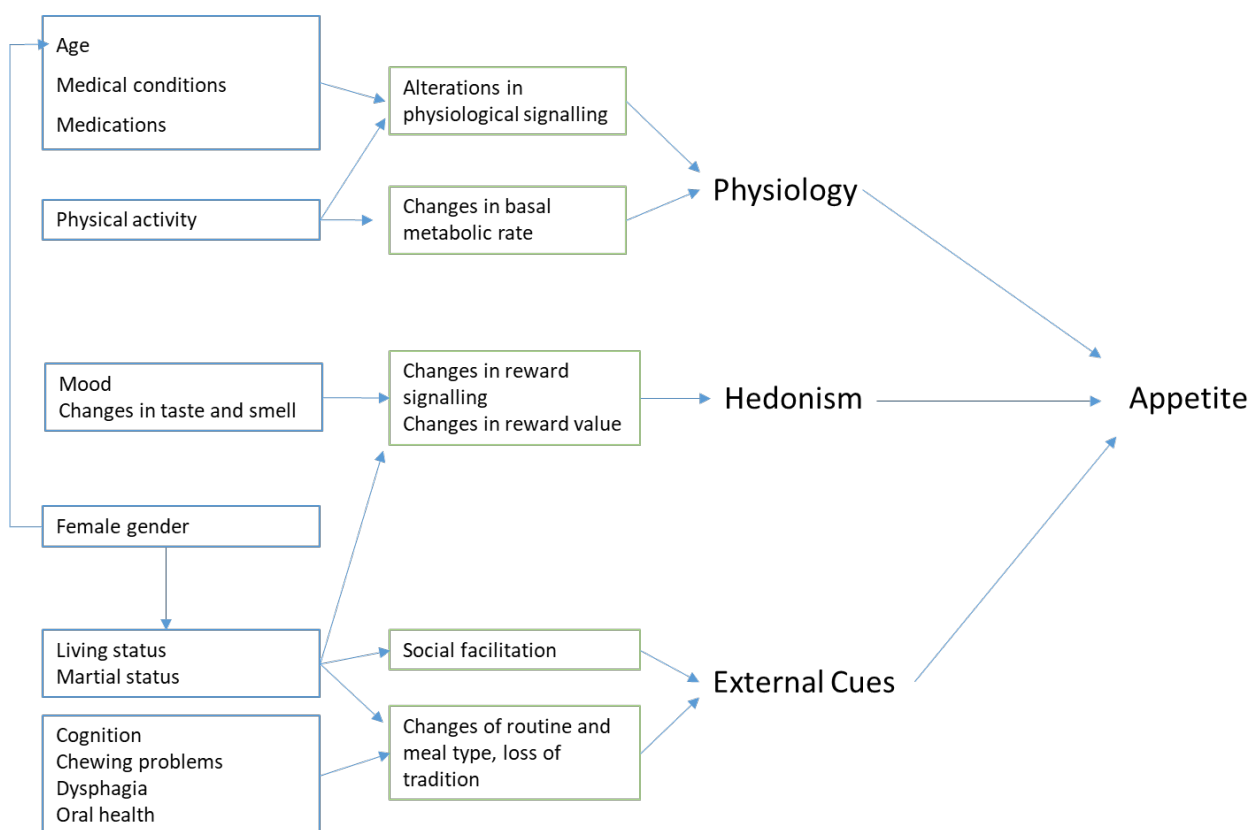
Figure 10   Theoretical model of relationship between influential factors and appetite

The framework is built upon the categories of influence on appetite as discussed in the introduction (section 1.3) and Cox et al [70].

4.2   Aims of the study

1. To describe levels of appetite in an older hospital population using the SNAQ score.
2. To explore the association between potential influential factors on appetite and SNAQ score.

4.3   Methods

4.3.1   Data collection

Three previous studies conducted within University Hospitals Southampton (UHS) on older hospital inpatients (aged over 70 years) have all included an assessment of appetite using the Simplified Nutritional Appetite Questionnaire (SNAQ):

1. The Cachexia: Skeletal loss and Inflammation in Older Women- the CaSIO study. This study aimed to determine the prevalence of cachexia in hospitalised older women and explore its role in six month outcomes [213].

2. The Southampton Mealtime Assistance Roll-out Trial-the SMART study. This study described the implementation of volunteer mealtime assistants in four hospital departments [214]

3. The Southampton Mobility Volunteer study- the SoMoVe study. This study assessed the feasibility and acceptability of implementing trained mobility volunteers on hospital wards [215].

All of these studies recruited from the same population (older hospital inpatients from the wider Southampton area served by UHS) [213-215]. The data were collected in the years 2010-12 (CaSIO), 2014-15 (SMART) and 2016-17 (SoMoVe). All three studies used the same data collection methodology for their core datasets, which were combined for this project. I combined the core datasets from separate databases into a single file for statistical analysis using SPSS software (SPSS IBM Corp version 24). The unique participant number was used to indicate which dataset they originated from and to enable sub-group analysis.

4.3.1.1 Participant characterisation

Demographic details recorded included age, gender, living circumstance (living alone, living with others, living in sheltered accommodation or living in a care home) and marital status (single, married, divorced/separated, widowed, cohabiting).

The Barthel index was used as a measure of physical function [216], which gives a score of 1-100, a higher score reflecting greater functional ability. Frailty was assessed using the FRAIL scale, which categorises the individual as being robust, pre-frail or frail [217], on the basis of screening questions relating to the Fried frailty phenotype of unintentional weight loss, self-reported exhaustion, weakness, slow walking speed and low physical activity. Grip strength was measured using a standardised approach [218], with a JAMAR Hydraulic Hand Dynamometer. Low grip strength was defined as <16 kg for women and <27 kg for men [219], and used as a marker for sarcopenia.

Markers of nutrition included body mass index (BMI), calculated by participants' weight (kg) divided by height squared (m²), and the Malnutrition Universal Screening Tool (MUST) category. The MUST categorises individuals into low, medium or high risk of malnutrition using scoring based on BMI, unplanned weight loss and acute illness, and demonstrates validity for use in hospitalised older people [220].

4.3.1.2   Outcome variable- appetite assessment

Appetite was assessed using the validated Simplified Nutritional Appetite Questionnaire (SNAQ) [134]. The SNAQ includes 4 questions each with 5 responses on a Likert scale, one of which the person selects. This questionnaire is scored out of 20 and a score <14 indicates poor appetite in community dwelling people aged >60 years and has been shown to be predictive of weight loss at six months [134]. In the hospital setting, the SNAQ has shown reliability, validity and ability to predict inadequate intake [179, 180]. A low SNAQ score during hospital admission has also been demonstrated to correlate with mortality six months in a female population [10], as well as reduced muscle strength post discharge [128] (see Chapter 3 section 3.2.2 for discussion on the development and use of the SNAQ in older populations).

4.3.1.3   Exposure variables- potential influences on appetite

Using my theoretical model of influences on appetite (Figure 10), I identified potential influential factors on appetite present within the dataset. The factors, including the tool used to assess them and presence within each individual study, are summarised in Table 4. Whilst a focus of the research in this thesis is to explore potentially modifiable influences on appetite, it is still important to understand association of appetite with other non-modifiable influences. This information will aid in determining co-variates to measure in future intervention studies. Therefore I included both modifiable and non-modifiable factors of interest in the analysis.

Table 4   Influential factors, assessment method and presence in the hospital based studies

Exposure Variables	Tool used to assess	Presence of measure in study		
		CaSIO (n=179)	SMART (n=201)	SoMoVe (n=100)
Age	Years	+	+	+
Gender	Categorised as male/female	+	+	+
Living circumstance	Categorised as: living alone, living with others, in sheltered accommodation, in care home	+	+	+
Co-morbidity	Charlson Co-Morbidity Index	+	+	+
Medication	Count	+	+	+
Physical activity level	Physical Activity Scale for the Elderly (PASE)		+	
Mood	Geriatric Depression Scale short form -15 (GDS-15)	+	+	+
Cognition	Mini-Mental State Examination (MMSE)	+	+	+

Age and gender were recorded for all of the participants, as well as their residence, which was categorised in all 3 studies as living alone, living with others, in sheltered accommodation or in care home. The number of medications and a list of co-morbidities were recorded in each study. The presence of certain co-morbidities had been used to calculate a co-morbidity index score (Charlson co-morbidity index) for the SMART and SoMoVe studies; age is also included in the scoring [221]. The index has been validated for use in identifying incident disability and also mortality in community dwelling older people [222, 223]. I derived the Charlson Index for one study (CaSIO) from the coded comorbidities to allow comparison with the other study sets. All other variables that needed to be derived from raw data had already been completed on data cleaning during the previous studies.

Physical activity was assessed in the SMART study using the Physical Activity Scale for the Elderly (PASE) questionnaire [224]. This is a 10 domain questionnaire covering leisure, household and work-related activity over the prior 7 days. A score can be derived based on activity frequency and a defined weighted value for that activity with a range between 0 and 793; a higher score indicates higher levels of activity. The SoMoVe study also included a measure of physical activity using pedometers, to measure in-hospital levels of physical activity. I did not select this for analysis as in-hospital levels of activity are not reflective of habitual levels of activity and older people are very sedentary when admitted to acute care [225]. The CaSIO study did not contain a measure of physical activity, therefore only the SMART study data were suitable for analysis of this variable.

The Geriatric Depression Scale short form (GDS-15) [226], was used to assess for low mood. This scale in the shortened form consists of 15 questions in a yes/ no format. A score of 0-4 indicates no depressive symptoms, 5-9 mild depressive symptoms and 10-15 moderate to severe depressive symptoms. This scale has been widely used in older people across settings [227].

Level of cognition was measured using the Mini-Mental State Examination (MMSE), which is a 30 point questionnaire covering different aspect of cognition with cut off values for mild (score 18-23) and severe (score ≤17) cognitive impairment [228].

Some theoretical influences on appetite identified in the appraisal of observational studies on correlates of appetite (see introduction to chapter section 4.1, Figure 10), such as dysphagia, oral health and marital status were not recorded within the 3 studies.

4.3.2 Statistical analysis

I analysed the data using SPSS statistical software (SPSS IBM Corp version 24), initially using descriptive statistics to characterise the population: mean and standard deviation for normally distributed data, frequency and percent for categorical, and median and inter-quartile range for skewed data. The levels of appetite in the population were described as mean and SD. Poor appetite was also described in categorical form, defined as a cut off of score <14, which has previously been shown to predict weight loss at six months in community dwelling older people [134]. To compare characteristics between participants with good (SNAQ score ≥ 14) and poor appetite (SNAQ score <14), I used independent samples T test for normally distributed data, Mann-Whitney U test to compare distributions for skewed data, and Chi Square for nominal data distributions. I used logistic regression to assess the association between poor appetite and death at six months post hospital discharge. Association between poor appetite and death were adjusted for gender, length of stay and Charlson co-morbidity index in multivariate analysis, as I considered these to be other important factors relating to mortality post hospital discharge. P values of <0.05 were considered statistically significant.

To assess the association between exposure variables present within the dataset and appetite, I utilised regression modelling. This was informed by the theoretical model derived from my review of observational studies and the concept of physiology, hedonism and external cues (Figure 10). The variables of age, gender, living circumstance, total number of medications, Charlson index, geriatric depression score and Mini-Mental State Examination were considered within the model. These variables were all considered with equal weighting as to their importance on their effects on SNAQ score. I initially used univariate analysis, then in multivariate analysis I built models determining the individual effects of including additional variables.

The PASE was used to assess the association between physical activity and appetite. This measure was included only in the SMART study, so sub-group analysis was performed to determine the association of this variable. The effects of variables associated with SNAQ in the whole group analysis were then adjusted for in a multivariate analysis of physical activity on SNAQ score.

4.3.3 Ethical considerations

All three of the studies had received ethical approval through the health research authority [213-215]. All participants from the included studies provided informed consent on recruitment to give permission that data collected with the study could be used in anonymised form for future research projects and analyses.

4.4   Results

4.4.1   Description of the study population

The total data set (Table 5) included 474 individuals who had a completed appetite assessment with SNAQ (completion rate of 98.75%), with more females (64%), which represents the sampling strategy of CaSIO (recruiting from a female only ward). The mean age was 84 years (SD 6.47); widowed females usually living alone represented the largest proportion of participants.

The participants represent a well-functioning sample of older people, cognitively with a median mini-mental state examination score of 27/30 (IQR 23-29), and physically with a median Modified Barthel Index score of 78/100 (IQR 53-91). The median comorbidity index score was 5 (predictive of a ten year survival of 34% [221]), and the mean number of medications was 9 indicating multi-morbidity. The median FRAIL scale score was 2 and grip strength median values of 24 kg for men and 13 kg for women indicating a pre-frail and sarcopenic population. The nutritional indicators BMI (median 24.9 kg/m^2 (IQR 21.7-28.3) and MUST screening score (70.5% were low risk) indicated that the majority of the population would be considered to have low clinical nutritional risk.

Table 5   Description of the hospital study population

Population descriptive. * mean (SD), $^\$$frequency (percent).

Variable	N (male, female)	Median (IQR)		
		Total	Males	Females
Age*	474 (169, 305)	84.13 (6.47)	82.49 (6.70)	85.03 (6.16)
SNAQ*	474 (169, 305)	13.87 (2.60)	14.05 (2.48)	13.77 (2.66)
Marital status$^\$$	461 (169, 305)			
Single		13/30 (6.5)	12	18
Married		153 (33.2)	95	58
Divorced/Separated		30 (6.5)	16	14
Widowed		245 (53.1)	44	201
Cohabiting		3 (0.7)	2	1
Unknown		13 (2.8)	0	13
Usual residence$^\$$	474 (169, 305)			
Private home alone		221	58	163
Private home with others		198	103	95
		37	4	33
Sheltered housing		15	3	12
Residential home		3	1	2
Barthel Index	472 (168, 304)	78 (53-91)	88 (70-100)	71 (45-86)
Cognition (MMSE)	473 (169, 304)	27 (23-29)	27 (24-29)	26 (23-28)
FRAIL scale	291 (165, 126)	2 (1-3)	2 (1-3)	2 (1-3)
Grip strength (kg)	442 (157, 285)	16 (12-22)	24 (19-30)	13 (10-17)
BMI (kg/m^2)	467 (169, 298)	24.9 (21.7-28.3)	25.3 (22.5-27.7)	24.9 (21.3-28.8)
MUST category$^\$$	472 (162, 278)			
Low risk		334 (70.5)	129 (79.6)	205 (73.7)
Medium risk		53 (11.2)	16 (9.9)	37 (13.3)
High Risk		53 (11.2)	17 (10.5)	36 (13.0)
Charlson Index	473 (169, 304)	5 (4-7)	6 (5-8)	5 (4-6)
N° medications	441 (136, 305)	9 (6-12)	8 (6-11)	10 (7-13)
Mood (GDS-15)	458 (166, 292)	4 (2-6)	4 (2-6)	4 (2-6)
PASE	200 (120, 80)	50 (25-114)	53 (25-132)	50 (25-76)
Length of stay (days)	473 (169, 304)	13 (7-22)	12 (6-20)	14 (8-23)
Deceased at six months$^\$$	472 (169, 304)	71 (15)	31 (18.5)	40 (13)

SNAQ= Simplified Nutritional Appetite Questionnaire; BMI= Body Mass Index; MUST=
Malnutrition Universal Screening Tool; GDS-15= Geriatric Depression Scale – 15;
PASE= Physical Activity Scale for the Elderly; MMSE= Mini-Mental State Examination

4.4.2 **Levels of appetite in the study population and characteristics relating to poor appetite**

The mean SNAQ score for the population was 13.87 (SD 2.6) and 195/474 people had a SNAQ score of <14. This shows that 41% of the population were suffering from poor appetite according to SNAQ. The characteristics of those with poor appetite (SNAQ <14) relating to characteristics of the population are summarised in Table 6.

Individuals in this hospital population with a poor appetite did not differ substantially from those with good appetite in terms of their demographic profile (Table 6). However, individuals with a poor appetite had a higher FRAIL scale score (p = .001) and Barthel Index (p = .007), indicating they were living with a greater degree of frailty and had higher levels of physical dependence compared to those with a good appetite. In addition, grip strength was weaker for individuals with poor appetite compared to those with good appetite and this difference reached statistical significance for women. Individuals with poor appetite also had a lower BMI (p = .006) and there was a trend towards a higher proportion of individuals meeting criteria for the high risk category on MUST scoring.

Table 6   Comparison of characteristics in those with good and poor appetite in the
            hospitalised study population

Characteristic	Good appetite (SNAQ ≥14); N=279	Poor appetite (SNAQ <14); N=195	P
Demographic			
Age*	84.29 (6.39)	83.89 (6.58)	.502
Female$	172 (61.65%)	133 (68.21%)	.143
Residence$ Living alone Living with friends/partner/family Sheltered/ warden controlled accommodation Care home	131 (46.95%) 119 (42.65%) 20 (7.17%) 9 (3.23%)	90 (46.15%) 79 (40.51%) 17 (8.72%) 9 (4.62%)	.828
Charlson Comorbidity Index^	5 (4-7)	5 (4-7)	.371
Number of medications^	9 (6-12)	10 (6-12)	.146
Grip strength^ Males Females	24 (19-30) 14 (11-18)	22 (18-28) 12 (9-17)	.144 **.014**
BMI^	25.58 (22.15-28.70)	24.20 (21.0-27.32)	**.006**
MUST category$ Low risk Medium risk High Risk	206 (73.83%) 27 (9.68%) 46 (16.49%)	128 (65.64%) 26 (13.33%) 41 (21.03%)	.153
FRAIL scale^	2 (1-3)	3 (2-3)	**.001**
Barthel Index^	80 (57.5-93.5)	72 (48-90)	**.007**
Length of stay^	13 (7-21)	14 (7-23)	.288
Deceased at 6 months$	28 (10 %)	43 (22.05%)	**<.001**

Population descriptive. * mean (SD), ^median (IQR), $frequency (percent). Bold indicates
statistical significance at <.05 level.

Seventy-one individuals (15%) were deceased at six months post-discharge among the hospital population, and included a higher proportion of individuals with poor appetite compared to those with good appetite (22% versus 10%; P<.001)

The CaSIO study data had been previously utilised to explore an association between poor appetite during hospital admission and mortality at six months following hospital discharge, highlighting a 2 fold increase in death for women with a poor appetite (SNAQ <14) [10]. To assess the reproducibility of this finding in a larger group including both genders I conducted logistic regression on the SoMoVe and SMART datasets. In this sub-group analysis, poor appetite (SNAQ score of <14) was associated with a 2.47 increase in odds of mortality at six month follow up (OR 2.47 (95% CI 1.27, 4.82) (Table 7). This association remained after adjusting for Charlson index, length of stay and gender (OR 2.62 (95% CI 1.30, 5.27) (Table 7).

Table 7   Analysis of associations with death at six months post hospital discharge

Variable	Unadjusted OR for death at six months (95% CI)	P	Adjusted OR for death at six months (95% CI)	P
SNAQ score <14	2.47 (1.27, 4.82)	**.008**	2.62 (1.30, 5.27)	**.007**
Charlson (per point increase)	1.25 (1.10, 1.44)	**.001**	1.22 (1.06, 1.41)	**.006**
Length of stay (per day increase)	1.02 (1.01, 1.04)	**.012**	1.02 (1.00, 1.04)	**.019**
Female gender	.42 (.20, .88)	**.021**	.423 (.20, .91)	**.028**

4.4.3 Association between potential influential factors and appetite as a continuous outcome

Categorical data can be useful to understand the characteristics of populations but is less powerful than continuous data to identify potential associations between factors. Therefore, I used linear regression to assess the association of measured potential influential factors with SNAQ score. This was performed in two ways, firstly assessing the association of variables present in all studies as one data set, then a sub-group analysis of the SMART dataset to assess the association of physical activity. The SNAQ scores displayed a normal distribution so was acceptable for use in regression analysis (Figure 11).
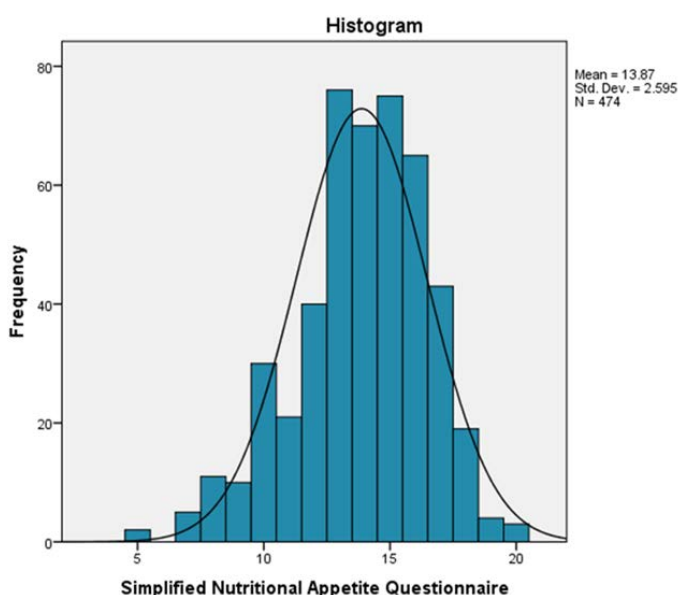
Figure 11   Distribution of SNAQ scores in the hospital study population

Univariate analysis of the whole dataset showed that the geriatric depression scale (GDS-15) score was associated with the SNAQ score (regression coefficient -.239, P<.001). The R^2 for GDS-15 was .065, indicating it explained 6.5% of the variance in SNAQ, (P<.001). None of the other identified exposure variables were associated with SNAQ score (Table 8).

Table 8   Association of potential exposure variables with Simplified Nutritional Appetite

               Questionnaire scores in the hospital study population

Independent variable	Univariate analysis		Multivariate analysis			
			Model 1 (n=458)		Model 2 (fully adjusted) (n=424)	
	Regression co-efficient (95% CI)	P	Regression co-efficient (95% CI)	P	Regression co-efficient (95% CI)	P
GDS-15	-.239 (-.323, -.156)	**<.001**	-.248 (-.332, -.164)	**<.001**	-.245 (-.336, -.154)	**<.001**
Age	.023 (-.01, .06)	.203	.031 (-.005, .067)	.093	.042 -.002, .085)	.062
Female gender	-.279 (-.768, .209)	.262			-.577 (-1.167, .012)	.055
Charlson comorbidity index	-.052 (-.166, .061)	.367			-.073 (-.208, .063)	.292
Total No medications	-.041 (-.1, .017)	.166			-.037 (-.097, .022)	.220
Living alone in own home	.118 (-.351, .588)	.588			.461 (-.082, 1.005)	.096
Living in care home	.305 (-.921, 1.531)	.625			.911 (-.506, 2.329)	.207
Living in sheltered accommodation	.079 (-.795-.953)	.860			.430 (-.569, 1.429)	.398
MMSE	.010 (-.053, .074)	.753			.012 (-.061, .085)	.754
R² for model			.071	**<.001**	.087	**<.001**

GDS-15= Geriatric Depression Scale – 15; MMSE= Mini-Mental State Examination

In multivariate analysis, I built models determining the individual effect of additional variables when included in the model. When added to the model following the removal of the effect of GDS-15, none of the other variables was significantly associated with SNAQ. Only age signalled an approach to significance when adjusted for GDS-15 (Table 8, Model 1). The model including GDS-15 and age explained 7.1% variance within SNAQ, P<.001.

Multivariate analysis including all variables was performed to assess the independent association of the GDS-15. In this model the independent association of GDS-15 with the SNAQ remained, with adjustment for the other independent variables having minimal impact (unadjusted co-efficient -.239, P<.001, adjusted co-efficient -.245 P<.001). The adjustment also had little impact

on the overall predictability of the model for the variance of SNAQ (8.3% of the variance P<.001, versus 6.5% in the univariate analysis) (Table 8, Model 2). Within the fully-adjusted model, only female gender and age approached significance (p=.055 and P=.062).

To test the association of physical activity levels with appetite I performed a sub-group analysis on the SMART study data. This was initially in univariate analysis and then adjusted for GDS-15 score in multivariate analysis. In initial univariate analysis, the PASE score was significantly associated with the SNAQ score (regression co-efficient .009, P=.001). GDS-15 again showed an association with SNAQ (regression co-efficient -.25, P<.001) (Table 9). In multivariate analysis GDS-15 remained associated with the SNAQ; (regression co-efficient -.198, P=.004), with PASE also continuing to be associated with the SNAQ (regression co-efficient .006, P=.024), showing independent effects. This model (n=198) (Table 9) explained 9% of the variance within SNAQ, P<.001.

Table 9   Association of physical activity and depression with appetite (Simplified Nutritional Appetite Questionnaire Score) in the hospital study population

Independent variable	Univariate Analysis Regression coefficient (95% CI)	P	Multivariate Analysis Regression coefficient (95% CI)	P
GDS	-.25 (-.38, -.12)	**<.001**	-.198 (-.333, -.063)	**.004**
PASE	.009 (.004, .014)	**.001**	.006 (.001, .012)	**.024**
R^2 for model			.092	**<.001**

GDS-15= Geriatric Depression Scale – 15; PASE= Physical Activity Scale for the Elderly

4.5   Discussion

This secondary data analysis described the level of appetite in a population of hospitalised older people and the association with potential influences on appetite present within the dataset.

The mean SNAQ scores in the study indicate that these cohorts of older people had a poor appetite during hospital admission. This was reflected in 41% of the population having a SNAQ score of <14 which has previously been defined as predictive of negative health outcomes in community dwelling older people [134]. In this group of hospitalised older people we observed that those with a poor appetite (score <14 on the SNAQ) had higher levels of frailty and physical dependence, a lower BMI and a trend towards weaker grip strength. We also confirmed the association between poor appetite during hospital admission and mortality six months post hospital discharge [10], with poor appetite associated with an over two fold increase in odds of mortality at six months in this sub-group analysis [11]. This finding adds to existing evidence in the literature by confirming this association in a larger group of hospitalised older people, which includes both genders.

Assessment of associations between potential influences on appetite in this population identified that lower mood as measured by the GDS-15 was associated with poorer appetite assessed using the SNAQ score. This effect remained relatively unchanged in a fully adjusted analysis, indicating an association independent of the other measured variables within the model.

As described in chapter 1 (part 1.2.2 and 1.3.1.2), mood has been previously identified as being influential on appetite in both older and younger individuals but that ageing appears to alter the nature of the relationship, with low mood potentially having more suppressive effects on appetite in older people. The association identified in this analysis in which a lower mood is associated with a lower level of appetite reflects the literature, which describes that older people when depressed tend to lose weight [115]. It is important to note that this was a hospitalised older population and so a major confounder for low mood and low appetite in this group is the effect of acute illness. However, a higher GDS-15 score (lower mood) has also been shown to correlate with poorer appetite in community dwelling older people, where the effects of acute illness would be less [191]. It is also noteworthy that in this hospitalised population the GDS-15 scores were low (3 - 4 out of 15) and would not be considered to represent clinical depression (a score of 5 or more out of 15 indicates depressive symptoms), but rather a low level change in mood.

In sub-group analysis, lower levels of habitual physical activity measured by the PASE was associated with lower level of appetite among 201 participants in the SMART study. This finding adds to an area with a paucity of research [96], despite popular belief and NHS guidance that

increasing levels of activity may combat poor appetite [229]. This association was independent of that between appetite and GDS-15. The fact that the PASE measures levels of habitual activity rather than exercise is noteworthy in relation to the results of the systematic review (see chapter 2 section 2.3), where exercise interventions did not show any effect on appetite. It reinforces the concept that these two different aspects of activity are likely to have differing effects on appetite (see introduction part 1.2.4), with habitual physical activity postulated to improve a person's response to their appetite physiological signalling mechanisms [63].

4.5.1 Study limitations

A limitation to this project is the cross-sectional methodology used to identify the potential influences on appetite. This means that although the study can determine that mood (measured by GDS-15) and habitual physical activity (measured by PASE) are associated with appetite (when measured with SNAQ) temporal sequence and causality cannot be determined.

Another limitation of this study is that it is a secondary analysis of existing core datasets, therefore these studies were not designed with the intent of understanding influences that may correlate with appetite. Therefore other potential variables, which were identified on my appraisal of observational studies on appetite and may be important confounders to appetite have not been measured for, such as presence of taste or visual disturbance (see Figure 10), which may have impacted on the associations observed.

4.6   Chapter summary and conclusions

This study encompassed a secondary data analysis on a hospitalised population of older people to assess the association of exposure variables with level of appetite during hospital admission. Variables of interest were those I considered to have a theoretical mechanism of action on appetite via physiology, hedonism or external cues. The hospitalised population included 474 individuals aged >70 years. Appetite was assessed during hospital admission using the Simplified Nutritional Appetite Questionnaire (SNAQ). Over 40% of the individuals had a poor appetite (SNAQ <14). These individuals had a higher degree of frailty and physical dependence as well as a lower BMI, and a trend to weaker grip strength. Poor appetite in hospital was also associated with increased odds of mortality at six months post hospital discharge.

In cross-sectional continuous analysis, mood measured by the geriatric depression scale (GDS-15) was associated with appetite measured by the SNAQ, in that higher mood was associated with better appetite. In sub-group continuous analysis both GDS-15 and level of physical activity measured by the physical activity scale for the elderly (PASE) were associated with the SNAQ, with both higher mood and higher levels of physical activity being associated with better appetite. In adjusted analysis these two correlates remained significant, suggesting independent effects.

Although this is a cross-sectional analysis and temporal sequence of associations cannot be determined, both mood and physical activity have theoretical mechanisms of influence on appetite, so warrant further exploration. However, a main potential confounder for the results of this analysis is the effect of acute illness on both mood and appetite of the population, which needs to be taken into consideration in future studies.

Chapter 5   Understanding individual's perceptions of appetite and its influences

5.1   Chapter Introduction

This chapter will describe a qualitative study undertaken to explore the perceptions of home-dwelling older individuals about appetite, its loss and influential factors. The main findings of this study have recently been published in Cox et al [230].

In this thesis I have previously grouped the multifactorial influences on appetite into those of physiology, hedonism and external cues. These influences are complex and likely individualised in older people (see Introduction section 1.3.2). This may be contributing to the current paucity of effective interventions for the anorexia of ageing (as highlighted in Chapter 3), as many of those trialled have looked at single strategies such as oral nutritional supplements. Of the three categories, the effects of hedonism and external cues are most likely to be individualised but remain key to understand if interventions for the anorexia of ageing are to be successful. In particular, little is known about the perspectives of older individuals on how they experience influences on their appetite. Additionally, there is little understanding of the older individual's perception of appetite itself, its loss and how influences on appetite may relate with these perceptions. Exploring this may provide greater clarity on factors which could be potential candidate interventions for reversing appetite loss. It may also inform the design of future interventions, including introduction of novel components but also critique of why existing interventions have had less success, to ensure effectiveness and relevance for older individuals [231].

Previous qualitative studies have largely discussed appetite in terminology relating to food choice, amounts consumed and practical aspects, such as the eating environment [117, 120, 182]. There is less exploration of what appetite means to older people, how they experience it, including loss of appetite and possible factors or events related to this. Wikby et al reported that feelings of independence, security, integrity and motivation, linked to health, wholesomeness and self-discipline, were related to a better appetite in older adults in residential care [117]. Holst et al also identified that wellbeing and hope had a positive effect on appetite in hospitalised older people [118]. However these may be situation specific as these studies are based in care settings.

The previous study in Chapter 4 has also highlighted that sub-clinical low mood and lower level of physical activity were associated with appetite scores in hospitalised older individuals. But it is also unclear whether these associations are also situation specific to care settings or the presence of acute illness. In addition, it does not explain if, or in what way, an individual may perceive any effects. Therefore, in line with pragmatic inquiry (see overview of methodology section 2.3), exploiting the strength of an alternative method (such a qualitative research) to explore potential factors related to appetite in later life and their effects, may produce results which contextualise the quantitative findings and improve understanding overall. Knowledge of the older individual's perceptions of appetite, its loss and influences affecting this experience may begin to answer important questions, for example whether factors described in hospital and care homes (such as wellbeing and mood) are also seen in home dwelling older people. It may also provide accounts as to what promotes some individuals to continue to eat well in later life when others do not. This may improve understanding of the pathway of appetite loss resulting in weight loss and subsequent malnutrition, and so may be a key target in potential supportive interventions to mitigate or treat poor appetite.

5.2   Aims of study

The aim of this study was to interview a purposive sample of home-dwelling older people and use reflexive thematic analysis to explore concepts around each individual's experience of appetite and its loss.

The specific research questions were -

- How do a group of own-home dwelling older people describe and think about appetite?
- How are the participants' experiences and thoughts about appetite shaped by factors they described as influential on their appetite?
- How do the participants experience and cope with appetite loss?

5.3   Methods

5.3.1   Methodological approach to the study

This project was undertaken using qualitative methods, which utilised my understanding and interpretation of data to synthesise it and create understanding through construction of a narrative of the data. I chose this method to answer the research questions and address the aims of this study, as they require production of an in-depth understanding of subjective individual experiences and interpretations of a phenomenon (appetite) within a socio-cultural context [137]. The strength of this method is that it allows a rich exploration of other meanings, processes or relationships which are important in appetite but were not possible to explore in the quantitative analysis of the previous study (Chapter 4) nor were identified in the systematic review. It may also expand upon and explain the potential relationships of mood and physical activity with appetite seen in the previous study (see section 4.4.3).

The qualitative method of analysis I used was reflexive thematic analysis, established through work by Braun and Clarke as a flexible qualitative method. Many qualitative methods are steeped in a particular epistemological, ontological stance or theory, however reflexive thematic analysis is not and so can be considered foundational for researchers learning qualitative methods [232, 233]. Despite reflexive thematic analysis being atheoretical, it is important to have clarity regarding the methodological or philosophical approach taken to this qualitative study. As discussed in the methodology overview (see section 2.3), this thesis overall utilises pragmatic inquiry, which enables use of the most appropriate paradigm to structure the approach to meet the research aims and objectives. It is particularly pertinent to be explicit about the research perspective for qualitative research, as it can relate to different paradigms, compared to quantitative methods which clearly align with positivism (see methodology overview section 2.2). In addition, the specific paradigm I utilised for this qualitative study has informed the research questions posed, the design of the study and the way in which I approached the subsequent analysis to answer these questions. For this qualitative study I drew on the critical realist perspective.

5.3.1.1   Critical realism

The critical realist perspective originates from the work of Roy Bhaskar who proposed there is a world independent of human consciousness (the intransitive dimension) as well as one which includes our socially and culturally influenced knowledge about reality (the transitive dimension) [234]. Critical realism considers that reality consists of three main domains. First is the domain of the

'real', which is made up of structures and mechanisms; these mechanisms sometimes go on to produce an event in the domain of the 'actual'. If this event is experienced by an individual this occurs in the domain of the 'empirical' and the event becomes an 'empirical fact' [234]. Importantly, in critical realism there is a focus around these mechanisms, events and experiences, as critical realists consider that if we are to understand causality then there needs to be focus on mechanisms which produce events, not just the empirically observed events themselves.

I felt this philosophical approach was useful for the aims of this research project, as it allows for exploration of the individual's personal lived (or empirical) experiences that may be shaped by their socio-cultural contexts, which influence a person's knowledge about their reality, and so would cover influences on appetite in a wider context. I also considered that a focus on mechanisms around an individual's experience would give greater insight into potential causative actions of influences on appetite. This meant that participants were actively probed to promote dialogue around their reasoning for certain thoughts or actions and the contexts of these, to attempt to understand experiences, events and potential mechanisms. I considered language as capturing the participants' lived experiences of reality of the phenomenon of appetite, whilst acknowledging this reality was produced and existed within broader social and environmental contexts.

5.3.2   Study Setting and participants

Participants were recruited from a study evaluating the feasibility of screening methods to identify frailty and sarcopenia among older people with an arm fracture attending a fracture clinic (the Southampton Arm Fracture Frailty and Sarcopenia Study (SAFFSS) [235]. This was a convenience sample in that we had access to the participants due to the existing study; however we purposely sampled within the participants (discussed in the next paragraph). We selected these participants to sample from as older people with a wide range of physical health states and social support requirements can suffer with a broken arm, therefore we would be able to explore the views of a diverse set of individuals to meet the research aims and objectives.

Participants were own-home dwelling individuals and sustained the fracture several weeks before being approached, ensuring that the potential effects of care settings or acute illness were reduced. Purposive sampling methodology was utilised, which is designed to concentrate on individuals with specific characteristics to provide rich information relating to the research [236]. The selection criteria included both genders and those living alone or with others, as I felt that these two factors may have affected experiences and so were important to take into account. Sampling continued

alongside analysis of the interviews and ceased when I felt my account of the data was comprehensive.

Participants with both good and poor appetite, with no cognitive impairment and able to provide written consent were approached when completing data collection for the arm fracture study. I then telephoned to arrange a convenient time for a home visit to undertake a semi-structured interview; an information sheet was sent in the post prior to interview. I decided to undertake the interviews in the participants' own homes as this was the location of most of their eating behaviour- so close to the situation of my phenomenon of interest. I also felt it would mean the participants were at greater ease and so would increase dialogue. At the beginning of the home visit I explained the purpose of the interview again and answered any questions, written informed consent was then taken prior to the audio recorder being turned on.

5.3.3   Data collection

Semi-structured interviews were used to enable in-depth discussion of individuals' subjective experience, which would not have been achievable through focus groups or observation. Using a semi-structured, rather than unstructured format to the interviews meant I was able to use questions and prompts to ensure discussion around thoughts, actions and contexts with the aim of understanding mechanisms. Data were collected in the form of an audio recording of each semi-structured interview. Following a review of the literature and discussion with two supervisors I created an outline interview schedule (Figure 12), covering the topics of thoughts about appetite, its influences and any experiences of its change. Attention was paid to ensuring questions were open ended such as 'when I say the word appetite what does that mean to you?', and with consideration that topics covered would also be guided by participants, sometimes with prompting to elaborate on a concept or idea mentioned by participants which was relevant to the research question. The iterative approach to data collection and analysis meant that in later interviews, topics and further questions were added, to expand on interpretation of the data. For example, the topic of mood and its relationship to appetite was identified in earlier interviews with the female participants and so I prompted subsequent male interviewees about this in later interviews to determine if it was a pattern specific to women. The iterative approach to data collection and analysis meant that I stopped recruiting participants for interview when I felt that I had a comprehensive account interpreted from the data.

When I say appetite, what does that mean to you? Could you tell me about your appetite? How much thought do you give to your appetite? How do you feel about food?

Some scientists describe appetite as a combination of three things - hunger- the desire or motivation to eat, satiation- becoming full during eating, which causes a person to stop eating, satiety- the feeling of fullness after food. What are your thoughts about this way of describing it?

Could you describe your eating routine? (When? How many? Where?) Can you describe what you are thinking or feeling leading up to a meal? Has breaking your arm affected your mealtime routine? If yes, How?

How do you feel when you are hungry? What would you say makes you feel hungry (or interviewee's term for increased appetite)? What do these things make you think or feel?

Can you recall a time when you felt very hungry? Can you tell me about that? What were you thinking and feeling at the time?

What would you say makes your appetite worse (or reduces your hunger)? What do these things make you feel?

Can you recall a time when you felt your appetite was poor? Can you tell me about that? What were you thinking and feeling at the time?

Do you feel your appetite has changed as you've grown older? How? What do you think is causing this? (If discuss practical/environmental things then prompt for why and thinking around this)

Has your appetite changed after having a fracture? How? Why do you think this has happened?

Figure 12   Schedule for interviews with community dwelling older adults

The interviews lasted between 30 and 90 minutes depending on the participant. Strict safety protocols were in place to ensure my lone worker safety with pre and post contact messages with a member of the research group. For five individuals, their spouse, family member or friend were present during the interview. These accompanying people did not actively partake in the discussion, and often were not present in the room the whole time. On occasion the interviewees referred to the accompanying people to clarify points that they had themselves raised, for example amount of weight loss when present. The responses by the family members or friends were not directly used in the analysis, rather, I used any re-iterations or clarifications by the participant themselves, in their own words.

I transcribed verbatim the audio recordings of the interviews, anonymised them using a participant ID number, removed any identifiable information, and then uploaded the transcript onto the NViVo 10 software platform to facilitate analysis.

I utilised quantitative data on the demographics of participants recently collected via the arm fracture study questionnaire, including age and frailty (assessed by the FRAIL questionnaire [217] (See section 4.3.1.1 for details on FRAIL scale) to characterise the participants. Appetite had also been assessed using SNAQ (See section 4.3.1.2 for details on SNAQ) [134].

5.3.4   Data Analysis

I analysed the interview transcript data using thematic analysis methodology. This method encompasses the creation of themes, which can be defined as "patterns of shared meaning, organised around a core concept or idea". Importantly they capture the essence or meaning within the data and conceptualise it, going further than a superficial summary of what the individuals have said [237]. Themes are established from coding of the data; a code can be defined as a word or phrase symbolising an attribute in a portion of data, whether summative, salient or essence capturing [238].

According to Braun and Clarke, the umbrella term of thematic analysis can be divided into three schools, including coding reliability, codebook and reflexive thematic analysis [237]. In reflexive thematic analysis, themes are an analytic output of the researcher's subjective interpretation of the data, created in an iterative way to provide knowledge grounded in the data. In this approach the codes are not pre-determined or fixed but are open and created in an iterative way. Codes may be subsequently split or amalgamated as the researcher continues their analysis to conceptualise the data, as Braun and Clarke write "to move beyond the surface or obvious content of the data and to identify implicitly or unexpected unifying patterns of meaning" [237]. This is opposed to coding reliability where themes are pre-determined, perhaps testing a hypothesis, often guided by a codebook and applied by more than one researcher to the data. 'Reliable codes' are prioritised based on levels of agreement between coders (sometimes established with quantitative methods). Codebook thematic analysis, which includes framework analysis, sits between coding reliability and reflexive analysis where there is a structured approach to coding, a codebook is often utilised and some codes are pre-determined, however the underlying philosophy is more in line with reflexive analysis, without stringent coding reliability measures [237].

In this study I utilised reflexive thematic analysis with an interest in the participant's account of appetite and concepts that related to this. I felt that the reflexive approach to thematic analysis was

most appropriate to the aims of the study, as I had no real preconceptions or hypotheses to test in the data and so the results I would generate would be open and interpreted from the data itself. My specific approach to data analysis followed the method for reflexive thematic analysis outlined by Braun and Clarke and was inductive and data driven [232, 237]. This involved my initial familiarisation with the data by conducting the interviews, transcribing the full interview audio recording and reading the transcripts, followed by initial descriptive coding. This enabled me to have deep active engagement with the data, with use of memos following each stage (post-interview, post-transcription, post reading and during the coding process) to note initial thoughts and questions raised.

My initial coding focussed on semantic content (i.e. surface level meaning) of the topics of interest-that of appetite and its influences, then onto latent constructs to explain the account I had interpreted from the participant's descriptions. As allowed by the flexible method of reflexive thematic analysis, I coded some elements of the data more than once if they pertained to different concepts, and others not at all, as they were not relevant to the research question, for example one participant spoke at length about the travelling logistics of a recent holiday they had been on.

I commenced data analysis and coding from the first interview. These codes were expanded upon in subsequent transcripts in an iterative way, with development of new codes, amalgamation of some codes into a more salient code and splitting of other codes. I undertook this using NViVo node classification and post-it notes to visualise and re-organise the data. This coding process enabled me to interpret and identify patterns within the data and establish candidate themes. These candidate themes were refined by myself in discussion with two of my supervisors (with some discarded as they were not of value to the research question) and through further iterative analysis of the data and active engagement and reflection by myself, with the aid of memos and thematic maps to visualise the data. The candidate themes were refined further during a number of active discussions with one of my supervisors in which themes were agreed upon and clarified to ensure they had a distinct organising concept, worked alongside each other and that the patterning was across the dataset and did not represent one individual account. I also utilised writing the results as an opportunity to further refine understanding and interpretation [232], again with discussions with my supervisors.

Finally, to assist in understanding the influences on appetite and appetite loss I had interpreted from the data, I went on to determine if these could be mapped onto my framework of physiology, hedonism and external cues (see introduction section 1.3). I undertook this to determine if the individual's experiences aligned with the way influences on appetite are described in the literature

and my categorisation. Ordering the influences on appetite in older people by physiology, hedonism and external cues reflects my subjective viewpoint of the phenomenon. Whilst this is an acceptable approach considering, as Braun and Clarke state, "any researcher will approach the data with preconceived ideas based on their existing knowledge and viewpoints" [237], it is important to note that the initial themes presented in the results were created inductively from the data. I then went on to map these themes onto my framework, to see if the influences interpreted from the data aligned with it, however they remain grounded in the data.

5.3.4.1   Reflexive commentary

Integral to the method of reflexive thematic analysis was to use my interpretation of the data, to synthesise it and generate (or construct) an account or version of knowledge [237]. It is fundamental therefore to acknowledge my role within this construction. So throughout the planning, data collection and analysis of the study it was important to consider my role in this and the assumptions, habits and socio-cultural values that I inherently hold as this affected my approach to the whole project.

The fact that I inherently sit in a positivist research paradigm (see methodology overview section 2.2.1) due to my medical training was important to recognise when planning this project. After conducting an extensive literature review and quantitative analysis, I was sensitised to the subject but in a positivist way, so planned direct questions and deductive codes addressing a number of hypotheses about possible relationships with appetite. This approach did not align with the aims of this study and so I undertook reflection and further reading, which introduced me to the critical realist perspective in relation to qualitative methods, and promoted the realisation of the inherent positivist paradigm medical training places you in. This 'habit of positivism' has continued to be a consideration and awareness throughout my analysis of the qualitative data, particularly in latter stages when constructing the narrative. I made the conscious decision not to present myself as a clinical doctor to the participants who knew only that I was a researcher and completing a PhD. I felt this was important as I wanted participants to feel they could have open opinions about the subject and not be concerned that I would be making judgements on this aspect of their health, hoping to reduce potential for social desirability bias where they might respond in a way they thought would be considered favourably.

My active interest in the subject of appetite and ageing as the subject of my PhD but also in relation to my clinical work means that I find it extremely important. This has had an effect on my approach to the data, where I was sensitised to concepts and discuss how important appetite and its change

was to individuals. This was evident in a candidate theme of "importance of appetite", which on refining and discussion with my supervisors was subsequently judged to be not a standalone concept, so was removed and integrated with other themes.

I grew up and attended further education in the South of England, following this I have spent all of my postgraduate training working in the local region of Southampton. Reflecting on where I sit socially and how this may have affected my data collection and analysis, I feel this has enabled me to understand nuances in language, colloquialisms and underlying meanings by the participants who are all from the Southampton region. Many of the participants were also of a working class background, and as the first generation of my family to complete further education, I felt familiarity in these individual's descriptions of life and also their use of language, as they mirrored those of my parents and older relatives. This may have sensitised me to their accounts but I think overall this has not affected the analysis, as the themes generated from across the data did not include a pattern for socioeconomic background.

My age, and gender for some, differing from my participants I feel affected my interpretation of their accounts. Although I am from a similar cultural background I have not lived through to later life to have my own version of ageing and appetite. Whilst this may be a strength, as it will mean I have not polarised the data with my own experience, it may also mean that I have less empathy with the accounts to fully understand them, and this may have most impact upon male accounts. I feel I overcame this with my prolonged engagement with the data such that the themes generated are grounded in the data.

5.3.5   Data quality

I took a number of measures to ensure the quality of the qualitative research data. These are underpinned by work from Yardley [239], who outlines the importance of sensitivity to context, commitment and rigour, transparency and coherence, and impact and importance [239], as well as reflections by Braun and Clarke specific to the reflexive thematic analysis method [240, 241].

Firstly with regard to sensitivity to context, the research aim and theoretical approach were compatible with my method (reflexive thematic analysis) and I had an awareness of the literature and previous work on the subject of appetite. As demonstrated in the reflexive commentary, my assumptions and views and how these might have impacted on the research were reflected upon during study planning, data collection and analysis and probed in regular debrief discussions with my supervisors. My characteristics as the researcher were also taken into consideration, with a decision to interview the participants in their own home to reduce any prospect of power-play. I also

approached the interview as a research fellow rather than health professional, which may have impacted on participant responses.

With regard to commitment, I had prolonged and active immersion in the data from the beginning of the data collection, through to writing of this thesis. Analysis involved thick description and movement from semantic to latent coding. Rigour was demonstrated through active engagement with the data, which was complemented by regular supervisory meetings to debrief, refine themes and reflect on potential assumptions. Data saturation is also referenced by others as a method to demonstrate rigour, however it is the subject of much debate [239], and is a term Braun and Clarke state is "perhaps best avoided" for reflexive thematic analysis [240]. This is largely because data saturation aligns more with the positivist paradigm for research- that there is a material truth out there that exists and can be sought and measured. Therefore, qualitative data becomes 'saturated' when there is 'information redundancy' i.e. there are no new parts or concepts relating to that 'truth' coming from the data. This is problematic for reflexive thematic analysis, which relies on my interpretation of the data to generate meaning, rather than a 'truth' already existing in the data. Therefore, depending on who and how the data are interpreted, additional and different meanings can be generated. Thus, instead of thinking about data saturation, it is perhaps more useful to state that the number of individuals I interviewed provided rich enough data to enable me to generate a comprehensive narrative, which could be considered as reaching 'theoretical sufficiency' [240].

Transparency within the study is demonstrated by my outlining the details of the methodological approach of a critical realist perspective, and my procedure of reflexive thematic analysis used with reflexive commentary. In addition, an audit trail is show in Appendix B as an example to demonstrate the inductive coding, sub theme and overarching theme of 'appetite reflects a physical need. Coherence of the data refers to whether the version of the phenomenon or reality is meaningful [239]. To test this, I discussed the narrative with public lay members (both older women living alone), who were able to engage with the account and also relate it to their own experience of appetite and it's change. I also discussed the findings with another researcher (separate to my own group) undertaking qualitative research in the field of older adults' nutrition, who fed back that the account chimed with findings within their own research.

Lastly, Yardley refers to impact and importance of qualitative research as a marker of its quality, referring to the ability of the work to provide a novel perspective or new understanding of a topic, including deeper explanation of effects observed in quantitative analyses [239]. Braun and Clarke also refer to the reported themes having the potential for "actionable outcomes" [241]. This aspect

of quality for this study is addressed as far as possible in the discussion and has undergone peer review for publication but is ultimately open to further review from others.

5.3.6   Ethical Considerations

This qualitative study was part of the Southampton Arm Fracture Frailty and Sarcopenia Study [235]. Ethical approval was granted by the health research authority North East- Newcastle and Tyneside 1 Research Ethics Committee 18/NE/0377 (see Appendix C).

5.4   Results

5.4.1   Demographics of the participants

I completed interviews with 13 individuals (5 men) with an age range of 69 to 83 years (Table 10). There were five individuals living alone, one of whom was a single man; all of the women living alone were widowed. Two participants (one man) were living with frailty according to the FRAIL questionnaire (score of 3 or more points).

According to the SNAQ questionnaire four individuals reported a poor appetite (score less than 14), however during the interviews it became apparent that some individuals with higher SNAQ scores were experiencing a current poor appetite. Individuals who expressed their current appetite was good reflected on instances when it was poor and their experience of this, and those with a poor appetite similarly reflected on times when it had been good. Therefore, data from all the individuals were used to understand experience, rather than a separation of those with 'good' or 'poor' appetite.

Table 10   Demographic details of interviewees- listed in chronological order of interview

Participant	Gender	Age	Living circumstance	Frailty (FRAIL)	Appetite (SNAQ)
01_M	Male	75	Living with spouse	1/ pre-frail	14
02_F	Female	72	Living with family	4/ frail	12
03_F	Female	71	Living alone- widow	0/ robust	18
04_F	Female	83	Living with family	0/robust	17
05_M	Male	71	Living with spouse	3/frail	17
06_M	Male	73	Living with spouse	0/robust	14
07_F	Female	77	Living alone- widow	0/robust	16
08_M	Male	78	Living alone- single	0/robust	14
09_M	Male	73	Living with spouse	1/pre-frail	16
10_F	Female	76	Living alone-widow	0/robust	16
11_F	Female	69	Living with spouse	1/pre-frail	12
12_F	Female	71	Living with spouse	2/pre-frail	13
13_F	Female	83	Living alone-widow	0/robust	13

5.4.2   Overview of main themes from the data

The data analysis produced three main themes with associated subthemes (three, one and two subthemes respectively). The main themes are 'appetite is an emotional experience', 'appetite reflects a physical need' and 'adaption to poor appetite aligns with perceptions of appetite and wider physical health'. The first two themes explore two narratives of appetite, its change or loss and perceived influences on this, interpreted from the data. Individuals tended towards coherently using one or other of the two narratives when talking about their appetite and appetite loss. However, some individuals drew on both narratives throughout their discussion and reflections, while others used each of them to describe different aspects of appetite (e.g. drawing on one

narrative to explain what they considered appetite to be, then changing to the other narrative to describe their experience of appetite loss). The third theme gives an account of adaptive behaviours to poor appetite and their relationship with the narratives of appetite loss but also the impact of wider perceptions of physical health.

5.4.3   Theme 1: Appetite is an emotional experience

In this narrative, appetite sits in the context of experience and thought. There is a build-up of thoughts and feelings about food in a positive way (pleasure and anticipation) prior to a meal, or sometimes expressed as continuous, driving desire to eat. For example, one lady with a current poor appetite recalled how appetite for her was related to fancying food.

> *"What I would like to have. Oh, my appetite is, oh I fancy that. That's appetite to me...*
> *Fancying for me, and appetite is way before I get hungry. Yeah, way before, I think to myself*
> *do you know what, 'cause we say oh what we fancy for tea tonight."* 02_F

Hunger in this narrative was a positive feeling encompassing pleasure and reward, relating to looking forward to food. Participants used words such as "nice" and "cosy" to describe feelings of hunger. But individuals also referred to a need to control this feeling and not let it get to far, as it then would turn into a drive towards what they considered to be unhealthy ways of eating.

> *"I think the danger of waiting until you really are hungry is when you eat the wrong things.*
> *Because you want to put that in there quickly other than wait for it to cook."* 03_F

The resulting fullness was then considered related to greed and overindulgence in a food, of going too far because of enjoying the experience, then linked to regret.

> *"…Somebody just being greedy and eating too much and then I'm full up, I can't finish eating it*
> *[laughs], I don't know… I've eaten too much and I wished I hadn't, and we all do that don't*
> *we?"* 03_F

Appetite loss was described as the struggle to initiate eating due to negative thoughts and feelings about food, including its sight, smell or taste. Individuals referred to their feelings about consumption of food having changed and a lack of pleasure in these thoughts and feelings.

> *"I cannot look at them now, I can't stand the smell of them… I cannot eat them."* 12_F

Negative thoughts and feelings around food occurred for some individuals even if they had taken the trouble to prepare a meal. For example, one individual with poor current appetite described that

although she knew she needed to eat, her negative feelings and dislike of food built up when preparing a meal stopping her from eating. So although she would initiate the task of preparing meals, she would not eat them. She described this in an interesting way, explaining that thoughts are not always mirrored by behaviour.

> *"I wish I hadn't started doing this, 'cause I don't' want it and I don't know why I'm doing it because I don't even like it, you know and by the time I've finished it's quite easy to throw it in the bin. [So what makes you prepare the food anyway?] Because you feel you should eat don't you?* ***... But the way you think is not always the way you can act is it?*** *So I, so sometimes I prepare a meal and I don't eat it."* 04_F

Whilst for other individuals, these negative feelings towards food fostered a general lack of interest in food and cooking, alongside descriptions of overall lack of interest in life activities.

> *"I think maybe the times I can't think of what to have to eat, and it's not because there's nothing out there, its um, I dunno just the motivation, I can't be bothered sort of going out there to cook. But as I say it's a difficult one I'm afraid."* 03_F

> *"I now think to myself its pointless cooking it, if I'm not going to eat it."* 02_F

5.4.3.1 Mood impacts appetite and has a relationship with food

Mood and wellbeing were important in the emotional experience of appetite. Typically females expressed opinions about a range of mood states, while men tended to link with a clinical diagnosis of depression or stress. Negative emotions were largely inhibitory to appetite, related to loss of the desire to eat or enjoyment of food they were eating and included descriptions of stress, feeling low, anger and anxiety.

> *"I mean that spell we were just talking about ['feeling very low'] I didn't really want food. I made myself eat something but I wasn't enjoying it. I was just thinking, I've got to, I've got to have something."* 13_F

A noteworthy point regarding low mood amongst individuals was that none were currently suffering from a clinical diagnosis of depression and when directly asked, people described themselves as happy. Despite this, fluctuations in mood were still described as an important influence on appetite but perhaps this reflects an overall sense of emotional wellbeing.

> *"I would say I was a happy person, I know I say I cry every day, that's a different matter, I am a happy person."* 03_F

"You worry about that, um and then you sort of paper over the crack and it sort of starts to crack a bit but we're all cool we're all ok." 02_F

The idea of comfort eating when upset was apparent amongst individuals, and for some there was a complex two-way relationship between mood and eating, where mood state affected the experience of appetite and food choice, and then the consumption of certain foods changed mood state. The most common instance of this was the consumption of liked food lifting the individual's mood in a positive way, but sometimes the reverse would happen with a lowering of mood.

"I can sit here nearly every day and for something just in there [points to head], something we've done, or something like that and I can cry. And I can then go and eat non-stop or maybe that's when I think oh I can't be bothered cooking anything you know...I think it's our mood swings that we eat with, or it's the eating that causes the mood swings" 03_F

"Having something that you fancy and it's lovely, it's a nice feeling. You fancy it and its good, fantastic." 12_F

5.4.3.2   The appeal of food is key to appetite

The appeal of food encompassed sensory appeal, such as presentation of the food, smell and taste, as well as thinking about food individuals liked all impacted upon appetite, aiding the build-up of a desire to eat. If food did not meet expectations or was disliked, the desire to eat was reduced due to negative thoughts and feelings.

"So when [daughter] is in there cooking I think mmm that smells nice, yeah that smells nice." 02_F

"Um, anti-climax I suppose. Oh its dinner time [rubs hands together], especially if you're in hospital, there's nothing else happening, look at the clock, the dinner trolleys coming and it arrives and you look at it, [raises up hands and blows out cheeks], I was expecting something nice and it's not." 03_F

The effects of illness and treatment also impacted upon the appeal of food through altered taste or where individuals described a lack of being in touch with their reality.

"I think they stopped my appetite yeah, maybe your senses a deadened down, because you're a bit out with the fairies maybe you're not so aware that your, I don't know but certainly I lost a lot of weight." 01_M

> *"I had influenza, the real thing... Erm, I had no appetite at all. I think I went down below ten stone then. It was about oh six, eight weeks to get on top of it. I couldn't eat, [husband] was making me meals… one meal he brought in I said [husband] it's full of salt, there's loads and loads of salt in there, he said no there's not, all I could taste was salt. It was the salt taste in that meal, made a lovely roast dinner, I couldn't, bleugh, I couldn't eat it."* 12_F

Certain appealing foods were often framed as 'naughty' when construed through typical public health messaging and so were eaten at the expense of 'health'. Consequently, individuals also downplayed negative thoughts about being overweight from unhealthy food choices, which they considered out of their control or too challenging to overcome, as these unhealthy but appealing foods were key to appetite.

> *"If I had a choice of food right now it would be a great big jammy donut or a lovely scone full of cream. You see I don't go for the things I should be going for!"* 04_F

5.4.3.3 Other people affect appetite through social interaction and life events

The role of pleasant social interactions with people, in the context of eating in a sociable way, was an important part of the build-up of a desire to eat. For some, this social interaction included the activity of cooking, which alongside a sense of accomplishment, produced pleasure and reward increasing desire to eat the food prepared. For these individuals, losing the ability to cook added to negative thoughts and feelings about food and lack of desire to eat. However, for others, the activity of cooking was not a pleasurable social experience, rather more a routine and so detached from appetite. For them, poor appetite due to negative thoughts and feelings about food and eating did not include any change in their cooking or meal preparation abilities.

> *"I've always cooked. Yes, always cooked, yes. The children cook and the grandchildren have always cooked with me as well, so that's great. Good fun, yes."* 10_F

> *"Well it's just, yeah I think before I broke me arm I used to do say 80% of the cooking, so I would prepare, I would get it ready ask the wife what she wanted, yeah give me something to do. But now I just [blows out cheeks]."* 05_M

When a participant's appetite was poor, people close to them (most often a spouse), would react by stating they had noticed a change or try to encourage eating. Sometimes these interactions fostered feelings of stress and guilt for the participant, as they felt unable to live up to a social pressure and expectation (often well-meaning) to eat a meal, with further escalation of negative feelings.

> *"I feel awful, but that, I don't, I feel a bit you know they stood out there all that time cooking and that you know."* 02_F

The loss of important people, whether through bereavement or geography, was clearly described by some, frequently via impacts on mood driving negative thoughts and feelings. However, amongst some individuals there was a sense of carrying on, being motivated when coping with loss, which most commonly coincided with reports of a good current level of appetite.

> *"'Cos if she was here she'd be saying you sit in this chair or you're coming down for a meal, you know. But I think that sort of kind of, kind of impacted a little bit but she's done the right thing [moving away]…"* 02_F

> *"It's not the same as being, having my husband here. But on the other hand you've got to make the most of it because I've got friends who've lost their husbands… but they are oh like this I can't carry on and I think oh for goodness sake you know and they've got family round them but it's what, you, you want to be strong yourself don't you?"* 13_F

Importantly, some individuals also did not see bereavement as negatively influential on appetite. This was in the context of having been a carer for the other person, or the other person having a more restrictive diet. They described a release to be able to suit themselves, with no worry about the other person.

> *"Now it's just me and so I can sort of please myself, if it's a roast or of it's a salad or if it's just a soup or something like that I haven't got to worry about the other person, yeah so that's all right yeah."* 03_F

> *"I'd gone from six years or whatever it was looking after XXX, the best meal, when I got a carer in once a week, I could go and nip out and I'd usually go up the XXX and have a carvery so at least I'd eaten properly one day, but then because it all changed because XXX is a good cook actually…"* 01_M

As an older age group, the participants discussed a wealth of different life experiences. This ranged from childhood experiences of eating and how their parents managed food, through working life and having young families themselves, to then further changes as they moved into retirement. Almost all individuals made some reference to the past, however, most of these life events and experiences appeared to affect the individual's eating habits, routines and food choice, rather than their perceptions of appetite.

This was a sense among some individuals of being motivated, resilient, keeping busy and coping with difficult times now they were in their later life and perhaps living alone. This mirrors findings on discussing coping with the loss of important people. These individuals were again almost exclusively those who reported that their current level of appetite was good.

> *"When you get low as well, you your days you're low. But erm you do, you've got to carry on, there's no, you don't want to be feeling sorry for yourself, you've gotta carry on and do things."* 13_F

5.4.4   Theme 2: Appetite reflects a physical need

This viewpoint regarded appetite as a way of meeting bodily requirements with physical descriptions of bodily need. Participants described planned practical ways of meeting this need, with an importance placed upon maintaining physical health.

The bodily sensations of hunger, such as a rumbling stomach, were described without emotion linked to them, whereas the sensation of feeling full was considered unpleasant. However, through proper planning of meal timing and size, often hunger was not felt and the occurrence of feeling full avoided. Individuals described appetite as a vehicle to consuming food in a practical sense, with no apparent build-up of thoughts and feelings towards food. Instead thought was given to practicalities around food preparation and fitting eating into schedules, pre-planned recipes and physical health needs.

> *"How much you eat a day, actually going into your body yeah, yeah…I've got to know that all those ones I have are good for me and I stick to those, um I don't venture out into other things, I don't know whether they're good or have got too much salt or sugar, so I need to know what I'm having is keeping in with the diabetes."* 08_M

> *"Appetite, it means wanting to eat… it's you know, a bodily function."* 10_F

Individuals described hunger as an "empty feeling" or "feeling cold", or that they did not feel it at all as they have a specific eating routine. Some also talked about how having health problems (such as diabetes and gallbladder removal) which would mean they could not miss meals, so for them hunger was rarely felt.

> *"I get tired and cold when I get hungry. I, my husband used to laugh because I'd say oh I'm tired and cold and he'd say no you're hungry, so I'd tend not always to recognise it."* 07_F

> *"Erm, I wouldn't go without a meal no, no. I have a hiatus hernia and erm I don't' have a*

> *gallbladder and so, because I had my gallbladder removed, because I had a stone, and so if, if I don't eat then that sort of becomes perhaps a bit uncomfortable."* 10_F

The feeling of fullness also has a practical identity in this narrative, individuals described it as either not felt due to proper planning of meal size or as a vehicle acting to stop eating.

> *"[Do you feel full after your meals?] "No not now no, I say, I know what I'm eating."* 08_M

> *"So when you get half way through your dinner and you've had enough stop, if you feel you've had enough, stop.*" 09_M

Appetite loss was described as a continued ability to initiate eating, with no negative thoughts about food itself, but a reduced capacity with fullness either following a small amount of food or constantly. Often individuals did not finish their meal, and some reasoned their fullness was from their "stomach shrinking". This feeling of fullness would then impact on how they prepared their next meal, often with reduced portions.

> *"I don't I don't eat as much, as we said, and I think that [spouse] has really hit it on the head in that the stomach shrinks doesn't it."* 01_M

> *"I got full much quicker than normal I think that is probably the best way to describe it. I just felt that I didn't want to eat as much as I normally would eat. So I was still eating at the same times, but you know, not as much."* 07_F

5.4.4.1 Appetite declines with age, illness and less activity

Within the reflections of bodily need, the effects of a physical state of ageing were considered detrimental with an expectation of appetite decline as individuals grew older. They were unable to fully quantify why they felt this was happening but it was drawn from experience or witnessing others, it did not appear to be related to social needs or requirements but rather a sense that the body required less.

> *"I find since your older you don't need as much to eat, you don't need it."* 12_F

Being physically active was important, where general declining levels of physical activity and using less energy were reported as reasons for poor appetite. In addition, improvements in activity level were seen as an avenue to "*build it [appetite] up*"

> *"You need to do a lot of exercise, you need to do work, as long as you're doing work. I did my own garden, so I, you build an appetite, you know. You don't eat between meals and you*

think cor we're hungry, enjoy whatever we had. But you don't do it, you don't do the exercise, you don't do the work, you know, you don't work up an appetite do you?" 12_F

"When my life gets back to being a bit more stable, a bit more energetic, then I'll have to start eating." 05_M

Physical illness, symptoms and treatment were also important, relating to activity and physical ability, including pain and the practicalities of eating and in food preparation.

"Say I was ill and didn't eat for three days… but it's rare, rare that that happens that I can't eat for three or four days, very rare I think it's I've got to be in bed and immobile not to eat." 08_M

Due to the nature of this study many views were expressed which related to the recent arm fracture participants had sustained. For a proportion of individuals, the event was seen as the cause for their appetite loss and was described as transient by some whereas others had not recovered. Many of these individuals utilised the physical narrative for appetite change, with reference to feeling full.

"I got full much quicker than normal I think that is probably the best way to describe it. I just felt that I didn't want to eat as much as I normally would eat. So I was still eating at the same times, but you know, not as much." 07_F

However, appetite change following arm fracture was not the case for all interviewees, with some describing appetite loss prior to the event. These individuals often described this appetite loss building up over time, but also that the arm fracture exacerbated it or heightened awareness of the problem.

"All of a sudden it was there and then you look back and it has been a very slow gradual… No I think this has been coming on slowly and for a long time. [The arm fracture] opened Pandora's Box, yeah it did, yeah." 02_F

Medical treatments for acute and long term conditions were described as affecting both the experience of appetite, where individuals described a lack of being in touch with their reality, and also in physical terms with acknowledgement that some drugs were bodily inhibitors of appetite.

"I think they stopped my appetite yeah, maybe your senses a deadened down, because you're a bit out with the fairies maybe you're not so aware that your, I don't know but certainly I lost a lot of weight." 01_M

> *"I think the drugs I was on, didn't help because they're, they are inhibitors for food, they warn you that. Um, basically I've just got no appetite."* 05_M

5.4.5   Theme 3: Adaption to poor appetite aligns with perceptions of appetite and wider physical health.

Individuals described adaptations to their eating behaviour in response to poor appetite, either as current actions or from memory. Three main adaptive behaviours were described- seeking out appealing food, eating and then preparing smaller meals or concealing the truth. The first two of these adaptive behaviours were closely linked to the two narratives of appetite, while the third, concealing the truth, also related to how appetite loss was prioritised by the individual and people close to them, which linked to perceptions of physical health.

5.4.5.1   Perceptions of appetite influence adaptive behaviour to poor appetite

When discussing appetite loss as a struggle to initiate eating due to negative thoughts and feelings about food, individuals would then most often describe seeking out food they found appealing. These foods were often considered as "*treats*" to "*tempt*" themselves and reignite their appetite.

> *"I might just go and have some cheese and biscuits instead of a cooked meal. But that's all I feel like eating."* 02_F

When appetite reflected a bodily need, individuals described reducing their portion size to combat appetite loss due to over or early fullness, initially eating and subsequently preparing less. In addition, priority in maintaining physical health drove decisions on food choice, often with reference to public health messaging or individual advice for chronic health conditions. This meant snacking or "treats" were held in a negative light and individuals with early or over fullness made no change to the type of foods they sought out.

> *"I was probably sort of dishing up what I normally eat and then thinking oh I don't want that and giving it to the foxes you know and then the next day perhaps putting a little bit less on the plate."* 07_F

In the main, there was consistency in how individuals expressed their appetite loss and then their adaption strategies to this. However, within the study one case used the narratives of appetite in a different way to others. She described her appetite loss as negative feelings towards food and eating, but then appetite overall as reflecting a physical need with snacking as "not good for you". Consequently, she attempted to eat the same food but with reduced portion size to manage her

appetite loss but still struggled to eat because the food was not appealing. This woman used the physical narrative of appetite in terms of perceptions and adaptations, but had an extra layer related to appeal of food, showing that for people like her, reducing portion size might not be enough to combat poor appetite.

> *"Just eating I suppose, just eating. Making sure that you eat something …I can't say I get full, no. I can't say I get full. But as I say I never feel hungry. So, I, I would be happy if I could be like a horse and graze all day long. You know picking at stuff, but you can't do that really, it's not good for you I don't think….I can't stand the smell of food cooking. It puts me right off, especially meat…You know I only put a tiny portion on my plate and sometimes I put that in my mouth and I, I get rid of it because I can't eat it…. I'll cook [spouse] a roast dinner and I'll try it, I'll have some on my plate and I'll try it, but I usually throw up afterwards …Well I think I might have changed, you know it might have changed, I'm hoping it might change but I don't expect it will now."* 11_F

5.4.5.2 Views on weight and other priorities can drive concern about appetite loss and adaption to poor appetite

All of the participants regardless of their use of appetite narrative saw being overweight in a negative light and often, a background of being overweight meant unintentional weight loss due to poor appetite was regarded positively. Consequently, individuals focussed on practical, often humorous aspects, making light of the situation and appeared largely unconcerned. There were several factors related to this lack of concern such as perceived control, lack of thought and prioritisation of appetite and a view that poor appetite produced a desirable health outcome- to be able to achieve a previous weight or a weight felt appropriate.

A sense of control over weight loss, even when unintentional, appeared to lead to a lack of worry. These feelings of control were often related to having lost weight intentionally in the past.

> *"My appetite wasn't great before, you know err, I did try to start losing some weight but it started coming off, so I didn't bother anymore [laughs], right do it on your own [laughs]."* 11_F

> *"[Do you think that you would have become worried about it?] I might have don't if I'd lost more weight than I wanted to lose, certainly. But I would have been quite happy if it had stayed away for a bit because I, I could have got back to the weight I should be."* 07_F

Interestingly for one individual (who was not overweight) her initial positive reaction to weight loss stimulated further reflection that weight loss was a negative thing for her health.

> *"[How did you feel about losing that weight?] Well I thought it was good! Yeah I thought it was good but then you see you're not toning, you're just losing and then that's flesh isn't it?"* 13_F

Another common reason reported by individuals rendering appetite loss less important was the lack of thought they gave to it. They talked about other priorities which they invested time and thought on instead and poor appetite was expected to be transient and not to be dwelt upon. Also, for one individual it was her spirituality and readiness for death, in her view considering her age, which made appetite a low priority.

> *"Don't worry me, not to say I, it's, it's just a passing thing that's all. It's just another thing in a long list of them…I just haven't got one, you know I don't walk around thinking oh food, I've gotta, I should, oh food, you know. Just don't think about it that's it."* 05_M

> *"Nothing matters now I am this age. 'cos you're just an old biddy and then you'll go. I don't mind, I don't mind when I'll go, I'll go tomorrow if I could but I can't. I couldn't do anything to myself that would be against my belief, I wouldn't even dream of it. So please don't think that… I would not do anything to myself at all. But if somebody said it's going to happen tomorrow or the next day, I'd say oh good let's get on with it then. Simply because I know where I'm going, my faith is so real to me."* 04_F

Of those with a current poor appetite, only one appeared to find it important and concerning. This individual talked about a feeling of powerlessness over her health and a struggle to understand why her appetite had changed, which appeared to heighten its importance.

> *"It's a lot and I read in there [gestures to medical record] why didn't anyone tell me about those, how did I not know?" "[Does it worry you? [Poor appetite]] It does because I don't know what it is and why, um, I should be able to sit down and eat the things that are there"* 02_F

For some individuals, who considered their poor appetite due to negative thoughts and feelings unimportant, difficult interactions with concerned family or friends led them to downplay or conceal their poor appetite. This was starkest for one woman, who described her poor appetite due to negative thoughts and feelings about food as a low priority; she also viewed her weight loss positively. This view was at odds to concerned family and friends, which led her to conceal uneaten

food in an attempt to hide the truth, as she considered that this would lessen the negative interactions and effects on others that her poor appetite had created.

> *"I think I'll get rid of that quick before [daughter] comes in so she won't know I've not had it. I've got to be honest that's what I would do at home and here I would just throw it away because [friend with dementia] ain't got a clue what I'm eating and what I'm not eating. And I lie and say I've had it... Because I know she'd be cross, well she'd be upset that I wasn't eating three meals a day and then she'd start to worry and I can't cope with her worrying."* 04_F

5.5   Discussion

The experiences described by individuals in this study give rich accounts of how these older people view appetite, its loss and their adaptations to this, with factors important in this experience. There were three main themes in the data, the first two were narratives regarding appetite, its loss and influences on this, the third theme discussed adaptions to a poor appetite and how these related to the narrative of appetite loss and wider perceptions of physical health.

5.5.1   Descriptions and thoughts about appetite

The first two themes interpreted from the data comprised of narratives the participants used to describe appetite. "Appetite is an emotional experience" encompassed pleasant thoughts and feelings building a desire to eat, such as anticipation and excitement. Loss of appetite in this narrative was negative thoughts and feelings about food and a struggle to initiate eating. The narrative of "Appetite reflects a physical need," described bodily sensations of hunger and satiety with loss of appetite attributed to a feeling of over or early fullness. Individuals tended towards coherently using one or other of the two narratives when talking about their appetite and appetite loss. However, some individuals drew on both narratives throughout, while others used one narrative to describe appetite and then the other for appetite loss. These narratives have not been described before in the current literature relating to appetite in older people. This may reflect that many prior qualitative studies have not had appetite itself as the focus of enquiry but rather subjects such as food choice, eating behaviour and undernutrition [117, 120, 182]. The two narratives do align with the concept of appetite as a psychobiological process [17] (see introduction section 1.2) but expand on this concept by demonstrating that individuals may tend to align their perceptions of appetite with one or other aspect (i.e. psychological or biological). This further insight is important for shaping management strategies for appetite change in later life as it highlights the need for

individualised approaches.

5.5.2   Factors influential on appetite and how these shaped perceptions of appetite

A wide range of influences on appetite and appetite loss were interpreted from the qualitative analysis and had distinct relationships with the two narratives of appetite loss. The influences described by participants include appeal of food, mood or wellbeing, other people, a physical state of ageing, using energy and being active and the effects of physical symptoms, illness and treatment. Mood states and the appeal of food, as well as the effects of social interaction, experiences and presence of other people linked with the narrative of appetite as an emotional experience, while a physical state of ageing, and using energy and being active were important in appetite reflecting a physical need.

I subsequently mapped these influences onto the framework of physiology, hedonism and external cues, and they were cohesive (Figure 13). The qualitative analysis has given further insight into these categories of influence, pointing to reciprocal effects of external cues and hedonic influences on one another which feed into the relationship with appetite. In this analysis the effects of hedonism and external cues relate to the emotional experience of appetite, whilst physiological influences (other than symptoms, illness and treatment) feed into appetite reflecting a physical need. The presence of physical symptoms, illness and treatment was a negative force for both emotional experience and physical need. This is likely to reflect the important physical as well as psychological impacts that states of illness have.
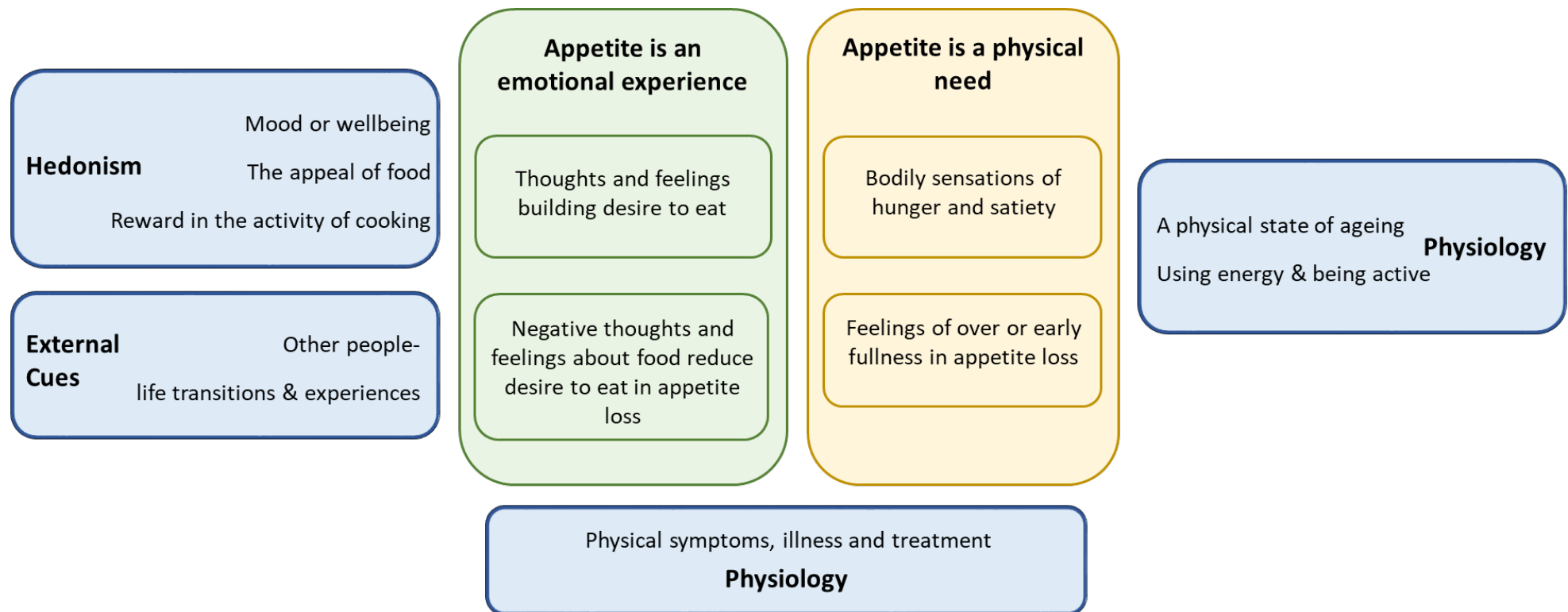
Figure 13   Influences on appetite interpreted from the qualitative data within the framework of physiology, hedonism and external cues.

The influences are depicted in blue alongside the narrative of appetite they relate to in the qualitative data.

Regarding the influences on appetite described in our study, a recent scoping review by Perrotta et al investigating older adult's opinions about their nutritional needs and malnutrition risk addressed themes relating to poor appetite as a consequence of ageing and reduced physical activity [242]. However, another recent systematic review by Clegg et al identified a lack of evidence around the relationship between level of physical activity and appetite in older individuals due to a paucity of robust research studies [96], so further investigation is required. Psychological influences on appetite in older people, including the role of health beliefs and awareness that appetite change is not necessarily normal or healthy, are under-explored. The clinical construct of depression and anxiety are observed to associate with appetite in community dwelling older adults [6, 7, 9, 113, 122, 123], however mood as a wider construct (encompassing both positive and negative affect) and wellbeing require further appraisal. Otherwise, much focus has been on identifying social factors associated with appetite, such as reduced social contact, poor communication with family [6], bereavement and eating alone [122]. Interestingly, when looking at social factors in our study, including people and life experiences and transitions, descriptions were more often about their effects on eating habits and food choice, rather than appetite. This finding is in line with previous qualitative research concerning factors affecting diet quality in older adults [243]. However, from our analysis, it appears that perceived motivation and ability to cope with any change in these external factors may be influential on appetite. Engel et al have identified that hardiness (encompassing the constructs of commitment, control and challenge) correlates with appetite in community dwelling older people [113]. This may align with our findings; however, motivational states and perceived ability to cope are under-researched in the context of appetite despite their potential importance in maintaining resilience to social and environmental change and thus sustained appetite. A movement towards maintaining resilience as a focus of enquiry, rather than the actual social or environmental changes, may therefore prove more fruitful in understanding potential supportive strategies for managing poor appetite in particular.

5.5.3   Coping with appetite loss

The experience of appetite loss in the two narratives appears to foster different adaptive behaviour to poor appetite, whether seeking out appealing food to attempt to re-ignite a desire to eat or reducing the size of meals eaten and then subsequently prepared to mitigate early or over fullness. Alongside this was the impact of wider physical health perceptions in driving food choice or positive feelings about unplanned weight loss as well as other priorities the individuals had relating to their health and life. Positivity about unplanned weight loss linked to an apparent unimportance of appetite loss for some individuals, which seems to impact on engagement with adaptive behaviour

alongside other health or life priorities. In the extreme this may promote concealing the truth from others who show concern. The lack of worry about poor appetite and unintentional weight loss in this group is contrary to a recent qualitative study in community dwelling older adults in the same region of the UK, where individuals had negative thoughts and a sense of resignation and inevitability about poor appetite and weight change [244]. However, in the study by Payne et al, participants were at nutritional risk, so perhaps had more advanced nutritional decline than our participants. Thus, it may be that older individuals initially have little concern over earlier stages of appetite loss, which then develops into resignation as their nutritional health deteriorates. This suggestion is supported by findings from Holst et al in hospitalised older people in Denmark [118], where individuals initially paid little attention to weight and appetite, which progressed to consideration that something was seriously physically wrong. Additionally, amongst interviews of community dwelling older individuals in New Zealand, Chatindiara et al [245] identified thoughts of eating less being the 'logical thing to do' due to reduced physical function with ageing, again suggesting a narrative of resignation rather than concern. This shows the need of robust health messaging to highlight that loss of appetite is not a normal part of ageing and so older people and those involved with their health and care should react early in response to its presence, as continued decline in health is not inevitable and is potentially reversible.

5.5.4 Relationships between influences on appetite, perceptions and adaptive behaviour to poor appetite

My analysis and interpretation of descriptions by the older individuals in this study has generated theoretical relationships between perceptions of appetite by older individuals, influential factors, and adaptions to a poor appetite centred on the two narratives (Figure 14). These hypothetical relationships can be brought together to explore how certain influential factors can be categorised into those of physiology, hedonism and external cues and how they relate to the different narratives of appetite loss, with some factors also having reciprocal effects on each other, or mediated by perceived ability to cope. In turn, the different experiences of appetite loss in each narrative foster distinct adaptive behaviours for poor appetite, alongside the impact of wider perceptions of physical health. These hypothetical relationships require testing in further studies, such as a deeper exploration focussed on adaptive behaviours to poor appetite in later life, to promote understanding and potentially generate a substantive theory for this. However, these findings also may help explain the paucity of evidence on effective interventions for appetite loss in older individuals ([96, 140], chapter 3 section 3.3.2) as they indicate that with distinct narratives of appetite loss, and individuality in the way some people use the narratives, single interventions for a population are

unlikely to be successful for everyone. Rather, person-centred, multi-component approaches with an understanding of the individual's view on appetite and their priorities around their physical health are likely to be more relevant and effective.

The qualitative analysis has also raised some potential limitations for current quantitative assessment methods for appetite in older people (see chapter 3 section 3.2.2), as these methods do not distinguish 'in what way' the individual has lost their appetite. Determining a way to distinguish this through quantitative means is important if, as this study indicates, different narratives of appetite loss have distinct relationships to influential factors and potentially foster different adaptive behaviours for poor appetite.
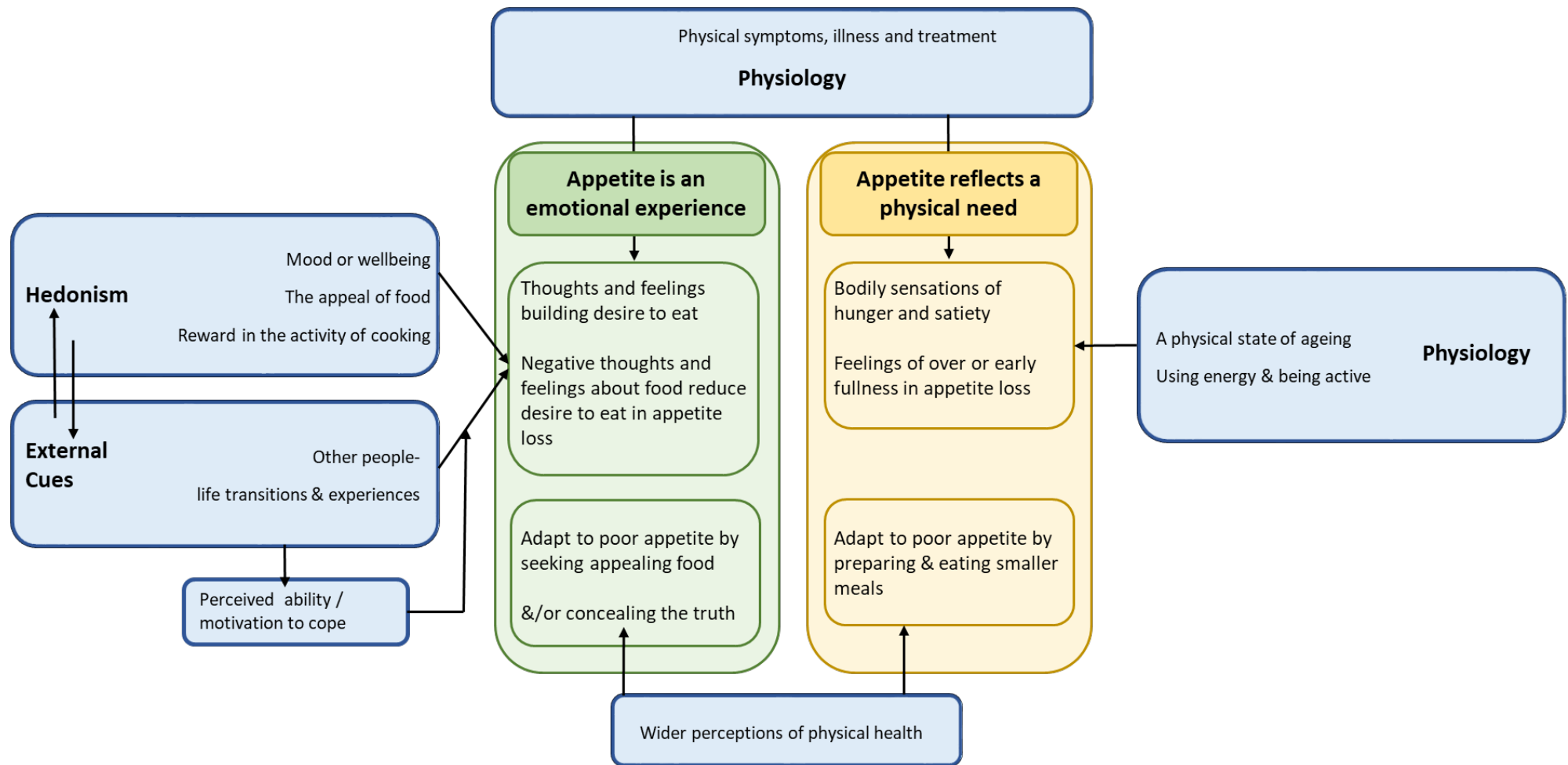
Figure 14   Hypothesised relationships between influences on appetite, perceptions of appetite and adaptions to poor appetite.

Influences on appetite and adaptive behaviour to poor appetite, depicted in blue, relate in distinct ways to the two narratives of appetite.

Adapted from Cox et al [230].

5.5.5 Potential clinical consequences of findings

The themes derived from interpreting the individual accounts of appetite and its influences have important implications for clinical practice and how potential interventions for the management of poor appetite might be shaped. It is clear that interventions will need to be person-centred as individuals perceive appetite loss and its influences in distinct ways, for the most part with a focus on either appetite as an emotional experience or reflecting a physical need. Therefore, clinicians need to make an assessment of the person's own account of their appetite loss, as this will affect approaches to management. For those who value appetite as an emotional experience, attention should be paid to food they like and to removing assumptions that these foods are 'bad' or 'naughty' when the goal is continued energy intake. Additionally, these foods may also be amenable to fortification to ensure appropriate nutrient diversity is achieved. For those who value physical needs, the focus may need to switch to meals with gradual increases in portion size or frequency, alongside discussions about increasing physical activity. It is also important to note that most of the individuals interviewed were overweight and so would not 'ring alarm bells' for the clinician regarding clinical nutritional risk, despite reporting weight loss due to their appetite change. This highlights a need to ask individuals about their appetite as part of a holistic assessment, taking note of changes regardless of the person's current weight. Development of a training tool to aid clinicians in identifying appetite change (making use of tools such as the Simplified Nutritional Appetite Questionnaire), as well as in recognising the narratives of appetite may aid appropriate tailoring of management strategies.

Certain accounts within the data are also noteworthy, such as the lady with poor appetite who continued to cook but then hid her lack of consumption from concerned family and friends, which shows that for some with poor appetite, engagement with cooking may not be an effective avenue to improve it, or be proof of consumption. The effect of encouragement and concern by family and friends may also be adverse for the individual with poor appetite, particularly those whose appetite loss is a negative emotional experience. Therefore, there may be instances when assessments should be made with the individual alone, to give them freedom to fully explain their experience. There is also a need to better understand the perceptions and experiences of the family/friends who make up the support network of older adults with poor appetite, as potentially interventions or resources aimed at assisting these people to provide meaningful and supportive help could be prove useful. Lastly, it was apparent in the data that for some individuals, bereavement did not impact negatively on their appetite but was instead a release often from being a primary caregiver. This finding echo's that of Chatindiara et al, who described accounts from older individuals who were primary caregivers, on difficulties with their diet and

intake due to the needs of the other person [245]. This is important as it counters an often held assumption that decline in appetite after widowhood is directly related to this event [242], especially if this had been preceded by caregiving. Therefore, there is a need to challenge these assumptions and ensure they are addressed appropriately in intervention development. For one woman, her narrative of appetite loss did not align with that of what appetite should be and she continued to try meals that had previously made her physically sick. This highlights how individualised and often nuanced experiences of appetite and its change are with sometimes seemingly illogical adaptions to poor appetite.

5.5.6 Study strengths and limitations

This study followed robust qualitative methods with attention to ensuring data quality, including the use of multiple researchers in the analysis at different stages and attention to reflexivity. This has provided a data-driven account of two narratives of appetite amongst a group of older adults and hypothetical interactions with influences and adaptions to poor appetite in later life. However, the sample was drawn from one outpatient clinic in a city, so when using the findings to shape potential future interventions for poor appetite they may not transfer to other contexts or settings. Some of the interviews were also conducted with family members present, which may have affected their responses giving variability with those interviewed alone. However, it may be that some of these individuals may not have felt confident to take part without the other person's presence and so their account would not have been heard if being interviewed alone was a requirement. Moreover, participating in a study around healthy ageing may have altered participant's interview responses due to social desirability bias, for example participants were aware of public 'healthy eating' messages and so may have shaped some responses around these. It is important to note that the participants had all sustained an arm fracture prior to interview; however the interviews covered timespans and experiences prior to this. In addition, three of the participants had sufficient weight loss for inclusion in a medium risk category for malnutrition. These individuals did not express differing views to those with lower malnutrition risk but their inclusion means the constructed account of appetite perceptions from the study cannot not be considered purely in terms of very early stages of appetite loss. Therefore, further enquiry and testing of these hypothetical relationships is needed in other community dwelling populations of older people to include different socio-cultural backgrounds and health and care needs.

5.6   Chapter Summary and conclusions

This study has provided an account of how older individuals perceive what appetite is or should be and how they experience its change, with broadly two different narratives of appetite: as an emotional experience or reflecting a physical need. These narratives foster different adaptive strategies for a poor appetite- commonly by seeking desirable food or reducing meal size. The study also provides hypothesised pathways for how influences on appetite are experienced by individuals, which relates to how they perceive appetite and its change. These influences on appetite align with the categories of physiology, hedonism and external cues. The themes and theoretical relationships from this study require further testing and can be used to inform quantitative methods of enquiry into influences on appetite in a larger cohort of older individuals, which will form the final part of this thesis. The study findings also have important implications for clinical practice to enable person-centred approaches for treatment for appetite loss.

Chapter 6   Analysis of a community population- examining the role of influences on appetite identified in the preceding studies

6.1   Introduction to chapter

Findings from the preceding studies have informed the research aims of this final study. The initial review of the literature identified multiple documented influences on appetite in older people, with a well-explored physiological basis but impacts of hedonism and external cues changing in later life also playing a key role. However, the systematic review forming Chapter 3 identified a current lack of evidence for effective management strategies for appetite loss in older people. Thus, greater insight into influences on appetite could potentially open up avenues for management.

The secondary analysis of datasets from a cohort of hospitalised older people identified an association between lower mood (measured by GDS-15) and lower levels of reported appetite (SNAQ) during admission (see Chapter 4 section 4.4.3). However as this was a hospitalised cohort, this relationship could be explained by effect of acute illness and unfamiliar environment, so mood and physical activity may not be an important influence in other settings. It is also important to note that the GDS scores were low (3 - 4 out of 15) and so the individuals had low level (or sub-clinical) changes in mood. Within the secondary data analysis, a lower level of habitual physical activity (measured using PASE) was also independently associated with poorer appetite (SNAQ) (See section 4.4.3). This could also be affected by the setting of hospital, as although the measure of habitual activity related to the two weeks prior to admission, the individuals may have reduced activity from their usual level due to illness. The very low level of activity seen could be indicative of this; the median PASE score of 50 (out of 793) for the group is lower than other community estimates for older people, which range from 114 to 155 [246-248].

Next, the qualitative study was designed to explore perceptions of appetite and appetite loss and the range of factors influential on their appetite in own-home dwelling older adults without acute illness (see Chapter 5). Analysis identified distinct narratives, which older adults used to describe perceptions of appetite; as either an emotional experience of thoughts and feelings building desire to eat, or reflecting a physical need with bodily sensations, planned eating and little attention to

thoughts or feelings about food. When exploring influences on appetite, participants in the qualitative study described different mood states including mild levels of low mood, anxiety, anger and upset, as detrimental to appetite, whereas excitement and happiness were a positive force. The relationship between appetite and level of physical activity was also described by individuals; less activity and not requiring energy was seen as a cause for appetite loss, whilst engaging in physical activity was also a potential avenue to improve their appetite or 'build it up'.

The qualitative study also highlighted a number of other factors that individuals related to their appetite including interactions with people and loss of people, the appeal of food, reward in cooking and the effects of life experiences and transitions. Perceptions of health were also important, not only in how individuals perceived appetite, but also in their responses to poor appetite. Other qualitative research studies have also described the importance of the eating environment for an older person's appetite [117, 120].

Taking the findings from these studies forward I firstly updated the theoretical model of potential influences on appetite, which guided my analysis of the hospital cohort data (chapter 4). This updated framework includes additional concepts informed by the qualitative study in chapter 5 (Figure 15). Translating these qualitative concepts to questions or scales means they can be tested in a measurable way to aid understanding of influences on appetite in different populations, at larger sample sizes and when planning potential intervention strategies for poor appetite. Whilst mood and physical activity were associated with appetite in hospitalised older people, it is important to know if these two factors are also determinants of appetite in the community, where the effects of acute illness are lessened. This is suggested in the qualitative study but needs examination in a larger sample with measurement of other factors. A focus on the community setting is also of value, as this has the potential to reach wider numbers of individuals who may be suffering from poor appetite, and at risk of malnutrition, sarcopenia and frailty. Therefore, this final study is an analysis of data from a community population of older people that provided an opportunity to assess correlates of appetite and to explore concepts highlighted in the qualitative study. The study participants were recruited from secondary care outpatient clinics, a similarity with the qualitative study and so a relevant population in which to explore the influential concepts on appetite identified in the qualitative analysis.

Figure 15   Updated theoretical model of influences on appetite

Qualitative findings (highlighted in purple)
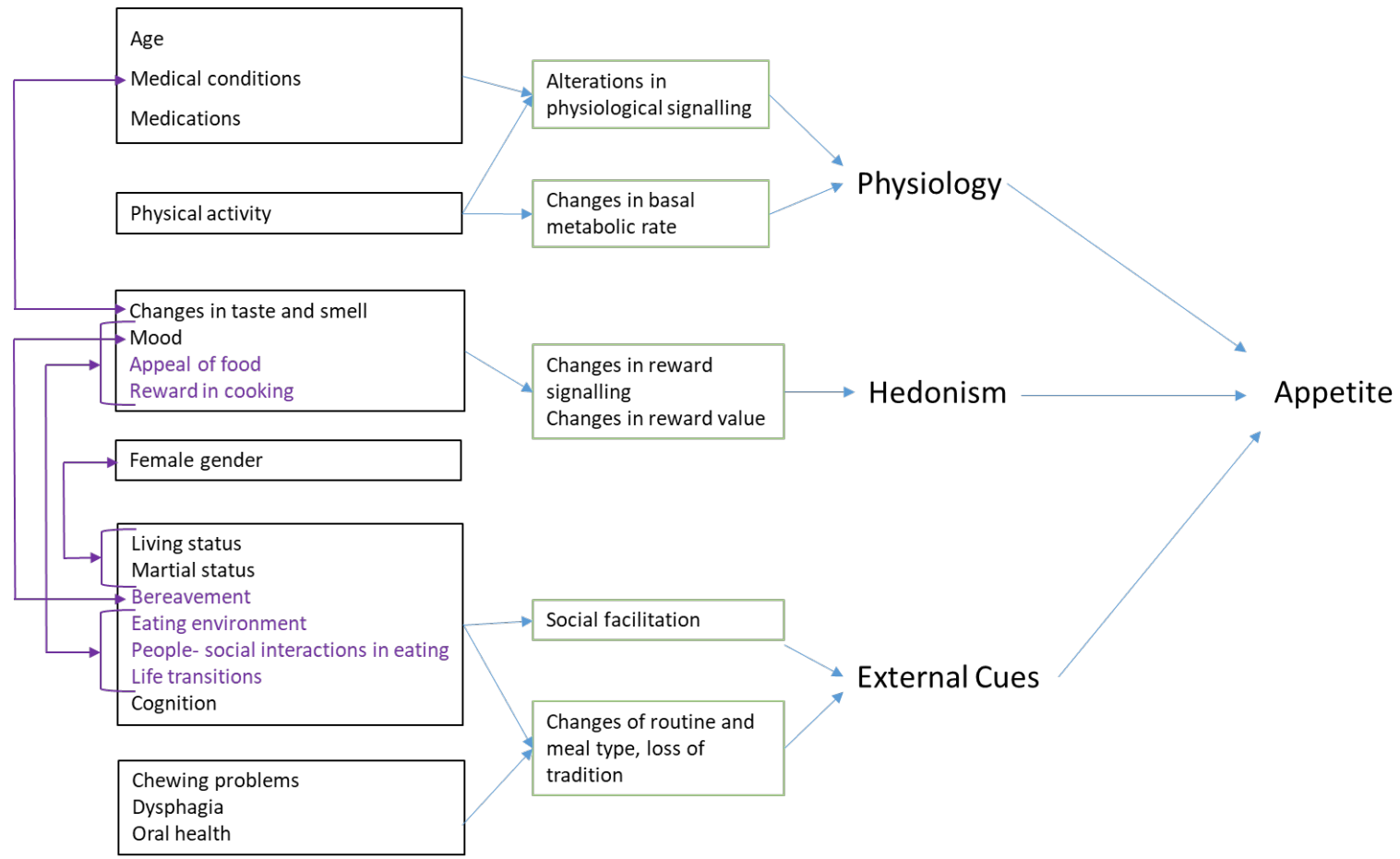
6.2   Aims of the study

- To examine levels of appetite in a community population of older people using SNAQ.
- To assess factors associated with appetite in this community group, with particular attention to-
    - o   Physical activity and mood as observed in the hospital setting.
    - O   Wider influences identified in the qualitative study in community dwelling older adults recruited from secondary care, and assessed in this community cohort

6.3   Methods

6.3.1   Data collection

The Lifestyle in Later Life (LiLL) study recruited 86 older individuals (aged over 60 years, not acutely unwell and capable of giving informed consent) from three outpatient clinics in University Hospitals Southampton (UHS) in 2015-2016 [249]. These clinics included a Comprehensive Geriatric Assessment (CGA) clinic, a syncope clinic and a fragility fracture clinic. The participants were visited by a researcher in their own home and assessed on a number of parameters using questionnaires and physical measurements. The primary aim of the study was to determine factors associated with poor dietary quality (including the role of appetite) and poor physical function in older adults accessing secondary care clinics.

All 86 of the participants recruited had a measure of appetite with the SNAQ (completion rate 100%) with other variables of interest for this analysis. The data were collated and had been cleaned by a statistician prior to this secondary analysis. However, I derived some variables from the data; these are specified in the methods.

6.3.1.1   Participant characterisation

Demographic details recorded included age, gender and living circumstance (living alone, living with others, living in sheltered accommodation or living in a care home).

Frailty was assessed using the Fried frailty phenotype. Individuals were considered as living with frailty if there were 3 or more of: self-reported unintentional weight loss, exhaustion, weakness,

slow walking speed or low physical activity. A standardised approach, with a JAMAR Hydraulic Hand Dynamometer was utilised to measure grip strength. Low grip strength was defined as <16 kg for women and <27 kg for men, and used as a marker for sarcopenia (see chapter 4 section 4.3.1.1).

Markers of nutritional status included body mass index (BMI), calculated by participants' weight (kg) divided by height squared (m²), self-reported amount of weight loss in the last year (kg) and the Malnutrition Universal Screening Tool (MUST) score (see chapter 4 section 4.3.1.1).

A short food frequency questionnaire (24 items), developed for the assessment of diet among community dwelling older adults, was administered by a researcher. A diet 'quality' score (termed prudent diet score) was calculated for each participant, based on the frequency of consumption of the listed foods, with a higher score indicating a diet characterised by more frequent consumption of fruit, vegetables and whole grains and lower consumption of processed meat and cereals, added sugar and full-fat dairy products [250].

6.3.1.2   Appetite assessment

The Simplified Nutritional Appetite Questionnaire (SNAQ) was utilised to assess appetite (see section 4.3.1.2 for details)

6.3.1.3   Potential influences on appetite present in the dataset

From the updated theoretical framework of influences on appetite (Figure 15) I identified the presence of variables of interest for analysis in the community dataset (Table 11).

Table 11   Theoretical influences on appetite (qualitative constructs in purple) in community study dataset and tool used to assess.

Category	Variable	Presence in dataset and tool to assess
Physiology	Age Comorbidity Medications Physical activity	Years Comorbidity count Medication count International Physical Activity Questionnaire, walking/exercise group attendance, time spent sitting
Hedonism	Mood Reward in cooking Gender	NICE screening questions for depression, Measure of National Wellbeing Likert scales Likert scale 'I enjoy cooking for others and myself' Recorded male, female
External Cues	Living circumstance Cognition Oral Health Dysphagia Eating environment People	Categories Mini Mental State Examination Difficulty eating due to problems with teeth Difficulty eating due to swallowing difficulty Eating out/alone/with family/with friends/at table/ watching TV, lunch club attendance. Lubben Social Network Score 6 item, leisure activities score

I derived medication and comorbidity counts from those listed in the dataset. There were two different measures for physical activity included in the dataset, firstly the International Physical Activity Questionnaire (IPAQ) short form telephone version [251]. This is a self-report of physical activity over the prior seven days and includes time spent on vigorous activities, moderate activities, walking and sitting. The score calculated is expressed in metabolic equivalent (MET)-minutes/week, which is MET level x minutes of activity x events per week, with a MET being the multiple of an individual's estimated resting energy expenditure (1 MET = expenditure at rest; 2 METS = twice what they expend at rest). Additional indicators of physical activity included self-reports of attendance at walking or exercise clubs.

Mood was assessed using two questions recommended by the National Institute for Health and Care Excellence (NICE) to screen for low mood in community settings; positive response to either indicates further diagnostic assessment is required [252]. These questions are 'during the past month have you often been bothered by feeling down, depressed or hopeless?' and 'during the past month have you often been bothered by having little interest or pleasure in doing things?' In this analysis, I used a positive response to either question as an indicator of low mood. Other questions for wellbeing and affect were included, these are used by the Office of National Statistics as measures of national wellbeing [253]. These were assessed using a Likert scale, which ranged 1-10 from 'not at all' to 'completely' and included satisfaction with life, feeling things you are doing in life are worthwhile, happiness yesterday, and anxiety yesterday. Reward in cooking was also assessed in this group by the responses to the statement 'I enjoy cooking for others and myself' on a 5-point Likert scale, with anchors of 'strongly disagree' to 'strongly agree'.

Cognition was assessed using the Mini Mental State Examination (MMSE (see chapter 4)). Participants were also asked whether they had difficulty eating and if so, if this was due to chewing or swallowing difficulties. Regarding the participant's eating environment, the frequency in a week of eating in a café/restaurant and eating a home prepared meal was recorded. Additionally, participants were asked about the regularity of environments in which they consumed their main meal, including eating at a table, eating watching TV, eating with other members of the family, eating with friends and eating alone, with responses of 'never, 'sometimes' or 'usually'. Any lunch club attendance in a usual week was also recorded.

I utilised the Lubben Social Network score six item (LSNS-6) [254], and reported leisure activities (which includes a social activities sub-score) to examine the effects of other people and social interactions. The LSNS-6 asks about the number of relatives/friends heard from at least once a month, the number of relatives/friends the person feels at ease with to talk about private matters and the number of relatives/friends the person feels close to call on for help. The total score is an

equally weighted sum of these items with a range of 0-30; a score of <12 implies risk of social isolation.

A leisure activities score was included, which was the sum of a number of 4 point Likert responses of 'never', 'less than monthly', 'monthly', 'weekly', (scoring 0-3 respectively), regarding frequency of reported leisure activities [255]. The activities covered religious activities/observance, positions of office (school governor, councillor etc.), involvement in clubs and organisations (voluntary or official), course and education/evening classes, social indoor games (cards, bingo, chess etc.), visiting friends and relatives, going to pubs and social clubs, individual occupations (e.g. reading, listening to music), household tasks (e.g. DIY, maintenance, decorating, practical activities), making things with your hands (e.g. pottery, drawing etc.), gardening and using a home computer for leisure. A subcategory of social leisure activities can be calculated separately by summing responses to positions of office, involvement in clubs and organisations, social indoor games, visiting friends and relatives and going to pubs and social clubs. These questions are based upon a questionnaire designed for a longitudinal study examining the socioeconomic gradient in health and disease (the Whitehall II study) [255]. In this present study, an original question regarding cultural visits to stately homes, present in the leisure activities and social activities sub score was omitted. Thus, the leisure activities score had a range of 0-36 in this study, whilst the social leisure activities subcategory range was 0-15.

6.3.2   Statistical analysis

I analysed the data using SPSS statistical software (SPSS IBM Corp version 24), initially using descriptive statistics to characterise the population: mean and standard deviation (SD) for normally distributed data, frequency and percent for categorical, and median and inter-quartile range for skewed data. Appetite in the population is described as mean scores and SD; appetite is also described categorised as good (SNAQ score ≥14) or poor (SNAQ score of <14) appetite (see chapter 4). To compare characteristics between the groups of good and poor appetite, I used independent samples T test for normally distributed data, Mann-Whitney U to compare distributions for skewed data, and Chi Square tests for nominal data distributions. P values of <0.05 were considered statistically significant.

I undertook regression analysis to assess the association between potential influences in the dataset with appetite, informed by the theoretical model (Figure 15). I considered the variables age, comorbidity count, medication count, IPAQ score, time spent walking, time spent sitting, attendance at walking or exercise clubs, presence of low mood, wellbeing Likerts, reward in

cooking Likert, gender, living circumstance, MMSE, eating difficulties, eating environments, LSNS-6 score and leisure activities score (with social activities sub-category) within the model. I considered all variables with equal weighting as to their importance on their association with SNAQ score.

I initially assessed variables in unadjusted analysis. Statistically significant variables ($P<.05$) were taken through to multivariate analysis, where I built a model using the stepwise approach. This assessed the effect of the addition of individual variables to the variance in the SNAQ (Criterion: Probability-of-F-to-enter model ≤.05, Probability-of-F-to-remove from model ≥.1)), to create a model optimised to explain the largest variance in the SNAQ score with all variables making significant independent contributions.

6.3.3 Ethical considerations

The Lifestyle in Later Life study had ethical approval from the UK National Research Ethics Service Committee Southwest, 14/SW/1129. All participants gave written informed consent for data collection, including use in future research on anonymised data; I conducted this secondary data analysis on anonymised data.

6.4 Results

6.4.1 Description of the population

The characteristics of the study population are summarised in Table 12. The participants had a mean age of 77.5 years and 62% were female. Fifty seven percent of participants were living in their own home with family or friends, 36% were living alone and six individuals (7%) were living in sheltered accommodation. They were a multi-morbid population with a median number of four comorbidities and a median of five medications but overall had good cognitive function with median MMSE of 29. Twenty-five (29%) participants were living with frailty according to the Fried phenotype. Mean grip strength was 30 kg (SD 8.7) for men and 19 kg (SD 6.6) for women. Using the EWGSOP II guidance (sarcopenia indicated with a grip strength of <27 kg for men and <16 kg for women) 10 (11.6%) men and 13 (15.1%) women were sarcopenic.

The BMI (median 26.4 kg/m^2; IQR 7) and MUST score (65% were low risk) indicate that the majority of the population would not be considered clinically to be at nutritional risk. However, 22 individuals (25.6%) reported the presence of weight loss in the last year and 19 (22%) reported some difficulty in eating. The mean prudent diet score was .172 (SD 1.34) for men and .919 (SD 1.70) for women: consistent with other studies [256], this indicates the women had diets of higher quality.

The participants had low median scores for physical activity on the IPAQ, with a median total time spent walking in a usual week of one hour, and 42 hours a week spent sitting (6 hours a day). Thirty-three individuals (39%) were suffering with low mood. On the social network score, 21 (24%) individuals scored <12 indicating a high risk of social isolation.

Table 12   Characteristics of the community study participants

Characteristic	Mean (SD)		
	Total (N=86)	Males N= 33 (38%)	Females N=53 (62%)
Age (years)	77.5 (8.1)	79.0 (8.28)	76.6 (8.2)
SNAQ	15.17 (1.8)	15.58 (1.79)	14.92 (1.85)
Grip strength (kg)		30 (8.7)	19.3 (6.6)
Prudent diet score	0.63 (1.6)	.172 (1.34)	.919 (1.70)
Lubben social network score 6 item	16.9 (6.9)	15.94 (7.73)	17.72 (6.24)
Leisure activities score	13.8 (5.7)	12.58 (5.86)	14.57 (5.55)
Social leisure activities score	4.9 (2.9))	4.36 (2.91)	5.2 (2.9)
	Median (IQR)		
Number of comorbidities	4 (3-6)	5 (3-7)	4 (3-6)
Number of medications	5 (2-9)	6 (3-9)	4 (2-10)
IPAQ score (MET-min/week)	404 (0-1538))	297 (0-1621.5)	412 (66-1449)
Time spent walking (min/week)	60 (0-891)	30 (0-360)	105 (5-240)
Time spent sitting (min/week)	2520 (1890-4200)	2940 (2280-5040)	2520 (1785-3570)
Cognition (MMSE)	29 (28-30)	29 (27-30)	29 (28-30)
Body Mass Index (kg/m^2)	26.6 (23.8-30.31)	27.69 (26.29-30.87)	24.76 (22.86-28.72)
	Frequency (%)		
Residence: Living alone	31 (36%)	8 (24%)	23 (43%)
Living with friends/partner/family	49 (57%)	24 (73%)	25 (47%)
Sheltered/ warden controlled	6 (7%)	1 (3%)	5 (9%)
Frailty (score ≥3 Fried)	25 (29%)	14 (42%)	11 (21%)
Low mood (positive response to NICE screening questions)	33 (38%)	12 (36%)	21 (40%)
MUST category	(N=74)	(N=28)	(N=46)
Low	56 (76%)	22 (79%)	34 (74%)
Medium	7 (9%)	2 (7%)	5 (11%)
High	11 (15%)	4 (14%)	7 (15%)
Presence of weight loss in the last year	22 (25.6%)	7 (21%)	15 (28%)
Amount lost (Kg) (median (IQR))	6.4 (3.2-9.5)	6.4 (3.2-9.5)	5.6 (3.2-6.4)
Difficulty eating any reason	19 (22%)	7 (21%)	12 (23%)
Difficulty eating due to dysphagia	4 (4.6%)	1 (3%)	3 (6%)
Difficulty eating due to poor oral health	10 (11.6%)	3 (9%)	7 (13%)
SNAQ <14	14 (16.3%)	4 (12%)	10 (19%)

MET Metabolic Equivalent, MMSE Mini-mental state Examination, NICE National Institute Health and Care Excellence, SNAQ Simplified Nutritional Appetite Questionnaire

Table 13 provides information on the eating environment for participants' main meals. Participants commonly ate home-prepared main meals (median 6.88/ week), for 70% this was usually seated at a table and for 54% usually eaten with family. However, 40% of participants usually ate their main meals alone and 40% usually ate them whilst watching television (TV).

Table 13   Eating environment of the community study participants

Location of main meals in a usual week	Median (IQR)		
	Total (n=86)	Males (n=33)	Females (n=53)
Home prepared meal	6.88 (6-7)	7 (6-7)	6.5 (6-7)
At café/ restaurant	0 (0-1)	0 (0-0.4)	0 (0-1)
Eating environment for main meal (usual week)	Frequency (%)		
At a table	Usually 60 (69.8%) Sometimes 7 (8.1%) Never 19 (22.1%)	Usually 24 (72.7%) Sometimes 2 (6.1%) Never 7 (21.2%)	Usually 36 (67.9%) Sometimes 5 (9.4%) Never 12 (22.6%)
Watching television	Usually 35 (40%) Sometimes 22 (25.6%) Never 29 (33.7%)	Usually 9 (27.3%) Sometimes 8 (24.2%) Never 16 (48.5%)	Usually 26 (49.1%) Sometimes 14 (26.4%) Never 13 (24.5%)
With family	Usually 46 (53.5%) Sometimes 18 (20.9%) Never 22 (25.6%)	Usually 24 (72.7%) Sometimes 4 (12.1%) Never 5 (15.2%)	Usually 22 (41.5%) Sometimes 14 (26.4%) Never 17 (32.1%)
With friends	Usually 1 (1.2%) Sometimes 33 (38.4%) Never 51 (59.3%)	Usually 0 (0%) Sometimes 9 (27.3%) Never 24 (72.7%)	Usually 1 (1.9%) Sometimes 24 (46.2%) Never 27 (51.9%)
Alone	Usually 34 (39.5%) Sometimes 11 (12.8%) Never (41 (47.7%)	Usually 9 (27.3%) Sometimes 2 (6.1%) Never 22 (66.7%)	Usually 25 (47.2%) Sometimes 9 (17%) Never 19 (35.8%)
Attend a lunch club	5 (5.8%)	1 (3%)	4 (7.5%)

Table 13 provides information on the eating environment for participants' main meals.

6.4.2   Level of appetite in the study population and characteristics relating to poor appetite

The mean SNAQ score was 15 (SD 8.1). When comparing men and women, there was a trend for a higher SNAQ score indicating better appetite in men (15.58 (SD 1.79), versus women (14.92 (SD 1.85), however this did not reach statistical significance (p= .11), so further analysis combined sexes.

Out of 86 participants, 14 had a SNAQ score of <14, indicating 16.3% of the population had poor appetite. The characteristics of those with poor appetite (SNAQ <14) relating to demographics of the population and sequelae of poor appetite are summarised in Table 14. Individuals with a poor appetite were older (age mean difference 5.92 years (95% CI 1.28, 10.57), p =.013) and more comorbid (median comorbidities 4 (IQR 3-6) with good appetite versus 6 (IQR 4-6.5) with poor appetite, P=.014). They had higher numbers of medications: median five (IQR 2-8.75) medications for those with good appetite versus nine (IQR 6-12.75) for those with poor appetite, P=.004). They also had a lower quality diet (prudent diet score mean difference 1.105 (95% CI .194, 2.01), p =.018) compared to individuals with a better appetite (SNAQ ≥14). Gender, living circumstance, presence of frailty and grip strength did not significantly differ between those with poor and good appetite, nor did markers of nutritional risk. However, there were trends towards a higher proportion of frailty, living alone and high-risk MUST category in the group with poor appetite, as well as lower grip strength.

Table 14   Comparison of participant characteristics in the community study according to reported appetite

Characteristic	Good appetite (SNAQ ≥14); N=72	Poor appetite (SNAQ <14); N=14	P
Demographic			
Age (years)*	76.57 (8.25)	82.49 (6.48)	**.013**
Female$	43 (60%)	10 (71%)	.410
Residence$ Living alone Living with friends/partner/family Sheltered/ warden controlled accommodation	24 (33%) 43 (60%) 5 (7%)	7 (50%) 6 (42%) 1 (7%)	.475
Number of comorbidities^	4 (3-6)	5.5 (4-6.5)	**.014**
Number of medications^	4.5 (2-8.75)	9 (6-12.75)	**.004**
Potential sequelae of poor appetite			
Grip strength (kg)* Males Females	31.39 (8.63) 19.67 (6.09)	25.75 (8.73) 17.90 (8.77)	.231 .450
Prudent diet score*	.819 (1.64)	-.287 (1.11)	**.018**
BMI (kg/m^2)^	26.30 (23.37-30.47)	26.40 (24.37-37.26)	.908
MUST category$ Low Medium High	(N=62) 48 (77%) 6 (10%) 8 (13%)	(N=12) 8 (67%) 1 (8%) 3 (25%)	.559
Presence of frailty (score ≥3 Fried)$	19 (26%)	6 (42%)	.240
Presence of poor function$	14 (19%)	4 (29%)	.442

*mean (SD), ^median (IQR), $Frequency (%), bold indicates significant at the <.05 level.

BMI Body Mass Index, MUST Malnutrition Universal Screening Tool

6.4.3   Association between potential influences and appetite as a continuous outcome

6.4.3.1   Univariate analysis

I examined the influences of selected factors (Table 11) on appetite, using continuous scores, initially in univariate regression analysis (Table 15). Mood, measured by depression screening questions showed a trend towards association with poorer appetite, but this did not reach statistical significance. However, the level of feeling that life is worthwhile was associated with SNAQ (co-efficient .199, P=.046), this was a positive association indicating higher levels of feeling life was worthwhile were linked with better appetite. Level of physical activity as measured by the IPAQ again showed trends with appetite score, but did not reach statistical significance in this group. However, time spent walking in the last week was positively associated with SNAQ in this univariate analysis (coefficient .002, P=.02).

A number of the factors identified in the qualitative study were associated with the SNAQ in univariate analysis. This included level of enjoyment in cooking for self or others (regression co-efficient .362, P=.041), which was positively associated with appetite. Eating environments of sitting at a table or watching TV for main meals (coefficients .502, P=.035; -.693, P=.002) also correlated with appetite, with sitting at a table having a positive association with appetite and watching TV having a negative association with appetite. The Lubben social network score and leisure activities score including the social activities sub-score, used to assess the effects of people being present, were also associated with appetite in the univariate analysis (coefficients- LSNS-6 .084, P=.003; leisure activities score .102, P=.004, social leisure activities .134 P=.05). These were all positively associated with SNAQ score, indicating that a better social network and higher engagement in leisure activities, including engagement in just social activities, were associated with a better appetite.

Within the univariate analysis of this population, some factors were consistent with the comparison of SNAQ categories of good and poor appetite (section 6.4.2). These included age (unadjusted coefficient -.056, P=.02), number of comorbidities and number of medications (unadjusted coefficients -.258, P=.016; -.266, P=.013). All these had negative associations with appetite, indicating increased age, greater comorbidity and medication counts were linked with poorer appetite.

Table 15   Association between factors and appetite (SNAQ score) in univariate analysis in the community study population.

Categorised by theoretical influential pathway

Theoretical category	Influential Factor	Regression co-efficient	P
Physiology	Age	-.056 (-.103, -.009)	**.02**
	Number of comorbidities	-.258 (-.361, -.037)	**.016**
	Number of medications	-.266 (-.184, -.022)	**.013**
	IPAQ score (Physical activity MET-min week)	.000 (.000, .001)	.073
	Time spent walking (min per week)	.002 (.000, .003)	**.02**
	Time spent sitting (min per week)	.000 (.000, .000)	.170
	Attendance at walking group	.510 (-1.653, 2.673)	.640
	Attendance at exercise group	.321 (-.866, 1.509)	.592
Hedonism	Presence of low mood	-.726 (-1.527, .076)	.076
	Level of feeling satisfied with life nowadays	.089 (-.096, .259)	.364
	Level of feeling things in life are worthwhile	.199 (.004, .395)	**.046**
	Level of happiness yesterday	.009 (-.165, .183)	.918
	Level of anxiety yesterday	.063 (-.110, .236)	.468
	Level of enjoyment cooking for self or others	.362 (.041, .684)	**.041**
	Female gender	-.651 (-1.456, .154)	.111
External cues	Living alone	-.525 (-1.345, .295)	.206
	Living in sheltered/warden accommodation	.529 (-1.026, 2.085)	.501
	Level of cognition (MMSE)	-.007 (-.181, .167)	.936
	Presence of poor oral health	-.763 (-1.992, .465)	.220
	Presence of dysphagia	-1.494 (-3.353, .365)	.114
	Eating environment of main meals[$]:		
	Eating alone	-.279 (-.702, .144)	.193
	Eating with other members of the family	.372 (-.091, .836)	.114
	Eating with friends	.542 (-.228, 1.31)	.166
	Sitting at a table	.502 (.037, .967)	**.035**
	Watching TV	-.693 (-1.13, -.256)	**.002**
	Attendance at lunch club	.240 (-1.458, 1.937)	.780
	Number main meals in a week:		
	At café/ restaurant	-.288 (-.997, .420)	.421
	Prepared at home	.093 (-.512, .698)	.760
	Lubben social network score (LSNS-6)	.084 (.029, .140)	**.003**
	Leisure activities score (total)	.102 (.034, .169)	**.004**
	Social leisure activities score	.134 (.000, .267)	**.05**

[$]Measured as increasing frequency; bold indicates significance at the 0.05 level. IPAQ International Physical Activity Questionnaire, MET Metabolic Equivalent, MMSE Mini-mental state examination.

6.4.3.2   Multivariate analysis

Factors that were associated with appetite in univariate analyses (P<0.05) were considered in a multivariate analysis to evaluate their independent effects. Assessment of these factors prior to model building identified no presence of strong collinearity (no variables had Pearson's correlation of r > 0.7 [257]). Regarding singularity, the social leisure activities score makes up part of the total leisure activities score, therefore I took the social activities score forward as I felt this was more reflective of interactions with people - the qualitative construct of interest.

Following stepwise regression, the model accounting for the largest variance in the SNAQ scores included three variables, which made independent contributions. These variables were eating main meal whilst watching TV, social network score and number of comorbidities (Table 16, Model 3; P <.001) and explained 25% of the variance within the SNAQ score (R^2 0.247). When comparing the standardised coefficients of the variables, they are making similar contributions but differing directions; a higher social network score linked with better appetite whilst a higher frequency of eating main meal whilst watching TV and greater number of comorbidities associated with poorer appetite, as seen in the univariate analysis. The other factors associated with appetite in the univariate analysis were not independently related to SNAQ when the effects of the variables in the final model were taken into account following stepwise regression.

Table 16   Stepwise regression analysis of factors associated with appetite (SNAQ score) in the community study population

Influential Factor	Model 1 Regression coefficients (95% CI)	P	Model 2 Regression coefficients (95% CI)	P	Model 3 Regression coefficients (95% CI)	Model 3 Standardised regression coefficients	P
Eating main meal whilst watching TV more often	-.730 (-1.18,-.284)	**.002**	-.655 (-1.09,-.224)	**.003**	-.602 (-1.02,-.179)	-.281	**.006**
Lubben Social Network Score			.078 (.023, .134)	**.006**	.075 (.021, .129)	.272	**.007**
Number of comorbidities					-.179 (-.332,-.026)	-.229	**.022**
R^2 for model	.116		.195		.247		

Figure 16 highlights the relationship between mean SNAQ score with frequency of eating main meal whilst watching TV and social network score using the LSNS-6. Indicating that individuals who usually ate their main meals whilst watching TV and had a social network score of <12 (which puts them at risk of social isolation) had the lowest mean SNAQ scores in the population.
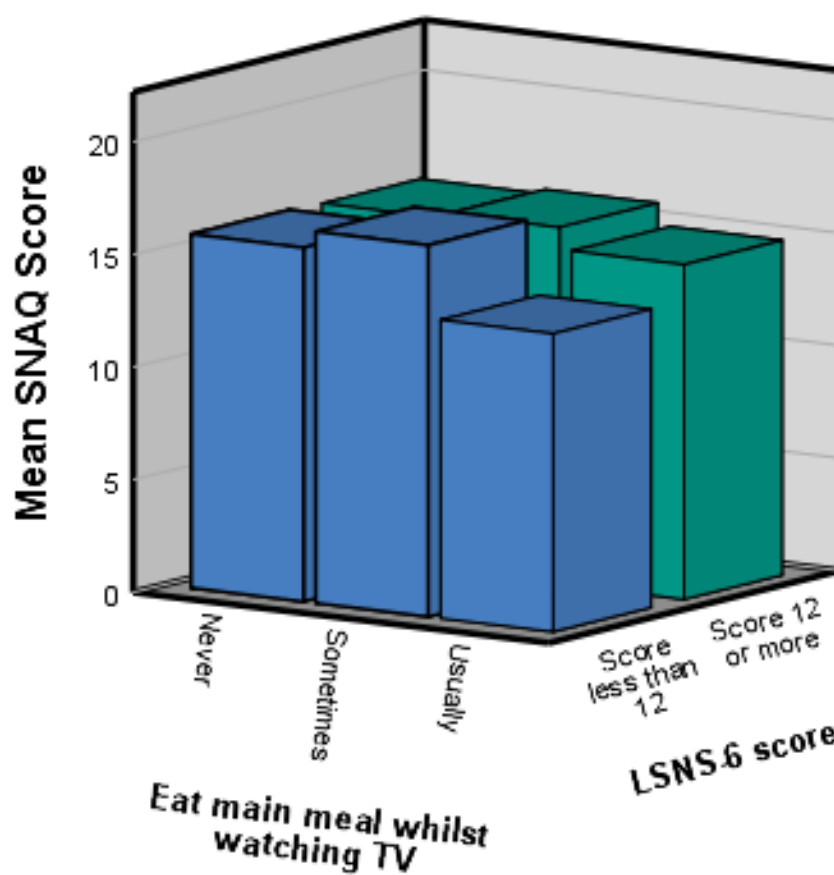

Figure 16   Mean SNAQ scores depending on frequency of eating main meal whilst watching TV and Lubben social network score in the community study

LSNS-6 Lubben Social Network Score 6. A score of <12 indicates risk of social isolation.

6.5 Discussion

In this study I aimed to examine levels of appetite in a community-dwelling population of older people and assess influences on appetite in this group, with particular attention to exploring factors identified from the prior two studies in this thesis, namely physical activity and mood as seen in the hospital setting and factors identified in the qualitative study.

The mean SNAQ score in the population was 15 and the prevalence of the population living with poor appetite was 16%. This is far lower than identified in the hospital population (over 40%) but sits within other community population estimates [126]. Categorising participants as having poor (SNAQ <14) or good (SNAQ ≥14) appetite to examine their characteristics highlighted that those with poor appetite were older, more comorbid and had higher numbers of medications, which fits with other descriptions in the literature [7, 8]. In addition, when examining theoretical sequelae of poor appetite, this study also identified that individuals with poor appetite had lower quality of diet and trends towards reduced grip strength, higher proportion of frailty and malnutrition risk, which is in line with the findings from the hospitalised population in Chapter 4. This study is cross sectional in design so the causation cannot be determined. However, longitudinal studies have shown a predictive association between low appetite and incident malnutrition, sarcopenia related outcomes and frailty [128-130].

Continuous univariate analysis highlighted a number of factors associated with appetite in this population (Table 15), which cover all of the theoretical categories influential on appetite - physiology, hedonism and external cues (See introduction section 1.3). In multivariate analysis Lubben social network score, watching TV whilst eating main meals and the number of comorbidities all made a significant independent contribution to the SNAQ in the final model (Table 16, model 3). In the multivariate analysis, age, medications, time spent walking, feelings of life being worthwhile, enjoyment in cooking, sitting at a table for main meals and social leisure activities were not associated with appetite, when the effects of the variables in the final model were taken into account. This is interesting when comparing the clinical characteristics of the population with poor appetite (categorised as SNAQ <14), who were older and had higher medication counts. This perhaps highlights the limitation of using SNAQ scores in a categorical way, as you are unable to assess effects of other variables. For example, it may be that older age as a characteristic in relation to appetite reflects social (or other) factors, which are influential on appetite. Therefore, while categorising individuals as having good or poor appetite is useful to broadly understand differences in population characteristics, perhaps for screening target populations at risk of poor appetite, digging deeper into those characteristics in continuous

analysis reveals a clearer picture of potential associations useful in examining for potential intervention strategies.

Regarding the factors of low mood and physical activity, which I considered of interest due to their association with appetite in the hospital cohort (see chapter 4 section 4.4.3), these associations were not observed in this study group when measured by the NICE depression screening questions or IPAQ short form. However, a trend for effects was seen in the direction expected from earlier analysis of the hospital cohort- low mood with poor appetite and physical activity with a small positive association. These trends are important to note as the differences in the findings may be explained by the small sample size of 86 in this study, meaning it was underpowered to determine statistical significance. Nevertheless, it may be that level of mood and physical activity have greater effects on appetite in hospital rather than community settings. Another possibility is that the difference in the effects seen between the two populations is related to limitations in using self-report data, as the data are subjective and require recall by the participant. It is important to note that these studies compared different tools, which have different wording and measure slightly different aspects of mood or physical activity, and this may have contributed to different findings. Interestingly, looking back to the hospital cohort, physical activity measured as 'amount of time spent walking in the last week' was also associated with appetite during hospital admission (regression coefficient adjusted for GDS score .002 (95% CI .000, .003; P=.017)), as seen in this study. In addition, a different measure relating to mood and wellbeing- feelings of life being worthwhile - was associated with a better appetite, as well as amount of time spent walking. This all adds to the hypothesis that mood and physical activity are factors of interest in terms of influences on appetite in older people.

In the continuous analysis, I aimed to explore other factors identified as important determinants of appetite in the qualitative study. I was able to translate some of these constructs to quantitative measures present in the community dataset and examine their association with appetite. In the univariate analysis correlates associated with appetite were reward in cooking, aspects of the eating environment such as sitting at a table or watching TV and effect of people-measured by Lubben social network score and engagement in social leisure activities. Interestingly, in the final multivariate model Lubben social network score, watching TV whilst eating main meals and the number of comorbidities all remained significant with an independent contribution to the SNAQ score. Prior observational studies have identified the socio-environmental factors of living and eating alone to be associated with appetite in older people [122-124] but measurement of social network has not been explored until now. This could be a

useful addition to understanding how the wider social environment in which an individual resides may affect appetite.

The external cue of eating environment, in particular watching TV whilst eating main meals, which was associated with lower appetite in univariate and multivariate analyses, may also be an indicator of differences in social network and activities. However, although it may indicate effects of poorer social interaction, it is important to note that the association of watching TV whilst eating to appetite was independent of the effects of social network in the final model. Another avenue which may be fruitful to explore is if eating environments such as watching TV may be related to reduced engagement with food eaten and so perhaps linked to reduced reward in the hedonic aspect of appetite. Whilst reward in cooking was measured in this cohort, the concept of appeal of food and eating was not covered and mood was not extensively explored, so their effects remain uncertain.

The multivariate model explaining variance in the SNAQ with each variable making an independent contribution included Lubben social network score, the environment of watching TV whilst eating main meal and number of comorbidities. This model contains variables from the physiological and external cue categories of influence. This shows the complexity of the influences on appetite in older people and the importance of a person's wider social and environmental context.

6.5.1 Study Limitations

The cross sectional nature of this study is a limitation to this project as I am unable to determine causation regarding potential influences on appetite. So, although associations between appetite and certain theoretically influential factors can be determined, temporal sequence is unclear.

The LiLL study provided an opportunity to explore a wide range of social and environmental factors relating to appetite in a study population similar to that of the qualitative study and collected in a standardised way by a trained researcher. This enabled me to examine influences on appetite identified in my earlier work. However, as this was a secondary analysis of data from a study designed with a different research aim compared with a study designed prospectively to examine influences on appetite, the nature of the data collected is limiting. The LiLL study had an aim of understanding factors associated with diet quality in older adults, so it focussed on mealtime environments. In terms of influences on appetite, there are additional variables that would have been interesting to examine but were not included. This has been particularly important when looking at the hedonic aspect of appetite, where fewer aspects were measured, such as sensory perception, the appeal of food and bereavement, and in the type of tools used to

measure certain variables of interest, namely mood and physical activity. These may all have had impacts on the findings and so further research is needed.

To determine quantitative variables to address the concepts I had interpreted in the qualitative study I ensured there was similarity between what the variable was measuring and the qualitative construct, including question wording. However, it is important to note that as this is a secondary analysis, I was utilising prior collected data rather than selecting questions or scales prospectively, so they may not always have been the best measure. This is particularly the case for the qualitative concept of the effects of people. In the qualitative study, this encompassed positive social interactions as a stimulant for desire to eat in the emotional experience of appetite but also the negative effects on a poor appetite through perceived social pressure to try to eat, as well as the effects of loss of important people. The Lubben social network score looks at the numbers of people within an individual's network who regularly visit and with whom they talk about private matters or feel close to call on for help. So while this score certainly relates to opportunity for social interaction and will likely relate to positive social interactions, it will not pick out the nuances around them, including potential perceived pressure to eat with a poor appetite and loss of important people. Similarly, the social activities score may identify opportunities for social interactions but not the type or perceptions of these.

The study sample size of 86 may also have limited statistical power and impacted on understanding potential significance of the association between correlates of appetite, particularly as some trends were observed which appear clinically meaningful and consistent with published data from other settings. However, a strength of the study was that the sample was representative of community dwelling older populations, including older adults of both sexes, with a prevalence of poor appetite within other community estimates and similar levels of comorbidity and polypharmacy, as well as typical numbers living with frailty. Therefore, the findings from the study relating to the social factors are important and should be relevant to the wider population. The findings need confirmation and to be assessed in larger population samples over time, alongside examination of the impact of variables missing from this analysis (as discussed above), to explore associations with appetite and address temporal sequence.

6.6 Chapter summary and conclusions

This study encompassed a secondary analysis of data from a population of community dwelling older adults to assess variables associated with appetite. The population comprised 86 individuals aged >60 years with appetite assessed using the SNAQ. The mean SNAQ score in the population was 15. Sixteen percent of the population had a poor appetite according to SNAQ and those with poor appetite were older, had more comorbidities with higher numbers of medications and lower quality of diet, with trends towards reduced grip strength, higher proportion of frailty and malnutrition risk.

Continuous analysis identified a number of factors associated with appetite, assessed with SNAQ, covering the different theoretical categories of influences (physiology, hedonism, external cues). In stepwise multivariate analysis, social network score, watching TV whilst eating main meal and number of comorbidities had independent associations with appetite score in this population. A higher social network score was associated with better appetite, whereas increased frequency of watching TV during main meal or higher number of comorbidities was associated with a poorer appetite. This identifies the importance of the wider social environment of an individual in relation to their appetite. However, the limitation of using existing data means that a number of potentially important factors (such as appeal of food and bereavement) were not assessed. Future studies should include larger population samples, alongside examination of the impact of factors missing from this analysis, and with longitudinal design to determine temporal sequence and potential for causality.

Chapter 7   Discussion

This research in this thesis explores influences on appetite in the context of ageing. Ageing populations are a global phenomenon, however, increased life expectancy does not infer extra years in good health. Rather, later life for many is associated with multimorbidity and poor health outcomes such as undernutrition, sarcopenia and frailty. Appetite loss is common amongst older people and, outside of a direct medical cause, often referred to as the anorexia of ageing. The anorexia of ageing is associated with undernutrition and related poor health outcomes, so identification and management of the condition could prevent these important health burdens in later life. The regulation of appetite is complex with wide ranging influences. A greater understanding of these influences might be key to providing insights for novel intervention strategies for the management of anorexia of ageing to the benefit of older people and those involved in their health and care. This chapter will summarise the key findings and implications drawn from the series of studies within the thesis exploring influences on appetite in older people.

7.1   Aims and objectives of the research within this thesis

The aims of the research in this thesis were to identify how best to assess appetite in clinical and research settings and then to explore potentially modifiable factors on anorexia of ageing in a series of studies. The specific research objectives for the studies were:

o To assess the current evidence for assessment and management of anorexia of ageing through a systematic review of the literature.

o To assess the association between appetite and potential influential factors through a secondary analysis of cross-sectional data from a cohort of hospitalised older people aged over 70 years.

o To explore perceptions of appetite, its loss and influences on the experience in a group of community dwelling older people aged over 65 years.

o To assess the association between appetite and potential influential factors (including translation of concepts from the qualitative study) through a secondary analysis of cross-sectional data from a cohort of community dwelling older people aged over 60 years.

Following a literature review of the current evidence for influences on appetite in older people when beginning this research, I suggested that influences in appetite could be organised into the

categories of physiology, hedonism and external cues around food and eating [70]. Structuring the influences in this way may aid understanding and benefit health and care of older people and future research. I utilised this structure to inform the series of studies within the thesis. The next section will discuss the main findings from the thesis contributing to knowledge about influences on appetite in older people.

7.2   Influences on appetite in older people

A main research aim was to explore potential influences on appetite in older people. Firstly, through a review of the literature on current evidence for interventions and then through a series of exploratory studies. I utilised a range of research methods to gain a more comprehensive picture. Figure 17 presents an overview of the influences, their relationships to one another, and proposed theoretical mechanisms of action generated from this research.
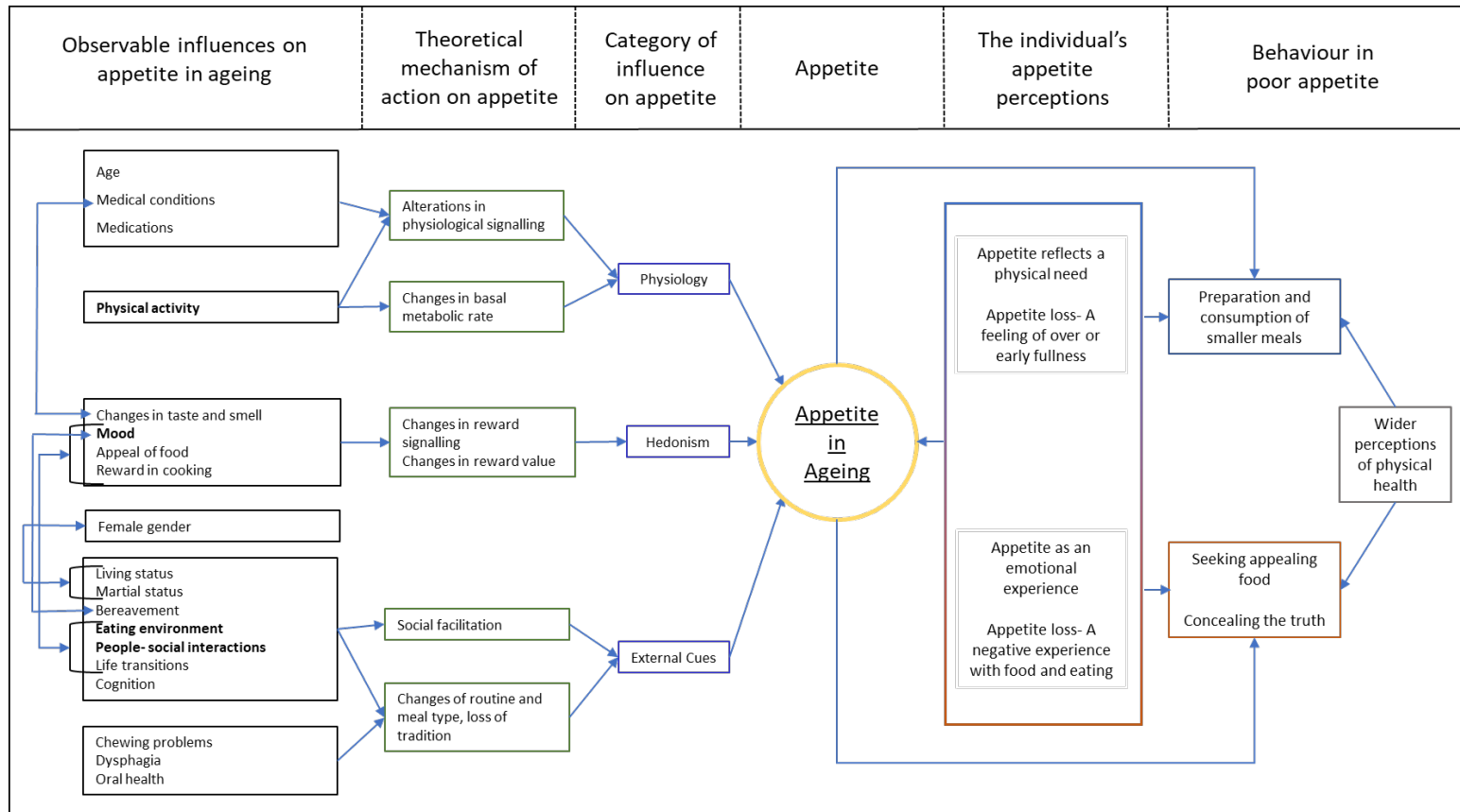
Figure 17   Overview the research findings within the thesis exploring influences on appetite in ageing.

Influences on and individual perceptions of appetite appear to interact in appetite in ageing, producing individualised experiences. Bold indicates the potentially modifiable influences emergent from the research in this thesis.

7.2.1   Mood and physical activity

The first exploratory study among the hospital study cohort identified mild low mood (hedonic category, measured by GDS-15) and lack of habitual physical activity (physiological category, measured by PASE) were associated with poor appetite during hospital admission (assessed using SNAQ). These hedonic and physiological influences were also identified in the subsequent two studies. In the qualitative study, participants described how both positive and negative mood related to their appetite and physical activity was seen as a cause for poor appetite as well as a means to improve it. In the community study cohort, the contribution of aspects of mood and physical activity were measured using different tools (NICE screening questions and the IPAQ respectively). Some comparable trends for association with appetite were still observed, including univariate associations between appetite (SNAQ score) and wellbeing and time spent walking in the last week, both of which could be considered proxy measures of mood and physical activity. However, the associations with appetite were less clear than in the hospital cohort study where I observed independent associations of mood and physical activity with appetite. The differences in observations between the studies may relate to sample size of the community study (being underpowered), nonetheless it may be those relationships were not as important or yet developed, as appetite was better in the community population and they had different characteristics. However, it is also recognised that mood and physical activity have a positive association (in particular that undertaking exercise improves mood) [258]. A more detailed assessment of their relationship with one another, with regard to appetite, is therefore required to determine if there is any evidence of mediation of effects on appetite. In addition, a greater understanding of optimum levels of physical activity to stimulate appetite would be invaluable, considering the observed differences between physical activity and anorectic effects of high intensity exercise. Still, the findings across the studies of mood and physical activity relating to appetite are of interest, as modifications in physical activity and/or strategies to improve mood may prove to be important interventions to maintain appetite in later life.

7.2.2   External cues

In the community population study, which had collected detailed data on environments and wider social aspects, there were clearer associations of external cues (the effects of people measured by the Lubben social network scale and the mealtime environment of watching TV) with appetite. A higher social network score was associated with better appetite, whereas eating meals whilst watching TV more often and having a higher number of comorbidities were associated with poorer

appetite. The findings relating to the wider social and environmental aspects of the individual were discussed by participants in the qualitative study and had otherwise only been explored in other qualitative contexts [117, 119, 120]. So, the opportunity to draw these concepts through to a quantitative analysis in the mixed-methods approach of this thesis has added to the evidence for socio-environmental contexts of the individual in relation to their appetite. This is important, as these aspects will need to be taken into consideration when assessing individuals with a poor appetite and in designing and trialling future management strategies, which may need to be adapted depending on socio-environmental contexts.

It is also interesting to note that inclusion of social and environmental factors in the model explaining the variance of SNAQ scores in the community study provided a higher R^2 value than the model for the hospital cohort. Twenty five percent of the variance in SNAQ scores was explained by social network, eating meal while watching TV and comorbidities in the community, versus 9% by mood and physical activity in hospital. There were also signals of the importance of socio-environmental contexts for interventions (and thus influences) on appetite in the systematic review. This was suggested by the different effects observed for mealtime adjustment interventions, with adjustments to meals in the individual's usual setting having a positive effect on appetite versus no effect for those conducted in research centres. However, the apparent importance of external cues assessed in the community study cohort in this thesis may also relate to study design, as the data collected were concerned with diet quality and so included a greater number of socio-environmental factors comparative to the hospitalised cohort. In addition, influences on appetite in the hospitalised cohort are likely to have been impacted upon by the effects of acute illness [259]. This is important as the qualitative study suggested that the effects of symptoms, illness and treatment were the only influences to affect both narratives of appetite loss, emphasising how it may have had an overarching impact on the results from the hospital setting. Moving forward, a measure of 'acute illness', perhaps through biochemical assessment of parameters such inflammation via C-reactive protein [259], would be invaluable in studies across settings.

7.2.3   Implications for future research

Elements of the three different categories of influence (physiology, hedonism and external cues) on appetite were observed across the hospital and community study cohorts but with some suggestion of differences depending on setting and context. Most importantly, the representation of all three categories of influence in the different cohorts highlights the complex nature of appetite and its loss

in ageing populations, so a multi-faceted approach to understanding influences and their potential for intervention development is integral. A next important step will be to combine observation of all of these influential factors within a longitudinal study to indicate temporal sequence and the potential of causality. It is also important that any future data collection has a unified minimum dataset and standardised data collection protocols, to ensure comparability of results and to start to test the effects of different environmental and situational contexts. The addition of biomarker measures, such as those of inflammation and metabolic pathways, would enable deep characterisation of a cohort of people and potentially gain mechanistic insight into the relationship between theoretical influences and appetite in the context of ageing.

7.3 Older individual's perceptions of appetite and appetite loss

The qualitative analysis undertaken as part of the research in this thesis outlined how older adults think about or conceptualise appetite and adds crucial context to explain and understand factors influencing its loss. The analysis constructed two narratives, which the individuals used to discuss appetite, as an emotional experience or reflecting a physical need (Figure 17). The participants used these narratives in different ways to discuss their experiences of appetite, many utilising one over another, some using aspects of both throughout their discussion and some switching between the two (such as using one to describe appetite and another appetite loss). Hedonic and external cue influences aligned with the emotional experience of appetite and with negative thoughts and feelings towards food, whereas the physiological influences appeared to relate to appetite as reflecting a physical need and feelings of early or over fullness. However, the different ways in which participants used the narratives in the qualitative study means not all fit 'neatly' into one narrative, rather an interaction of perceptions and influences produce individuality of experiences of appetite and appetite loss (Figure 17).

7.3.1 Implications for future research

The individuality of experience in appetite and appetite loss means that an important part of assessment of those with a poor appetite will be to hear and acknowledge their perceptions, to guide meaningful management strategies. However, it is important to initially understand whether the concepts of the two narratives of appetite seen in this qualitative study are transferrable to other older people from different social and environmental circumstances. There is also a need to understand which potentially modifiable influences individuals with poor appetite prioritise, and how these might align with their current adaption strategies. This would help to ensure that

potential intervention targets and approaches are optimally meaningful and engaging for all older individuals with poor appetite. Within this, the perspectives of family, friends and in particular caregivers of those with poor appetite are also important to understand, especially in relation to the role(s) they may undertake in supporting those with poor appetite, as this may also impact on how potential interventions are received. Knowledge on these wider perspectives may also aid our understanding of how some of the influences on appetite appear to be mediated through other perceptions, such as motivation to cope or maintaining resilience through life transitions, and what affects this.

The findings of the two narratives that participants used to discuss appetite (an emotional experience or reflecting a physical need) suggests a need for a quantitative measure to ascertain whether larger groups of individuals also relate to them. This measure would need to be quick and scalable. A quantitative measure such as this would assist in understanding if there were distinct mechanistic pathways associated with these narratives; it would also be an important step for focusing future management strategies for poor appetite.

7.4 The importance of identifying poor appetite in older people

The series of exploratory studies in the thesis provides further evidence of the importance of assessing appetite in older people. In the acute setting of the hospitalised cohort, a low SNAQ score during hospital admission was associated with increased risk of death over 6 months post discharge [11], confirming findings in the previous female-only study [10]. In addition, individuals with poor appetite during hospital admission had higher levels of frailty and functional dependence, and a lower body mass index, with trends towards lower grip strength. This was echoed in the community-based cohort where individuals with low SNAQ score trended towards a higher degree of frailty and reduced grip strength. These findings are in line with growing evidence that poor appetite is associated with malnutrition, sarcopenia and frailty, all of which entail poor and costly health outcomes [3, 4, 260]. However, an important and not fully answered question is to what extent poor appetite is a direct cause or correlate of these poor health outcomes. It is most likely to be both, but knowledge is restricted by a lack of longitudinal evidence to determine the nature of associations. There is limited longitudinal evidence of a role for poor appetite in subsequent weight loss [134], as a determinant of incident undernutrition [129, 195] , and as a factor in incident disability mediated through its relationship with frailty [130] in different older populations. Poorer appetite has also

been shown to predict lower muscle strength, mobility and physical performance [128], and importantly mortality across a range of settings, including post-discharge from acute care in our hospital cohort and from a rehabilitation setting [261], as well as in nursing home [131] and own-home dweller [132] populations. The main theoretical causal relationship between poor appetite, undernutrition and associated health burdens is that of alteration in dietary pattern and reductions in overall intake due to poor appetite, leading to weight loss. However, despite cross sectional evidence of the association between poor appetite and reduced intake and poorer diet quality [124, 132, 262] (evidence added to by the same observation in this community study analysis), just one study has investigated in a longitudinal fashion. Huang et al identified that diet quality moderated the effects of poor appetite on mortality [132], indicating the potential of this theoretical causal relationship but this continues to be an important area for future research.

Poor appetite as a correlate of poor health outcomes also seems likely, due to the multi-faceted nature of its influences and regulation, meaning effects of poor health will be present. This was suggested by the qualitative analysis where illness, physical symptoms and treatment appeared to impact upon both narratives of appetite loss (both the emotional experience and reflection of a physical need). The cross-sectional nature of much of the evidence for poor appetite and ill health, (including in this thesis) means that further prospective longitudinal evidence is important and required to develop further the themes identified in this research between poor appetite and poor health outcomes. However, regardless of the work still needed to understand potential causal mechanisms, assessing appetite in the older population is still timely and of great utility. This is because it is easy to assess (such as with SNAQ) and with links to morbidity and mortality, has the potential to indicate individuals who may be developing undernutrition and poor health. Furthermore, the older community dwelling populations studied in this thesis who were accessing secondary care outpatient clinics had a high prevalence of poor appetite, which was in line with other community estimates [126]. However, interestingly, they did not have a high prevalence of clinical malnutrition risk, which may underline the role of identifying early appetite change in the recognition of trajectories towards ill health. This echoes the study by Schilp et al who identified poor appetite as an early determinant of undernutrition [129]. Early identification of reduction in appetite therefore may offer opportunity for intervention to mitigate against poor health outcomes, particularly in community settings. The hospital cohort within this thesis had a higher prevalence of both poor appetite and nutrition risk than in the community, a finding also reflected in the literature, which highlights a need for routine assessment in health and social care practice to identify those at risk before reaching a state of undernutrition.

7.5   Approach to assessment of appetite in older people

Within the research in this thesis, appetite was assessed using the SNAQ tool in busy clinical settings, including during hospital admission or attendance at a fracture clinic, as well as in participants' own homes. The SNAQ was also highlighted in the results of the systematic review, as an evolution of the most robustly validated tool used amongst the included intervention studies- the AHSPQ. Other Likert scale or visual analogue scale responses to questions on appetite are also currently used in intervention studies for the anorexia of ageing. However, a standardised approach to measurement of appetite in intervention studies is required, to enable pooling of results.

7.5.1   Implications for future research

A standardised approach to measurement of appetite could be by consistent use of Likert scale responses, such as those in the SNAQ, which is being increasingly utilised particularly in clinical studies [131, 259, 263]. Use of the SNAQ may also have an additional benefit, as it has potential for use in routine clinical practice to assess appetite because of its simple structure and links to health outcomes, which are of interest to clinicians. Whilst there have been no studies purely focused on assessment of feasibility and acceptability of using SNAQ in clinical settings, our results show high completion rates (98.75% for the hospital study and 100% for the community study). This indicates feasibility of researchers using SNAQ in different environments as a way to assess appetite in older people, which could be utilised by those involved in their health and care. An important next step would be to understand the acceptability of implementing assessment of appetite routinely in practice, particularly barriers and enablers for its use. This would need to take in the views of key stakeholders, such as older people and clinical and care staff, as to how routine use of SNAQ could be operationalised, which could then be piloted and evaluated.

It is important also to note the qualitative study findings of two narratives for appetite perception (an emotional experience and reflecting a physical need), which the participants used in different ways. This finding raises the question as to whether tools to assess appetite are capturing the full experience of appetite for all older individuals. The SNAQ is comprised of questions on feelings of fullness, which may reflect the perception of physical need and food taste, which may reflect the emotional experience, as well as amounts consumed and a global assessment. However the extent to which it captures the different aspects of appetite needs further assessment as, for example, individuals who have negative feelings about food may be overlooked if they do not have altered

taste. It is also important to note that the SNAQ is a shortened more widely used version of the Council of Nutrition Appetite Questionnaire (CNAQ) [134]. The CNAQ includes an additional 4 questions covering the domains 'I feel hungry', 'compared to when I was younger, food tastes', 'I feel sick or nauseated when I eat' and 'most of the time my mood is'. On the validation study, these domains were removed to form the SNAQ without any impact on the reliability of the tool [134]. Use of the more extensive CNAQ may broaden its scope to individuals with mood change and so potentially changes in the emotional experience of appetite, however feelings about food is still not represented in the questioning. In addition, if appetite is perceived in different ways, then individuals may interpret questions on appetite (such as in the SNAQ) in different ways. This could be explored through techniques such as cognitive interviewing [264], which examines through interview and qualitative analysis how individuals process and respond to questionnaires, to assess if there is misrepresentation or failure to measure what was intended. A better understating of how questions relating to appetite are interpreted by older individuals, particularly with a poor appetite, could indicate if there is a need for additional questions to ensure their full range of experience is captured.

7.6   Management of the anorexia of ageing

The systematic review of evidence for interventions addressing the anorexia of ageing identified 21 studies with few focussed on appetite; for many it was a secondary outcome with the primary focus on undernutrition. The overlap between appetite and undernutrition in terminology use and markers of measurement, such as weight loss or oral intake, is likely to limit further research. This is because appetite loss is a probable precursor to undernutrition as well as an aspect of it, so a focus purely on undernutrition risks limiting the potential scope of older individuals who could benefit from interventions. Therefore, clarity of the target of interventions, with a move away from inclusion of appetite loss under the umbrella of undernutrition, may provide wider ranging benefits and potentially act to prevent onset of undernutrition for some. The importance of separating appetite loss and undernutrition to ensure all relevant individuals are captured is further suggested by the other studies in this thesis. Appetite loss had a greater prevalence than high malnutrition risk (according to MUST score) in both cross sectional studies and in the qualitative study many individuals who were suffering from poor appetite were overweight or did not have a degree of weight loss that would trigger a risk score.

The systematic review also identified a lack of evidence for management strategies for the anorexia of ageing. There was a signal for the potential benefits of additional flavouring, fat emulsion ONS or

fortified cookies. However, these positive results were from small single studies without replication. The qualitative study in the thesis gives some suggestion as to why this may be the case, as individuals perceived appetite and its loss in different ways (summarised by use of the two narratives of emotional experience and reflecting a physical need). Thus, interventions based upon the experience of appetite loss for the individual and what they prioritise (perhaps guided by their narrative), may provide more effective strategies for management of appetite loss. In the analysis of the qualitative study, it was clear that those participants with poor appetite were already engaged in adaptive behaviours to mitigate this, largely through smaller portions and seeking appealing food. This appeared to be influenced by the individual's perception of appetite as well as wider perceptions about physical health: smaller portions when appetite reflected a physical need, or seeking appealing food or concealing the truth in the emotional experience (Figure 17). These behaviours offer an opportunity for interventions, perhaps by fortifying foods the individuals are seeking or ensuring nutrient density in smaller portions. Holistic assessment of the individual, including their perceptions, is likely to be key to management strategies, as apparent differences in adaptive behaviours according to the narrative of appetite loss suggests potential for lack of engagement in 'one size fits all' strategies. However, for nutrition-based interventions that do require a one-size fits all approach (as individualised, holistic assessment may not always be feasible or practicable), knowledge about these narratives of appetite loss and adaptive behaviours is still an important avenue for optimising engagement. For example, it would be useful to ensure that communication of any guidance acknowledges and uses the different narratives, to maximise the likelihood that individuals will identify with what is being said, thus optimising engagement.

7.6.1 Implications for future research

When looking forward to development and trialling of future management strategies for the anorexia of ageing, this research highlights level of habitual physical activity, mood, eating environment and social interaction as a potential focus. These factors can also be assessed in a clinical setting with relative ease (summarised in Table 17). Successful interventions are likely to need to be multi-component and selected based upon the individual's experience and also socio-environmental context, following a conversation about their appetite. Taking the approach of a partnership with the older person to manage their appetite with due attention to their needs and priorities is also likely to prove most beneficial; an approach that aligns with the principles of a cornerstone in geriatric medicine- the comprehensive geriatric assessment

Table 17   Updated table of potential intervention targets for appetite loss in ageing and examples of clinical assessment strategies

Narrative of appetite loss	Category of influence	Potential target for intervention	Examples of assessment tool with potential to translate into clinical practice
A physical feeling of early or over fullness	Physiology	Habitual physical activity	Time spent walking in the past week Step count
A negative emotional experience with food and eating	Hedonism	Low mood	Geriatric Depression Scale-15
	External Cues	Eating environment Social network	Questions as part of social history in clinical assessment

7.7   Strengths and limitations

7.7.1   Strengths relating to the mixed-methods design

The aim of taking an open and mixed-methods approach to exploring influences on appetite was to exploit the strengths of different methodological approaches and integrate their results, to give insights into a phenomenon where "the whole is greater than the sum of its parts" [137]. This has be achieved by providing a comprehensive overview of the phenomenon, as well as insights into the range of different influential factors on appetite in later life, highlighting their broad scope but also with suggestions of how they may relate to the individual's experience of appetite loss.

Certain aspects have really benefitted from the mixed-methods approach, such as insight of the importance of different personal and socio-environmental aspects, where factors initially identified in the qualitative study then demonstrated measurable associations with SNAQ score in subsequent quantitative analysis. In addition, the perceptions of appetite explored in the qualitative study provide some suggestions for the current lack of evidence for effective interventions for the

anorexia of ageing in the systematic review and point towards person-centred approaches to management. Finally, factors such as mood and physical activity were identified throughout the different studies and settings within the thesis in their association to appetite. The appearance across settings and methods strengthens the suggestion of the need to focus on these factors more closely and over time in future research.

7.7.2   Strengths relating to the data collected

The populations studied in the thesis were from different settings- hospital and the community. The groups were similar in characteristics to other cohorts in the literature having a similar prevalence of poor appetite. This has produced interesting insights into differences between the populations studied but also similarities. These different settings aid in the generalisability and transferability of findings observed across the studies; this is important for research in older people who are often considered a very heterogeneous group to study.

A second strength relating to the nature of the data collection is that the majority can be collected routinely in ageing studies (as demonstrated by the ability to combine the hospital datasets). Much of the data could also potentially be collected in clinical practice (although in a briefer fashion for some items) and do not require physical assessment. This means that the findings of these studies will be easier to test in different populations and due to the simplicity of tools, such as the SNAQ, has real potential to be applied to large cohorts of older individuals. Utilising measurement tools often used in clinical practice, such as the GDS-15 for low mood, also makes the findings of the studies more relevant and understandable to those involved in the care of older people, aiding their translation into clinical practice.

7.7.3   Limitations relating to the data collected

Both quantitative analyses were conducted on existing datasets, where the data had been collected for different primary outcomes to that of appetite; they were also both cross sectional in design. The limitations of secondary analysis mean that the data collection tools may not be designed for exploring associations with appetite. Additionally, variables of interest in relation to appetite were not all measured, especially those factors which became apparent after conducting the qualitative analysis, particularly around certain hedonic aspects of appetite such as taste and smell perception. This lack of variable measurement may mean some important influential factors or potential confounders were likely not measured and so unaccounted for. The inclusion of BMI to characterise

clinical state of nutrition in both cohorts is also a limitation, as it can be inaccurate in older people due to loss of height, for example due to osteoporotic fractures. The difficulties in calculating accurate BMI may thus have led to its overestimate. The limitations of the cross-sectional design of the studies means that although important insights into theoretical influences on appetite have been obtained from the research, their potential for causality cannot be determined. This remains an important point for much of the research on appetite in ageing, as discussed earlier.

The final analysis at the end of the thesis was an alteration in the planned research due to the COVID-19 global pandemic, since prospective in-person data collection on older individuals was not feasible. This may have yielded different results, as the original proposed study focussed upon appetite and was designed to assess theoretical influences identified from literature review and the hospital cohort analysis. Instead however, the opportunity to carry out secondary analysis did provide further insights relating to socio-environmental context and identified that data which will be important to collect prospectively and in a longitudinal fashion in future studies.

Another limitation to address relates to sample size. This was partly mitigated for in the hospital population by studying a larger group, as I was able to combine data collected using the same methods. However, the number of different potential influences on appetite in ageing meant that further exploration, such as potential mediation of effects, could not be assessed. The qualitative study might be considered to have a very small sample in quantitative terms. However, this sample is acceptable for qualitative research, which has a focus on the depth and nature of the data collection and analysis, but it does limit the transferability of the constructed account to other older populations.

7.7.4 Potential sources of bias

The exclusion criteria placed on the studies included in the secondary analysis may have produced selection bias, as the participants were likely to have been less unwell and less cognitively impaired than the older populations they were recruited from. Included within this was the fact that all of the participants across the studies volunteered to take part and the ability or willingness to volunteer may entail having different characteristics to the rest of the population, such as motivational attitude or better cognition. Any effects of this bias are mostly likely to have been evident in an underestimation of the prevalence of poor appetite in the different settings. It is unlikely that participant selection would explain the findings in the studies; however, as indicated by the observations that those with poor appetite differ in certain characteristics from those with good appetite, selection bias may limit the generalisability of the results.

Many of the tools used in the two observational studies were also self-report, including for variables of interest such as physical activity and so may be more open to recall bias. This may have affected the results, for example by an underestimation of physical activity level if individuals were unable to recall all their activity. However, the physical self-report tools used in the analyses, particularly the PASE are widely used and show good validity in older populations comparative to other questionnaires, against more objective measures such as accelerometers [265].

With regard to the qualitative study, the constructed account of the narratives of appetite is inherently biased, as it was my interpretation of the data. However, this is embraced in the qualitative method as the way in which 'sense' is made from the data. Nevertheless, it does limit the account to the group studied and so can only be used to hypothesise potential relationships, which then need to be tested in further research and in other groups. It is also important to note that this was my first qualitative analysis, which may add some limitation to the quality of the account I constructed. This is particularly in relation to having the confidence and experience in analysis to draw out latent meaning (underlying patterns and ideas) from the data, rather than just description. However, my learning and inexperience was mitigated by input and guidance from my two supervisors experienced in qualitative research.

7.7.5   Sequence of the studies

Finally, a reflection relating to the sequential nature of the studies within this thesis is appropriate. The qualitative study findings regarding individual's perceptions of appetite and links with influences and adaptive behaviour were so rich that I identified further avenues of research (as discussed). Had I conducted this study earlier on I may have altered the path of the research towards understanding the potential importance of these perceptions of appetite, their influences and adaptive behaviours. In this, I may have changed the design to creating and evaluating a potential quantitative measure of these perceptions and tested this in relation to theoretical influences. However, as further prospective data collection was unachievable over the COVID-19 pandemic this may also not have been feasible during the period of my PhD research.

7.8 Future research recommendations

The research in this thesis has identified a number of areas for future research; these are listed in the following bullet points:

7.8.1 Influences on appetite in older people

- Gain mechanistic insight into the relationship between theoretical influences and appetite in the context of ageing. The approach with greatest potential to achieve this would be through measurement of all theoretical influences on appetite in a longitudinal design with a unified minimum dataset and standardised data collection protocols.

7.8.2 Older Individual's perceptions of appetite and appetite loss

- To understand if concepts arising from the qualitative study relating to narratives of appetite in this thesis are transferable to older people with different socio-demographic characteristics and living in different regions of the UK.
- To understand which potentially modifiable influences individuals with poor appetite prioritise, and how these might align with their current adaption strategies.
- Explore the perspectives of family, friends and in particular caregivers of those with poor appetite in relation to the role(s) they may undertake in supporting those with poor appetite.
- Creation and evaluation of a novel quantitative measure of the narratives of appetite in older people (an emotional experience or reflecting a physical need). To ensure the measure is meaningful to older people, a co-production approach to its development with patient and public members would be of value.

7.8.3 The importance of identifying appetite in older people

- To understand more fully, through longitudinal study, the extent to which poor appetite is a direct cause or correlate of poor health outcomes such as malnutrition, sarcopenia and frailty.

7.8.4 Approach to assessment of appetite in older people

- A standardised approach to measurement of appetite in relation to intervention studies, to enable pooling of results across studies.

- Improve understanding of interpretation of the SNAQ by older people, such as through cognitive interviews, to determine whether alterations are required to capture their full experiences of appetite.

- Trial and evaluate the acceptability of implementing assessment of appetite routinely in clinical practice. Quality improvement methods such as plan, do, study, act (PDSA) cycles [266], may be of most use as it enables rapid and repeated refinement to address situation specific issues, then evaluation of those changes through the cycles.

7.8.5   Management of the anorexia of ageing

- For future intervention studies greater clarity of the primary outcomes are required, with a move away from inclusion of poor appetite under the umbrella of undernutrition.

- Future development and trialling of multi-component interventions to manage poor appetite in ageing effectively, based on the older individual's experience of appetite.

- Level of habitual physical activity, mood, eating environment and social interaction are potential avenues to focus on for multi-component interventions. These factors can be assessed in a clinical setting with relative ease.

Chapter 8   Conclusion

In conclusion, this thesis describes a series of studies using a range of methods to explore influences on appetite in ageing. Appetite loss attributable to the ageing process (the anorexia of ageing) is associated with a number of major health burdens in the older population including undernutrition, sarcopenia and frailty. Thus, identification and management of poor appetite may be a useful approach in preventing onset or progression of these conditions. A series of studies were undertaken, in hospital and community settings, to assess the current evidence for assessment and management of the anorexia of ageing. These aimed to explore potentially modifiable influences on appetite in ageing within the categories of physiology, hedonism and external cues, and to understand older persons' perceptions of appetite.

Assessing older individual's appetite by researchers was feasible in clinical and home settings. Mood, level of habitual physical activity and eating environment as well as the effects of other people and social interaction were theoretical influences associated with appetite in the different observational studies. In addition, through the qualitative analysis it appears that these influences also shape individuals' experience of appetite and behaviours in response to appetite loss, alongside their perception of what appetite is and the role it serves.

The research within this thesis has important clinical implications. Firstly, it demonstrates a need for timely translation of appetite assessment into routine clinical evaluation of older people, due to the association of poor appetite with worse health outcomes. The research includes participants identified through clinical encounters as an outpatient or during hospital admission, suggesting utility in these environments as a beneficial starting point to instigate routine appetite assessment. The findings in the thesis also highlight the need for clinicians to consider poor appetite as separate from undernutrition. Implementing scales into clinical practice, such as the Simplified Nutritional Appetite Questionnaire, which focus upon appetite alone rather than as part of nutrition-risk screening would aid clarity of the two concepts. Taking a structured approach to managing poor appetite is also important and exploring the person's individual experience presents an opportunity on which to base this. Management strategies are likely to be most effective when multi-component and with attention to the role of potential changes in physiology, hedonism and external cues of the individual, alongside their needs and priorities.

Finally, there are a number of future research implications relating to this work. Main themes include how our understanding of influences on appetite in ageing is currently limited by lack of integrated longitudinal evidence. Thus, investigation in cohorts with standardised data collection

procedures and over time is required. An important part of this is to address the need for consensus on a unified approach to defining appetite in ageing and its assessment. In addition, the qualitative study has also suggested the presence of distinct narratives of appetite loss, aligning with different influences and behaviours. Future research is necessary to understand the translatability of these concepts to groups with different socio-demographics and develop potential ways to characterise the appetite narratives in a scalable fashion.

Influences on appetite in ageing are complex and wide-ranging. Continued progress in our understanding of these will greatly aid management of poor appetite with a view to promote health ageing and delay onset or progression of poor health outcomes in later life.

Appendix A Example search strategy for systematic review

MEDLINE via OVID

1. exp AGED/

2. elder*.mp.

3. older.mp.

4. geriatric*.mp.

5. 1 or 2 or 3 or 4

6. exp THERAPEUTICS/

7. Disease Management/

8. treat*.mp.

9. interven*.mp.

10. manag*.mp.

11. 6 or 7 or 8 or 9 or 10

12. APPETITE/

13. Appetite Regulation/

14. ANOREXIA/

15. appetite.mp.

16. anorexia.mp.

17. unplanned weight loss.mp.

18. 12 or 13 or 14 or 15 or 16 or 17

19. 5 and 11 and 18

20. exp NEOPLASMS/

21. cancer*.mp.

22. neoplas*.mp.

23. malignan*.mp.

24. carcinoma*.mp.

25. 20 or 21 or 22 or 23 or 24

26. 19 not 25

27. Anorexia Nervosa/

28. anorexia nervosa.mp.

29. 27 or 28

30. 26 not 29

31. child*.mp.

32. 30 not 31

33. Animals/ not (Animals/ and Humans/)

34. 32 not 33

Appendix B Audit trail for theme 'Appetite as a physical function'

Raw Data	Codes
Um how well or bad you eat. Because if you eat or you don't eat, or if you eat the right stuff or the wrong stuff, whatever, or when do you eat? 05_M	Appetite as a planned need to eat food
I think it was the weekend, one of the weekend days, I was doing something around here and then I was in the kitchen doing things, then I thought better get washed and dressed and all of that and I could hear my stomach rumbling and it was getting on for ten o'clock and I thought I haven't even had my breakfast yet. So if that rumbles I think, yeah you are hungry and I, it was then I thought yes you are hungry, so I had brunch as I call it, mix the two. 03_F	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)
[Would you say that that feeling of hunger is a common thing for you?] No, no rare, rare. 03_F	
Well I wasn't feeling hungry and therefore I wasn't eating. 01_M	
[How do you feel when you feel hungry?]Um well I don't know how to describe that, an empty feeling in ones stomach I suppose. Not to the extent of rumbling and thinking what's going on down there, or not going on because you've had nothing 01_M	
I, I would, hmmm appetite, to me it would be something like feeling hungrier than I normally do but that's not the case. 06_M	
[Do you think, do you feel hungry very often?] No I don't, no, well I only around mealtimes yes. 06_M	

Raw Data	Codes
I feels like I'm wanting dinner [laughs], no it erm I never feel ravenous, no I just sort of mmm, where's those sausages. [So is it a thought of eating?] I suppose it is, I could go and not bother about it until I fell over [laughs] 06_M	
I suppose it really is just keeping everything in line, you know like when you are working, oh yeah I'll do that and then you see its lunch time and you say no ill meet you at 2 o'clock, that sort of thing. [So you've always been planning it in?] Well yeah, is that annoying? 06_M	Appetite as a planned need to eat food
[When you know meal time is coming or she is preparing food, are there any particular thoughts that normally go through your head?] Well one of them, which is a silly one I know but I have to think in terms of vitamin K, because I take Warfarin erm so if somebody says oh there is a so and so with Brussel sprouts, I [whistles], I like Brussel sprouts but I think vitamin K and I have to sort of count them so I say I never want any more than three. 06_M	
Well the there's three categories, mmm, like its stages, but erm, I must admit I'm not particularly worried, I do say oh I fell hungry but I wait 'til food comes I'm not banging on, it doesn't affect me in that way 06_M	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)
So after, satiety, after a meal sort of saying like [blows out cheeks] well that's all right but I could do with some more, no I don't ever feel that I don't think. 06_M	Feeling of fullness (not felt through planning or stops meal)
[So relate that back to feelings of satiety then, you think that's changed?] I think so, where sometimes you don't, you don't say it because there's not enough food around or you do say it- no I don't want any more thanks [blows out cheeks] that's me done, I don't say that. 06_M	

Raw Data	Codes
How much you eat a day, actually going into your body yeah, yeah. 08_M	Appetite as a planned need to eat food
[Would you describe yourself and somebody who loves food?]		
No [laughs]. No		
[OK, so what is food to you, if you don't love it?] Well as I say I have porridge in the morning, a ham sandwich and two yoghurts at lunchtime, main meal in the evening. 08_M	
[And do you looks forward to your meals?] No, I wouldn't say I look forward to them I think that they've got to be done, yeah. Yeah, yeah, a job it is. If I had it all cooked for me I might say right, but actually you do it yourself and that's err you know, you've got to work for it. 08_M	
[When you are thinking about what you are going to cook, um in the day, do you sort of plan your meals over the week?] Yes, yes. Yeah it's basically the same week in, week out. I get the ingredients, make sure I've got it in that's all.	
[What makes you decide that you're going to choose those meals?] I just have it all printed out and err, and so I know what I'm having each day and make sure I've got it all there and. 08_M	
[Ok, would you say that you feel hungry at all?] No. No, no as I say it's just a thing to do. 8 o'clock in the morning its breakfast, midday, midday news is on hang on and same with evening, evening news is on, you don't mind missing a bit of news, you can have it on in the background without concentrating on what is going on in the programme and so I have those set time and set time to go to bed [laughs]. 08_M	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)

Raw Data	Codes
I know if I'm, if I'm out somewhere where in I haven't had those meals in the right time, why am I not quite right, because I haven't eaten at the time I expected to be. See I Don't feel hungry I just feel, what have I done, what have I missed out? And that's a meal. [Ok, so it's a sort of funny feeling?] Yeah, yeah so you start to feel not quite right. But not hungry, just not right. 08_M	
[Do you feel full after your meals…?] No not now no, I say I know what I'm eating [You know what you're doing?] That's it. 08_M	Feeling of fullness (not felt through planning or stops meal)
[And so have you always been somebody who feels full and then stops eating?] No, no. [So what would normally stop you eating?] The plate was empty yeah. 05_M	
[Would you say you feel hungry much?] No I've never felt hungry, I can't remember the last time I felt hungry. 05_M	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)
Yeah, it wasn't necessarily because erm I was on a diet. I reduced the quantities because I found that it was bulking me up too much, I was, every time I was, she would bring a dinner out for me, I'd eat it and afterwards I'd feel full up. And I didn't like that feeling, you know, and because I had been on a diet before and I'd got my weight right down, I'd I realised that by doing that type of eating isn't good for you, you know. So when you get half way through your dinner and you've had enough stop, if you feel you've had enough, stop. And, and that's the way my mind thinks now, I thinks that way all the time so when I'm full up, you know the wife says oh you bloody waster, but pfftt if I don't want it, I don't want it, you know. 09_M	Feeling of fullness (not felt through planning or stops meal)
Appetite means to me that erm, there are certain times of the day when you got to eat, you know and you can go past those times. 09_M	Appetite as a planned need to eat food

Raw Data	Codes
Well I guess if it's changed at all, you know, the amount you eat and how you feel about food in general. Err, I try to eat sensibly, cooking for yourself is a bit boring sometimes but I tend to batch cook and freeze things. So I have two, probably two meals a day, sort of brunch and then a meal about seven in the evening. And sometimes a later snack, but err, I eat well. 07_F	
Yes, yes. To eat healthily and to eat regularly erm not to binge, not to starve I think that's always been quite important. 07_F	Feeling of fullness (not felt through planning or stops meal)
Yeah that's, that's a very scientific description of it. Yeah but that's it isn't it, you eat when you're hungry, I tend to do that, erm, yes and stop when your full. That's how I fell, because I stopped when I was full and I gave the rest to the foxes and fell when I came back up from the garden! If I'd eaten it all I'd still be fine [laughs]. 07_F	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)
I get tired and cold when I get hungry. I, my husband used to laugh because I'd say oh I'm tired and cold and he'd say no you're hungry, so I'd tend not always to recognise it. That's was perhaps more when I was busier, when I was working. Now I tend to not want to eat until I'm hungry, when I get up, even if I get up early I rarely eat until about 11, 12, I have like a brunch and then in the evening if I'm not hungry I don't cook until later, so I usually wait until I think I need something. [OK, do you wait until, so is it a feeling of being cold and tired or...] Not so much now just sort of your tummy feels a bit empty doesn't it? Yes. [Ok so a sort of tummy rumble then?] Yes, yes, an empty feeling. 07_F	Appetite as a planned need to eat food
Just eating I suppose, just eating. Making sure that you eat something. Yeah, I make sure I have a good breakfast, I have porridge or cereal in the morning. But if I have a good breakfast I can go all day without having something else to eat. 11_F	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)
[Do you think about food very much?] No, I don't get hungry, I've never got hungry. I eat because I have to, you know erm, or he [husband] makes me. [Ok, and has that always been the case?] Yeah. Well I do eat. Because he [husband] makes me. Ok, but erm	

Raw Data	Codes
he'll come along and say 'its about time you had something to eat, I'm having something now it's about time you had something to eat.' But if I'm doing something like if err, like I do a lot of sewing erm, I can get quite engrossed into doing that and then I, I don't get hungry, I just don't get hungry, that's all there is to it, so unless he comes and says it about time you had something to eat it could be five o'clock at night before I so. So I don't get hungry, I've never got hungry. [So you can't really remember a time when maybe you thought….?] No, not ever 11_F	Appetite as a planned need to eat food
[Is looking forward to your meals, looking forward to food, is that an important thing for you?] No 11_F	
[When you're cooking, cooking a meal, preparing a meal. Would you say your thoughts are on the food that you are cooking, or are you thinking about other things?] Thinking about other things, really, yeah. 11_F	
I have a look in the fridge, see what we've got. You see it happens, Wednesday we do our shopping. I get the shopping and I get home and think what the hell am I going to have for tea tonight? The other night it was err, I don't know I can't be bothered to cook anything se we had erm a bowl of soup with mashed potato and bread, that was nice, I enjoyed that. So, and that was filling, so it was quite good. 11_F	Feeling of fullness (not felt through planning or stops meal)
[Do you feel full up, or…?] Yeah, well I don't. I can't says I get full, no. I can't says I get full. But as I say I never feel hungry. So, I, I would be happy if I could be like a horse and graze all day long. You know picking at stuff, but you can't do that really, it's not good for you I don't think. You know. 11_F	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)
[Ok, another thing I wanted to ask is that although you say that you don't ever remember feeling hungry, if I asked you to described what you think feeling hungry should feel like, what would that be?] Well, you were ready for food sort of thing. You know, and I just don't get that way. Yeah, I would have thought you wold have a rumbling stomach or something would have told you you needed something to eat. But as I say I can be concentrating on something, I used to make cards and things like that and I could be in the	

Raw Data	Codes
craft room all day long. And I would have anything, if I've had a good breakfast, like a good bowl of porridge in the morning or a good bowl of cereal, err cup of tea and erm maybe a biscuit and err the rest of the day I'd go to get a drink out of the fridge, a handful of grapes, back, but I don't have any signs to tell me I'm hungry. No, no people say to me oh I don't know, I need something to eat, I never feel like that. Not ever, I can't ever remember feeling like that. 11_F	
[And when you have been say gardening, and you feel peckish, what, describe what you mean by that.] Well I just feel like, just need to go in and have a little something and a cup of tea or something. Maybe a cup of tea and a biscuit, or, or a biscuit and cheese or something like that. [So is it that you sort of think about food? Perhaps at that moment?] Erm, no I can't says that I actually think about it, erm, I might think oh maybe it's about time I did go in and have something. But that's, I can't say I was feeling hungry or anything. 11_F	Feeling of fullness (not felt through planning or stops meal)
[So feeling full during eating, which causes you to stop eating.] No, no I don't get that either. [No, so what normally causes you to stop eating?] Well, when everything is gone on the plate. 11_F	Appetite as a planned need to eat food
Appetite, it means wanting to eat 10_F	
But no I eat. I think that's the one thing about living alone and this might be people. There, it's not social, it's you know, a bodily function. 10_F	
Erm I think oh I'd better have something to eat now, you know I have breakfast and I have lunch, I have a snack at lunch time and I have an evening meal. 10_F	

Raw Data	Codes
I wouldn't go without a meal no, no. I have a hiatus hernia and erm I don't' have a gallbladder and so, because I had my gallbladder removed, because I had a stone, and so if, if I don't eat then that sort of becomes perhaps a bit uncomfortable. So yes I do try and keep a normal, I don't eat late because that's really difficult, because you can't lie down after, you know, that there's one of the things where you get the reflux. So we tend to eat early. 10_F [What has food always been for you, sort of throughout your life, have you been a lover of food?] Erm, I enjoy cooking and being creative. I think, I think I would say that erm I eat to live rather than I live to eat, yes. I enjoy food but it's not the most important thing in my life. 10_F Oh I plan them out more or less for the week erm and I batch cook. So there's casseroles and things in the freezer. I do a lot of fish because it's quick and easy to do. Erm, so yes, so things, so I know what I'm going to eat today, tomorrow and over the weekend because I needed to get that planned because I know I'm going to be tired when I get home. Erm so consequently I want to have something absolutely ready yeah. 10_F [And so for you when you're thinking about meals, is it that you will be thinking oh I will be tired so I want something easy to do or that you fancy that particular thing?] Erm no its organisation of what I'm going to have and that, I say I don't eat much red meat, so I'd do it up and it would be chicken or fish or I mean I do have a beef casserole but no it's a sort of planning. And also having grown up in the era of having never wasted anything, that you, so err, once, at least once a week I would have some sort of Spanish omelette, using up everything that's around, all the vegetables and things, something like that, so erm yes, frugal [laughs]. We yes after the war you just ate what was on your plate or you didn't get anything else, you weren't fussy. That's why we're all slim. We didn't have a lot of food, we didn't have any fizzy drinks, we didn't have sweets and things. A very different regime. 10_F [Is there any thoughts or feelings that go through your mind, know that you are about to eat?] Erm, well I usually listening to the radio when I do it and erm thinking about what I'm going to do next. 10_F	

Raw Data	Codes
No, no that's been planned in advance. I mean I try to eat a healthy diet, I reckon 90% of the time it's quite healthy. Occasionally you have to have a bit of beef don't you [laughs]. 10_F	
By about 1 o'clock my tummy is rumbling and it'll be like lunch something or other and I'll look forward to that. But we've done something. 12_F	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)
That's the diabetic sensation. If I've gone over the time and you get an instant hunger feeling and then I have to have erm a biscuit or something to, because I get a slight shake, and I'm fine then. 12_F	
I don't feel full anymore. 12_F	Feeling of fullness (not felt through planning or stops meal)
Its feeling hungry, I know what it's like to feel hungry, I know if I go past one o'clock I need to eat and it tells me, diabetes tells you instantly that you're hungry and you've got your, gone over. Erm. 12_F	Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)
Well your stomach tells you when you're hungry. It rolls doesn't it, it makes gurgling sounds to say you need something down in your tummy. 13_F	
Well I, the only thing, because I live out of the freezer because erm I haven't got the big upright freezer in my kitchen where we had before at the other house. So I eat out the freezer so I really decide in the morning that what's got to come out and then I can build my freezer up again. And then I do that for the simple reason in the winter time if I don't have to go out I don't, and the weathers bad, I don't go out. I've always got a backup and as long as you keep fresh fruit and vegetables and milk of course is most important.	Appetite as a planned need to eat food

Raw Data	Codes
That the three things I always have, and extra milk in the freezer and stuff like that and so I, and by the time you cook it it's defrosted. 13_F	
No sometimes I don't even think like that, then I might have something on toast or something. Erm, it all depends. If I don't feel like cooking and I don't feel particularly hungry I might have something on toast, it's mainly an egg on toast or well I have, I don't know, or I'll have some soup. So I'll think that I'm not that hungry today so I'll have, I'll bypass it. I don't go [puffs cheeks out] I can't and don't feel I want to bloat out or anything now. [Ok, so you don't like the feeling of fullness?] No, no oh God no. That's to me an awful feeling. I'll always leave the table, for years now, with just feeling that little bit I could eat a little bit more but I don't. 'cause you just get uncomfortable. It's all right if you're running a home because you're moving around. But as you're retired you're sitting down a lot aren't you and that's uncomfortable. To me it's uncomfortable. 13_F	Feeling of fullness (not felt through planning or stops meal)
Well I'll look in the fridge and think oh I'll have you know, it all depends, I mean I, I did in the past before I broke my arm I used to make a lot of stews and then put them in separate dishes and then freeze them and think oh I'll take one out and that'll be ok, all I have to do is make mashed potatoes up with it or something like that. Because with the stew you put a numerous amount of vegetables in and in the meat and it, that was sufficient for me. But now erm, no I, I think I, what I have and I never go to bed hungry, if I feel hungry through the middle, if I haven't had a proper meal I might have a bowl of cornflakes you know, with plenty of milk on it. But I never go to bed hungry. And I don't honestly say I really get hungry, you get a 'oh I could eat something' but it's not hunger. 13_F	Appetite as a planned need to eat food Feeling hungry as a physical sensation (nothing, empty, rumbling, odd cold)

Appendix C Ethical approval for qualitative study

NHS
Health Research Authority

North East - Newcastle & North Tyneside 1 Research Ethics Committee

NHSBT Newcastle Blood Donor Centre
Holland Drive
Newcastle upon Tyne
NE2 4NQ

Tel: 0207 104 8089

07 May 2019

Professor Helen Roberts
Professor of Medicine for Older People
University of Southampton
Academic Geriatric Medicine, Mailpoint 807
Southampton General Hospital
Southampton
SO16 6YD

Dear Professor Roberts

Study title:	Assessment of patients aged 65+ years with an upper limb fracture for frailty and sarcopenia for the prevention of future falls and fractures: a feasibility study
REC reference:	18/NE/0377
Protocol number:	MED1580
Amendment number:	Substantial Amendment 1 - 26.03.2019
Amendment date:	26.03.2019
IRAS project ID:	247077

The above amendment was reviewed at the meeting of the Sub-Committee held on 15 April 2019 by correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Interview schedules or topic guides for participants [Amendment1_Provisional semi-structured interview guide V2-dated 26.03.2019.docx]	v2	26 March 2019
Interview schedules or topic guides for participants [Amendment1_Interview (patient) PIS V3-dated 26.03.2019.docx]	v3	26 March 2019
Notice of Substantial Amendment (non-CTIMP)	Substantial	

A Research Ethics Committee established by the Health Research Authority

		Amendment 1 - 26.03.2019	

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

18/NE/0377:	Please quote this number on all correspondence

Yours sincerely
pp

Mr Paddy Stevenson
Chair

E-mail: nrescommittee.northeast-newcastleandnorthtyneside1@nhs.net

Appendix D Scientific output from thesis

Peer-review publications

- Cox NJ, Ibrahim K, Sayer AA, Robinson SM, Roberts HC. Assessment and treatment of the anorexia of ageing. A systematic Review. *Nutrients*. 2019 Jan; 11(114).

- Cox NJ, Morrison L, Ibrahim K, Robinson SM, Sayer AA, Roberts HC. New horizons in appetite and the anorexia of ageing. *Age and Ageing*. 2020 Jan; 00:1-9 afaa014.

- Cox NJ, Lim SER, Howson F, Moyses H, Ibrahim K, Sayer AA, Roberts HC, Robinson S. Poor appetite is associated with six month mortality in hospitalised older men and women. *Journal of Nutrition Health and Aging* 2020 Jul; 24, 1107–1110.

- Cox NJ, Morrison L, Robinson SM, Roberts HC, Ibrahim K. Older individual's perceptions of appetite, its loss, influencing factors and adaptions to poor appetite. A qualitative study. *Appetite* 2021 Dec; 167(1).

Conference abstracts

- Cox NJ, Ibrahim K, Sayer AA, Roberts HC. Anorexia in older people and its treatment. A systematic review. Age and Ageing. 2019 Feb. 48(Supplement_1):i26-i26. Also presented as poster at Federation of Nutrition Societies (FENS) International meeting. 2019 Oct, Dublin Ireland.

- Cox NJ, Lim S, Baylis D, Howson F, Sayer AA, Robinson SM, Robert HC. Poor appetite is common in hospitalised older people and associated with subclinical low mood. Age and Ageing. 2020 Feb. 49(Supplement_1):i34-i36.

- Cox NJ, Ibrahim K, Morrison L, Robinson SM, Roberts HC. How do older people perceive appetite and its loss? A qualitative study. European Geriatric Medicine. 2020 Dec 11, 255.

- Cox NJ, Ibrahim K, Morrison L, Robinson SM, Roberts HC. What influences loss of appetite in older people? A qualitative study. Age and Ageing. 2021 Mar. 50(Supplement_1):i1-i6.

Invited speaker
- 'The anorexia of ageing and the obesity paradox' British Dietetic Association Older Persons Specialist Group Webinar. 2020 November; Virtual

- 'Potentially modifiable influences on appetite and anorexia of ageing' the MRC UK Nutrition Research Partnership (NRP) workshop- Nutrition and Frailty: Opportunities for Prevention and Treatment. 2020 November; Virtual.

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