Poor vitamin D status, obesity and associated health outcomes: focus on groups at risk

PhD by prior output

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Declaration

I am submitting the following five original peer reviewed journal articles for the award of PhD by prior output.

List of original publications

The thesis consists of the following publications referred to in the text with the roman numerals (I-V).

I. Hirani V and Primatesta P. Vitamin D concentrations among people aged 65 years and over living in private households and institutions in England: population survey. Age and Ageing 2005 34(5):485-491; doi:10.1093/ageing/afi153. July 25, 2005.

II. Hirani V, Tull K, Ali A, Mindell J. Urgent action needed to improve vitamin D Status among older people in England! Age Ageing. 2010;39 (1):62-8.

III. Hirani V, Mosdol A , Mishra G. Predictors of 25-hydroxyvitamin D status among adults in two British national surveys. Br J Nutr. 2008; 17:1-5.

IV. Stewart R and Hirani V. Relationship between depression and vitamin D levels in older residents from a national survey population. Psychosom Med. 2010; 72(7):608-12.

V. Hirani V. Generalised and abdominal adiposity are important risk factors for chronic disease in older people: results from a nationally representative survey. J Nutr Health Aging. 2011;15(6):469-78. Available online at http://precedings.nature.com/users/e6d3fc64c08fb5cee67e27ba8be5a4ce).

The aims of this submission are to ensure that it fulfils the criteria for a PhD in both volume and academic content. This sub-set of my publications constitutes a coherent whole, and includes independent and original contribution to knowledge.

A full list of my publications including Government commissioned reports is available in Appendix 9.

This body of work that is in the public domain demonstrates that poor vitamin D status, obesity and associated chronic diseases, are areas of public health concern among particular groups of the population such as older people and deprived populations. It highlights that policies to address these problems are urgently needed to improve quality of life, reduce morbidity and mortality, and be cost-effective for health care.

CONTENTS

Abbreviations

BMI	body mass index
CI	confidence interval
GDS10	10-item Geriatric Depression Scale
HSE	Health Survey for England
IU	international unit
LIDNS	Low Income Diet and Nutrition Survey
NDNS	National Diet and Nutrition Survey
$NDNS_B$	National Diet and Nutrition Survey-on benefits
$NDNS_{NB}$	National Diet and Nutrition Survey-Not on benefits
OR	odds ratio
PTH	parathyroid hormone
RCT	randomized controlled trial
RNI	recommended nutrient intake (United Kingdom)
UVB	ultra-violet B radiation
VDR	vitamin D receptor
WHO	World Health Organisation
25(OH)D	25-hydroxyvitamin D
$1,25(OH)_2D$	calcitriol

Glossary of terms

Body composition	proportions of fat, muscle and fluid
Body mass index	index of weight in relation to height (weight (kg)/height (m^2))
Nutritional intake	intake of nutrients from all sources including food and supplements
Obesity/obese	classified as a BMI of ≥ 30kg/m^2
Over nutrition	a result of an excessive food intake and/or restricted or limited activity
Overweight	classified as a BMI of 25 – 29.9kg/m^2
Under nutrition	a result of an inadequate food intake and/or the presence of metabolically active disease
Underweight	classified by WHO as a BMI of <18.5kg/m^2.

1 Abstract

Vitamin D deficiency affects many population groups; but there are some groups that are at increased risk such as older people. It has been shown that obesity may influence vitamin D status. There is also emerging evidence linking poor vitamin D status to obesity related chronic diseases. This collation of original published work submitted in this thesis includes studies focusing on older people and deprived groups in areas of current public health concern and presents the prevalence and trends in vitamin D status among older people, examines the influence of poor vitamin D status with deprivation, obesity and other health outcomes such as depression. It also examines prevalence and trends in overweight and obesity and associated risk factors among older people.

Particular issues that have been identified in this collation of research are that older people, especially those living in institutions are at a high risk of vitamin D deficiency and that there have been no improvements in vitamin D status among older people living in the community since 1994. The research also shows that poor vitamin D status is associated with obesity among older people living in the community, and prevalence of obesity is increasing among this group. Poor vitamin D status is associated with many risk factors including season, ethnicity, poor health status and depression in older people. It has also been identified that the low income/deprived population is another group at high risk of poor vitamin D status and findings from this study show inverse associations between 25(OH)D levels and body mass index.

Overall the thesis shows that there are population groups at high risk of vitamin D deficiency and obesity. Both of these areas are of public health concern that can impact health outcomes. There is some potential to address and improve the situation through public health policies such as appropriate vitamin D supplementation and food fortification, interventions for the prevention and management of overweight and obesity, and optimising the management of chronic diseases. Policies that include strategies to prevent and address these areas of concern have the potential to improve the quality of life, reduce morbidity and mortality, can be cost effective for the health service and can have an impact particularly on groups at risk.

2 Introduction

Although there are commonly used definitions to classify the 'older population', there is no general agreement on the age when individuals can be classified as 'old' since this differs according to country or context, e.g. the World Health Organisation (WHO,2011) uses the definition of aged 60 and over. In the UK, the Office of National Statistics (ONS, Bayliss and Sly, 2010) uses the age 50 and over, but age 65 and over is the definition commonly used in the context of 'pensionable age'. Despite differences in the definition, globally the proportion of older persons (aged 60 and over), has risen from 8% in 1950 to 11% in 2007, and is expected to reach 22% in 2050 (United Nations, 2009).In the UK the ageing population is increasing rapidly and this trend is likely to continue (Bayliss and Sly, 2010). Age is by far the biggest risk factor for a wide range of clinical conditions that are prevalent today influenced by environmental and lifestyle factors (Kirkwood, 2008).Ageing is associated with physical, mental, social and environmental changes (Gariballa and Sinclair,1998) as well as age-related functional decline of many physiological systems that can affect the nutritional status (Ahmed and Haboubi, 2010).

Vitamin D deficiency affects many population groups; the older population is especially vulnerable to poor vitamin D status due to reduced capacity to synthesise vitamin D from sunlight (Maclaughlin and Holick, 1985), lack of sun exposure as well as lowered renal conversion of vitamin D to its active form (Holick *et al.*, 1989; Holick, 2006). Dietary intake and supplement use are also low among older people in the UK (Finch *et al.*, 1998). It was also important to look at vitamin D status among the low income or deprived population, since there are many factors that may affect their vitamin D status.

The prevalence of overweight and obesity is increasing in all age groups, including among older people (Han *et al.*, 2011). There are direct negative effects of obesity on vitamin D status, since vitamin D is stored in the adipose tissue: there is reduced bioavailability with increased fat mass (Wortsman *et al.*, 2000). Serum levels of 25(OH)D and $1,25(OH)_2D$ are inversely correlated with body mass index (BMI) and fat mass in populations (Konradsen *et al.*,2008; Lagunova *et al.*,2011). Both obesity and poor vitamin D status can be associated with chronic health outcomes, (Stein and Colditz 2004; Holick,2004; Holick,2006) disability, (Zamboni,2002) as well as depression (Lee *et al.*,2010) and other mental health problems (Dening and Barapatre, 2004).

The increase in the ageing population predicts an overwhelming demand on social and health care systems that is likely to increase substantially in the future (Wanless, 2004; Gariballa and Sinclair, 1998). Research into prevention of and interventions for age-related nutrition related conditions to improve the quality of life are important (Franco *et al*, 2009) The purpose of this thesis was to evaluate the vitamin D status of people in the community and institutions, examine trends in vitamin D status and look at associations with risk factors. It also investigates the influence of low income/material deprivation on vitamin D status and examines the associations of poor vitamin D status with depression. It also looks at the prevalence and trends in overweight and obesity and associated risk factors among older people.

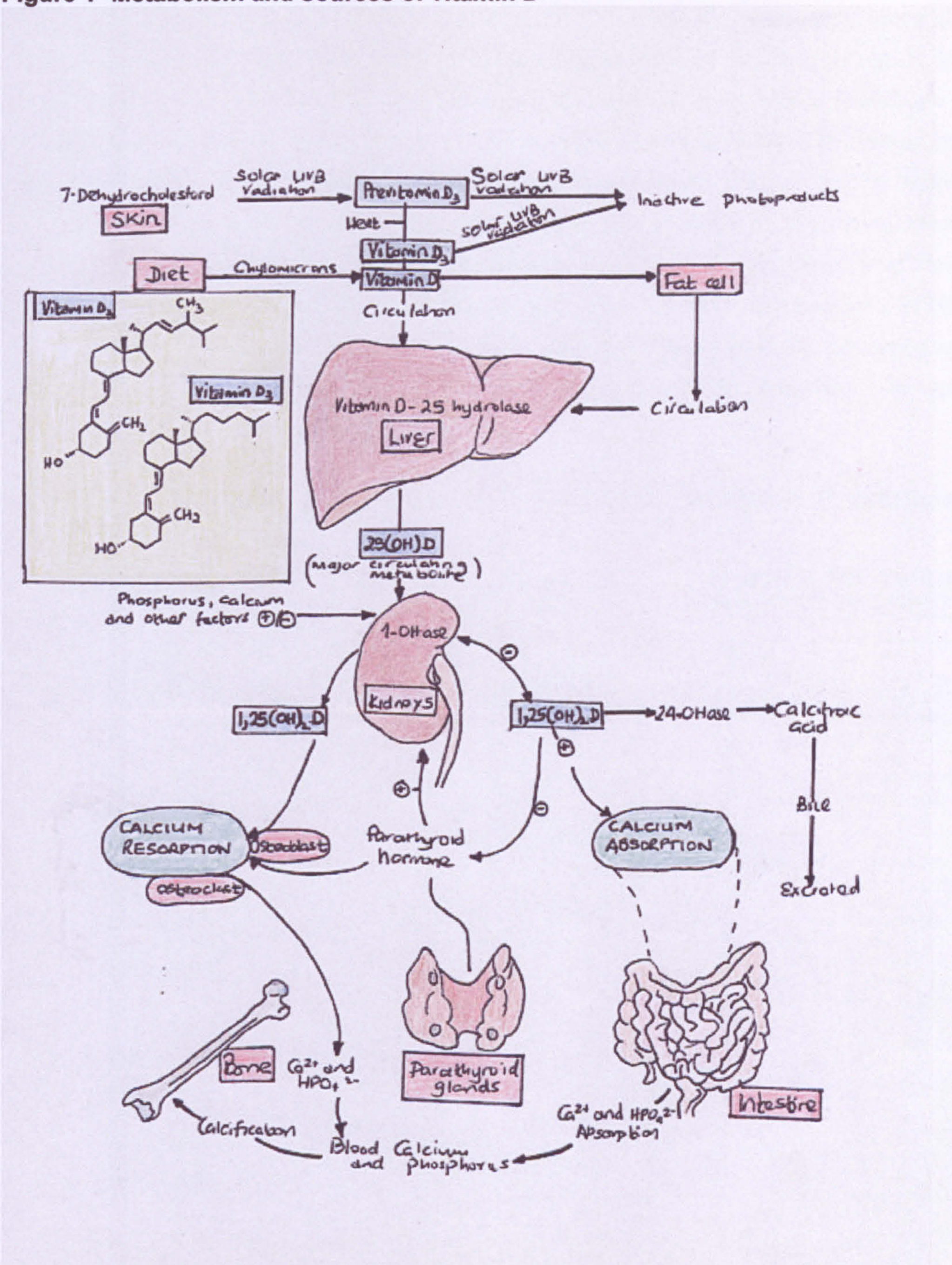
3 Literature review

The following literature review provides a summary of vitamin D metabolism, prevalence of vitamin D status, impacts of vitamin D status on health, and other nutritional risk factors such as obesity.

3.1 Vitamin D metabolism

There are two main forms of vitamin D: vitamin D_3 (cholecalciferol) and vitamin D_2 (ergocalciferol). From this point onwards reference to vitamin D includes both forms. Vitamin D is transported to the liver and metabolised to 25-hydroxyvitamin D (25 (OH)D) the major circulating form of vitamin D and the form measured in most assays. A second hydroxylation takes place in the kidney to the active form 1,25-dihydroxyvitamin ($1,25(OH)_2$)D, also known as calcitriol. Therefore, impaired renal function results in reduced production of $1,25(OH)_2$ D and can effect vitamin D metabolism. The activated form of vitamin D and has three main functions: enhancing absorption of calcium and phosphate from the small intestine, inhibiting parathyroid hormone synthesis and secretion and mineralising the bone matrix (Holick, 2007, Figure 1).

Figure 1- Metabolism and sources of vitamin D



Source: adapted from Holick 2007

Over the past decade there has been an increase in the understanding of the many biological actions for the active form of vitamin D ($1,25(OH)_2$ D). Vitamin D receptors (VDR) have functions both in the cell nucleus as a transcriptional factor to influence the human genome, and in the plasma membrane as a modulator of signal transduction pathways (Norman and Bouillon, 2010). VDRs have the enzymatic actions to convert the primary circulating form of vitamin D, 25(OH)D, to the active form (Holick, 2007). VDRs are expressed throughout the body, including major organs such as the brain, heart, muscle, skin and pancreas, the immune system (both the innate and adaptive), and more classical target tissues such as the intestines and bone (Norman and Bouillon, 2010). This suggests wide-ranging influences for health. Figure 2 below shows the physiological systems, biological responses and vitamin D-deficient related diseases that are associated with an inadequate vitamin D status.

Figure 2- Physiological systems, biological responses and vitamin D deficiency related diseases

PHYSIOLOGICAL SYSTEMS	BIOLOGICAL RESPONSES	VITAMIN D DEFICIENCY RELATED DISEASES
ALL CELLS	Cell cycle regulation Cell proliferation inhibition	Cancer Prostate, breast, colon cancer (prevention) leukemia and other cancers
CALCIUM HOMEOSTASIS	Intestinal calcium absorption & Bone remodeling	Rickets, osteomalacia, osteoporosis
IMMUNE SYSTEM INNATE ADAPTIVE	Stimulate macrophage function & synthesis of antimicrobial peptides Dendritic and T-cell function	Increased prevalence of infection e g. tuberculosis Increased autoimmune diseases; e.g. type 1 diabetes, multiple sclerosis, inflammatory bowel disease, psoriasis
PANCREAS β Cells	Facilitate insulin secretion	Impaired glucose tolerance and diabetes / metabolic
HEART & CARDIOVASCULAR	Renin-angiotensin regulation, coagulation, fibrinolysis, heart muscle function	High renin hypertension, increased cardiovascular risk , increased thrombogenesis
MUSCLE	Promote normal skeletal muscle development; improve muscle strength	Muscle myopathy; increased falls
BRAIN	*In progress* Brain has VDR & 1α-Hydroxylase	Vitamin D deficiency *in utero* alters adult behavior (mice)

Source: adapted from Norman and Bouillon, 2010

3.2 Assessment of Vitamin D Status

Vitamin D status is considered to be reliably determined by assay of serum 25(OH)D concentration as it reflects both synthesis in the skin and that which is absorbed from the diet, a process which is not regulated (Weaver and Fleet, 2004). The half-life of 25(OH)D was previously thought to be in the order of 3 months (Preece *et al.*, 1975) but more recently serum 25(OH)D has been shown to have a half-life of 15 days. Levels of $1,25(OH)_2D$ have a shorter half-life of only 15 hours, therefore 25(OH)D is a better marker for the measurement of vitamin D status (Jones, 2008).

While population-based reference ranges for 25(OH)D have been used for defining vitamin D status, it is more appropriate to define vitamin D status using clinical or functional markers of health risk, because vitamin D status varies so much between countries and populations (being dependent on UV exposure, vitamin D intake, and other factors). There is no consensus on interpretive criteria to define the minimum concentration of 25(OH)D associated with maximal risk reduction. Estimated cut-offs for 25(OH)D concentration are generally based on studies that include case control and cohort studies, randomized controlled trials and small metabolic studies. Although there has been a poor consensus in defining vitamin D status, the following cut-offs have been used (Pearce and Cheetham, 2010, Table 1).

Table 1 Serum 25 (OH) D concentrations, health and disease

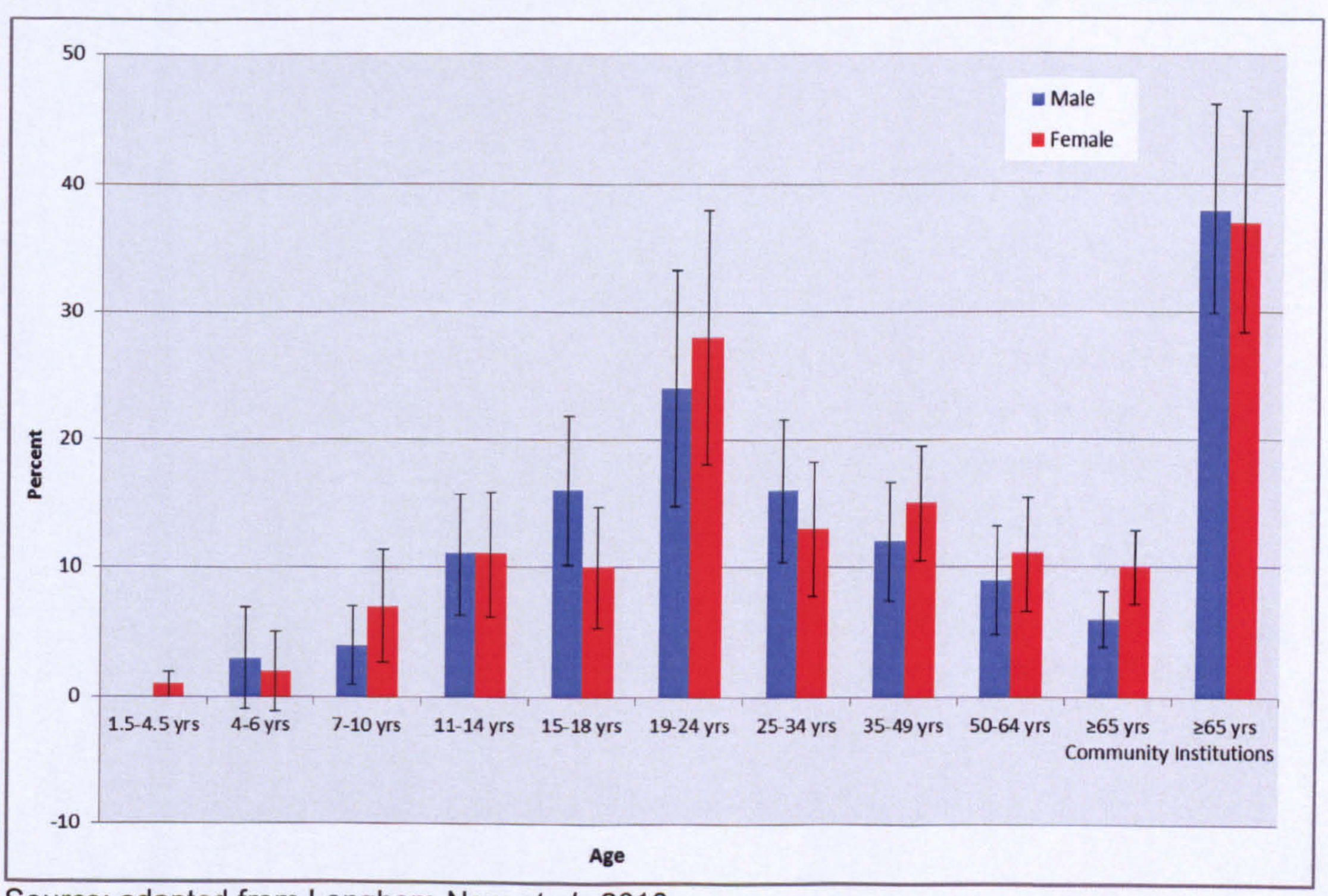
Serum 25 (OH)D concentrations, health and disease	Vitamin D status	Manifestation
<25 nmol/L.	Deficient	Osteomalacia Rickets
25-50 nmol/L	Insufficiency	Associated with disease risk
50-75 nmol/L	Adequate	Healthy
>75 nmol/L	Optimal	Healthy

Source: Pearce and Cheetham 2010.

3.3 Prevalence of vitamin D status

Vitamin D deficiency is the most common nutritional deficiency worldwide (Holick, 2007). Prevalence is dependent on the definition of vitamin D deficiency that is used. Serum 25 (OH)D levels below 75 nmol/L are common in most populations. The percentage of the population with vitamin D insufficiency (25(OH)D concentrations between 25nmol/l and 50nmol/l) is high or very high in most European countries (Mithal *et al.*, 2009). A large proportion of the UK population (about 50% in spring) have vitamin D insufficiency (Hyppönen and Power, 2007). The prevalence of vitamin D deficiency in the UK (based on the current definition of plasma 25(OH)D concentration <25nmol/L) is a common problem among all population groups, as shown in Figure 3 (Gregory *et al* ., 1995; Finch *et al*., 1998; Gregory and Lowe, 2000; Ruston *et al*., 2004), but is severe among ethnic minority groups (Lawson and Thomas,1999; Das *et al*.,1999; Ladhani *et al*., 2004; Bodnar *et al*., 2007; SACN,2007) and older populations. It is particularly severe among older people living in institutions, (Finch *et al*., 1998).

Figure 3: Prevalence of Vitamin D deficiency, by sex and age groups: (data from the NDNS: Gregory *et al*., 1995; Finch *et al*., 1998; Gregory and Lowe, 2000; Ruston *et al*., 2004)



Source: adapted from Langham-New *et al*., 2010

The National Diet and Nutrition Survey (NDNS) shows that mean serum 25(OH)D concentrations in older people in the UK are around 55 nmol/L among those living in the community and 33 nmol/l in institutions (Finch *et al.*, 1998). A high prevalence of vitamin D deficiency in older people is also shown in other countries (Haller, 1999; Passeri *et al.*, 2003). Concerns over vitamin D deficiency worldwide have prompted the WHO to produce guidelines on vitamin D and supplementation (WHO, 2004). In the UK there is renewed government interest in healthy lifestyles (Department of Health, 2008), the role of vitamin D in prevention of osteoporosis (SACN,2007) and initiatives to achieve adequate vitamin D status in older people (Department of Health, 1998).

3.4 Sources of vitamin D

3.4.1 Sun exposure

The primary source of vitamin D is synthesis in the skin under the influence of sunlight. The amount of sun exposure necessary to meet vitamin D requirements depends on factors such as age, latitude, season, time of day, time of year, clothing and skin pigmentation (Holick, 2003). As a result of limited sunlight exposure and reduced capacity of the skin to produce vitamin D, deficiency may occur in healthy older people (Lips *et al.*, 2001).

3.4.2 Dietary Vitamin

In the UK, there are a few dietary sources of vitamin D: these include oily fish (e.g. salmon, mackerel, sardines). Smaller amounts are available from red meat and egg yolks. Other sources of vitamin D are from fortified foods e.g. margarines in which fortification with vitamin D is mandatory (Department of Health, 1998), in order to increase the vitamin D concentration of margarines closer to that naturally found in butter. Some low fat and dairy spreads, low fat milk, powdered milks and breakfast cereals are also fortified with vitamin D but this is not mandatory. The UK Reference Nutrient Intake (RNI) is 10µg/day (400 international units (IU)) for men and women over 65 years. However dietary intake is shown to play a small part in vitamin D status. The NDNS for people aged 65 and over found that vitamin D intake was well below requirements in both men and women at 3.4ug/day (Finch *et al.*, 1998).

3.4.3 Supplement use

Vitamin D is currently prescribed and also available without prescription as a dietary supplement. The vitamin D present in supplements contains both vitamin D_2 and vitamin D_3, but vitamin D_3 has been shown to be more potent than vitamin D_2 (Armas *et al.*, 2004). Most commercial multivitamins contain vitamin D, and many vitamin D supplements are found in combination with calcium, which can have adverse side effects such as constipation.

The UK Government (Department of Health, 1998) recommends that all adults over 65 years should consume 400 IU (10µg) of vitamin D daily. More recently the Scientific Advisory Committee on Nutrition (SACN, 2007) reiterated this advice and further recommended that all adults over 65 years should take a vitamin D supplement to enable them to meet the requirement of 10µg vitamin D daily. Even though there is clear evidence to support this recommendation, there is concern that these recommendations are being overlooked by both health professionals and the general public (SACN, 2007).

It has been recommended by the International Osteoporosis Foundation (IOF) in their 2010 position paper that 800 to 1,000 IU of vitamin D per day for people age 60 years and older (Dawson-Hughes *et al.*, 2010) is sufficient to achieve serum 25(OH)D levels at a threshold of 75 nmol/l, optimal for fall and fracture reduction. In contrast to this, recently, the Institute of Medicine (IOM, 2010) recommended that for older people, a vitamin D intake of 600-800 IU/day is adequate to achieve a threshold of 50 nmol/l. There is clearly some controversy regarding doses of vitamin D Intakes that are recommended.

3.5 Risk factors for poor vitamin D status

In the UK (as mentioned in section 2.3), older people, particularly those living in institutions, are at higher risk of vitamin D deficiency in comparison with other age groups (Figure 3). This may be because of a decline in efficiency of vitamin D synthesis due to decreasing concentrations of 7-dehydrocholesterol (vitamin D precursor) in the skin (Maclaughlin and Holick, 1985) and lowered renal conversion to its active form as people become older (Holick *et al.*, 1989; Holick, 2006). It has been suggested that the lower vitamin D status of older age groups is predominantly due to decreased sun exposure, for example being housebound or institutionalised (Web *et al.*, 1990; Wolpowitz and Gilchrist, 2006). Low endogenous production during winter months can be compensated for by dietary intake and supplement use, but vitamin D intake among older people is also low in the UK (Finch *et al.*, 1998).

Older people living in institutions or in hospital long term are at high risk of vitamin D deficiency due to other factors such as malabsorption (Holick, 2007; Bhutto and Morley, 2008), liver/kidney disease, and use of antiepileptic agents (secondary hyperparathyroidism with these drugs) and glucocorticoids, which can affect vitamin D status (Holick and Chen, 2008).

3.5.1 Season, Climate and Latitude

Synthesis of vitamin D_3 in the body depends upon solar radiation of the skin. Factors that affect solar radiation include atmospheric ozone, angle of the sun, ground elevation, and cloud cover. At greater latitudes, sunlight reaches the earth at a more oblique angle, thereby reducing the potential for vitamin D synthesis; this effect becomes more pronounced as latitude increases, particularly in winter months (Holick, 2004). In most locations in the world around the equator (between latitudes 42°N and 42°S), approximately 30 minutes of skin exposure (without sunscreen) of the arms and face to sunlight can provide adequate vitamin D (WHO/FAO, 2004). However, in many regions of Britain, above latitudes of 37° N, the sun is not strong enough to provide any vitamin D in winter. Even during the remainder of the year, cloud cover can block up to 99% of vitamin D production (Engelson *et al.*,2005). The literature reports strong evidence that vitamin D insufficiency is greater in winter months in the UK (Hyppönen and Power, 2007). Climate and other environmental conditions such as air pollution can also affect dermal vitamin D synthesis.

3.5.2 Sun exposure, Sunscreen and Clothing

Sunscreen use (Matsuoka *et al.*, 1998), urban living associated with an indoor lifestyle, being housebound or deliberately avoiding the sun due to either a preference for fair skin or awareness of advice for skin cancer prevention reduces dermal synthesis of vitamin D. The link between excessive sunlight exposure and skin cancer risk has been clearly established. Campaigns to reduce skin cancer risk in the UK (Cancer Research UK, 2009) may have contributed to reduced opportunities for sun exposure to ensure optimal vitamin D status. These campaigns have advised regular use of sunscreen which may have adversely influenced skin synthesis of vitamin D and vitamin D status among groups at risk of poor vitamin D status. Cancer Research UK recognises the need to balance skin cancer prevention with generation of adequate vitamin D, and has now specified that 'little and often' sun exposure is best i.e. for a few minutes around the middle of the day every day without using sunscreen (Cancer Research UK, 2009). Cultural practices such as complete clothing cover effectively minimise sun exposure (Matsuoka et al., 1999); veiled women have low vitamin D concentrations (Gannage-Yared *et al.*, 2000).

3.5.3 Ethnicity / Skin pigmentation

A genetic influence on dermal vitamin D synthesis is natural skin pigmentation, with melanin acting as a natural sunscreen (Holick, 2004). Therefore, people with darker skin require a longer period of UVB exposure to produce an equivalent amount of vitamin D than a fairer skinned person (Matsuoka *et al.*, 1991), but the capacity to produce vitamin D is not different in Asian than in white skin (Lo *et al.*, 1986). It has also been suggested that altered vitamin D metabolism i.e. increased 25(OH)D -24 hydroxylase activity may be responsible for the high prevalence of low 25(OH)D concentration observed in South Asians (Awumey *et al.*, 1998).

3.5.4 Vitamin D and toxicity

Vitamin D toxicity is rare. There is evidence that up to 250 µg (10,000 IU) per day of vitamin D can be tolerated, (Vieth, 1999) but controversy exists regarding the strength and adequacy of the evidence supporting this conclusion. Ingestion of excessively high doses (>50,000 IU per day) can be associated with hypercalcemia and hyperphosphatemia (Holick, 2007). In the UK, the Expert Group on Vitamins and Minerals (FSA, 2003) concluded that a level of 25µg per day (1,000 IU) of supplementary vitamin D would not lead to adverse effects when consumed regularly over a long period. At present, there is concern about the lack of knowledge and limitations in the available evidence regarding vitamin D toxicity.

3.6 Vitamin D and health outcomes

The importance of vitamin D for bone health is well known. Prolonged vitamin D deficiency in adults clinically manifests itself as osteomalacia and osteoporosis. A growing body of evidence suggests that people who are deficient in 25(OH)D have higher risks for numerous chronic medical conditions (Holick, 2007). Table 2 provides a summarised overview of recent meta-analyses examining the associations between vitamin D and health outcomes such as musculoskeletal conditions, cardiovascular diseases, and cancer.

Table 2: Meta-analyses of vitamin D and health outcomes

Author, year, age	Outcomes	No of studies	Sample size	Dosage	Main results	Conclusion
Musculoskeletal :fractures						
DIPART Group Abrahamsen *et al.*, 2010 Mean age 69.9 years, range 47-107 years	Fractures	7 RCTs	n=68,500	Vitamin D 400IU(10 µg)/day or 800IU(20 µg/day) with 1000 mg calcium or vitamin D alone	Trials using vitamin D with calcium showed a reduced overall risk of fracture: hazard ratio 0.92(95% CI 0.86 to 0.99, P=0.025) Hip fracture All studies: 0.84 (0.70 to 1.01, P=0.07) Studies using 400 IU of vitamin D given with calcium: (0.74, 0.60 to 0.91, P=0.005). For vitamin D alone in daily doses of 400 IU or 800 IU, no significant effects were found.	Vitamin D alone at doses of 400-800IU is not effective in preventing fractures. Co-administration of 1000 mg calcium/day is required for fracture prevention
Bischoff-Ferrari *et al.*, 2009 Older adults aged ≥65 years	Low dose : Non-vertebral fractures Hip fractures High dose : Non-vertebral fractures Hip fractures	12 RCTs 8 RCTs 9 trials 5 trials	n = 42, 279 n = 40, 886 n = 33, 265 n = 31, 872	Vitamin D with or without calcium vs. vitamin D with calcium or placebo ≤400 IU/day vs. ≥400 IU/day	For the lower dose: prevention of non-vertebral fractures: the pooled relative risk (RR): 0.86 (95% CI, 0.77-0.96) Prevention of hip fractures: and 0.91 (95% CI, 0.78-1.05) Non-vertebral fractures: For the higher dose, the pooled RR was 0.80 (95% CI, 0.72-0.89; Hip fractures: 0.82 (95% CI, 0.69-0.97;	The higher dose reduced non-vertebral fractures in community-dwelling individuals (-29%) and institutionalized older individuals (-15%), and its effect was independent of additional calcium supplementation.

Continued

Table 2 continued

Author, year, age	Outcomes	No of studies	Sample size	Dosage	Main results	Conclusion
Musculoskeletal: falls						
Bischoff-Ferrari *et al.*, 2009 Older people aged ≥65 years	Falls	8 RCT	n=2,426	Dose of vitamin D (700-1000 IU/day vs. 200-600 IU/day	High dose supplemental vitamin D reduced fall risk by 19% (pooled relative risk (RR) 0.81, 95% CI 0.71 to 0.92; serum 25(OH)D concentrations of 60 nmol/l or more resulted in a 23% fall reduction (pooled RR 0.77, 95% CI 0.65 to 0.90). Falls were not reduced by low dose supplemental vitamin D (pooled RR 1.10, 95% CI 0.89 to 1.35 or serum 25 (OH)D concentrations of < 60 nmol/l (pooled RR 1.35, 95% CI 0.98 to 1.84). Active forms of vitamin D reduced fall risk by 22% (pooled RR 0.78, 95% CI 0.64 to 0.94).	Supplemental vitamin D at doses of 700-1000 IU a day reduced the risk of falling among older individuals by 19% Doses of supplemental vitamin D of less than 700 IU or serum 25 (OH)D concentrations of less than 60 nmol/l may not reduce the risk of falling among older individuals.
Stockton *et al.*,2010 Adults>18 years	Muscle strength	17 RCT	n=5,072	All forms and doses of vitamin D supplementation with or without calcium supplementation were included	No significant effect of vitamin D supplementation on grip strength (SMD −0.02, 95%CI −0.15,0.11) or proximal lower limb strength (SMD 0.1, 95%CI −0.01,0.22) in adults with 25(OH)D levels >25 nmol/L. Large effect of vitamin D supplementation on hip muscle strength (SMD 3.52, 95%CI 2.18, 4.85) in vitamin D deficient adults(25(OH)D <25 nmol/L)	Vitamin D supplementation does not have a significant effect on muscle strength in adults with baseline 25(OH)D >25nmol/L. However, a limited number of studies demonstrate an increase in proximal muscle strength in adults with vitamin D deficiency.
Kalyani *et al.*, 2010 Older adults aged ≥60 years	Falls	10 RCT	n=2,932	Vitamin D at doses 200-1,000 IU	Vitamin D therapy (200-1,000 IU) resulted in 14% (relative risk (RR) =0.86, 95% CI=0.79-0.93) fewer falls than with calcium or placebo. Subgroups had significantly fewer falls: community-dwelling (aged <80), adjunctive calcium supplementation, no history of fractures or falls, duration longer than 6 months, cholecalciferol, and dose of ≥800 IU.	Vitamin D treatment effectively reduces the risk of falls in older adults.

Table 2 continued

Author, year, age	Outcomes	No of studies	Sample size	Dosage	Main results	Conclusion
Cardiovascular disease(CVD)						
Parker J, *et al.*, 2010 Mean age 40.5-74.5 years	Cardio-metabolic disorders	28 studies (19 cross-sectional, 3 case–control 6 cohort studies)	n=99,745	Highest vs. lowest 25(OH)D	**Overall cardiometabolic disorders** :OR 0.57, 95% (CI 0.48–0.68 **Cardiovascular disease:** OR 0.67 (0.55–0.81) **Metabolic syndrome** OR: 0.49 (95% CI 0.38–0.64) **Diabetes** OR 0.45 (95%CI 0.25–0.82)	High levels of vitamin D are associated with a reduced prevalence of cardiovascular disease, metabolic syndrome and diabetes.
Pittas *et al* ., 2010 Mean age 40 to 70 years	Cardio metabolic outcomes (Type 2 diabetes hypertension, or cardiovascular disease).	13 observational studies, 14 cohorts and 18 RCTs	Vitamin D and type 2 diabetes (n=95, 243)	Highest vs. lowest vitamin D status groups(doses differed)	Analyses (4 cohorts) reported a lower incident diabetes risk in the highest vs. lowest vitamin D status. 8 trials found no effect of vitamin D supplementation (400 to 5714 IU/d) on glycemia or diabetes.	The association between vitamin D status and cardiometabolic outcomes is uncertain. Trials showed no clinically significant effect of vitamin D supplementation at the dosages given. Large Heterogeneity between studies
			Vitamin D and hypertension (n=32 181)	Lowest(<37 to 51 nmol/L) vs highest (>75 to 81 nmol/L)	3 cohorts, lower 25 (OH) D concentration category was associated with incident hypertension (relative risk, 1.8 [95% CI, 1.3 to 2.4]).	
				Vitamin D alone or with calcium at dosages :400 to 8571 IU/d.	Analyses of 10 trials, supplementation non significantly reduced systolic blood pressure (weighted mean difference, -1.9 mm Hg [CI, -4.2 to 0.4 mm Hg]) and did not affect diastolic blood pressure (-0.1 mm Hg [CI, -0.7 to 0.5 mm Hg]).	
			Vitamin D and CVD (n=43, 527)	Lowest vs highest	Lower 25(OH)D concentration was associated with incident CVD in 5 of 7 analyses (6 cohorts).	
			4 RCT(n=37,162)	Vitamin D doses differ (with/without calcium) 700IU/d-5714IU/d	Four trials found no effect of supplementation on CVD outcomes	

Table 2 continued

Author, year, age	Outcomes	No of studies	Sample size	Dosage	Main results	Conclusion
Cardiovascular outcomes: hypertension						
Burgaz *et al.*,2010 Adults>18 years	Hypertension	18 studies	78 028	Highest versus the lowest category of blood 25(OH)D concentration	Prospective and cross-sectional studies with blood 25 (OH)D concentrations as the exposure and hypertension as the outcome The pooled odds ratio of hypertension was 0.73 [95% confidence interval (CI) 0.63-0.84] for the highest versus the lowest category of blood 25-hydroxyvitamin D concentration. In a dose-response meta-analysis, the odds ratio for a 40 nmol/l (16 ng/ml) (approximately 2 SDs) increment in blood 25(OH)D concentration was 0.84 (95% CI 0.78-0.90).	Findings from this meta-analysis indicate that blood 25 (OH)D concentration is inversely associated with hypertension.
Wu *et al.*, 2010 Mean age 64 years	Blood pressure	4 RCTs	429	The vitamin D dose used in one RCT was 200 IU/d, while the other three RCTs used 400 IU/d or above. Between 600 mg/d and 1200 mg/d of calcium supplementation was used with vitamin D supplementation in 3 RCTs.	Vitamin D supplementation reduced systolic blood pressure (SBP) by 2.44 mm Hg (weighted mean difference [WMD]: -2.44, 95% confidence interval [CI]: -4.86, -0.02), but not diastolic blood pressure (DBP) (WMD: -0.02, 95% CI: -4.04, 4.01) compared with calcium or placebo	Oral vitamin D supplementation may lead to a reduction in systolic blood pressure but not diastolic blood pressure. Only four trials and small but statistically significant reduction in systolic blood pressure.

Table 2 continued

Author, year, age	Outcomes	No of studies	Sample size	Dosage	Main results	Conclusion
Cancers						
Gandini *et . al.*,2011 Mean age 50-74 years	Cancers: Colorectal Breast Prostate	Case-control/cohort 9 studies 10 studies 11 studies	 2,630 cases 6,175 cases 3,956 cases	Serum 25(OH)D* : Upper bound of lowest quantile or group vs lower bound of lowest quantile or group	The summary relative risk (SRR) and (95% CI) for a 10 ng/ml (25 nmol/l) increase in serum 25(OH)D was 0.85 (0.79; 0.91) for colorectal cancer; 0.89 (0.81; 0.98) for breast cancer; and 0.99 (0.95; 1.03) for prostate cancer.	A consistent inverse relationship between serum 25-hydroxyvitamin D levels and colorectal cancer was found. No association was found for breast and prostate cancer.
Yin *et al.*, 2010 Mean ages 20-90 years	Breast cancer	10 case - control studies	6147 cases 6754 controls	An increase of 25(OH)D by 20ng/ml (50nmol/L)	Summary RRs (95% CI) for an increase of 25(OH)D by 20ng/ml (50nmol/l) were 0.59 (0.48-0.73), 0.92 (0.82-1.04) and 0.73 (0.60-0.88) with P values of <0.001, 0.164 and 0.001 for case-control studies, nested case-control studies and both study designs combined, respectively Large heterogeneity between studies	Case-control studies with measurement of 25(OH)D after diagnosis suggest an inverse association. Prospective studies with measurement of 25(OH)D years before diagnosis show a statistically significant inverse association that remained unconfirmed .

*Lower quantile was used as reference category; upper bound in ng/ml and mean values when upper level not available.
Lower bound in ng/ml and mean values when lower level not available.

Table 2 continued

Author, year, age	Outcomes	No of studies	Sample size	Dosage	Main results	Conclusion
Cancers						
Fedirko *et al.*, 2010 Age 30–74 years	Colorectal cancer	3 case-control studies	616 colorectal adenoma cases and 770 polyp-free controls.	Highest versus lowest quartiles of circulating 25(OH)D concentrations	Higher circulating 25(OH)D) concentrations were statistically significantly associated with decreased colorectal adenoma risk (highest vs. lowest quartile odds ratio = 0.59, 95% confidence interval: 0.41, 0.84). The observed inverse association was stronger among adults who used non steroidal anti-inflammatory drugs regularly (highest vs. lowest quartile OR = 0.33, 95% confidence interval: 0.19, 0.56).	These findings support the hypothesis that greater vitamin D exposure may reduce the risk of colorectal adenoma and suggests that the association is stronger in participants using anti-inflammatory agents.
Stolzenberg *et al.*, 2010 Median age 56-68 years	Pancreatic cancer	8 cohorts	952 cases and 1,333 controls	25(OH)D concentrations (≥100 nmol/L) or low (<25 nmol/L) 25(OH)D concentrations compared with the reference category (50–<75 nmol/L).	No significant associations were observed for participants with lower 25(OH)D status. However, a high 25(OH)D concentration (≥100 nmol/L) was associated with a statistically significant 2-fold increase in pancreatic cancer risk overall (odds ratio = 2.12, 95% confidence interval: 1.23, 3.64).	A high 25(OH)D concentration ≥100nmol/L) was associated with a statistically significant two-fold increase in pancreatic cancer risk overall., Recommendations to increase vitamin D concentrations in healthy people for the prevention of cancer should be carefully considered.

Table 2 continued

Author, year, age	Outcomes	No of studies	Sample size	Dosage	Main results	Conclusion
Mortality						
Grandi *et al.*,2010 Mean age 59 to 78.6 years (4 studies) Mean age 44.8 to 74 years (5 studies)	CVD mortality	Prospective studies: 4 incident studies on on CVD events 5 mortality studies on CVD death	n=24387 n=5253	Lowest vs. highest 25(OH)D	Meta-analysis indicated a significant association of low 25(OH)D with CVD mortality (HR = 1.83 [1.19–2.80]; Combining estimates from incidence and mortality studies yielded a pooled hazard ratio of 1.64 [1.27–2.11], supporting an association of low 25(OH)D with CVD outcome.	Meta-analysis shows an inverse association between 25(OH)D and cardiovascular risk. However, given the heterogeneity of eligible studies in terms of study population, outcome and exposure level definitions, there remains an urgent need for additional large-scale studies to further elucidate the role of vitamin D as a potential risk marker and maybe even a modifiable risk factor for CVD.
Semba *et al.*,2010 Adults aged ≥ 65 years	CVD mortality	1 longitudinal study InCHIANTI (Invecchiare in Chianti, Aging in the Chianti Area) study	n=1006	Highest (>66nmol/L) vs lowest (<26nmol/L) quartiles of serum 25(OH)D	Participants in the lowest quartile of serum 25(OH)D had increased risk of all-cause mortality (Hazard Ratio (H.R.) 2.11, (95% C.I: 1.22-3.64, P=0.007) and cardiovascular disease mortality (H.R. 2.64, 95% C.I.: 1.14-4.79, P=0.02), in multivariate Cox proportional hazards models that adjusted for age, sex, education, season, physical activity and other potential confounders.	Older community-dwelling adults with low serum 25(OH)D levels are at higher risk of all-cause and cardiovascular disease mortality

Vitamin D and falls and fractures

Evidence from meta -analysis of fall prevention trials, among older individuals (aged 65 or more) showed that vitamin D supplementation at doses of 700-1,000 IU per day reduced falls (Bischoff-Ferrari *et al.*, 2009; Kalyani *et al.*, 2010) and 25(OH)D levels of 75-112nmol/L were required for non-vertebral fracture prevention (Bischoff-Ferrari *et al.*, 2009) Vitamin D at doses of 10µg with calcium significantly reduced the risk of fracture (Abrahamsen *et al.*, 2010).

Evidence from a meta-analysis of RCTs does not support the effect of vitamin D supplements on muscle strength and function in the elderly with baseline 25(OH)D greater than 25 nmol/L, but in a limited number of studies an increase in proximal muscle strength was shown in adults with vitamin D deficiency (Stockton *et al.*,2010).

CVD and other health conditions

Evidence from meta-analysis among older people (Parker *et al.*, 2010) shows a significant association between high levels of vitamin D and a decreased risk of developing cardiovascular disease (33% reduction compared with low levels of vitamin D), type 2 diabetes (55% reduction) and metabolic syndrome (51% reduction). Another meta-analysis by Pittas et al., (2010), shows association between vitamin D status and cardiometabolic outcomes to be uncertain with no clinically significant effect of vitamin D supplementation at the dosages given, which varied between the studies. There is weak evidence to support the effect of vitamin D on blood pressure (Pittas *et al.*, 2010; Burgaz *et al.*,2010; Wu *et al.*,2010).

Mortality

Older adults living in the community with low serum 25(OH)D levels are at higher risk of all-cause and cardiovascular disease mortality (Autier and Gandini, 2007; Ginde *et al.*, 2009). Ginde *et al.* (2009) highlighted that randomised controlled trials of vitamin D supplementation in older adults are warranted to determine whether this association is causal and reversible.

Cancer

Table 2 shows overall that low vitamin D status is associated with a higher risk of colorectal cancer (Gandini *et al.*, 2010), but the evidence is contradictory for breast cancer (Yin *et al.*, 2010; Gandini *et al.*, 2011) and there is a lack of association for prostate cancer (Gandini *et al.*, 2011). A pooled analysis of 10 cohort studies found that levels of 25(OH)D >75nmol/L do not reduce the risk of uterine, oesophageal, stomach, kidney or ovarian cancers, nor non-

Hodgkin lymphoma, (Helzlsouer, 2010) but a high 25(OH)D concentration (≥100nmol/L) was associated with a two-fold increased risk of pancreatic cancer (Stolzenberg *et al.*, 2010).

Vitamin D and depression

Cohort and cross-sectional studies (Hoogendijk *et al.*, 2008; Ganji *et al.*, 2010) have shown that depression may be associated with vitamin D deficiency. This may reflect influences of depressive states on sunlight exposure, diet and nutritional supplementation. However, there are also plausible biological pathways for a role of vitamin D deficiency in the pathogenesis of depression, including effects on nerve growth factor synthesis, (Wion *et al.*,1991) and a variety of potential neurotransmitter targets (Stumpf,1995).

Other diseases

Other diseases considered to be related to vitamin D deficiency include multiple sclerosis in younger people aged 18-48 years, (Mungar *et al.*,2006), lower respiratory diseases such as influenza and pneumonia (Cannell *et al.*, 2008), and septicaemia (Jeng *et al.*,2009). A disease with limited support is dementia, based in part on studies on mood and cognitive impairment (Wilkins, 2006; Llewellyn *et al.*, 2009).

3.6.1 Changes in body composition among older people

Aging causes a decline in the basal metabolic rate (mainly due to decreased fat-free mass), total body weight, height, and skeletal mass (Roberts and Rosenberg, 2006). This can result in a loss of up to 3 kg of lean body mass per decade after the age of 50 (Prentice and Jebb, 2001).

Overweight and obesity

Overweight or obesity occurs when energy intake exceeds energy expenditure (through metabolism and daily physical activity). Older people expend less energy as a result of lower metabolic rates and changes in lifestyle with increased levels of sedentary behaviour (Phillips, 2003) resulting in weight gain. Obesity has additional problems which are of particular concern for older people as ageing results in sarcopenia (loss of muscle mass). Older people who are obese can develop sarcopenic obesity and this is a major determinant of poor health status in older people (Zamboni et al., 2007).

Sarcopenia and vitamin D

Sarcopenia is also associated with a reduction in muscle strength (Thomas, 2007). Vitamin D has direct effects on muscle strength modulated by specific vitamin D receptors present in human muscle tissue (Bischoff-Ferrari *et al.*, 2004). Myopathy from severe vitamin D deficiency has been shown to be reversible with vitamin D supplementation (Glerup *et al.*, 2000). A meta-analysis of trials in older people with vitamin D deficiency has shown that vitamin D supplementation improved proximal muscle strength (Stockton *et al.*, 2010).

Obesity and vitamin D

Vitamin D is fat soluble therefore some of it is stored in the adipose tissue. An inverse correlation exists between body fat content and serum 25(OH)D concentrations in healthy older men and women (Arunabh *et al.*, 2003; Lucas *et al.*, 2005; Bolland *et al.*, 2006; Lagunova *et al.*, 2011). In the obese, adipose tissue may serve as an 'irreversible sink' for vitamin D (Wortsman *et al.*, 2000; Holick, 2004). Wortsman and colleagues (2000) showed that obesity affects the release of vitamin D into the circulation. This association may exacerbate the reported relationships between low vitamin D status and common chronic conditions which occur more commonly in obesity (Field *et al.*, 2001).

3.6.2 Prevalence of overweight, obesity and underweight in older people

Prevalence of obesity

The global prevalence of obesity has been increasing rapidly in all age groups, including older people, and is a cause for major concern (Haslam, 2006). The World Health Organisation has described the situation as an epidemic (WHO, 2011). In England in 2009, 66% of men and 57% of women were either overweight or obese (Craig and Hirani, 2010) It has been reported that England has some of the highest levels of obesity in Europe (Foresight, 2007) but recently there are indications that the trends in obesity may be levelling off in adults and even declining in children (Craig and Hirani, 2010).

Association with health outcomes

Obesity is an important public health burden among older people due its association with poor health and well-being (Kopelman, 2000) reduced life expectancy (Corrada *et al.*, 2006) and premature death (Jonsson *et al.*, 2002) due to associated co-morbidities such as cardiovascular disease (CVD), diabetes, hypertension, stroke, and certain forms of cancer (Stein and Colditz 2004). The literature shows quite conflicting associations between obesity and mortality in older people (Janssen *et al.*, 2005; Corrada *et al.*, 2006); Flegal and Graubard, 2009). A systematic review (Heieat *et al.*, 2001) showed the overall association between BMI and all-cause mortality in people over 65 as a flat-bottomed U-shape curve, with increased mortality in those with BMI above 30-31 kg/m^2. It has also been suggested that associations of BMI with mortality are at least in part due to confounding factors such as physical activity, diet, body composition or fat distribution, so it is difficult to isolate the causal effects (Candiff, 2006; Flegal, 2006).

A recent meta-analysis has shown that there is very little research on the benefits of weight reduction in older obese people, though intentional weight loss has been shown to reduce all-cause mortality in males aged 56-75 years (Witham and Avenell, 2010). There seem to be a limited number of good quality studies of older people that have compared diet and exercise interventions with diet alone but the greater benefits of combined diet and exercise regimes found in this analysis were consistent with studies using a similar design in younger subjects. Studies with specific goals achieved greater weight reduction though no significant improvements in exercise capacity, physical function, quality of life or in cardiovascular events or risk factors emerged from the meta-analysis (Witham and Avenell, 2010).

A previous systematic review (Bales and Buhr, 2008) that included weight reduction studies for a short duration showed probable clinically beneficial outcomes in physical activity, osteoarthritis and hypertension and possibly also in type 2 diabetes and coronary heart disease. This review excluded studies in which the weight loss achieved was <2kg or 3% of baseline over 6 months, suggesting that achieving greater weight loss is more likely to have significant benefits. However the benefits shown in shorter duration studies may not be sustainable.

3.6.3 Assessment of overweight and obesity

Body mass Index (BMI) and waist circumference (WC)

Body Mass Index (BMI) is a widely accepted measure of weight for height.

The WHO (WHO, 2000) and the National Institute for Health and Clinical Excellence guideline (NICE, 2007) classifies BMI into the following groups (Table 3):

Table 3 BMI classification

BMI (kg/m^2)	Description
Less than 18.5	Underweight
20 to less than 25	Normal
25 to less than 30	Overweight
30 or more	Obese
40 or more	Morbidly obese

Source: WHO (2000) and NICE (2007)

There is currently no consensus on an appropriate cut off for underweight in people aged ≥65. Less than 20 kg/m^2 is often used to define underweight in older people (Price *et al.*, 2006).

Waist circumference

Despite BMI being regularly used to in the assessment of nutritional status, it is a crude marker that does not take into consideration body composition or where fat is stored. This is important as visceral abdominal fat (i.e. fat stored around the abdominal area) is associated with increased risk of cardiovascular disease and type 2 diabetes (Cook *et al.*, 2005). It has therefore been postulated that waist circumference may be a better measure than BMI to identify those with a health risk from their body shape (WHO, 2000). Waist circumference can be considered an appropriate indicator of body fatness and central fat distribution (Pouliot *et al.*,1994). Among older people, the fat distribution changes considerably and abdominal fat tends to increase with age (Kyle *et al.*, 2001). The definition of raised WC is, in accordance with the ATP (Adult Treatment Panel) III (National Institutes of Health, 2001), >102cm in men and >88cm in women.

3.6.4 Common factors affecting nutritional status

Low income

In 2008/2009, 22% of the UK population were living in poverty, defined as living below 60% of the median net disposable household income before housing costs (ONS, 2010). Although the level of older people living in poverty has fallen in the past decade, 17% of pensioners continue to live in poverty (ONS, 2010). This age group suffers declining health and poor nutritional status, as identified in the Low Income Diet and Nutrition Survey (LIDNS, Nelson *et al.*, 2007). Further analysis of the LIDNS data found that older men and in particular those who live alone may be at even more risk of an inadequate diet (Holmes et al., 2008). Diet has been known for many years to play a key role as a risk factor for chronic diseases such as cardiovascular disease, hypertension and some forms of cancer that can continue into later life (WHO, 2003).

Dental Health

Dental health affects the nutritional status of older people. Studies using data from the National Diet and Nutrition Survey (NDNS) showed the effects of being edentulous on nutritional status among older people. Intakes of non-starch polysaccharides, protein, calcium, iron, niacin and vitamin C were significantly lower in the edentulous individuals, (Sheiham *et al.*, 2001) and having few or no natural teeth was associated with a greater risk of both being underweight and obese (Sheiham *et al.*, 2002). Another study among older people using the HSE 2000 data showed strong associations between dental status and cognitive impairment, important determinants of nutritional status (Stewart and Hirani, 2007).

Depression

Depression in older people is common and substantially disabling (Moussavi *et al.*, 2007). It is associated with worse general health, probably both as a cause and consequence (Prince *et al.*, 1998). Micronutrient deficiencies (whether relatively low levels or clinical deficiency states) are related to depression (Moussavi *et al.*, 2007; Jacka *et al.*, 2009) and are likely to be particularly important in older people because of higher levels of morbidity and frailty. However it is not known whether a nutritional deficit is the cause or the consequence of impaired cognition (Del Parigi *et al.*, 2006).

4 Aims and objectives

4.1 Aim

To investigate vitamin D status and obesity and identify the extent of these public health problems among population groups

4.2 Objectives

1. To determine the prevalence of poor vitamin D status among older people in England living in institutions and in the community
2. To examine trends in vitamin D status in older people in the community since 1994.
3. To examine vitamin D status in low income groups
4. To examine associations of poor vitamin D status with other risk factors
5. To examine overweight and obesity and risk factors among older people:
   a. trends in obesity 1993-2008
   b. obesity and risk factors for chronic diseases
6. To highlight the policy implications of the findings

5 Methods

In this section, an overview of surveys will be provided, followed by a brief description of the sample (Table 4). Common factors in all these surveys are that they are based on a random probability sample of private household addresses (except that HSE 2000 also included institutions) using multi-stage stratified sampling. Data on socio-demographic information was collected by face-face computer aided personal interviewing (CAPI) in the household. The study methods for original papers (I-V) are described in detail in the papers. Further information can be found in the Appendices 2-7.

A summary of the details for studies included in this thesis are outlined in Table 4 below:

Table 4 Information about the nationally representative cross-sectional surveys included in the thesis

Study	Objectives addressed	Age	Study information	Dates of Fieldwork	Data Collection	Study Participants (N) (with valid measurements) Response rates (%) for measurement of interest
HSE 2000 Prior *et al.*,2002 **(I)**	1,2,4,5,6	≥65 years	Health of older people living in private households and Institutions, England 2000.	January 2000 - March 2001	Self-completion; Clinical measurements; Physical measurements.	***Private households***
						322 men 320 women Valid vitamin D: 64%
						Institutions
						201 men 454 women Valid vitamin D: 61%
HSE 2005 Craig and Mindell,2007 **(II,IV and V)**	1,2,4,5,6	≥65 years	Health of older people: living in private households, England 2005.	January 2005-June 2006	Self-completion; Clinical measurements; Physical measurements.	***Private households:*** 950 men, 1,120 women Valid vitamin D: 66% BMI,1512 men, 1,747 women WC, 1393 men, 1,617 women Valid BMI:76% Valid WC:96%

Continued...

Table 4 continued

Study	Objectives addressed	Age	Study information	Dates of Fieldwork	Data Collection	Study Participants (N) (with valid measurements) Response rates (%) for measurement of interest
NDNS Finch *et al.*, 1998 **(II)**	1,2,6	≥65 years	Nutritional status of older people living in private households and institutions in the UK	October 1994-September 1995	Health-and-lifestyle interview, a four-day weighed diet record, anthropometric measurements and a fasting blood sample for biochemical indices.	***Private households:*** 476 men, 451 women Valid vitamin D:57%
NDNS Ruston *et al.*, 2004 **(III)**	3,4,6	19-64 years	Nutritional status of a sample of people aged 19-64 living in private households in UK.	July 2000 - June 2001	Interview on general eating habits and health. Record of food eaten and drank at home and outside of home, over a seven-day period. Anthropometric measurements and a fasting blood sample for biochemical indices.	***Private households:*** Not on benefits, 508 men, 546 women On benefits, 84 men,159 women Valid vitamin D:60%
LIDNS Nelson *et al.*,2007 **(III)**	3,4,6	19 and over	Nutritional status of a sample of low-income or materially deprived people aged 19 and over living in private households in UK.	November 2003 - January 2005	Self-completed questionnaire four 24-hour recalls of diet. Physical measurements, height, weight and blood pressure. A blood sample for those aged eight years old and over.	***Private households:*** 246 men, 546 women Valid vitamin D:51%

5.1.1 HSE 2000 (I)

The HSE 2000 (Prior *et al.*, 2002) was designed to provide data at both national and regional level from a sample of older people (aged 65 and over). For the institution sample, 677 care homes were selected. Interviews were achieved with 1,217 residents. The private household sample (6,800 addresses) was drawn from the Postcode Address File (PAF). 1,677 residents aged 65 and over were interviewed. A blood sample was obtained from 61% of the total institution sample (1,217) and 64% of the private household sample (1,677) aged 65 and over. A valid 25(OH)D sample was obtained from 1,766 participants (708 men and 1,058 women).

5.1.2 HSE 2005 (II, IV and V)

In 2005, the HSE included a nationally representative general population sample of English people aged ≥65, living in private households: 1,897 men and 2,372 women were interviewed (Craig and Mindell, 2007). The sampling design included the PAF as the primary sampling frame. It comprised a core (general population) sample and a boost sample (interviewers screened households to increase the sample of people aged ≥65). The overall response rate was 71% in the general population sample and 74% in the boost sample.

Data collection (I, II, IV and V)

Interviewers collected data from participants by computer-aided personal interview (CAPI) on socio-demographic aspects (e.g. age, sex, ethnicity and region), health behaviours (e.g. general self-reported health, smoking etc) and doctor-diagnosed health conditions (ischaemic heart disease, stroke and diabetes). In HSE 2005 (II and IV) additional measures about depressive symptoms were included using the 10-item Geriatric Depression Scale (GDS10), with a score of three or more defined as case level, according to usual practice (Yesavage,1998; Stewart *et al.*, 2001). Height and weight measurements were taken according to the HSE standardised protocol (see Appendix 7) to calculate BMI.

After the interview, those who agreed had a nurse visit. Nurses collected information including current medication and vitamin supplement usage; took measurements such as waist circumference, demi-span, and blood pressure; and obtained non-fasting blood samples (see Appendix 6). Generalised obesity refers to BMI ≥30 kg/m^2 and abdominal obesity was defined in accordance with the ATP (Adult Treatment Panel) III (National Institute of Health, 2001) as WC >102cm in men and >88cm in women (V).

Detailed information on data collection can be found in Appendix 4.

Non-response weighting

Non-response occurs when selected individuals or households decline to take part in the study or cannot be contacted. This can introduce bias as some groups are more likely to decline than others. Additionally, those who are not eligible (e.g. unable to give informed consent or to understand and answer the questions, due to cognitive or language problems) are also defined as non-responders in HSE. Non-response weighting is a statistical calculation that improves the precision of survey estimates, giving greater confidence that the estimate presented is reflective of the general population. In 2003, the HSE introduced non-response weighting for the first time. Data from HSE 2003 onwards are weighted for non-response (different weights are applied for non-response to each stage i.e. for the interviewer, nurse visit and blood samples). However, non-response weights are not available for previous HSE data sets (1993 -2002).

The detailed methods and further information for HSE 2000 can be found in Appendix 3, and HSE 2005 in Appendix 4.

5.1.3 NDNS (I, II, III)

The NDNS sample design included using all postal sectors within mainland Britain. In Paper II, the NDNS sample included participants aged 65 and over living in private households. It included analyses of serum 25(OH)D concentrations for (927 people:476 men and 451 men) and). The NDNS was carried out from October 1994 to September 1995.

In paper III, the NDNS sample included people aged 19-64 years (excluding pregnant or breastfeeding women). Data were collected 2000-2001. There were 3,704 eligible respondents; 61% completed the dietary interview. Participants were asked to provide measurements, including anthropometry, blood pressure, and urine sample. Blood samples were obtained from 61% of men and 59% of women in the dietary sample. A valid serum 25(OH)D sample was obtained from 592 men and 705 women.

5.1.4 LIDNS (III)

Data were collected 2003-2005. Participants aged ≥19 years consisted of 1,048 men and 2,019 women. Of these, 96% started the individual questionnaire or the first of four dietary recalls. Ninety percent agreed to be visited by a nurse, 81% were successfully revisited.

The detailed methods and further information on areas regarding sample design, protocols etc. for the NDNS and LIDNS can be found in the Appendix 5.

5.2 Vitamin D analysis (I, II, III, IV)

5.2.1 Laboratory analysis of the serum 25(OH)D

Vitamin D analyses in HSE and LIDNS were carried out at the Royal Victoria Infirmary (RVI) in Newcastle upon Tyne using the DiaSorin radio immunoassay (RIA) kit (DiaSorin Inc., Stillwater, MN, USA, formerly known as INCSTAR). The vitamin D analysis for the NDNS was carried out using the same methods. Quality control procedures comprised both internal and external procedures. Detailed information on internal and external quality control procedures are available in the reports (Finch *et al.*, 1998; Ruston *et al.*, 2004, FSA 2004, Craig and Mindell, 2007).

Internal quality control (IQC)

The purpose of internal quality control (IQC) was to ensure reliability of an analytical run, identify, and prevent the release of any errors in an analytical run.

The laboratory obtains a supply of quality control materials, usually at more than one concentration of the analyte. Target (mean) values and target standard deviations (SD) are assigned for each analyte. Target assignment includes evaluation of values obtained by the laboratory from replicate measurements (over several runs) in conjunction with target values provided by manufacturers of IQC materials. The standard deviation and the coefficient of variation (CV) are measures of imprecision. Internal QC values are assessed against an acceptable range for the analyte.

External quality assessment (EQA)

The laboratories performing the 25(OH)D analyses took part in the Vitamin D External Quality Assessment Scheme (DEQAS). EQA permits comparison of results between laboratories measuring the same analyte. An EQA scheme for the analyte distributed aliquots of the same samples to participating laboratories, which were blind to the concentration of the analyte. Samples were assayed shortly after arrival to the laboratory. Results were returned to the scheme organisers, who issued a laboratory specific report.

Tables 5A -14A in Appendix 8, show internal and external quality assessment results for vitamin D in the NDNS (1994/95 and 2000/2001), the HSE 2000, the HSE 2005 and the LIDNS. The assayed values for each of the surveys were assessed from the quality

assurance parameters. The CV for assays in the NDNS in waves 1-4 (1994/95) ranged from 12.1%-17.1% and in the NDNS 2000/2001 ranged from 7.2% -16.7%. In the HSE 2000, HSE 2005 and the LIDNS, analyses was carried out monthly, CV ranged from 0.3%-20.6% in HSE 2000, from 4.4%-21.9% in HSE 2005 and 5.3%-21.9% in LIDNS (Tables 9A, 11A and 13A, Appendix 8).

Cut-offs and optimal levels of 25(OH)D (I,II,III,IV)

In Papers I, II and IV, vitamin D deficiency was defined as serum concentrations 25(OH)D <25nmol/L (Department of Health 1998). Two other deficiency states are defined as levels less than 50 nmol/L (hypovitaminosis), which has been associated with slightly high serum parathyroid hormone concentration and mildly high bone turnover (Zitterman, 2003; Holick, 2006) and optimal levels, which are currently considered to be 75 nmol/L or greater (Vieth *et al.*,2007). In paper II, both <25nmol/L and < 50 nmol/L was considered when looking at prevalence of vitamin D status; < 50 nmol/L was the cut-off used as the dependant variable in the multivariate analysis. In paper III, serum 25(OH)D concentrations were considered as a continuous outcome measure in simple and multiple regression analyses used to model the relationships between serum 25(OH)D and covariates including age group, ethnicity, sex, region of residence, dietary intake, and dietary supplements use. In paper IV, it was decided to consider definitions of low vitamin D levels separately (<25.0 nmol/L, <50 nmol/L, <75 nmol/L) as independent variables. There is also a difference in the preference of units that are used for presenting 25(OH)D concentrations in different countries, in the UK, more commonly, nmol/L are used, but for example in paper IV that was published in an American journal, the preferred units are ng/mL (2.5 nmol = 1ng).

5.3 Research ethics approval and written consent

Ethical approval for the HSE was obtained from North Thames (I,V,VI) and London (II,IV) Multi-centre Research Ethics Committee (MREC) and from all Local Research Ethics Committees (LRECs) in England. The NDNS survey (I, III) was approved by the South Thames MREC and National Health Service LRECs. The LIDNS survey (III) was approved by the North London MREC. Participants gave verbal consent for the interview and measurements and written consent to have blood samples taken.

6 Statistical analysis

6.1 Data analysis

Data was analysed using various versions of SPSS (v10 (I and IV), v15.0 (II, IV, V) and Stata v10 (I,V) and v9 (II and IV). The statistical methods used in the original papers (I-V) are described in detail in the papers. In all the publications, data was checked for normality using the appropriate statistical methods.

Mean levels (SD) and prevalence were described for the HSE,NDNS and LIDNS data. Categorical data were described using percentages and 95% confidence intervals when applicable. The appropriate statistical tests were used to assess statistical differences between groups e.g the t-test was used to test the difference between two means and one way Analysis of Variance (ANOVA) was used to assess differences in mean serum 25(OH)D across more than two different groups (used in papers I and II). The chi-square test was used to examine the association between the categorical data e.g. used to test differences in prevalence of vitamin D deficiency by sex and age group.

Regression models were used to investigate the relationship between the dependant and independent factors, adjusting for confounders such as socio-demographic and lifestyle factors. Linear regression was used where the variables were continuous and logistic regression was used when there were binary outcomes.

7 Results

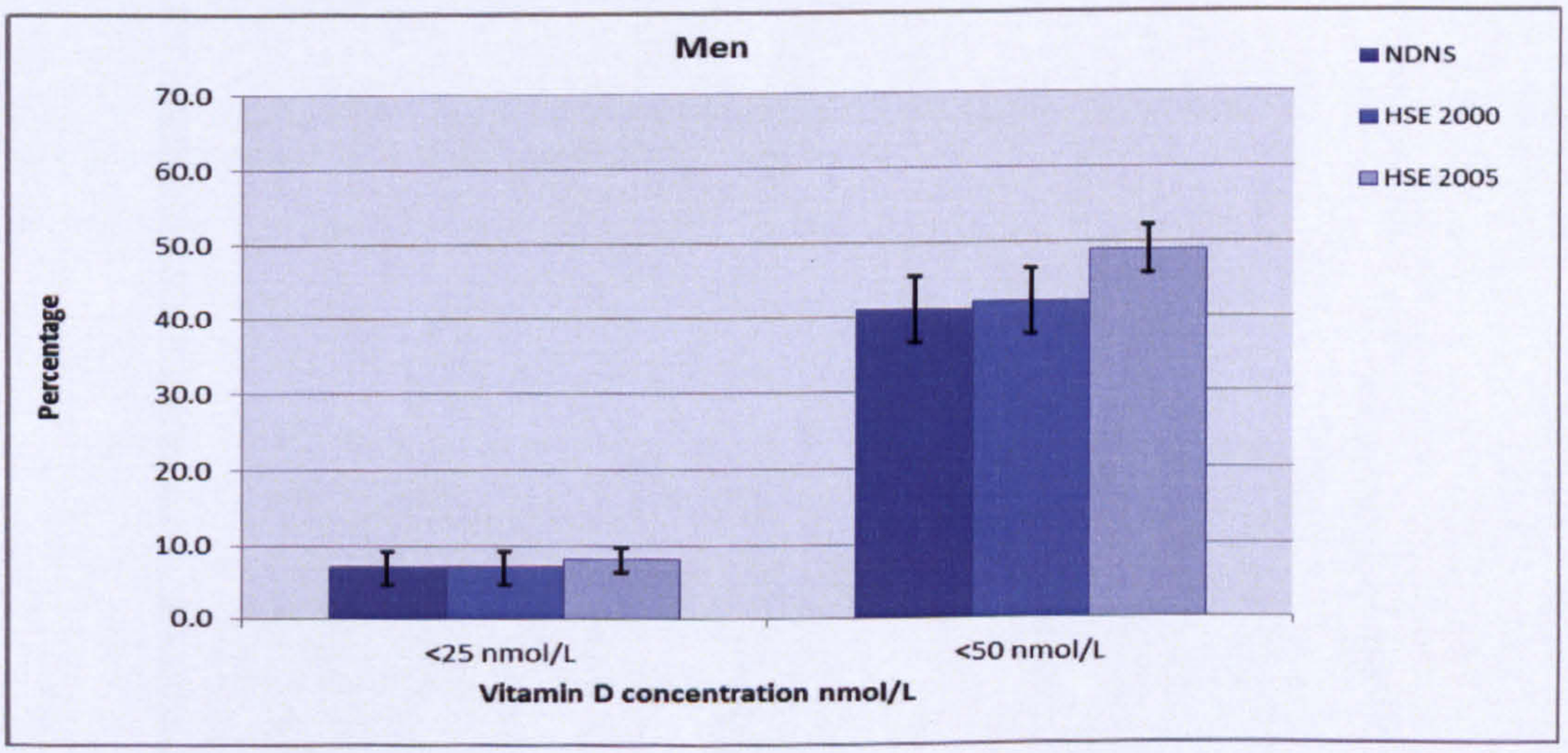
7.1 Prevalence of vitamin D status among older people in the community and in institutions HSE 2000 (I)

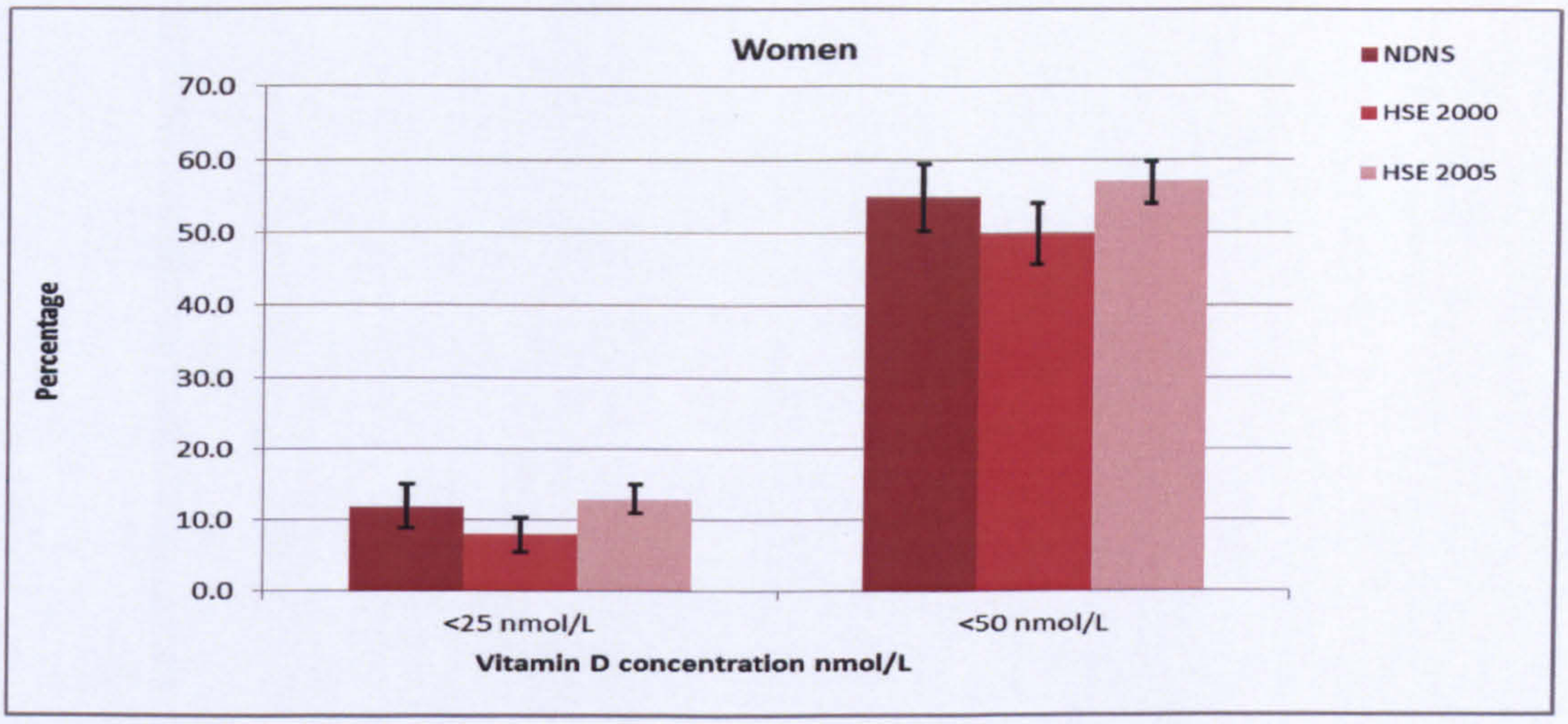
The results show that in institutions, the prevalence of vitamin D deficiency was similar in both men and women (30.2% in men and 32.5% in women), while in private households women were significantly more likely to be deficient than men (15.0% vs 9.6%). Full results for paper I can be found on pages 2-3.

7.2 Trends in vitamin D status among older people in the community since 1994 (I,II)

Figure 4 shows that there have been no significant improvements in vitamin D status among older people since 1994/95. Full results for paper II can be found on pages 64-66.

Figure 4 - Prevalence of age standardized vitamin D deficiency (<25 nmol/L) and hypovitaminosis (<50 nmol/L) in private households by sex in NDNS, HSE 2000 and HSE 2005.

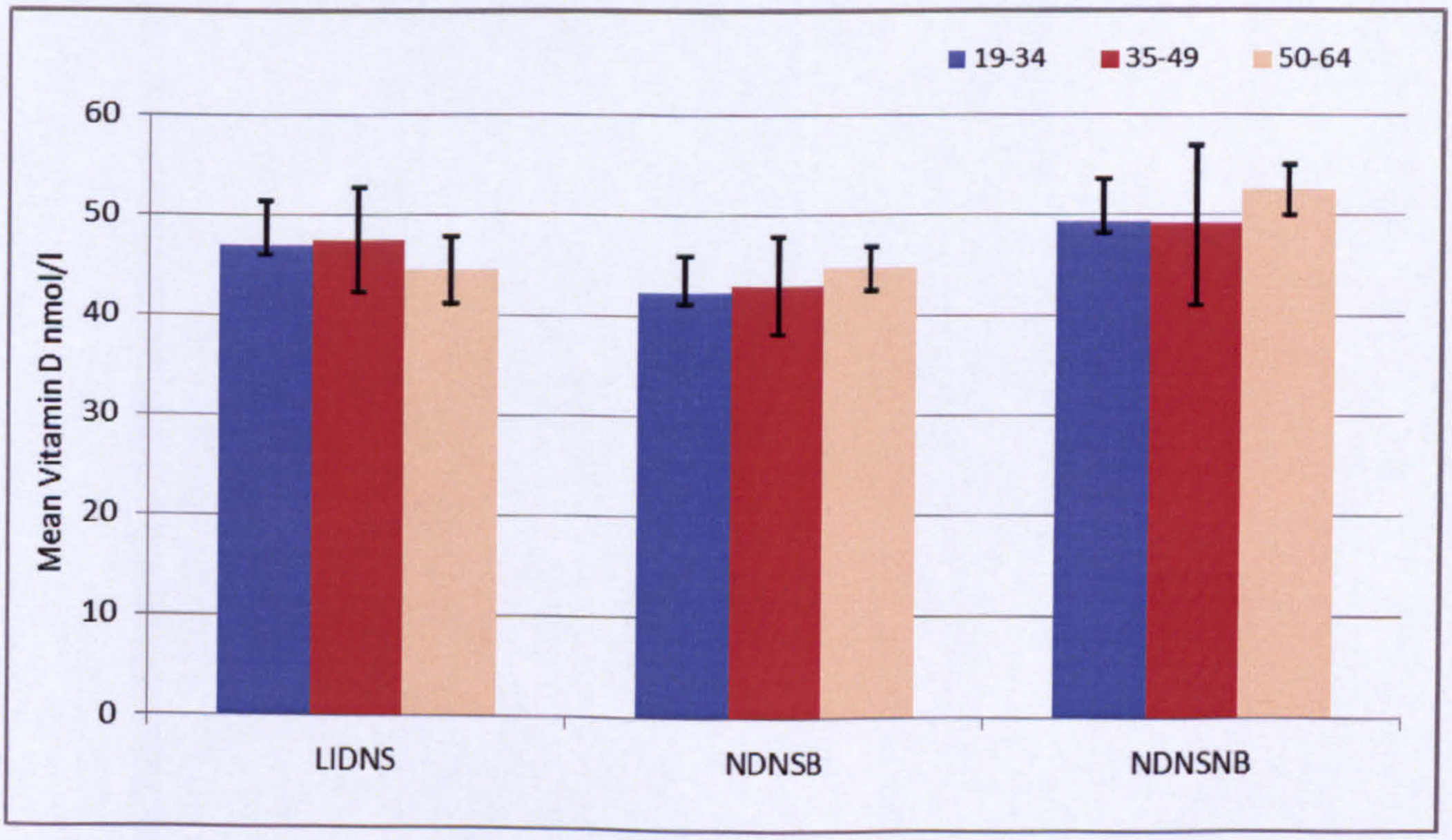




Vitamin D status among low income groups: in the community (III)

The full results for Paper III, can be found on pages 761-762. Among all age groups in the National Diet and Nutrition Survey-on benefits ($NDNS_B$) sample and the LIDNS sample, mean 25(OH)D levels were significantly lower than among the National Diet and Nutrition Survey-not on benefits ($NDNS_{NB}$) sample (Figure 5).

Figure 5– Mean vitamin D concentrations among people aged 19-64 years living in private households in LIDNS, $NDNS_B$, $NDNS_{NB}$.



7.3 Associations of vitamin D status with risk factors among older people in Institutions and the community (I, II, III IV)

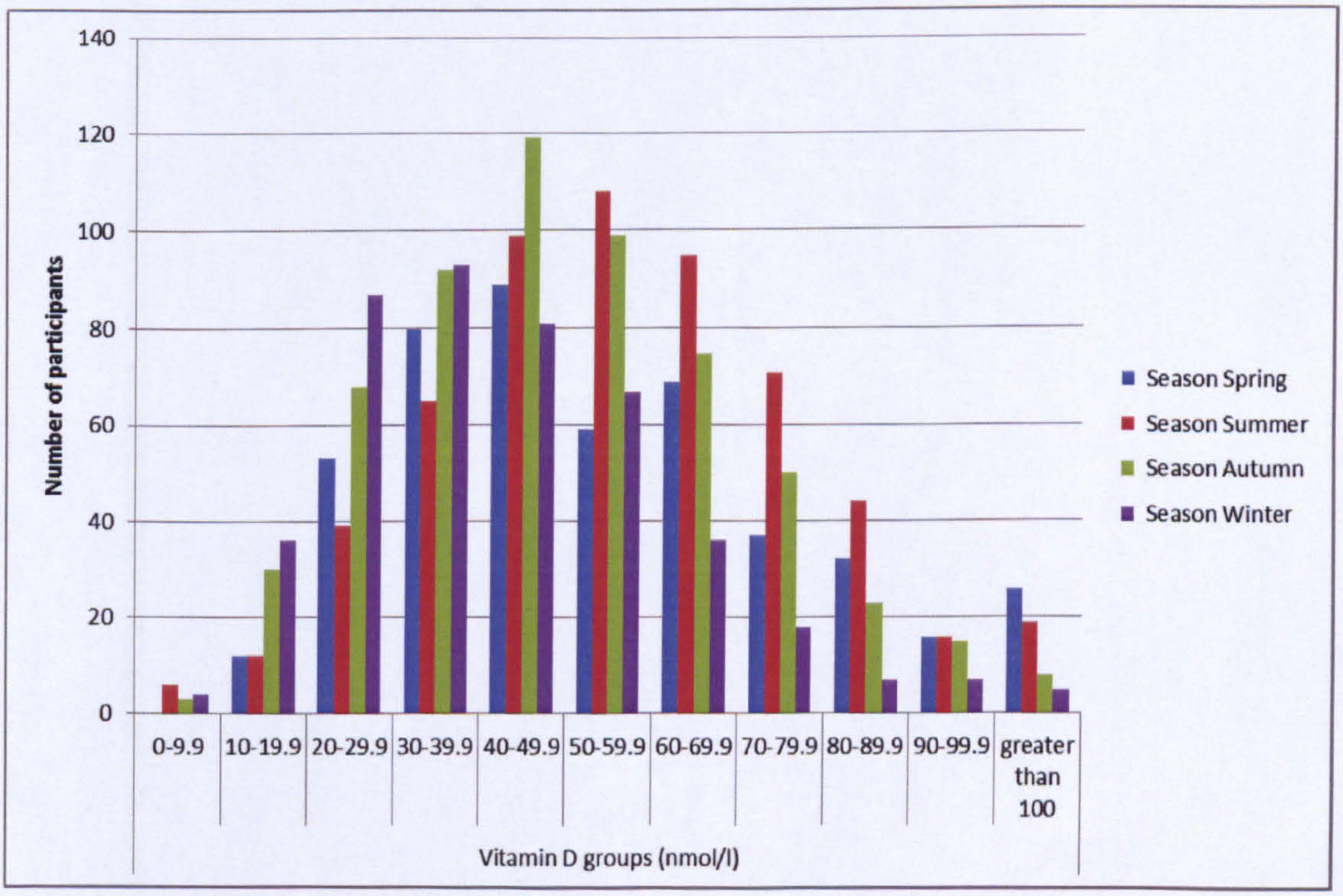
Vitamin D deficiency and possible risk factors, in the institution and private household sample of older people in HSE 2000 (I)

See full results for paper I on pages 2-3.

Season (paper II)

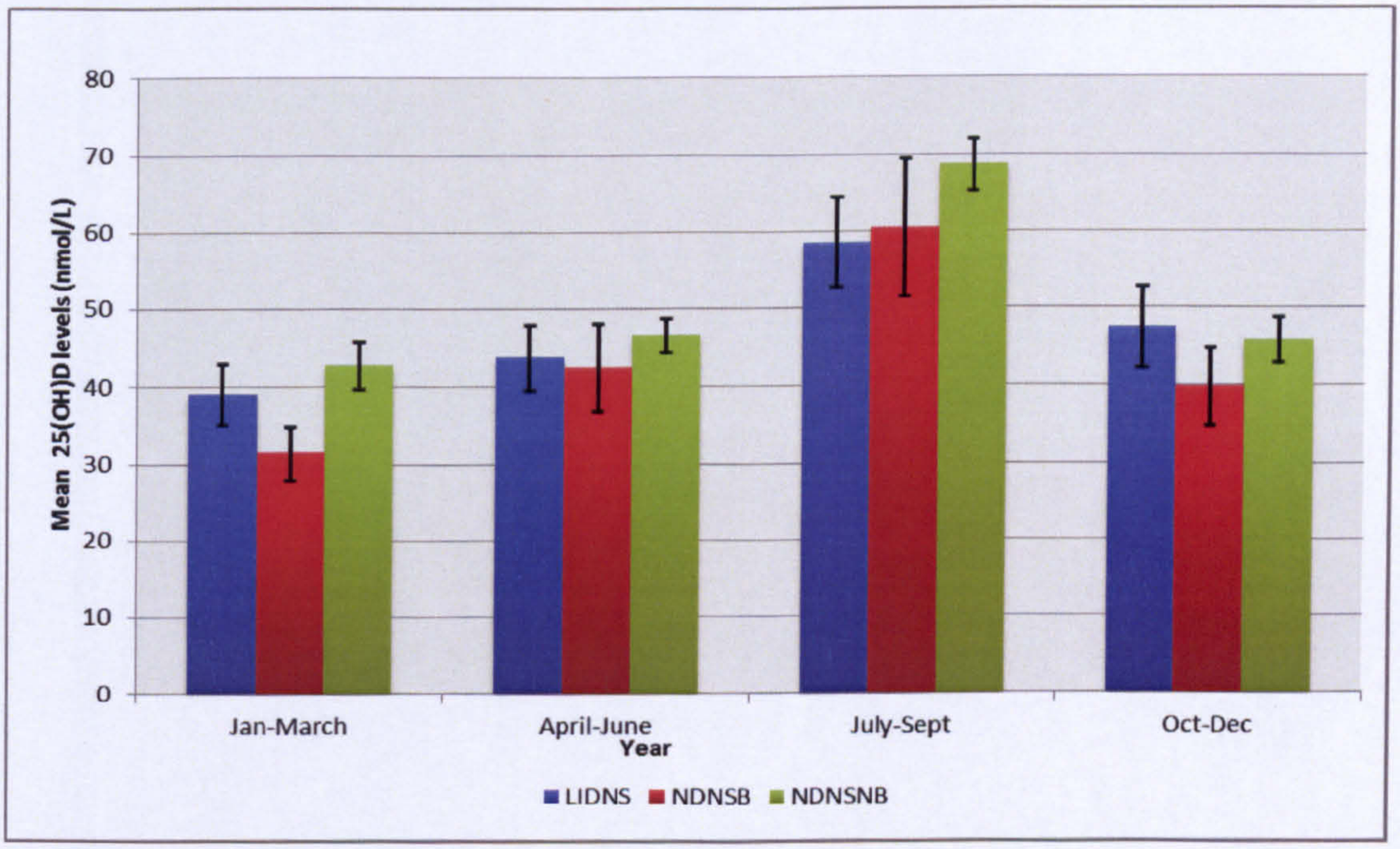
Seasonal differences in serum 25(OH)D levels <50nmol/l are shown in Figure 6. HSE 2005 participants with blood samples collected in the winter had lower serum 25(OH)D levels than those collected in the spring or summer. This was also shown in the multivariate analysis for the associations between vitamin D deficiency and hypovitaminosis D, respectively (papers I,II). See full results for paper I page 3 and paper II on pages 65.

Figure 6-Seasonal variations in serum 25(OH)D levels (II)



There was also marked seasonal variation in all three populations: LIDNS, $NDNS_B$ and $NDNS_{NB}$ (III), with the mean levels being approximately 50% higher for blood samples collected in July-September compared with January –March (Figure 7). Full results can be found in paper III, pages 761-762.

Figure 7-Seasonal variations in mean serum 25(OH)D levels in LIDNS, $NDNS_B$ and $NDNS_{NB}$ samples (III)



Vitamin D, season and depression (IV)

The results from multivariate analysis showed that association between vitamin D status and depression was not modified when adjusting by season. See results section in paper IV, page 2 for detailed results.

7.4 Vitamin D and BMI (I, II III, IV)

Findings from papers I and II show that vitamin D was associated with normal/under nutrition and obesity. In study I, participants from both private households and institutions with a BMI <25 kg/m^2 were at a higher risk of vitamin D deficiency than those with a BMI above 25 kg/m^2. In contrast, with study II, participants who were obese were at a higher risk of hypovitaminosis D than those that had a 'normal' BMI. In addition, an inverse association was found between 25(OH) D levels and BMI (adjusted regression coefficient -0.6 (-0.9,-0.2) for participants from the materially deprived population from the LIDNS sample (III)). In study III, participants with a normal BMI (18.5-24.9 kg/m^2) had higher mean 25(OH)D levels (49.3 nmol/l) than those in the other categories (p=0.03); those with a BMI of 30-34.9 kg/m^2 had the lowest levels (41.8 nmol/l). In paper IV (see section 7.6) there were marked reductions in the strength of association between depression and low vitamin D status (<25 nml/L) when adjusted by BMI, suggesting that BMI affects both depression and vitamin D levels (Tables 2 and 3, paper IV, page 3).

7.5 Vitamin D and depression (IV)

Prevalence of depressive symptoms was 22.6% among 85% of participants with 25(OH)D levels below 75 nmol/l (30ng/ml); in participants with 25(OH)D levels below 50 nmol/l (20ng/ml, 51.4%), prevalence of depression was 25.8%; and in participants with 25(OH)D levels below 25 nmol/l (10ng/ml, 9.8%), prevalence of depression was 35.0%. See results for paper IV on pages 2-3.

7.6 Obesity and risk factors for chronic disease in older people (V)

In 2005, the HSE focussed on older people. 72% of men and 68% of women aged over 65 were either overweight or obese. Prevalence of raised WC was higher in women (58%) than in men (46%). Generalised obesity and abdominal obesity increased among men and women from 1993 to 2008. See detailed results for paper V on pages 3-6.

8 Discussion

8.1 Vitamin D status among older people in the community and institutions (I,II)

These original research papers included secondary analysis of the HSE datasets. Data on vitamin D among older people was collected for the first time in the HSE series in 2000. The annual HSE report had not included the findings on this topic even though they were very important and the results had not been disseminated elsewhere. Paper I presenting results from the HSE 2000 captured a sample of care home residents, a group often under-represented. The evidence showed widespread vitamin D deficiency in older adults, and despite a number of initiatives (Department of Health, 1998, Department of Health, 2008) there had been no improvement since the previous large study in the UK, the NDNS in 1994/95 (Finch *et al.*, 1998).

This research was initiated because it was an important and much needed area of investigation. A report on the NDNS among older people had presented results on this topic but there had been no further investigation into vitamin D status in older people since 1994/95, nor examination of associations of vitamin D status with health outcomes. It was shown in paper I that vitamin D deficiency existed at worrying levels among people aged ≥65 living in the community and is even higher among people living in institutions. Comparisons with the earlier 1994/95 NDNS data (Finch *et al.*, 1998) showed similar findings. However, even with the recognition that this problem existed, no improvement in prevalence was found. The multivariate logistic regression analysis in paper I showed that vitamin D deficiency (levels below 25 nmol/L) was more common in women than men and among those in manual social classes. It was also associated with limiting longstanding illness and poor general health: those with poor health may have limited mobility, being unable to go outdoors and therefore lacking exposure to sunlight. Overall it highlighted that older people from poor socioeconomic backgrounds and poor physical health are at risk of vitamin D deficiency.

8.2 Trends in vitamin D status among older people (II)

It was important to look at trends in vitamin D status among older people when data from HSE 2005 became available, to examine whether there were any improvements in vitamin D status with the emergence of increasing interest in this topic, especially in relation to chronic conditions. In a subsequent analysis of the HSE 2005 among people living in the community, it was important to expand this area of research by considering factors that had not been available to include in the earlier publication. Research was indicating that a higher threshold of serum 25(OH)D <50 nmol/L (hypovitaminosis D) could have implications for health (Zitterman, 2003; Holick, 2006). Therefore the analysis was conducted using this level, (in paper I, a lower threshold of <25 nmol/L had been used in the analysis) and extended to include investigating poor vitamin D status and associations with chronic diseases such as diabetes and cardiovascular diseases as well as musculoskeletal diseases. However, it was taken into consideration that the direction of causality cannot be determined in a cross-sectional survey.

To compare prevalence of poor vitamin D status in 1994/95, 2000 and 2005, the data was age-standardised using the 2001 census data to provide accurate interpretation of changes with time in prevalence of vitamin D deficiency. This showed that there was still no improvement in vitamin D status in HSE 2005 compared with the earlier HSE 2000 and showed a significant decline in vitamin D status among men in 2005 compared with the 1994/95 NDNS results. Hypovitaminosis D was worse among those aged ≥75 years. Both studies I and II showed that poor vitamin D status in older people continues to be a public health problem in England. Vitamin D deficiency and hypovitaminosis D are associated with many risk factors and poor health outcomes. An equivalent survey to the HSE, the Third National Health and Nutrition Examination Survey (NHANES III, Ginde *et al* .,2009), has shown that vitamin D deficiency (<25 nmol/l) increased and the prevalence of optimal vitamin D status (> 75 nmol/l) decreased in the USA between 1988 and 2004.

Secular trends in Vitamin D status.

In this thesis it has been shown that poor vitamin D status is highly prevalent in the UK population and I have initiated and carried out research (paper II) that shows secular trends in vitamin D status highlighting that the situation does not seem to be improving among older people. The advantages of the findings from this paper are that they have not been examined before among older people in England. This strongly suggests that there is an

urgent need for action to improve the situation. There was also an importance to address poor vitamin D status due to emerging evidence of its association with chronic diseases. This is important since it is known that with ageing diseases become more prevalent, but poor vitamin D status and obesity may accelerate the onset of diseases, in addition to other related risk factors and co morbidities. Associations between vitamin D deficiency and diseases cannot be interpreted as a cause and effect relationship at present since the mechanism of action of vitamin D in the prevention or progression of various diseases has not been firmly established, aside from osteoporosis and falls. There is potential, however, for future research to focus on disease causality and test appropriate vitamin D supplementation and fortification for disease prevention. As the ageing population is increasing, these areas are of great concern for current and future public health.

8.3 Risk factors associated with poor vitamin D status (I, II, III)

Season (I,II,III)

This research showed seasonal differences in serum 25(OH)D levels <25 nmols(I) and levels <50nmol/l (II). The surveys included in these papers had collected data on the month that the blood sample had been collected to enable analysis by season. Our data showed that participants with blood samples collected in the winter had lower serum 25(OH)D levels than those collected in the spring or summer. Similar findings have been shown in the 1958 birth cohort in the UK (Hyppönen and Power, 2007). Housebound older people, especially those living in institutions are shown to be at increased risk of poor vitamin D status and need to spend more time outdoors in all seasons. However, older people also have lowered capacity to synthesize vitamin D when exposed to sunlight, so it may also be difficult for them to meet their requirements via sunlight exposure alone (Holick, 2006). There is relatively little known specifically about the recommended amount of time that older people need to spend in sunlight to synthesise optimal levels of vitamin D. There were also differences in mean levels of 25 (OH)D levels by season in all three populations (LIDNS, $NDNS_B$ and $NDNS_{NB}$ (III)), with the highest levels for blood samples collected in July-September compared and the lowest in January –March.

Supplement use (II,III,IV)

Papers II, III and IV showed that older people not taking vitamin supplements were more likely to have hypovitaminosis D. The use of vitamin D supplements (~800 IU) is effective in reducing falls and fractures among older people and is recommended in those at high risk of deficiency to preserve muscle strength and functional ability (Bischoff-Ferrari *et al.*,2006). It

has also been suggested that vitamin D intakes higher than 800 IU are required to increase serum levels to the desirable levels (Vieth *et al.*, 2007) but there is little evidence on long-term compliance of vitamin D supplementation among older adults living in the community as a health improvement strategy. There is also a need to review the evidence related to vitamin D dosage that is effective to replenish vitamin D levels to optimal levels and the amount that is beneficial to prevent chronic diseases (Calvo *et al.*, 2006). When reviewing the literature, it was clear that there is a large disparity between vitamin doses tested in the studies looking at vitamin D and associated health outcomes. This may be due to the controversy relating to appropriate and recommended vitamin D doses. As with other medications that undergo stringent trials and regulations before they are available for use, it is necessary that the same procedures are followed for vitamin D supplements. Clinical trials to assess the benefits of vitamin D for chronic conditions including cardiovascular diseases and cancer are now urgently needed since the current evidence is mainly from observational studies that does not provide adequate information on the benefits of vitamin D supplementation on health outcomes. The evidence from studies evaluating vitamin D supplementation have not consistently shown benefit, but this may also be due to suboptimal levels of vitamin D or due to the other many factors that affect vitamin D status. In the UK, in recent years there has been a problem with the availability of vitamin D preparations at appropriate doses. Hospital pharmacies have had preparations imported from Europe that are unlicensed and therefore not available for prescription outside of hospitals. This may have been a logistical issue that has affected provision of appropriate doses of vitamin D to high risk groups in the community.

Ethnicity (II, III)

Although the sample sizes were small for non-white ethnic groups in our studies, the findings (II, III) are consistent with other studies that also found a greater risk of vitamin D deficiency and hypovitaminosis D in people with darker pigmented skin (Matsuoka *et al.*, 1991; Dawson-Hughes,2004). The reasons as already mentioned in the introduction are likely to be multi-factorial, including skin pigmentation and melanin concentration (Matsuoka *et al.*, 1991) and lifestyle factors such as cultural differences for example clothing, but there are no national data for these high risk groups in the UK. Previous studies of vitamin D status among minority ethnic groups have focused on particular age groups, areas of the UK, or small subgroups, compromising the quality and power of the studies (Roy *et al* ., 2007;Ladhani *et al.*, 2004; Ford *et al.*, 2006). Vitamin D deficiency is more prevalent among African Americans than the white population (Harris, 2006) but there is also no data on vitamin D levels among Black Caribbean and African groups in the UK. A cross-sectional study, assessing the vitamin D status of a nationally representative sample to establish the

vitamin D status of males and females of different age groups within the South Asian and Black Afro-Caribbean populations in England is clearly needed in order to fully quantify the problem in the UK and to be able to audit the progress of measures for improving vitamin D status. It is important, interesting and unknown at present regarding the extent to which health inequalities between minority ethnic groups can be explained by vitamin D status considering the link between vitamin D status, obesity and predisposition to increased risk of CVD and other chronic diseases that are highly prevalent in some minority ethnic groups.

Obesity (II, III, IV)

Obese participants (BMI ≥ 30 kg/m^2) had more than a 50% increased odds of having hypovitaminosis D compared with those with a normal BMI (20-25 kg/m^2). Other studies also show this association (Snijder *et al.*, 2005), suggesting that this results from decreased bioavailability of vitamin D due to its deposition in fat. Exposure to the same amount of UV radiation raised plasma 25(OH)D concentration by only 50% in obese subjects compared with non-obese subjects (Wortsman *et al.*, 2000). If participants in the sample were taking weight loss medications like orlistat or cholesterol-lowering drugs like cholestyramine that can reduce the absorption of vitamin D, this may have affected the findings. These potential confounders were not taken into account in the analysis. In contrast to these findings, in paper I, people aged ≥ 65 living in both institutions and private homes with a BMI below 25 kg/m^2 had increased risk of vitamin D deficiency than those with a BMI above 25 kg/m^2. This analysis included the sample of older people living in institutions, a group who were likely to have the poorest health. This association may have been affected by unmeasured potential confounding factors such as those affecting both sun exposure i.e. poor mobility, lack of time spent outdoors, travel to overseas destinations with higher sunlight exposure and unmeasured factors affecting BMI such as a poor diet, undiagnosed illness, and poor appetite. There is only one other study that shows that a low BMI was associated with low serum 25(OH)D levels.(Hintzpeter *et al.*,2007). There was an association between depression and low vitamin D status (<25nmol/L) that remained even after adjusting for BMI. There is a need for more evidence to understand the effects of adiposity on circulating 25-hydroxyvitamin D concentration and its implications for vitamin D requirements.

Poor general health and longstanding illness (I, II)

Vitamin D deficiency (I) and hypovitaminosis D (II) are associated with poor general health and having a longstanding illness, whether limiting or non-limiting. This may be due to many factors: longstanding physical health problems may influence access to sun exposure, by affecting mobility. Direction of causation is perhaps the most important consideration and cannot be concluded from a cross-sectional design.

Poor socioeconomic status (I,III)

In study I, both men and women in manual social classes had double the odds of being vitamin D deficient than those in non-manual social classes. In another UK study, the prevalence of vitamin D deficiency was shown to be particularly high, especially in the winter and spring, in poor socioeconomic groups (Hyppönen and Power, 2007). Study III, that included analysis on vitamin D status using data from the NDNS (adults aged 19–64 years) and LIDNS (adults aged ≥ 19 years in the UK, screened to identify low-income/materially deprived households) showed that people who were not receiving benefits had higher mean 25(OH)D than NDNS participants receiving benefits and the LIDNS sample. This may be due to lack of sun exposure due to spending limited time outdoors, inability to afford to go abroad on holiday in hotter countries and poor dietary intake of vitamin D rich foods such as oily fish. This has also been shown among low income groups in another study (Harris *et al.*, 2000). A European study (Dean *et al.*, 2009) showed that older people's overall variety of food intake depends on material resources (e.g. monthly income, access to a car, living arrangement, physical and mental health): this may have an impact on including vitamin D rich foods such as oily fish. This research highlights that national prevention and treatment strategies of poor vitamin D status need to include the adult population, particularly deprived populations.

Health outcomes

Recent reviews suggest that suboptimal vitamin D status has wider adverse effects than those on bone structure and skeletal integrity, and may play a role in the development of many chronic diseases. Evidence from epidemiologic studies and small clinical trials suggests an association between 25(OH)D concentrations and systolic blood pressure, risk for CVD, related deaths, symptoms of depression, cognitive deficits, and mortality (Barnard and Colón-Emeric, 2010). Recent meta-analysis (Pittas *et al.*, 2010) shows that lower 25(OH)D concentration or vitamin D intake may be associated with higher risk for incident hypertension and cardiovascular disease, but the association with diabetes-related outcomes remains unclear. As a whole, the trials showed no statistically significant effect of

vitamin D supplementation on cardiometabolic outcomes. This is due to large heterogeneity among studies, especially in vitamin D thresholds used, doses analyzed, outcomes specified, and confounders adjusted for.

We examined the relationship between serum 25(OH)D and various chronic diseases in multivariate analysis (II). In adjusted models, hypovitaminosis D did not show an association with any of the chronic diseases included in the model. This may be due to this data having limitations i.e co morbidity relied on self-reported information which is subject to measurement inaccuracy. The results from meta-analyses of RCTs from a large number of emerging studies can provide more reliable evidence. Recently the IOM 2011 report concluded that evidence of the benefits of vitamin D are convincing only for bone health. It was reported that the evidence for other health outcomes was inconsistent and inconclusive regarding a cause-and-effect relationship, and not yet sufficient to inform nutritional requirements for vitamin D. Further randomised controlled trials are required in this area to confirm causal associations of vitamin D with health outcomes in order to allow implementation of vitamin D supplementation at appropriate dosages in the prevention of diseases.

There is some debate on optimal serum 25(OH)D levels. Older people are at increased risk of being vitamin D deficient because dietary intake and endogenous production decrease with age. At present, there is some debate on the optimal serum 25-hydroxyvitamin D levels which offer maximum preventative action in relation to various diseases.

The International Osteoporosis Foundation (IOF), in their 2010 position paper on vitamin D, recommended that an intake of 800 to 1,000 IU of vitamin D per day is sufficient to achieve a serum 25(OH)D level of 75 nmol/l, considered optimal for fall and fracture reduction for older people age 60 years and older. It has also been suggested that a higher amount is required to achieve desirable 25(OH)D concentrations of ≥75nmol/L (Dawson-Hughes *et al.*,2010). However, the IOM recommendation (IOM,2011) for older people is that a vitamin D intake of 600-800 IU/day is adequate to achieve a threshold of 50 nmol/l but this threshold recommendation may be too low even for optimal bone health in adults (Bischoff-Ferrari *et al.*, 2004). Trivedi *et al.*, (2003) examined the effect of vitamin D supplementation on risk of fracture in the elderly. Participants aged 65-85 years, were provided with 100,000 IU of vitamin D, or a placebo, every 4 months for a 5-year period. The study showed a reduction in fracture risk in the hip, wrist/forearm and vertebrae by 33% in the group receiving the vitamin D supplementation. However, the RECORD (Randomized Evaluation of Calcium and/or vitamin D) trial compared the effects of 1,000 mg calcium carbonate, 800 IU vitamin D_3,

combined 800 IU vitamin D_3 and 1,000 mg calcium carbonate or a placebo in participants aged 70 years with a previous fracture, during a 2 year period (Grant *et al.*, 2005) and showed no significant differences between the various groups with regards to bone fractures.

The IOM (2011) vitamin D recommendations may be adequate for older people at low or moderate risk but may not meet the needs of those at high risk. This includes older people with limited sunlight exposure (i.e. institutionalized, homebound), the obese, those with osteoporosis, those with malabsorption, those living in regions known to be at high risk for vitamin D deficiency such as the Middle East and South Asia, immigrants from these regions living in Europe and people living in northern areas of Britain with low levels of sunlight.

Vitamin D and Depression (IV)

Although vitamin D deficiency has been investigated in relation to mental disorders in younger adults (Schneider *et al.*, 2000), relatively little research had been investigated in older people, despite the higher potential impact. A case control study of older people with or without mild Alzheimer's disease, showed lower 25(OH)D levels were associated with mood disorder as well as with cognitive impairment (Wilkins *et al.*,2006). A longitudinal study of ageing found lower 25(OH)D levels, as well as higher parathyroid hormone levels, to be associated with both major and minor depression (Hoogendijk *et al.*, 2008). Findings in paper IV show associations between vitamin D deficiency and depressive symptoms but only for clinically defined vitamin D deficiency (levels <25 nmol/l), and not for milder categories of vitamin D status. The association was not accounted for by physical health or other potential confounding factors and was not substantially modified by the season at which the examination was carried out. Particular advantages of this study were the presence of directly measured serum 25(OH)D levels, a widely used scale for measuring depressive symptoms in older people, and a large and nationally representative sample. The findings in other literature are consistent with these results. It should be taken into consideration that participants were from the community which represents a relatively healthier sub-population of older adults in comparison to those in institutional care with poorer health who were not included. This does compromise the findings for this sub-population – it simply restricts the generalisability to more dependent groups. Conventional confounding factors were taken into account in this analysis. Other unmeasured potential confounding factors might include general lifestyle (for example, the ability/willingness to travel to overseas destinations with higher sunlight exposure) and cognitive impairment (for example, causing both depressive symptoms and vitamin D deficiency), neither of which were measured in this study. However, were data to be present for cognitive function, its role would probably be difficult to determine since cognitive impairment could also be a consequence of both vitamin D deficiency and depression. Dietary intake of vitamin D was also not measured and it was not possible to determine vitamin D supplementation (because of varying doses in multivitamin preparations) but these are likely to be important, particularly in people with less than adequate sun exposure/absorption. However, the role of diet, if causal, is potentially complex because of the difficulty distinguishing micronutrients of interest. For example, oily fish are key sources of vitamin D but are also of interest in depression as a source of essential fatty acids. Longstanding illness which was present in a large proportion and which was potentially associated with both depression and (through reduced sunlight exposure) vitamin D deficiency, did not appear to have a substantial

influence on the association of interest. The data shows that the association between vitamin D deficiency and depression is reduced when adjusting by BMI, i.e. BMI influences both vitamin D levels and depression. There are many possible explanations. Depression is the most common cause of weight loss in older adults (Wilson *et al.*,1998) but it is also commonly predictive of obesity, as shown in a recent meta-analysis by Luppino *et al.*, 2010; this may be due to factors such as overeating and reduced physical activity. Depression due to lower vitamin D levels may be as a consequence of staying indoors and lack of sunlight exposure. In addition, weight gain is a common side effect associated with taking anti-depressant medications. It was also shown that being obese increases the risk of suffering from depression (Luppino *et al.*, 2010).

If vitamin D deficiency is demonstrated to be a cause of depression, addressing vitamin D deficiency could be an effective public health measure to reduce depression prevalence in later life. There are also plausible biological pathways for a role of vitamin D deficiency in the pathogenesis of depression, including effects on nerve growth factor synthesis, (Wion *et al.*,1991) and a variety of potential neurotransmitter targets (Stumpf,1995). At present, this paper shows an important association between vitamin D deficiency and depression despite the direction of causation not being entirely clear. Further prospective studies are required to prove the direction of the association but if vitamin D deficiency is demonstrated to be a cause of depression, correcting the problem could be an effective public health measure to reduce depression prevalence in later life. There is also insufficient evidence at present from RCTs to support vitamin D supplementation in patients with depression; it is mainly from observational studies that cannot establish causality.

8.4 Overweight and obesity and chronic disease (V)

This thesis also shows that the prevalence of obesity has been increasing and is a public health burden that can lead to morbidity, premature death and poor quality of life. Both generalised and abdominal obesity among older people are associated with increased risks of diabetes, hypertension and arthritis, in both sexes. Obesity is a well-known contributing factor to the development of type 2 diabetes, which itself can increase the risk of cardiovascular disease and can lead to other complications that can affect the quality of life. The results of this study are in agreement with other studies providing evidence of both types of obesity being associated with hypertension (Harris *et al.*, 2000; Greg *et al.*, 2005; Yalcin *et al.*, 2005). The data shows that arthritis was more common in those with generalised and abdominal obesity, which has also been shown in other studies (Leveille *et al.*,2005; Sarzi- Puttini *et al.*,2005). An effective treatment for severe arthritis is joint replacement, which we found to be more likely in people categorised as overweight or with raised waist circumference. Multivariate analysis, adjusting for other factors, showed that in women only, joint replacement was common only in women with abdominal obesity. It was surprising that the data in this study did not show any association between abdominal or generalised adiposity and heart disease. The explanation for this may be that overweight/obese individuals and those with diabetes have a higher incidence of, and also higher mortality from, circulatory diseases (Rogers *et al.*, 2003) and are probably less likely to survive to be included in this survey, compared with overweight and obese individuals without diabetes. Another survey has shown that overweight and obesity as well as raised waist circumference were related to increased prevalence of cardiovascular disease, diabetes, hypertension and arthritis in men and women (Turley *et al.*, 2006). These conditions are known to improve with weight loss even in old age. Policies on treatment strategies to address these conditions such as, weight management and prevention of overweight and obesity are important.

8.5 Vitamin D status, obesity and chronic disease (II, III)

Obesity is a rapidly increasing public health problem and is associated with cardiometabolic outcomes. Vitamin D is stored in adipose tissue and therefore may have reduced bioavailability, resulting in the direct negative effect of obesity on vitamin D status that is also a public health issue. The findings of the studies (papers II, III and IV) in this thesis show that poor vitamin D status is associated with obesity. Other literature also shows that serum 25(OH)D levels are inversely correlated with body mass index (BMI) and fat mass in

populations (Konradsen *et al.*,2008). Overweight and obesity may be the cause of chronic diseases but people with chronic conditions may be at a higher risk of becoming overweight or obese due to an inability to be physically active due to their condition and also unable to access sunlight exposure due to this same reason increasing the risk of vitamin D deficiency which has been shown (paper II) to be reduced in people with a BMI of >30 kg/m^2. Prevention and management of overweight and obesity and ensuring adequate vitamin D status in the population remains promising in reducing the risk of cardiometabolic disease. At present, there is a need for adequate randomised controlled trials conducted in well-defined populations to test the potential role of vitamin D in primary and secondary prevention or therapy.

The findings from papers I and II show that women are at a greater risk of vitamin D deficiency and hypovitaminosis D than men. Vitamin D deficiency is often seen in post-menopausal women and has been associated with greater incidence of hip fractures (Gillespie *et al.*, 2003). It was also shown in paper V that in women only, those with generalised obesity had an increased risk of falls, after adjusting for other factors. Muscle weakness and a poorer sense of balance are more common in those leading sedentary lives (Singh, 2002) and also associated with poor vitamin D status (Holick, 2009). Vitamin D deficiency has been shown to be highly prevalent in older people (I, II). It is important that regular assessment for vitamin D deficiency is provided, followed by appropriate interventions such as vitamin D supplementation that may help in the management of sarcopenia (Morley *et al.*,2010). Obesity and poor vitamin D status are therefore additional indirect risk factors for falls. Encouraging physical activity, such as incorporating it into daily life by walking or cycling, and ensuring an adequate vitamin D status may help reduce risk of falls (Bischoff-Ferrari *et al.*, 2009; Kalyani *et al.*, 2010). Physical activity can also contribute to curbing or reversing the obesity epidemic.

8.6 Strengths and limitations

The strengths of the original publications included in the thesis are that they are studies from large scale surveys conducted using similar sampling designs, recruitment, data collection, laboratory methods (I-IV), and designed to give a nationally-representative picture of the health and nutritional status of the population groups examined. Specific statistical weighting was included in the surveys to correct for sample selection and from HSE 2003 onwards, also to attempt to correct for non-response. The surveys also had stringent quality assurance techniques that included field staff being trained on how to collect information using computer aided personal interviewing (CAPI) and on taking measurements and samples according to standardised protocols. This included for example taking repeated measurements (such as height and weight) on individuals during the training days, to test the repeatability of measurements (which were taken again by the trainer to check for accuracy). Staff also had regular refresher training annually, as well as periodically being observed in the field by nurse supervisors, who are very experienced.

The advantages of the surveys were that they all had data collected on the month that the blood sample had been taken to enable vitamin D analysis (in papers I-IV) to be carried out by season as well as allowing the multivariate analysis to be adjusted by season. Many other studies in the literature are limited in this aspect because data is only collected in one particular season.

Paper III was the first study in the UK comparing data collected in two large national surveys (LIDNS and NDNS) that showed a higher prevalence of vitamin D deficiency among low income households in comparison to those not on benefits. These two independent survey samples also show very similar risk factors for vitamin D deficiency as reported in other studies, in specific groups (Clemens *et al.*,1982; Holick, 1994; Pal *et al.*,2003; Holick, 2004).

Paper V was the first investigation in England that used data collected over a period of 15 years in large, nationally representative samples to look at trends in generalised and abdominal obesity and examined the risk of chronic conditions in older people. The findings showed that both generalised and abdominal obesity are associated with increased risks of chronic conditions such as diabetes, hypertension and arthritis. These are important findings highlighting that there is a need to address this area with public health interventions that can promote and preserve the health of older people.

A limitation of the data used in the papers are that they are cross-sectional, so associations may be due to reverse causality e.g. low vitamin D status may be causing poor health or poor health may be limiting outdoor activity and sun exposure, leading to low vitamin D status. However, the findings from these studies can allow generation of hypotheses for further research in these areas that can then be carried out in prospective studies. In papers I, II, III and IV, some potential confounders could not be accounted for in the analysis because data was not available, for example, data on sun exposure (time spent outdoors) and ability to travel abroad to access higher sunlight exposure. There was also a lack of information on the dietary intake of vitamin D (papers I, II and IV).This information could have been useful to include in the multivariate analysis to look at impact of dietary intake of vitamin D rich foods on vitamin D status among older people. This data was available in the NDNS and LIDNS in paper III and the results showed that people not on benefits had a higher dietary intake of vitamin D from food in comparison to those on low incomes.

The assessment from quality assurance parameters showed that there was no significant change in vitamin D assay's performance in the surveys throughout its use. In the surveys, the quality control assessment results for the assayed values were within the target/acceptable levels in each of the surveys. The precision of vitamin D assays was comparable for each of the surveys as indicated by the CV ranges. A recent study evaluating the precision of 25 (OH)D, showed that CVs ranged from 4.8% to 18.3% (Wallace *et al.*, 2010). Imprecision has been a challenge for vitamin D assays, but it has improved within the past decade, decreasing from an average CV across all methods of 32% to 15%, with some assays having much better precision than others (Carter *et al.*, 2010). The advantages of the studies in this thesis was that the laboratories performing the 25(OH)D analyses took part in the DEQAS that has been monitoring 25(OH)D assay performance since 1989. The scheme has expanded rapidly in recent years and DEQAS is the only specialist international Proficiency Testing Scheme for 25(OH)D. The overall performance of 25(OH)D assays has improved greatly, but it is noted that further improvements are warranted.

Data on vitamin supplement use was available for the studies (II, III and IV), but the dosage of vitamin D in the supplements could have varied and this information was not available. Although the studies (II, III and IV) showed that taking a vitamin supplement had an impact on vitamin D status, this may have to some extent reflected the fact that supplement users may also generally have a healthier diet and lifestyle. In all the surveys, there was no information collected on factors that affect vitamin D status such as the amount of time spent in the sun, sunscreen usage, skin coverage and skin type. Information on all these aspects,

including asking participants about holidays abroad has now been included in the current NDNS rolling programme.

When examining the relationship between serum 25(OH)D and various chronic diseases in the multivariate analysis in paper II, the findings did not show any association between low vitamin D status and chronic diseases. An explanation for this may be due to the data being reliant on self-reported information which is subject to measurement inaccuracy. This may also apply to some extent in paper V.

All surveys included in the thesis had only small samples of non-white participants which was a limitation since it could not allow separate examination of factors associated with poor vitamin D status by ethnic group. This is an important and emerging area of research that is needed in order to gain an understanding and address the challenges in reducing health inequalities among minority ethnic groups in the UK. Further research specific to ethnic populations using RCTs are required to establish whether causal links between 25(OH)D and obesity-related chronic disease exist, and whether vitamin D supplementation could be valuable in the prevention or treatment of obesity-related diseases that are highly prevalent in some ethnic groups.

In paper V, BMI, the most commonly used anthropometric index of obesity was used. However, BMI has been questioned in nutritional assessment of older populations as it is not a good indicator of body fat distribution, since it does not take into consideration body composition or where fat is stored. A limitation was that measurements of body composition that are a better indicator of fat mass were not collected in the HSE series which would have allowed further investigation of the link between fat percentage (that increases with ageing) and risk of chronic disease.

In paper I, the analysis did not include age standardisation, because the results were shown by age group but in the subsequent paper II, the data was age-standardised to enable comparisons between the surveys in the assessment of differences in trends of vitamin D status. In the multivariate analysis, in addition to the sequential adjustments for other covariates, BMI could have been included into the model when looking at the association between depression with vitamin D categories and adjusting by limiting long standing illness and general health.

9 Public health policy implications

Prevalence of vitamin D deficiency and the implications for public health policy

The studies in this thesis show that there is a high prevalence of poor vitamin D status in some population groups in England and the UK. However, there is no consensus currently on optimal vitamin D levels, prevalence varies depending on the cut-offs used to define vitamin D deficiency. This research has highlighted that further action is needed to alert health professionals about the high prevalence of vitamin D deficiency, inform them about the related risks, and how to detect and treat it. There is an urgent need for investment in national awareness programmes to educate the public and health professionals about the health importance of vitamin D. In the UK, at present there is no consensus on advice on vitamin D supplementation that should be given to many groups of the population, nor any formal guidelines to assist health care professionals in dealing with this health problem. Lack of consistent guidance results and conflicting messages make it difficult to implement strategies for the primary prevention of vitamin D deficiency effectively. Thus, SACN has currently recruited additional expertise to their committee and will continue to be proactive in investigating current strategies to overcome the many problems related to vitamin D status in the UK among the different population groups.

In most countries, dietary intakes of vitamin D are far lower than recommended levels (Mosekilde 2008). As a consequence, options for optimizing vitamin D status in the absence of sun exposure depend largely on vitamin D supplements or vitamin D enriched food products (Weggemans *et al.*, 2009). This could be more easily achievable in the UK if food manufacturers were able, in collaboration with the scientific community, to provide suitable fortification of appropriate foods such as milk, yogurts, fruit juice and breakfast cereals at desirable and safe levels, in addition to adequate sun exposure. Meta-analysis has shown that such vitamin D-fortified foods (including dairy products such as fortified milk and cheese, fortified orange juice, and fortified bread) have been shown to improve vitamin D status in adults. (O'Donnell *et al.*, 2008). A recent Finnish experience of voluntary food fortification has also been encouraging (Lanham-New *et al.*, 2011).

Although ensuring that adequate vitamin D containing foods are consumed and promoting more exposure to sunlight seem like natural beneficial interventions, these may be less effective for certain groups such as older people since absorption of vitamin D has been shown to decrease with age. Vitamin D is important throughout the lifecycle but emphasis on vitamin D supplementation at appropriate doses should focus on older people with limited sun exposure (SACN, 2007; Souberbielle *et al.*, 2008). It has been emphasised that

supplementation with 800-1,000 IU of vitamin D per day may be the best cost effective option (Dawson-Hughes *et al.*, 2005; Dawson-Hughes *et al.*,2010). It has also been recognised that this approach has its disadvantages, such as poor compliance. Food fortification of common foods consumed may be a more promising method to achieve optimal levels of vitamin D in groups with such barriers. There is also a need to standardise methods of testing 25(OH)D and to provide high-potency vitamin D_3 preparations (Hollis, 2004) as well as further studies to establish optimal dosing recommendations.

Vitamin D supplementation and food fortification could benefit all age groups of the UK population but current recommendations for dietary intake and supplementation for vitamin D are not being followed even among groups at highest risk such as older people. A feasible approach may be to start off by targeting those at highest risk i.e. older people that are housebound or living in institutions and treat them appropriately and then extend this practice to wider population groups.

It is important to consider that certain groups such as vegetarians (that do not eat fish) may not be able to get enough dietary vitamin D since oily fish (tuna, salmon and mackerel) has the highest natural content of vitamin D. Some vitamin D supplements may not be halal or contain gelatin so may be unsuitable for some ethnic groups.

Consideration should be given to how to enhance the uptake of public health messages. There is an urgent need for a uniform policy on assessment and dietary supplementation of vitamin D, particularly among older people, to prevent poor vitamin D status and its negative consequences. Future research should include dose-response studies, and trials of vitamin D supplementation and food fortification on different age groups, and populations such as ethnic groups. It is also important that policies are implemented effectively, a matter that will require regular assessment of vitamin D status in representative samples of the population.

Vitamin D and its association with deprivation, obesity and chronic disease and implications for public health policy.

Large scale studies (papers I and III) showed vitamin D deficiency to be associated with socioeconomic status. In paper I, older people in manual social classes had an increased risk of vitamin D deficiency than those in non-manual social classes and paper III identified low income vulnerable groups being at high risk of low vitamin D status. Paper III also shows an inverse association between 25(OH) D levels and BMI in the low income samples. There is broad evidence in the literature that suggests that poor socioeconomic groups are at higher risk of overweight/obesity due to a poor lifestyle. The LIDNS findings (Nelson *et al.*, 2004) identified low income groups as having poor diets, reduced physical activity, higher levels of smoking and increased alcohol intake, all of which are established risk factors for chronic disease. It is interesting to note that obesity has been shown to be linked with poor vitamin D status and both have been shown to be associated with an increased risk of chronic diseases and its consequences. It is evident that there are many economic constraints that may influence both poor vitamin D status and overweight/obesity. There may be an inability to afford to eat a healthy diet, due to lack of cooking facilities or cooking skills and instead consuming cheaper unhealthy fast foods. Lack of ownership of a car affects the ability to shop at large supermarkets and markets where food may be more fresh, and affordable. Living in a property with a lack of storage space for food can prevent being able to buy in bulk (which is often cheaper) and leads to reliance on frequent purchases at small corner shops that may not sell fresh foods and may actually be more expensive than in a supermarket. In addition, among low income groups, there may also be an inability to go outdoors and access sunlight and be physically active i.e. go for walk due to living in unsafe areas, or due to an extra expense to get to places where it is safe to take part in physical activity. In addition, there is an inability to afford to travel to sunnier destinations (lack of holidays abroad) and have higher sun exposure. The findings from this research (paper III) could support policy development by prompting a need to increase awareness and impact the delivery of support programmes appropriate and achievable for people living in deprived areas. This research highlights that certain targeted communities need to be provided with guidance on weight management and on how to achieve optimal vitamin D status. The findings can be used to inform policy to design and implement interventions such as how to manage to eat a healthy diet on a limited budget, improve lifestyle, and appropriate provision of vitamin D supplements, tailored to meet the needs of these population groups. Interventions may in the long-term reduce morbidity and mortality and address health inequalities.

10 Conclusions

This thesis highlights that both vitamin D deficiency and obesity are areas of concern for older people and the low income/deprived population, which are, in many respects, already identified in the general population, although appear to be a problem at a greater degree among these groups. There are important associations between 25(OH)D levels, obesity and poor health outcomes. It is evident that there is a need for policies to address these important public health issues since they are common and can have substantial adverse health consequences that may be potentially reversible. These areas need to be addressed urgently in order to improve quality of life, reduce morbidity and mortality, and be cost-effective for the health services.

My contribution to this field of research shows that both vitamin D deficiency and obesity is a continuing public health problem among older people in England and the deprived population in the UK. Research in this area suggests that both poor vitamin D status and obesity are associated with poor health outcomes. Although further prospective research is required to establish the direction of causation between 25(OH) D and obesity-related chronic disease and to determine whether vitamin D supplementation/fortification could be valuable in the prevention or treatment of obesity-related diseases, research included in this thesis could be useful in informing policy.

11 Reflection – links between publications

This submission includes publications that use data that is nationally representative of mainly older people living in the community and in care home settings and other high risk groups such as the deprived population. It provides an original independent contribution to increase knowledge in the area relating vitamin D status and obesity to health outcomes and disease status. The aim of this submission was to include publications that considered a focus on vitamin D status, obesity and chronic diseases, issues of public health concern for health and disease status.

The principal data sources for the publications included are the Health Survey for England 2000, 2005, NDNS and LIDNS. The main topic areas that link these publications is vitamin D status, obesity and associations with chronic diseases among groups at high risk such as older people and the deprived population living mainly in the community but for some topics also including those living in institutions. The ideas for these publications came from becoming familiar with the data and identifying where there were gaps in the literature that could be investigated using the available data and following these ideas by the process of planning the papers with co-authors.

These topics were important to investigate at the time of preparation but there have been many developments in ideas for prospective research since these outputs have been published. Research has advanced in some of the areas covered since these publications.

12 Prospective follow up research

There have been many ideas generated to further develop and continue with research in the areas covered, following on from the publications presented in this thesis. Due to the large number of barriers to achieving an optimal vitamin D status, this area was important to investigate and we are currently writing a paper titled 'vitamin D for health: barriers to adequate intakes and how the issue is currently addressed by UK policy. I am also working on a series of publications using HSE 2005 data to study associations of vitamin D status with respiratory disease. I am also working in collaboration with colleagues to examine associations between vitamin D status and mortality. There has also been a publication that has been accepted focusing on associations between vitamin D status and hyperglycaemia (Hirani 2011 in press JAGS) and vitamin D status and pain (Hirani 2011 in press BJN). Further research is planned using the HSE 2010 vitamin D data which will be available in March 2012.

13 Appendices

13.1 Appendix 1 Planning process for papers included in the thesis

Ideas were initiated and a literature search of the topic area was carried out. After planning the analysis with co-author(s) and producing draft table outlines, the analysis was commenced using statistical packages SPSS (paper I,V) or STATA (papers II,IV,V). As a routine for all papers, initially a check for outliers in the data was carried out and the data was checked for normality as this would affect the analysis procedure. Analysis was carried out to determine the characteristics of the sample, and analysis to get an idea of what the data was showing was carried out using specific tests. It was decided to include multivariate logistic regression analysis (Papers I,II and IV) to look at the association between the dependant variables with the independent variables, adjusting for covariates such as sex, age, social class etc.

The analysis was re-checked and tables were produced in the correct format. After the tables were produced an Introduction to the paper was written, with further literature search as needed. The methods and results were then written up, highlighting the key findings and referring to the tables. Throughout the writing up of the paper it was important to discuss the findings with the co-authors to ensure that interpretation of the results had been agreed. The discussion was written by initially inserting headings for the main key paragraphs referring to what the results were highlighting. After writing the first draft it was important to email it to the co-author(s) so that they could comment. There was a need to look at literature again when reviewing the paper. Each point in the discussion needed to include references that showed similar or different findings to what was found in the study and support the discussion with a critical view. After receiving the comments from the co-author(s) this was followed by editing and re-writing of sections, including suggestions highlighted or to clarify thoughts or if there was a need to change the paragraphs to allow logical flow. The text was checked overall for .e.g. correct numbering of tables referred to in the text. It was decided early on which journal the paper would be appropriate to submit the paper to. At the final editing stage the text, tables, figures and references were formatted and checked to ensure that they were correct for the selected journal for submission. After submission the papers were sent to reviewers. The reviewers provided comments that were responded to and the papers were re-submitted until accepted. On some occasions the papers had to be resubmitted to a different journal.

13.2 Appendix 2 Health Survey for England (I, II, IV, V)

The Health Survey for England (HSE) is an annual survey of a nationally-representative sample of the general population. The initial survey was in 1991, and was part of a surveillance programme comprising a number of government-funded repeated surveys that aimed to describe and monitor the 'state of the nation's health including disease-related outcomes, general health and health-related behaviours in the general population and major sub-groups to improve targeting of nationwide health policies' (Department of Health, 1992).

The aims of the HSE are shown in the Table 1A below:

Table 1A The aims of HSE
Provide annual data about key indicators of the nation's health;
Estimate the proportion of the population with specific health conditions;
Estimate the prevalence of risk factors associated with those conditions;
Assess the frequency with which combinations of risk factors occur;
Examine differences between population sub-groups; and
Monitor progress towards selected health goals
Describe the health status of certain population groups that are difficult to study, e.g. minority ethnic groups and elderly people living in care homes.

Objectives of the initial surveys were to monitor progress towards the *Health of the Nation* (Department of Health, 1992) cardiovascular disease targets (to reduce systolic blood pressure and to reduce obesity prevalence, in adults aged 16-64y). Subsequent targets (since 1995) were to include the height of children and monitor the prevalence of child overweight and obesity.

The HSE has a series of core elements that are included every year, such as general health; smoking, drinking and fruit and vegetable consumption; height; weight; blood pressure measurements; and blood and saliva samples. Special topics are included in selected years, such as cardiovascular disease; physical activity; accidents; lung function measurement and measurements of certain blood analytes.

13.3 Appendix 3 HSE 2000 (Paper I)

Survey design

The HSE is an annual survey designed to measure health and health related behaviours in a representative English sample of adults and children. HSE 2000 was designed to provide data at both national and regional level about the population aged two and over living in private households in England. In addition, a separate sample of older people (aged 65 and over) resident in care homes was included. As in previous years, the sample for the 2000 survey included a cross-section of the population living in private households for which over 6,800 addresses were drawn from the Postcode Address File (PAF). The private household sample was set at about half the size of those in most previous years of the Health Survey, so that resources could be devoted to the sample of older people resident in care homes. The care homes sample was selected from the Laing and Bussion database.The sample contained nursing, residential, dual-registered and small residential homes and covered local authority, voluntary and privately-owned care homes. 677 care homes were selected. Up to six residents at each care home were selected for interview, and interviews were achieved with nearly 2,500 care home residents. Residents who were capable of completing a full interview were interviewed in person; other residents were interviewed by proxy. As in previous years, in the private household sample all persons aged 2 and over were eligible for inclusion in the survey. At addresses where there were more than two children aged 2-15, two children were selected at random. Information was obtained directly from persons aged 13 and over. Information about children aged 2-12 was obtained from a parent, with the child present. For all participants, there was a computer-assisted interview by an interviewer with each eligible person (Stage 1).

Main Topics:

The interview with participants from the general population sample included the question modules included in most years in the Health Survey ('core' modules), such as general health and longstanding illnesses, use of health services, cigarette smoking, psycho-social health (GHQ12) and accidents. Also included in the 2000 survey were questions on disability, the Short-Form Health Outcomes (SF-12) questionnaire (and for participants aged (16-64) a new module on social capital and social exclusion). In addition to the 'core' question modules outlined above, participants in care homes were asked questions about cardiovascular disease (CVD) and respiratory symptoms, eating habits, physical activity and activities in the care home. The disability module was also included in the care home sample

interview. A short interview with home managers included details about the type of care home, the number of residents and the availability of services and specialised equipment.

Participants aged 16 and over in private households, and participants completing personal interviews in the care home sample, were also visited by a nurse (Stage 2) who made a number of measurements and in some cases obtained a blood sample or a saliva sample. Nurses also used computer-assisted interviewing. Blood and saliva samples were sent to a laboratory for analysis. Interviewing was conducted throughout the year to take account of seasonal differences. The sampling design, methods and full protocol for measurements have been described in detail in the HSE methodology report (Prior *et al.*, 2002).

Blood Sample

Blood samples were collected non-fasted and analysed for serum 25(OH)D by the Diasorin Kit. The laboratories performing the 25(OH)D analyses took part in the Vitamin D External Quality Assessment Scheme (DEQAS).

Those who gave a blood sample were representative of those interviewed both in institutions and private households (mean age of those interviewed in institutions was 85.0 in comparison to 84.6 for those who gave a blood sample). For those in private households the mean age among those interviewed was 74.3 in comparison to 74.1 for those who provided a blood sample.

Statistical analysis

Analysis was carried out using SPSS v10. The normality of the data were confirmed using both the Kolmogorov Smirnov-test and the "Skewness index". Differences in mean serum 25(OH)D level by age and sex between people living in institutions and private households were compared using ANOVA. The Chi square test was used to test differences in prevalence of vitamin D deficiency by sex, age group and risk factors between those living in institutions and private households. A logistic regression model was developed to examine associations between vitamin D deficiency and possible risk factors. The dependant variable was vitamin D deficiency (serum concentrations of 25-hydroxycholecalciferol below 25 nmol/l). The independent variables included were household type (i.e. institution or private household), sex, general health, season, cigarette smoking status, social class, body mass index (BMI), longstanding illness, musculoskeletal condition and disability.

13.4 Appendix 4 HSE 2005 (Papers II,IV)

Survey design

HSE 2005 was designed to provide data at national and regional level from a representative sample of older adults. The survey was commissioned by the NHS Information Centre. The 2005 survey drew its sample of older people only from those living in private households, and introduced a number of new areas of questioning and physical performance measures. The general household sampling method does not yield sufficient numbers of older people to allow the detailed analyses required. Therefore, only half of the usual sample number of adults and children was selected in the usual way. This provided a representative sample of the whole population at both national and regional level, including older people who were included in this general sample. 7,200 addresses were selected in 720 postcode sectors issued over twelve months from January to December 2005. At each address, all households, and all persons in them, were eligible for inclusion in the survey. Where there were three or more children aged 0-15 in a household, two of the children were selected at random. A nurse visit was arranged for all participants who consented. In addition to the core household sample, a boost sample of older people was selected using 11,520 additional addresses at the same 720 sampling points as the core sample. Households were screened to identify whether older people were resident, and in these cases interviews and nurse visits were conducted. For some months of the year (January, February, October, November and December), this same boost sample was also used to identify households with children aged 2-15, and interviews were conducted with up to two children when such households were identified. There was no nurse follow up for this child boost sample. The boost sample of children was taken to increase the number of children available for analysis as part of the monitoring of the government target on obesity in children. Data collection involved an interview, followed for all participants in the core sample, and for older people in the boost sample, by a visit from a specially trained nurse, if the informant agreed. The nurse visit included measurements and collection of blood, urine and saliva samples as well as additional questioning. Both interviewers and nurses used computer assisted interviewing. The sampling design and methodology have been described in more detail in the report (Craig and Mindell,2007).

Data collection

Eligible participants were all those living at 18,720 private addresses randomly selected in a two-stage stratified sampling process from the Postcode Address File. 4,269 were aged 65 years and over. An interview with each eligible older person was followed by a nurse visit. Questions asked include: smoking; consumption of alcohol, fruit and vegetables, and medications (including dietary supplements). Equivalised household income was also measured (total household annual income taking account the number of adults and children in the household). Participants were asked whether they had "any longstanding illness, disability or infirmity". Those who reported an illness, disability or infirmities were then asked whether it limited their daily activities or the work they could do, in any way. Self-reported illnesses were coded into broad categories, and then further aggregated into groups which corresponded as far as possible with the chapter headings of the International Classification of Diseases (ICD-10) (WHO, 2005).

A large number of quality control measures were built into the survey at both data collections and subsequent stages to check on the quality of interviewer and nurse performance (Craig and Mindell, 2007).

Method

Representativeness of the data included in the analysis (II and IV)

The participants were asked to comply with many components in the survey in addition to the nurse visit. These included giving a blood sample, which contributed to differences in response rate. However, specific statistical weighting were used to attempt to correct for the non-response at each stage, in addition to unequal sample selection, using information available about responders and non-responders. Further confirmatory analysis showed that the participants from whom vitamin D data were obtained were representative of those interviewed. For example, mean age was 74.5 years in those interviewed and 73.7 in those who gave a blood sample; 44% of those interviewed, and 46% of those providing a blood sample were male. Similar comparisons for income, region, and social class all confirmed the representativeness of the data.

Description of variables included in the regression analysis (II)

Vitamin D was assesses in relation to the following variables:

Age: Age was grouped into five age groups: 65-69, 70-74, 75-79, 80-84 and 85+.

Sex: The analysis was adjusted to take sex differences into account.

Ethnic group: Self-defined ethnic group was categorised as: White, Black or Black British, Asian or Asian British, and Chinese or other ethnic group.

Social class:

Social class was assigned on the basis of occupation of the head of the household, with the Registrar General's standard classification (OPCS,1991). 11 Social classes were further grouped into manual (skilled manual, partly skilled, and unskilled occupations) and non manual (professional, managerial and technical, and skilled occupations).

Cigarette smoking status: Participants were asked if they smoked or had ever smoked. The answer was categorized as never smoker, former/ex smoker, or current cigarette smoker.

Body mass index (BMI): Height and weight in the HSE were measured by a trained interviewer and those where reliable/valid measurements were taken were included in the analysis. BMI was calculated as kg/m^2 and categorised as underweight (less than 20), normal weight (20-24.9), overweight (25.0–29.9), obese (30.0 or over).

Season: the month in which participants had a blood sample taken was categorised as spring (March, April, May), summer (June, July, August), autumn (September, October, November), or winter (December, January, February).

Region: There are nine Government Office Regions (GOR) in England: the categories included were North East, North West, Yorkshire and the Humber, East Midlands, West Midlands, East of England, London, South East and South West.

General health: Participants were asked the question 'How is your health in general? Would you say it was 'very good', 'good', 'fair', 'bad', or 'very bad'? In the table, the five categories are combined to present as, 'very good'/ 'good'; 'fair'; 'bad'/'very bad '.

Limiting longstanding illness: Participants were asked whether they had any longstanding illness. Those who reported such an illness were asked whether the condition limited their activities in any way. Participants were categorised as 'not having a longstanding illness', 'having a limiting longstanding illness' and having a 'non-limiting longstanding illness'.

Self-reported doctor diagnosed conditions:

Coronary heart disease: Participants were classified as having coronary heart disease if they reported ever having angina or a heart attack, confirmed by a doctor.

Diabetes: Participants were classified as having diabetes if they reported diabetes that was doctor diagnosed. The Health Survey for England interview makes no distinction between type 1 and type 2 diabetes. Diabetes that occurred only during pregnancy was excluded.

Stroke: Participants were classified as having a stroke if they reported ever having a stroke, diagnosed by a doctor.

Current musculoskeletal condition: Participants were classified as having a musculoskeletal condition if they reported ever having this condition, diagnosed by a doctor.

Multivitamin Use: This information was collected by a nurse who asked participants if 'At present, are you taking any vitamin or mineral supplements or anything else to supplement your diet or improve your health, other than those prescribed by your doctor?' This was categorised as 'Yes' or 'No'.

Blood pressure: This was measured three times after a five minute rest by a trained nurse according to standardised procedures. Participants were classified as having high blood pressure (BP) if they had a systolic blood pressure (SBP) of 140 mmHg or above, or a diastolic blood pressure (DBP) of 90 mmHg or above, or were currently taking medication specifically prescribed to treat their high blood pressure. Those with hypertension were further divided into the following categories:

Controlled	SBP below 140 mmHg/ DBP below 90 mmHg but taking medication for blood pressure
Treated but uncontrolled	SBP at or above 140 mmHg/ DBP at or above 90 mmHg and taking medication for blood pressure
Untreated	SBP at or above 140 mmHg/ DBP at or above 90 mmHg and not taking medication for blood pressure

Thiazide use: The information about the use of any prescribed medicines that are being taken at present

Vitamin D and calcium: Participants who reported having osteoporosis, diagnosed by a doctor were asked if they were taking vitamin D and calcium.

Statistical analysis

Paper II

Analysis was carried out using SPSS v15 and STATA v9.0. Descriptive data were analysed by five-year age bands to calculate age-specific mean 25(OH)D and prevalence of vitamin D deficiency and hypovitaminosis. The normality of the data were confirmed. Comparisons across the three surveys used data age- standardised to the mid-2000 population estimates. Participants with missing information were excluded from analysis. Differences in mean serum 25(OH)D level between HSE 2005, HSE 2000 and NDNS 1994/95 were compared using ANOVA. The Chi square test was used to test differences in prevalence of vitamin D deficiency and hypovitaminosis D between the years.

A logistic regression model was developed to examine associations between hypovitaminosis D and possible risk factors. The dependant variable was hypovitaminosis D. The independent variables were: age group; BMI; cigarette smoking status; chronic diseases (hypertension, coronary heart disease, diabetes, stroke); ethnicity; general health; longstanding illness; current musculoskeletal condition; multivitamin supplement use; use of thiazide diuretics; vitamin D and calcium taken for osteoporosis; region; sex; season, and social class. Analyses were conducted in SPSS and in STATA to enable statistical adjustment for the complex (clustered and stratified) survey design.

Paper IV

Analysis was carried out using STATA v10.Following a description of the sample, associations between case-level depressive symptoms and the three 25(OH)D deficiency categories were analysed in logistic regression models with sequential adjustments for demographic factors, season, supplement intake, and smoking status, followed by further separate adjustments for BMI, reported long-term illness and subjective general health status.

The 10-item Geriatric Depression Scale (GDS10) was used which is a shortened version of the 30 –item Geriatric Depression Scale, designed to diagnose depression in older people. The questionnaire comprises 10 questions, which measure depressive symptoms, such as feeling unhappy, feeling helpless, or hopeless. The GDS10 was self-completed by participants aged 65 and over. A score of 3 or more was defined as having depression.

Further information on the sampling design and methodology have been described in more detail in the report (Craig and Mindell, 2007).

13.5 Appendix 5 NDNS and LIDNS (Paper I,II,III)

13.5.1 NDNS(I, II, III)

The NDNSs were funded jointly by the Food Standards Agency (FSA) and the Department of Health (DH) until 2011; currently the rolling programme of the NDNS is funded by DH alone. NDNS provides cross-sectional information on the dietary habits and nutritional status of nationally representative samples of the UK population (FSA, 2010).

Table 2A National Diet and Nutrition Survey	
Survey	***Year survey conducted***
Dietary and Nutritional Survey of British Adults	1986/87 (Gregory *et al.*, 1990
National Diet and Nutrition Survey: Children aged 1.5 to 4.5 years	1992/93 (Gregory *et al.*, 1995)
National Diet and Nutrition Survey: Young People aged 4 to 18 years	1997 (Gregory and Lowe, 2000)
National Diet and Nutrition Survey: People aged 65 years and over	1994/95 (Finch *et al.*, 1998)
National Diet and Nutrition Survey: Adults aged 19 to 64 years	2000/01 (Ruston *et al.*, 2004)

Previous surveys have collected quantitative information on food consumption (weighed records over seven days (Gregory *et al.*,1995) or four days (Finch *et al.*, 1998); physical measurements (e.g. height, weight and blood pressure); blood samples for analysis of nutritional status indices; a detailed interview to collect information on socio-economic, demographic and lifestyle characteristics; a physical activity record (Gregory and Lowe, 2000); a urine sample (24-hour sample, Gregory *et al.*,1990); and an assessment of oral health/dental examination.(Hinds and Gregory,1995; Steele *et al.*, 1998 ; Walker *et al.*,2000). The key objectives of the NDNS are outlined in Table 3A below:

Table 3A Objectives of the NDNS
Provide detailed and robust food consumption data for individuals (>5,000 foods);
Provide information on nutrient intakes
Provide data on participants' diet, nutritional status and related characteristics to allow analysis of the links between them.

13.5.2 LIDNS (III)

This survey, of a national sample of the most materially deprived households, provides nationally representative baseline data on the dietary habits and nutritional status of the part of the UK population that has a low income. The specific aims of LIDNS are shown in Table 4A below:

Table 4A The aims of the LIDNS
Provide quantitative data on the food and nutrient intakes, sources of nutrients and assess the nutritional status of the low income population.
Describe the characteristics of individuals with intakes of specific nutrients above or below the national average.
Evaluate the extent to which the diets of the low income population vary from recommendations.
Provide physical measurements of health-related factors closely associated with diet, such as height, weight and other anthropometric measurements and blood pressure.
Measure blood indices that provide evidence of nutritional status or dietary biomarkers.
Assess physical activity levels of the low income population.
Provide basic information on smoking and oral health status in relation to diet.
Examine the relationship between dietary intake and factors associated with food choice in the low income population.

The LIDNS sample selection included all regions of UK. The target population was the 15% most deprived households in the UK and participants were selected based on screening questions aimed at identifying low-income or materially deprived households (combination of questions on type of housing, car ownership, employment status, receipt of certain benefits or pensions). Up to two respondents (one adult and one child) were selected from a household, excluding pregnant women. Data were collected 2003-2005. Participants aged ≥19 years consisted of 1048 men and 2019 women. Of these, 96% started the individual questionnaire or the first of four dietary recalls. Ninety percent agreed to be visited by a nurse, 81% were successfully revisited and 51% (both sexes) provided a blood sample. A valid serum 25(OH)D sample was obtained from 246 men and 546 women (Nelson *et al.*, 2007).

The aim of the NDNS was to provide a comprehensive cross-sectional picture of the dietary habits and the nutritional status of the population of Great Britain. The survey gave valuable information on adults aged 19 to 64 years to provide guidance for future food policy, and for

the development of nutrition education programmes. The survey examined the relationship between diet and health and also included information on physical activity and oral health in relation to dietary intake and nutritional status.

Fieldwork for the survey began in July 2000 and finished in June 2001. This fieldwork period of a year consisted of four waves to take account of seasonal variation. The survey was conducted in 152 areas covering Scotland, England and Wales. The survey was based on a random sample of the population of Great Britain living in private households. The households taking part in the survey were sampled from the PAF in Great Britain. One adult aged between 19 and 64 years per household is selected at random and then invited to take part in the survey.

The survey initially comprised a face-to-face interview to collect information on general eating habits and health, and some basic information about the individual and their household. The adults involved are then asked to keep a record of everything they eat and drink, while they are at home and when they are out, over a seven-day period.

Adults are also invited to take part in the remaining survey components, and if one is refused, then co-operation with the other components was still sought:

- a seven-day record of physical activity;
- an eating behaviour questionnaire;
- blood pressure and anthropometric measurements (height, weight, waist and hip);
- a 24-hour urine collection;
- a seven-day record of bowel movements;
- a blood sample taken by qualified phlebotomists;
- an oral health component with self-tooth and amalgam filling count.

Blood collection and analysis

Blood samples were collected non-fasted and analysed for serum 25(OH)D by the Diasorin Kit for both the National Diet and Nutrition Survey (NDNS) and the Low Income Diet and Nutrition survey (LIDNS). The laboratories performing the 25(OH)D analyses took part in the Vitamin D External Quality Assessment Scheme (DEQAS).

Anthropometry and other covariates

In both studies, interviewers collected data on socio-demographic aspects (including age, sex, ethnicity, region of residence, and season of data collection) and health behaviours (including the intake of vitamin supplements). Height and weight measurements were taken

in light clothing without shoes, and body mass index (BMI: m/kg^2) was calculated. Dietary vitamin D intakes were obtained from four 24-hour recalls on random days (including at least one weekend day) in the LIDNS sample (Nelson *et al.*, 2007) and by 7day weighed dietary records in the NDNS sample (Ruston *et al.*, 2004)

Statistical analysis

Simple and multiple regression analyses were used to model the relationships between serum 25(OH)D as a continuous outcome measure and covariates including age group, ethnicity, sex, region of residence, dietary intake, and dietary supplements use. For the NDNS sample, significant interactions were found for benefit status and season of data collection, BMI, ethnicity, dietary vitamin D intake, and supplements use ($p<0.01$). Therefore the NDNS sample was divided into those receiving benefits ($NDNS_B$) and those who did not ($NDNS_{NB}$). To assess if the predictors of serum 25(OH)D in the LIDNS sample were similar to those in other low income groups analyses carried out separately for the three samples, LIDNS, $NDNS_B$, and $NDNS_{NB}$. Descriptive statistics were weighted to correct for the sampling probabilities and non-response in the two surveys (FSA, 2004). For all the three samples, the "Skewness index" for the distribution of serum 25(OH)D were between 0.5 and 0.8 samples, and hence there was no need to transform the variable prior to analysis.

13.6 Appendix 6 HSE 1993-2008, main focus HSE 2005 (Paper V)

Sample

The HSE is a continuous series of large, cross-sectional annual surveys in a representative sample of the non-institutionalised English population designed to provide health related information on the general population in England. From 1991 to 2004, it was commissioned by the English Department of Health, and since 2005 by the NHS Information Centre. The survey has a series of core elements that are included every year and special topics that are included in selected years. The annual household response rate for adults varied between 76% (1993) and 68% (2008), depending on the survey year. The trends data is presented for people aged ≥65 with valid height, weight and waist circumference data from the annual surveys over the period 1993 to 2008 (The Information centre, 2009). A majority of the sample (~94%) in each of these years was of self-defined 'white' ethnic group. The main focus of this paper is on chronic disease among older people. In 2005, the Health Survey for England (HSE) included an additional, nationally representative general population sample of English people aged 65 and over, living in private households. Like previous surveys in the HSE series, the 2005 survey adopted a multi-stage stratified probability sampling design using the English Postcode Address File (PAF) as the primary sampling frame. It comprised a core (general population) sample randomly selected using 7,200 addresses in 720 postcode sectors, and a boost sample of people aged 65 and over, selected using 11,520 additional addresses at the same 720 postcode sectors as the core sample. Households were screened to identify whether older people were resident and, in these cases, interviews and nurse visits were conducted. The total sample aged 65 and over who were interviewed included 4,269 residents (723 men, 873 women in the general population sample and 1,174 men and 1,499 women in the boost sample). The overall response rate among men and women aged 65 and over was 71% in the general population sample and
74% in the boost sample.

Statistical analysis

Analysis was carried out using SPSS v15 and STATA v10.0. In 2003, non-response weighting was introduced for the first time in the HSE series. Trend data presented in Figures 1 and 2 before 2003 is not weighted for non-response. Data for other analyses were weighted appropriately to take into account non-response and to correct for unequal sample selection. Data on prevalence of chronic diseases by overweight/obesity and raised WC was age- standardised to the mid-2000 population estimates and the Chi square test was used to test differences in prevalence of disease by BMI or raised waist circumference. To further investigate the link between different fat patterns and risk of chronic disease, sex-specific logistic regression models were developed. The dependant variables in the two models were BMI ≥ 25 kg/m^2 and WC >102cm in men and >88cm in women which were run separately, adjusted simultaneously by the independent variables included in the models. These were age group, smoking status, region, social class, general health, longstanding illness, hypertension, self-reported chronic conditions (such as heart disease, stroke, diabetes, cancer, arthritis, osteoporosis, joint replacement, chronic lung disease) and reporting having a fall in the last year. The analysis was run in STATA to enable statistical adjustment for the complex (clustered and stratified) survey design.

Representativeness of the data included in the analysis

The participants were asked to comply with many components in the survey in addition to the nurse visit. These included giving a blood sample, which contributed to differences in response rate. However, specific statistical weighting were used to attempt to correct for the non-response at each stage, in addition to unequal sample selection, using information available about responders and non-responders. Further confirmatory analysis showed that the participants from whom a valid waist circumference (nurse visit) was obtained were representative of those interviewed. For example, mean age was 74.5(SD 6.8) years in those interviewed and 74.0 (SD 6.6) in those who had a valid waist circumference measurement; 44% of those interviewed, and 46% of those providing a valid waist circumference measurement were male. Similar comparisons for income, region, and social class all confirmed the representativeness of the data.

Description of variables included in the regression analysis

Overweight, obesity and raised waist circumference was assessed in relation to the following variables:

Age: Age was grouped into five age groups: 65-69, 70-74, 75-79, 80-84 and 85+.

Sex: The analysis was adjusted to take sex differences into account.

Social class:

Social class was assigned on the basis of occupation of the head of the household, with the Registrar General's standard classification. 11 Social classes were further grouped into manual (skilled manual, partly skilled, and unskilled occupations) and non manual (professional, managerial and technical, and skilled occupations).

Cigarette smoking status: Participants were asked if they smoked or had ever smoked. The answer was categorized as never smoker, former/ex smoker, or current cigarette smoker.

Body mass index (BMI): Height and weight in the HSE were measured by a trained interviewer and those where reliable/valid measurements were taken were included in the analysis. BMI was calculated as kg/m^2 and categorised as underweight (less than 20), normal weight (20-24.9), overweight (25.0–29.9), obese (30.0 or over).

Region: There are nine Government Office Regions (GOR) in England: the categories included were North East, North West, Yorkshire and the Humber, East Midlands, West Midlands, East of England, London, South East and South West.

General health: Participants were asked the question 'How is your health in general? Would you say it was 'very good', 'good', 'fair', 'bad', or 'very bad'? In the table, the five categories are combined to present as, 'very good'/ 'good'; 'fair'; 'bad'/'very bad '.

Limiting longstanding illness: Participants were asked whether they had any longstanding illness. Those who reported such an illness were asked whether the condition limited their activities in any way. Participants were categorised as 'not having a longstanding illness', 'having a limiting longstanding illness' and having a 'non-limiting longstanding illness'.

Self reported doctor diagnosed conditions:

Coronary heart disease: Participants were classified as having coronary heart disease if they reported ever having angina or a heart attack, confirmed by a doctor.

Diabetes: Participants were classified as having diabetes if they reported diabetes that was doctor diagnosed. The Health Survey for England interview makes no distinction between type 1 and type 2 diabetes. Diabetes that occurred only during pregnancy was excluded.

Stroke: Participants were classified as having a stroke if they reported ever having a stroke, diagnosed by a doctor.

Current musculoskeletal condition: Participants were classified as having a musculoskeletal condition if they reported ever having this condition, diagnosed by a doctor.

Joint replacement: Participants were classified as having a joint replacement if they reported ever having this condition, diagnosed by a doctor.

Cancer: Participants were classified as having cancer if they reported ever having this condition, diagnosed by a doctor.

Falls: Participants were classified as having a fall if they reported having a fall in the last 12 months.

Chronic lung disease: Participants were classified as having a this condition if they reported ever having chronic bronchitis, or emphysema, diagnosed by a doctor.

Blood pressure: This was measured three times after a five minute rest by a trained nurse according to standardised procedures. Participants were classified as having high blood pressure (BP) if they had a systolic blood pressure (SBP) of 140 mmHg or above, or a diastolic blood pressure (DBP) of 90 mmHg or above, or were currently taking medication specifically prescribed to treat their high blood pressure. Those with hypertension were further divided into the following categories:

Controlled	SBP below 140 mmHg/ DBP below 90 mmHg but taking medication for blood pressure
Treated but uncontrolled	SBP at or above 140 mmHg/ DBP at or above 90 mmHg and taking medication for blood pressure
Untreated	SBP at or above 140 mmHg/ DBP at or above 90 mmHg and not taking medication for blood pressure

13.7 Appendix 7 HSE measurement protocols

Height

Height was measured using a portable stadiometer with a sliding head plate, a base plate and three connecting rods marked with a metric measuring scale. Participants were asked to remove their shoes. One measurement was taken, with the informant stretching to the maximum height and the head positioned in the Frankfort plane. The reading was recorded to the nearest millimetre. Participants who were ill, chairbound, unsteady on their feet etc. to obtain a reliable height measurement were not measured.

Weight

Weight was measured using Soehnle, Seca or Tanita electronic scales with a digital display. Participants were asked to remove shoes and any bulky clothing. The reading was recorded to the nearest 100g. Participants who were chairbound, or unsteady on their feet were not weighed. Participants who weighed more than 130 kg were asked for their estimated weights. Participants who were chairbound, or unsteady on their feet were not weighed. Height and weight measurement were used to calculate body mass index (BMI, the weight in kilograms divided by the square of the height in metres). Participants in the sample who had estimated weights were excluded from the BMI calculation.

Waist circumference

Waist circumference was defined as the midpoint between the lower rib and the upper margin of the iliac crest. WC was defined as the midpoint between the lower rib and the upper margin of the iliac crest. It was measured using a tape with an insertion buckle at one end. The measurement was taken twice, using the same tape, and was recorded to the nearest even millimetre. Those whose two WC differed by more than 3 cm had a third measurement taken. The mean of the two valid measurements was used in the analysis. Participants with measurements considered unreliable by the nurse, for example due to excessive clothing or movement, were excluded from the analysis.

13.8 Appendix 8 Internal and external assessment results for vitamin D in NDNS (1994/95 and 2000/2001), HSE 2000, HSE 2005, and LIDNS

Quality control procedures for the NDNS comprised both internal and external procedures. The DiaSorin (previously Incstar, Minnesota, USA) 25(OH)-vitamin D radioimmunoassay (RIA) kit assay was used.

Quality control assessment results for vitamin D, NDNS 1994/95 and 2000/2001

Table 5A Internal Control results for vitamin D, NDNS 1994/95

Wave*	Mean	SD	CV (%)	N
1	50.0	7.79	15.6	62
2	51.0	7.22	14.2	62
3	50.9	7.85	15.4	66
4	49.7	7.88	15.9	32

Table 6A Kit **Control results for vitamin D, NDNS 1994/95

Wave*	Target range	Observed mean(nM)	SD	CV (%)	N
1	17.5-52.5	33.4	5.14	15.4	31
2	17.5-52.6	31.5	4.45	14.1	22
3	17.5-52.7	30.7	3.71	12.1	18
4	17.5-52.8	33.7	5.75	17.1	22

*Fieldwork wave
1: Oct-Dec 1994
2: Jan-March 1995
3: April-June 1995
4: July-Sept 1995
**Kit QC had target ranges based on Diasorin (Incstar) kit.

External Quality Control.

Data is not published but the laboratory participated in the DEQAS scheme: for 24 samples the analysis showed an overall mean deviation index of -0.51.

Table 7A Internal Control results for vitamin D, NDNS 2000/2001

Wave*	Mean	SD	CV (%)	N
1	67.7	6.9	10.2	24
2	60.6	10.1	16.7	38
3	61.5	8.7	14.2	31
4	51.9	5.9	11.4	39

Table 8A Kit Control results for vitamin D, NDNS 2000/2001**

Wave*	Target range	Observed mean(nM)	SD	CV (%)	N
1	24.3 - 50.8	38.2	2.9	7.6	15
2	23.8 - 50.8	38.7	4.3	11.1	15
3	23.5 - 50.0	34.6	3.1	9.0	31
4	23.5 - 50.0	36.3	2.6	7.2	35

*Fieldwork wave
1: July-Sept 2000
2: Oct-Dec 2000
3: Jan-March 2001
4: April-June 2001
**Kit QC had target ranges based on Diasorin (Incstar) kit.

External Quality Control.

Data is not published, but the laboratory participated in the DEQAS scheme: for 24 samples the analysis showed an overall mean deviation index of -0.4.

Quality control assessment results for vitamin D HSE 2000 and HSE 2005

Table 9A Internal quality control results for Vitamin D, HSE 2000

Date[a]	Level (mg/l) Target/Achieved	Acceptable Range	S.D.(mg/l) Achieved	C.V (%) Achieved
May	42.0/41.7	30.0-52.0	5.05	12.1
	149.0/145.8	111.0-186.0	18.58	12.7
June	42.0/46.3	30.0-52.0	3.89	8.4
	149.0/158.8	111.0-186.0	12.80	8.1
July	42.0/38.7	30.0-52.0	5.6	14.5
	149.0/140.2	111.0-186.0	19.37	13.8
August	37.0/36.4	24.0-49.0	36.4	20.6
	144.0/151.3	109.0-179.0	151.3	7.9
September	37.0/40.1	24.0-49.0	4.80	12.0
	144.0/150.0	109.0-179.0	25.22	16.8
October	37.0/36.1	24.0-49.0	5.10	14.1
	144.0/137.7	109.0-179.0	13.38	9.7
November	37.0/32.7	24.0-49.0	5.00	15.3
	144.0/133.0	109.0-179.0	7.13	5.4
December	38.0/40.8	24.0-51.0	4.98	12.2
January 2001	37.0/39.3	24.0-50.0	2.2	5.6
	132.0/140.8	84.0-179.0	5.7	4.0
February	37.0/34.3	24.0-50.0	6.4	18.7
	132.0/119.5	84.0-179.0	0.7	0.6
March	37.0/37.8	24.0-50.0	0.1	0.3
	132.0/132.5	84.0-179.0	17.7	13.4

a Vitamin D analysis did not start until May 2000.

Table 10A External quality assessment results for Vitamin D, HSE 2000

Date[a]	Target value[b] (nmol/L)	Assayed value (nmol/L)
October	30.3	35.0
	13.9	16.0
	50.9	53.0
	25.7	31.0
	25.5	32.0
January 2001	15.0	19.0
	46.5	51.0
	32.4	44.0
	15.5	19.0
	49.7	54.0

a Assay did not start until May 2000 and there were only two EQA distributions over the period of the Health Survey 2000.

b All laboratory trimmed mean.

Table 11A Internal quality control results for Vitamin D, HSE 2005

Date	Level (nmol/L) Target/Achieved	Acceptable Range	S.D. (nmol/L) Achieved	C.V (%) Achieved
January 2005	37.0/39.2	22.0-52.0	8.60	21.9
	142.0/143.6	85.0-199.0	21.10	14.7
February	37.0/42.4	22.0-52.0	7.90	-
	142.0/143.0	85.0-199.0	19.40	13.6
March	37.0/40.1	22.0-52.0	6.60	16.5
	142.0/151.2	85.0-199.0	26.8	17.7
April	37.0/40.5	22.0-52.0	2.8	6.9
	142.0/134.9	85.0-199.0	10.1	7.5
May	37.0/38.2	22.0-52.0	7.8	20.4
	142.0/138.5	85.0-199.0	35.7	20.8
June	37.0/40.2	22.0-52.0	6.60	16.4
	142.0/139.2	85.0-199.0	15.3	11.0
July	38.0/37.6	24.0-51.0	5.90	15.7
	136.0/142.6	87.0-184.0	8.40	5.9
August	38.0/38.6	24.0-51.0	7.10	18.4
	136.0/129.5	87.0-184.0	20.50	15.8
September	38.0/36.1	24.0-51.0	4.60	12.8
	136.0/136.3	87.0-184.0	21.10	15.5
October	38.0/38.2	24.0-51.0	4.90	12.8
	136.0/133.5	87.0-184.0	7.10	5.3
November	38.0/36.2	24.0-51.0	3.20	8.8
	136.0/137.1	87.0-184.0	9.80	7.1
December	38.0/41.0	24.0-51.0	5.50	13.4
	136.0/146.9	87.0-184.0	12.20	8.3
January 2006	38.0/37.4	24.0-51.0	5.30	14.2
	136.0/145.1	87.0-184.0	15.50	10.7
February	38.0/42.3	24.0-51.0	4.80	11.3
	136.0/149.3	87.0-184.0	18.80	12.6
March	38.0/36.0	24.0-51.0	2.60	7.2
	136.0/136.0	87.0-184.0	6.00	4.4

Table 12A External quality assessment results for Vitamin D, HSE 2005

Date	Target value (nmol/L)[a]	Assayed value (nmol/L)
April 2005	62.8	64.0
	72.6	68.0
	41.6	34.0
	28.4	26.0
	27.4	22.0
July	42.0	35.0
	80.2	65.0
	76.5	69.0
	117.6	112.0
	74.5	73.0
October	80.6	83.0
	36.6	39.0
	91.8	78.0
	29.9	29.0
	65.3	61.0
January 2006	44.9	40.0
	45.8	45.0
	21.3	20.0
	68.7	72.0
	67.8	57.0

[a] Overall mean.

Quality control assessment results for vitamin D LIDNS

Table 13A Internal quality control results for Vitamin D, LIDNS

Date	Level (nmol/L) Target/Achieved	Acceptable Range	S.D. (nmol/L) Achieved	C.V (%) Achieved
January 2004	16.0/17.4	13-19	1.0	5.8
	72.0/76.7	62-82	6.3	8.2
	96.0/105.0	82-110	5.7	5.4
February	16.0/17.5	13-19	0.5	2.9
	72.0/78.8	62-82	3.8	4.8
	96.0/105.6	82-110	6.8	6.4
March	16.0/17.9	13-19	1.0	5.6
	72.0/80.9	62-82	2.0	2.5
	96.0/110.6	82-110	1.9	1.7
April	40.0/40.8	25-54	6.3	15.5
	122.0/131.1	78-166	13.8	10.5
May	37.0/35.8	24-50	3.2	8.9
	126.0/114.9	81-171	6.1	5.3
June	37.0/34.9	24-50	5.9	16.9
	126.0/117.7	81-171	13.7	11.6
July	37.0/37.0	24-50	6.5	17.6
	126.0/139.8	81-171	18.1	13.9
August	35.0/38.5	23-48	2.6	6.7
	129.0/143.5	82-175	8.6	6.0
September	35.0/38.2	23-48	2.5	6.5
	129.0/114.0	82-175	10.3	7.2
October	35.0/41.4	23-48	3.6	8.7
	129.0/140.4	82-175	9.3	6.6
November	37.0/43.5	22-52	7.1	16.3
	142.0/136.0	85-199	8.4	6.2
December	37.0/36.6	22-52	7.9	21.6
	142.0/142.1	85-199	16.4	11.5
January 2005	37.0/39.2	22.0-52.0	8.60	21.9
	142.0/143.6	85.0-199.0	21.10	14.7
February	37.0/42.4	22.0-52.0	7.90	-
	142.0/143.0	85.0-199.0	19.40	13.6
March	37.0/40.1	22.0-52.0	6.60	16.5
	142.0/151.2	85.0-199.0	26.8	17.7

Table 14A External quality assessment results for Vitamin D, LIDNS

Date	Target value (nmol/L)[a]	Assayed value (nmol/L)
January 2004	31.6	31.0
	59.5	58.0
	87.4	78.0
	107.2	80.0
	69.0	65.0
April	50.2	49.0
	49.6	42.0
	15.9	17.0
	58.2	55.0
	50.5	51.0
July	87.1	80.0
	46.5	41.0
	86.0	87.0
	24.6	27.0
	48.9	43.0
October	46.5	56.0
	125.7	116.0
	26.2	25.0
	71.1	68.0
	60.6	69.0
January 2005	32.2	27.0
	44.3	37.0
	56.3	45.0
	68.6	58.0
	80.4	77.0

[a] Overall mean.

13.9 Appendix 9 Full list of publications and selected Government commissioned reports

Hirani V. (2011). Vitamin D status and pain: analysis from the Health Survey for England (HSE) among English adults aged 65 and over (accepted in press *BJN*)

Hirani V. (2011).Relationship between vitamin D and hyperglycaemia in older people from a nationally representative population survey (accepted in press *J Am Geriatr Soc.*)

Hirani V. (2011).Generalised and abdominal adiposity are important risk factors for chronic disease in older people: results from a nationally representative survey (accepted in press *J Nutr and Ageing*).

Stewart R and **Hirani V.** (2010).Relationship between depression and vitamin D levels in older residents from a national survey population. *Psychosom Med.*72(7), p608-12.

Hirani V, Tabassum F, Aresu M, Mindell J.(2010). Development of new demi-span equations from a nationally representative sample of adults to estimate maximal adult height . *J Nutr.* 140(8),p1475-80.

Hirani V, Tull K, Ali A, Mindell J.(2010). Urgent action needed to improve vitamin D Status among older people in England! *Age Ageing.* 39(1), p62-8..

Tull K, **Hirani V,** Ali A ,Mindell J.(2009). Prevalence of anaemias and use of serum transferrin receptor protein in anaemia diagnosis in older adults. *Age Ageing.*38(5), p609-13.

Stewart R and **Hirani V.**(2009). General health status and vascular disorders as correlates of late-life depression in a national survey sample .*Int J Geriatric Psychiatry.* 25, p483–488.

Hirani V, Tull K, Ali A. (2008).Vitamin D deficiency among older adults in England remains a cause for concern! *Proc Nutr Soc.* 67(OCE),E45.

Stamatakis, E, **Hirani V,** Rennie K.(2008). Different physical activity types and sedentary behaviour and in relation to body mass index-defined obesity and raised waist circumference. *Br J Nutr.* 5, p1-9.

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Publications in preparation/ submitted

Hirani V, Aresu M. Vitamin D and mortality from a nationally representative sample of older people (in prep).

Hirani V, Aresu M, Mindell J. Development of new demi-span equations from a nationally representative sample of adults to estimate maximal height in older people (submitted *J Am Geriatr Soc*).

Stewart R and **Hirani V**. Relationship between depression, anaemia and iron status in older residents from a national survey population (submitted to *Int J Geriatric Psychiatry*).

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13.10 Appendix 10 Statement from co-authors of the papers submitted in the thesis

The statements from co-authors regarding my contribution corresponding to papers I, II and IV included in the thesis are underlined. For paper III my role is indicated in the paper page 763.

2.4. Collaboration

Where any of the work to be submitted has been carried out in collaboration with other persons, a statement should be made here of the extent of the applicant's contribution to the work, and appropriate evidence should be appended.

1. **Hirani V** and Primatesta P. *Vitamin D concentrations among people aged 65 years and over living in private households and institutions in England: population survey.* Age and Ageing 2005 34(5):485-491; doi:10.1093/ageing/afi153 July 25, 2005.

V. H. initiated the idea of the paper, designed and conducted the analyses, interpreted the results, prepared the first draft and had responsibility in preparing the final draft with co-authors for submission.

2. **Hirani V**, Zaninotto P, Primatesta P. *Generalised and abdominal obesity and risk of diabetes, hypertension and hypertension- diabetes co-morbidity in England* Public Health Nutr. 2007; 4:1-7.

V. H. initiated the idea of the paper, designed the analysis, carried out the initial analyses and with co-authors interpreted the results, prepared the first draft and with co-authors had responsibility in preparing the final draft for submission.

30/04/2010

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2.4. Collaboration

Where any of the work to be submitted has been carried out in collaboration with other persons, a statement should be made here of the extent of the applicant's contribution to the work, and appropriate evidence should be appended.

Hirani V and Mindell J. The effect of using demi-span in the assessment of body mass index among people aged 65 and over in England. Age Ageing. 2008 May;37(3):311-7.

V H reviewed the literature, designed the analysis, conducted the analyses, interpreted the results, prepared the first draft and had responsibility in preparing the final draft for submission.

Hirani V, Tabassum F, Aresu M, Mindell J. New demi-span equations from a nationally representative sample of adults to estimate maximal adult height (accepted by J Nutr).

VH initiated the idea of the paper. VH designed and contributed to the analyses, wrote the first draft of the manuscript and had responsibility in preparing the final draft for submission.

Hirani V, Tull K, Ali A, Mindell J. Urgent action needed to improve vitamin D Status among older people in England! Age Ageing. 2010;39(1):62-8. Epub 2009 Nov 23.

VH initiated the idea of the study, designed and conducted the analyses, interpreted the results, prepared the first draft and final draft for submission.

I am confirming that Vasant Hirani contributed fully to the following chapter :

Falaschetti,E, **Hirani V**, Mindell,J. Chronic diseases and quality of care (Volume 2, Chapter 3): In Craig R, Mindell J. (ed.) Health Survey for England 2005. The health of older people. London: National Centre for Social Research, 2007.

Dr Jennifer Mindell, BSc MBBS PhD FFPH FRCP

4th May 2010

2.4. Collaboration

Where any of the work to be submitted has been carried out in collaboration with other persons, a statement should be made here of the extent of the applicant's contribution to the work, and appropriate evidence should be appended.

Hirani V, Tull K, Ali A, Mindell J. *Urgent action needed to improve vitamin D Status among older people in England!* Age Ageing. 2010;39(1):62-8. Epub 2009

VH initiated the idea of the study, designed and conducted the analyses, interpreted the results, prepared the first draft and final draft for submission.

Tull K, Hirani V, Ali A ,Mindell J. *Prevalence of anaemias and use of serum transferrin receptor protein in anaemia diagnosis in older adults.* Age Ageing. 2009 Sep;38(5):609-13.

V. H. contributed to the design of the analysis, conducted the multivariate regression analyses, interpreted the results, and contributed to the preparation of the manuscript.

I agree that Vasant Hirani contributed to the papers above as described above.

Kerina Tull

2.4. Collaboration

Where any of the work to be submitted has been carried out in collaboration with other persons, a statement should be made here of the extent of the applicant's contribution to the work, and appropriate evidence should be appended.

Hirani V, Tull K, Ali A, Mindell J. *Urgent action needed to improve vitamin D Status among older people in England!* Age Ageing. 2010;39(1):62-8. Epub 2009

VH initiated the idea of the study, designed and conducted the analyses, interpreted the results, prepared the first draft and final draft for submission.

I agree that Vasant Hirani contributed to the papers above as described above.

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28th April 2010

To Whom It May Concern

I am writing to confirm the contributions of Vasant Hirani to the following three papers which I have co-authored with her.

1. Dental health and cognitive impairment in an English national survey population.
Robert Stewart[1] and Vasant Hirani[2]
1 King's College London (Institute of Psychiatry), London, UK
2 University College London Medical School, University College London, London, UK

Journal of the American Geriatric Society. 2007 Sep;55(9):1410-4.

2. General health status and vascular disorders as correlates of late-life depressive symptoms in a national survey sample
Robert Stewart[1] and Vasant Hirani[2]
1King's College London (Institute of Psychiatry), London, UK
2 University College London Medical School, University College London, London, UK

International Journal of Geriatric Psychiatry. 2010 May;25(5):483-8.

For the above two papers, V. H. contributed to the design of the analyses, conducted the analyses, contributed to the interpretation of results and to the preparation of the manuscript. V.H had full access to the survey data.

3. Relationship between depression and vitamin D levels in older residents from a national survey population
Robert Stewart[1] and Vasant Hirani[2]
1King's College London (Institute of Psychiatry), London, UK
2 University College London Medical School, University College London, London, UK

Psychosomatic Medicine (in submission – revision requested)

V. H. initiated the idea for the paper, contributed to the design of the analysis, conducted the analyses, contributed to the interpretation of results and to the preparation of the manuscript. V.H had full access to the survey data.

I am very happy to be contacted should any of the above information need clarifying

Yours

R. J. Stewart

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Clinical Reader and Head of Section of Epidemiology

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I would like to thank and acknowledge co-authors for their collaboration and contributions to the publications included in this thesis.

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May 2011

Hirani

Vasant Hirani

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16 Original publications

The thesis consists of the following publications

I. Hirani V and Primatesta P. Vitamin D concentrations among people aged 65 years and over living in private households and institutions in England: population survey. Age and Ageing 2005 34(5):485-491; doi:10.1093/ageing/afi153. July 25, 2005.

II. Hirani V, Tull K, Ali A, Mindell J. Urgent action needed to improve vitamin D Status among older people in England! Age Ageing. 2010;39(1):62-8.

III. Hirani V, Mosdol A, Mishra G. Predictors of 25-hydroxyvitamin D status among adults in two British national surveys. Br J Nutr. 2008 ;17:1-5.

IV. Stewart R and Hirani V. Relationship between depression and vitamin D levels in older residents from a national survey population. Psychosom Med. 2010; 72(7):608-12.

V. Hirani V. Generalised and abdominal adiposity are important risk factors for chronic disease in older people: results from a nationally representative survey (accepted in Press June 2011 J Nutr and Ageing Available online at http://precedings.nature.com/users/e6d3fc64c08fb5cee67e27ba8be5a4ce).

PAPER I

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Vitamin D concentrations among people aged 65 years and over living in private households and institutions in England: population survey

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Abstract

Background: vitamin D deficiency among older people results in poor bone and muscle health and an increased risk of fractures. In the UK, government initiatives and the launch of the Osteoporosis Strategy have been in place since 1998, highlighting the importance of adequate levels of vitamin D for its prevention. The aim of this analysis is to assess vitamin D status and examine associations of deficiency with risk factors among older people in England.
Methods: a valid vitamin D sample was obtained from 1,766 informants as part of the Health Survey for England (HSE) 2000, a nationally representative survey of people aged 65 and over living in institutions and private households in England.
Results: among both men and women in institutions, the prevalence of vitamin D deficiency was higher and mean serum vitamin D levels were significantly lower than among those in private households. Regression analyses showed that women were more likely to be vitamin D deficient than men (odds ratio (OR) 2.1) and deficiency was associated with limiting long-standing illness (OR 3.57), manual social classes (OR 2.4), poor general health (OR 1.92) and body mass index <25 kg/m^2 (OR 2.02), and was 67% more likely among informants in the winter/autumn. Overall, the results show no significant improvements in vitamin D status in comparison to earlier National Diet and Nutrition Survey (NDNS) results.
Conclusion: vitamin D deficiency exists at worrying levels among those aged 65 years and over. Further action is needed to alert health professionals about the risks related to vitamin D deficiency and extend the provision of prevention and treatment programmes targeted to those in need.

Keywords: *vitamin D deficiency, older people, England, population survey*

Introduction

It is well recognised that vitamin D deficiency in adults clinically manifests as osteomalacia and osteoporosis, characterised by muscle weakness, skeletal pain, deformed and brittle bones, and an increased risk of fractures. The risk of deficiency has important implications for general health. It increases as a result of an age-related reduction in bone mass (particularly after the menopause), with obesity [1], and among cigarette smokers, although it has been suggested that this could be due to the association with poor diets [2]. It also increases during the winter [3], and due to factors that effect adequate sun exposure and therefore formation of vitamin D by the skin [4].

In 1998, the UK government introduced new clinical guidelines on strategies for the management and treatment of osteoporosis [5]. The guidelines' key messages were on prevention and treatment to help primary care teams develop consistent, evidence-based practice for diagnosing and managing osteoporosis. The COMA (Committee on the Medical Aspects of Food and Nutrition Policy) report on nutrition and bone health highlighted the importance of ensuring enough calcium and vitamin D in the prevention of osteoporosis [5, 6].

Although the efficacy of vitamin D supplementation as a health improvement strategy in the healthy community-dwelling elderly is not proven, it has been recommended that older people at high risk, i.e the frail, housebound or institutionalised and those with restricted mobility, should receive routine supplementation of vitamin D [6, 7] this can preserve muscle strength and functional ability [8–12]. In a recent meta-analysis [13], vitamin D supplementation between 700 and 800 IU/d appears to reduce the risk of hip and any non-vertebral fractures in ambulatory or institutionalised elderly persons.

The aim of this paper is to assess vitamin D status among older people in England by means of the Health Survey for England (HSE) 2000, a continuous survey carried out on behalf of the Department of Health to look at the health of people living in England. In 2000 it included a

nationally representative sample of people aged 65 and over living in institutions and in private households in England [14].

Methods

The HSE 2000 was designed to provide data at both national and regional level from a sample of older people (aged 65 and over) resident in private households and care homes.

For the institution sample, 677 care homes were selected. Up to six residents at each care home were selected for interview, and interviews were achieved with 1,217 residents. Residents who were capable of completing a full interview were interviewed in person; other residents were interviewed by proxy. The private household sample included 1,677 residents, aged 65 and over, who were interviewed. As in previous years, the general population sample for the 2000 survey included a cross-section of the population living in private households for which over 6,800 addresses were drawn from the Postcode Address File (PAF). The private household sample was set at about half the size of those in most previous years of the Health Survey, so that resources could be devoted to the sample of older people resident in care homes.

A blood sample was obtained from 61% of the total institution sample (1,217) and 64% of the private household sample (1,677) aged 65 and over who gave written consent. A valid 25-hydroxycholecalciferol (vitamin D) sample was obtained from 1,766 informants (708 men and 1058 women). Those who gave a blood sample were representative of those interviewed both in institutions and private households (the mean age of those interviewed in institutions was 85.0 in comparison to 84.6 for those who gave a blood sample). For those in private households, the mean age among those interviewed was 74.3 in comparison to 74.1 for those who provided a blood sample. Of those with a valid vitamin D sample, 1,297 informants were included in the analysis; 466 informants taking medications that would affect their vitamin D status and/or taking vitamin supplements were excluded. Vitamin D analyses were carried out at the Royal Victoria Infirmary (RVI) in Newcastle upon Tyne using the Diasorin Kit. Comparisons of the vitamin D results were made with the National Diet and Nutrition Survey (NDNS) [15], a survey nationally representative of older people aged 65 and over living in institutions and in private households in Great Britain. It included plasma vitamin D analyses for 1,185 people (927 free-living, 258 in institutions). The survey was carried out from October 1994 to September 1995; the methods by which vitamin D was analysed in both surveys were comparable. Vitamin D deficiency was defined as serum concentrations of 25-hydroxycholecalciferol <25 nmol/l [16, 17].

Results

Table 1 shows mean, lower and upper percentiles of vitamin D concentrations by sex and age group. Mean vitamin D levels declined with age and were higher among men than women, although the sex differences were only significant for those living in private households.

The mean serum vitamin D levels were significantly lower for both men (38.1 nmol/l) and women (36.7 nmol/l) in institutions than among men (56.2 nmol/l) and women (48.4 nmol/l) in private households ($P<0.05$). This was comparable with the NDNS results for both sexes. Both surveys also showed a decline in vitamin D levels with age, but not among those in institutions (NDNS data not shown).

Figure 1 shows the differences in prevalence of vitamin D deficiency by sex and age group between those in institutions and private households. In institutions there was little difference overall in the prevalence of vitamin D deficiency between men (30.2%) and women (32.5%), while in private households women (15.0%) were significantly ($P<0.001$) more deficient than men (9.6%). In the NDNS, no sex differences were observed.

Seasonal differences were observed among men in institutions only: 37% of men whose blood sample was collected in winter and autumn were vitamin D deficient in comparison to 22% of those whose sample was collected in the spring and summer.

Social class differences were observed for men living in private households and women living in institutions. Among men in private households, those from manual social classes (13%) were more likely to be vitamin D deficient than those from non-manual social classes (5%, $P<0.05$). Women living in institutions, from manual social classes, were more likely to be vitamin D deficient (40%) in comparison to those from non-manual social classes (23%).

Table 1. Distribution of vitamin D concentrations among older people aged 65 years and over living in private households and institutions by sex and age group (HSE 2000)

Private households		Age					Age		
Men	Vitamin D (nmol/l)	65–79 ($n=260$)	80+ ($n=62$)	All ($n=322$)	Women	Vitamin D (nmol/l)	65–79 ($n=249$)	80+ ($n=71$)	All ($n=320$)
	Mean (SE)	58.3(1.7)	47.5(3.0)	56.2(1.5)		Mean (SE)	49.4(1.6)	44.7(2.4)	48.4(1.3)
	Median	53.5	44.5	50.5		Median	44.0	39.0	43.0
	Upper 2.5th percentile	132.0	120.9	131.5		Upper 2.5th percentile	114.5	95.2	104.0
	Lower 2.5th percentile	19.0	15.2	18.1		Lower 2.5th percentile	16.0	10.4	16.0
Institutions		Age					Age		
Men	Vitamin D (nmol/l)	65–79 ($n=73$)	80+ ($n=128$)	All ($n=201$)	Women	Vitamin D (nmol/l)	65–79 ($n=85$)	80+ ($n=369$)	All ($n=454$)
	Mean (SE)	40.0(2.8)	37.1(1.8)	38.1(1.5)		Mean(SE)	37.4(2.0)	36.6(1.0)	36.7(0.9)
	Median	32.0	33.0	32.0		Median	33.0	32.0	32.0
	Upper 2.5th percentile	108.1	79.8	85.9		Upper 2.5th percentile	86.3	94.8	93.3
	Lower 2.5th percentile	11.6	11.0	11.1		Lower 2.5th percentile	13.2	10.0	11.0

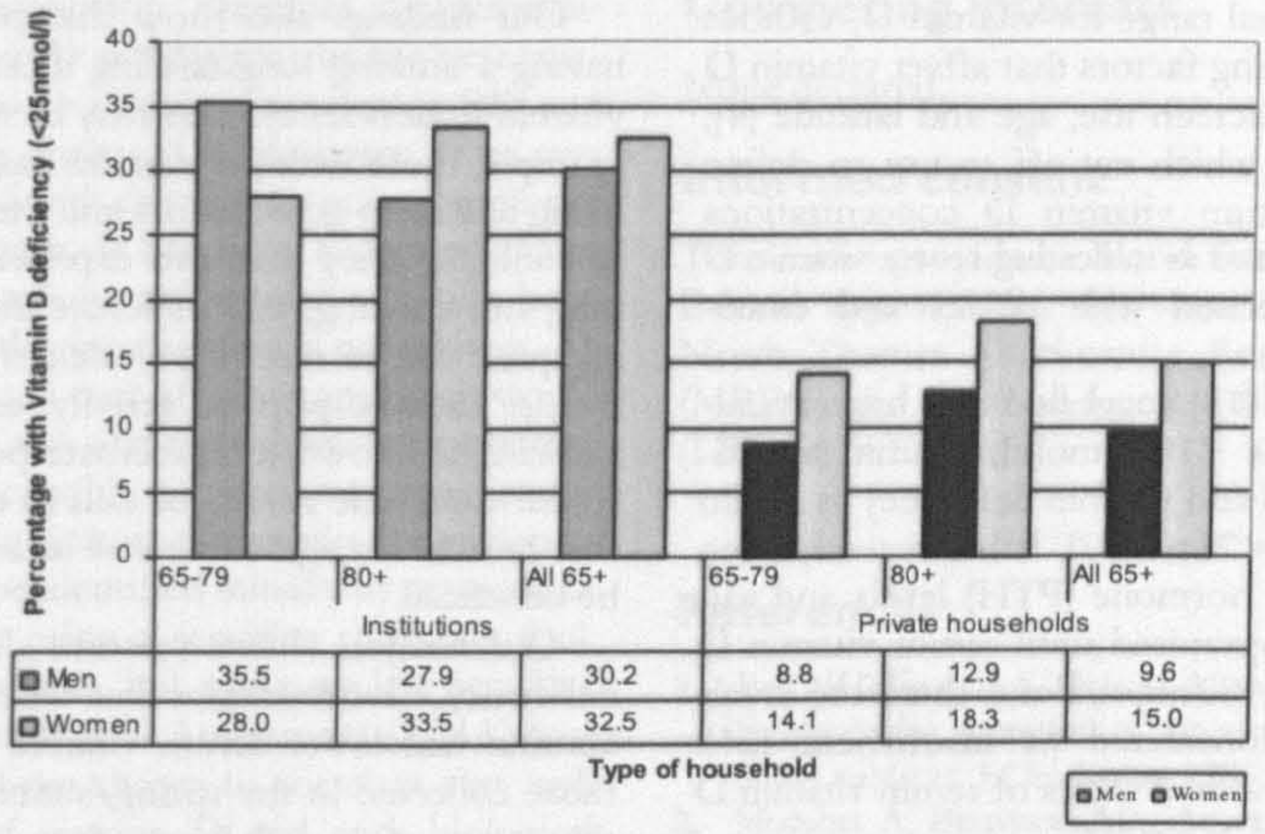

Figure 1. Percentage of older people aged 65 years, living in institutions and private homes, with vitamin D deficiency by sex and age group.

Among both men and women living in private households an association between vitamin D deficiency and poorer self-reported general health was observed. Women with vitamin D deficiency were twice as likely (66.7%) to have moderate or severe disability in comparison to those with no disability (33.3%).

To examine further the link between vitamin D deficiency and possible risk factors, a logistic regression model was developed (Table 2). The dependent variable was vitamin D deficiency (serum concentrations of 25-hydroxycholecalciferol <25 nmol/l). The independent variables included were household type (i.e. institution or private household), sex, general health, season, cigarette smoking status, social class, body mass index (BMI), longstanding illness, musculoskeletal condition and disability.

Household type, disability and cigarette smoking did not show an association with vitamin D deficiency, once the other independent variables were included in the model. Sex was associated with vitamin D deficiency: women had double the odds in comparison to men (odds ratio (OR) 2.1). Vitamin D deficiency was 67% more likely among informants whose samples were collected in winter/autumn in comparison to those collected in the spring/summer. There was an association between those suffering from a limiting longstanding illness and vitamin D deficiency (OR 3.57). Being from manual social classes and having poor general health more than doubled the odds of deficiency. BMI of <25 kg/m^2 (underweight or normal weight) was significantly associated with vitamin D deficiency. Those who were underweight or normal weight were twice as likely to be vitamin D deficient in comparison to those who were classified as overweight and obese (OR 2.02).

Table 2. Estimated odds ratio for vitamin D deficiency (serum vitamin D concentrations <25 nmol/l) by associated risk factors and sex among older people aged 65 years and over living in private households

Variable	*N*	OR	95% CI[a]
All *Base (weighted) 714*			
Sex ($P<0.001$)			
Men	353	1	
Women	361	2.1	1.40,3.0
Season ($P=0.007$)			
Spring and summer	345	1	
Winter and autumn	369	1.67	1.15,2.42
Social class ($P<0.001$)			
Non-manual	332	1	
Manual	382	2.4	1.61,3.57
BMI status ($P<0.001$)			
Over 25 kg/m^2	471	1	
Below 25 kg/m^2	243	2.02	1.39,2.93
General health ($P=0.04$)			
Very good/good	432	1	
Bad/very bad	58	1.92	1.04,3.57
Longstanding illness ($P<0.001$)			
No longstanding illness	254	1	
Limiting longstanding illness	291	3.57	2.06,6.20
Condition of musculoskeletal system ($P=0.03$)			
No condition present	517	1	
Has condition	197	0.62	0.40,0.96

[a]Confidence interval.

Discussion

The results from the HSE 2000 confirm the high prevalence of low vitamin D concentrations in the older general population in England and an even higher prevalence among those in institutions, where about one in three men and women were vitamin D deficient, using the cut-off level of <25 nmol/l. Vitamin D deficiency also exists at high levels among older populations in other European countries and the USA [18–21].

There is no generally accepted criterion for vitamin D deficiency. This, together with differences in serum vitamin D measurement, can make comparisons between studies and the interpretation of results problematic. Studies have previously measured serum vitamin D in 'healthy' human

subjects to define the normal range for vitamin D, without taking into account underlying factors that affect vitamin D status such as lifestyle, sunscreen use, age and latitude [4], hence the controversy on which cut-off to use to define deficiency. In general, serum vitamin D concentrations <20 nmol/l have been regarded as indicating severe vitamin D deficiency, clinically associated with rickets and osteomalacia [22, 23].

McKenna and Freaney [16] suggested that hypovitaminosis should be defined as <100 nmol/l, vitamin insufficiency as levels <50 nmol/l and vitamin deficiency as serum vitamin D concentrations <25 nmol/l. It has recently been proposed that parathyroid hormone (PTH) levels and calcium absorption are not optimised until serum vitamin D levels reach approximately 80 nmol/l and therefore levels <80 nmol/l should be considered as insufficient [24]. Holick [25] suggested that normal values of serum vitamin D should be between 75 and 125 nmol/l.

In our study the proposed threshold of <25 nmol/l to indicate vitamin D deficiency was used, in accordance with the Department of Health recommendations [6], and to enable comparisons with the NDNS. Further analysis of the HSE 2000 data showed that when a higher threshold of <50 nmol/l is used, around 80% (80.7% for men and 81.5% for women) of those in institutions are vitamin D deficient; the figures for those in private households are 50 and 62.2%, respectively. At a threshold of <75 nmol/l, 97.9% of men and 93.9% of women in institutions are vitamin D insufficient, whereas the figures for those in private households are 79.5 and 86.6%, respectively. These results suggest that such groups of individuals require careful surveillance in order to prevent their vitamin D levels declining even further and increasing their risk of poor bone health.

Our findings show that women were more likely to be vitamin D deficient than men. Vitamin D deficiency is often seen in post-menopausal women and has been associated with a greater incidence of hip fractures [26]. The Decalyos II study examined the effect of combined calcium and vitamin D supplementation in a group of older women studied for 2 years, and results suggested that such supplementation could reduce the risk of hip fractures in this population [27]. However, these results were contradicted by two studies that showed no evidence that calcium and vitamin D supplementation reduces the incidence of fractures in patients with a history of previous low-trauma fracture [28] and among women at high risk of fracture [29]. It could be argued that both these studies had quite a few limitations though, such as poor compliance, and that serum vitamin D levels were not measured in the study population at baseline.

In our study, for both sexes, those with vitamin D deficiency were twice as likely to be in manual as in non-manual social classes. Poor socieconomic status among older people has been shown in other studies as a risk factor for vitamin D deficiency [30]. In addition to this, those living in deprived areas often have little access to a wide variety of good quality foods [31]. This suggests that government initiatives to tackle social inequalities could also potentially influence vitamin D status among older people.

Our findings also show that poor general health and having a limiting longstanding illness were associated with vitamin D deficiency. This may be due to many factors; for example, those with poor health may have limited mobility, being unable to go outdoors and therefore lacking exposure to sunlight. They may also experience difficulties in shopping and cooking, and therefore be unable to consume an adequate diet to meet their calcium and vitamin D requirements. Lack of physical activity, especially weight-bearing exercise, is known to exacerbate poor bone health [32]. A recent Cochrane review of falls in older people [33] shows that muscle strengthening and balance training are likely to be beneficial.

Our analysis shows seasonal differences in vitamin D deficiency. Blood samples that were collected in the winter/autumn had lower serum vitamin D concentrations than those collected in the spring/summer. The evidence states this as one of the risk factors for poor bone health [34]. It is suggested that housebound older people and those in institutions should be encouraged to spend more time outdoors, but the precise dose and duration of exposure are not yet clearly established. Recommended levels are about 5–10 min of sun exposure on bare skin, two or three times per week [4]; however; this is not always possible especially in the UK. In addition older people have an age-related lowered capacity to synthesise vitamin D when exposed to sunlight.

In our analysis, those with a BMI <25 kg/m^2 (underweight/normal weight) had double the odds to be at risk of vitamin D deficiency in comparison to those with a BMI >25 kg/m^2 (overweight and obese), suggesting that nutritional status and dietary vitamin D levels among those who are underweight/normal weight are inadequate, possibly due to lack of overall food consumption and low bone density. A BMI <18.5 kg/m^2 has been shown to be one of the strongest risk factors for poor bone health [35]. Due to small numbers of individuals with a BMI <18.5 kg/m^2, the analysis could not be carried out separately in this subgroup.

The analysis fails to show any significant improvement in vitamin D status in England with comparison to earlier NDNS [15] results. Even with the government initiatives in place [36] and the launch of the Osteoporosis Strategy, vitamin D deficiency, a preventable public health problem, still exists at worrying levels.

As the number of older people in the population continues to rise, the future impact is likely to be phenomenal, resulting in a poor quality of life and major cost implications to the National Health Service. The question to ask then is whether enough is being done in primary care to prevent vitamin D deficiency. There are very few published evaluations of interventions carried out at the primary care level. Improving the diet to ensure that adequate vitamin D-containing foods are consumed and promoting more exposure to sunlight seems like a natural beneficial intervention, but may be less effective since absorption of vitamin D has been shown to decrease with age. Therefore, early detection and treatment for those with sub-optimal levels of vitamin D may be necessary.

Our data suggest that people aged 65 living in institutions are at a higher risk of vitamin D deficiency and insufficiency

than other groups in the population. Therefore, supplementation with 800 IU of vitamin D per day may be the best cost-effective option, shown to be effective in reducing falls and fractures among high-risk groups [12]. However, there may be disadvantages associated with this such as poor compliance and problems in distribution. It has been suggested that a better option could be supplementation once a month; however, the effectiveness of this intervention is not proven.

Within the community, a cost-effective approach would be to target those at high risk and treat them appropriately. The elderly are more susceptible to poor nutritional status and low BMI, which are indicators of vitamin D deficiency. Individuals at risk could be identified initially by assessment of their nutritional status using a sensitive screening tool. There are many tools available, but some are less sensitive than others. The Mini Nutritional Assessment (MNA) tool [37] is validated and has been shown to correlate very well with nutritional intake of vitamin D and with biological parameters such as serum vitamin D levels. Even though the tool only provides an indication of dietary vitamin D intake without taking exposure to sunlight into account, it may be useful to identify individuals who may benefit from further assessments. Among individuals who are only 'marginally' deficient, vitamin D supplementation may not be necessary. Interventions that include education and advice about consuming vitamin D-fortified foods, and increased exposure to sunlight may be sufficient to prevent vitamin D levels from declining any further.

In addition, in order to target appropriate interventions, health professionals should be alerted to complaints presented to them by older people, such as muscle weakness, muscle and bone pain, and a history of falls and fractures, which are indicators of vitamin D deficiency.

In conclusion, vitamin D deficiency exists at worrying levels among those aged 65 years and over, especially in institutions. Further research is required to monitor the provision of interventions over time, with clear guidelines that include awareness, evidence-based advice and education in the primary care setting.

Key points

- Vitamin D deficiency in England is higher among those living in institutions than in private households.
- Increased odds of vitamin D deficiency are seen among women and in the winter/autumn. It is associated with manual social classes, low/normal BMI, poor general health and existing longstanding limiting illness.
- No significant improvements in vitamin D status were seen in comparison with earlier NDNS results.
- Further action is needed to alert health professionals of the risks related to vitamin D deficiency and extend the provision of interventions to those in need.

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Competing interests

None declared.

Informed consent

Those who provided a blood sample gave written consent. Ethical approval for the survey was obtained from the North Thames Multi-centre Research Ethics Committee (MREC) and from all Local Research Ethics Committees (LRECs) in England.

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PAPER II

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Urgent action needed to improve vitamin D status among older people in England!

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Abstract

Background: the importance of vitamin D for bone health is well known, but emerging evidence also suggests that adequate vitamin D status may also be protective against non-communicable diseases. In the UK, government initiatives highlighting the importance of adequate vitamin D among older people have been in place since 1998.
Objectives: the aim of this analysis is to assess vitamin D status in people aged ≥65, living in private households in England, 2005 and make comparisons with the Health Survey for England (HSE) 2000 and the National Diet and Nutrition Survey (NDNS), 1994. We also examine associations of hypovitaminosis D [serum 25(OH)D <50 nmol/l] with demographic, geographic, lifestyle and health risk factors.
Design and setting: a nationally representative sample of older people living in England in 2005.
Participants: 2,070 adults aged ≥65, living in private households taking part in the HSE 2005.
Results: in the HSE 2005, mean serum 25(OH)D levels were 53 and 49 nmol/l in men and women, respectively, these levels are significantly lower than currently recommended at ≥75 nmol/l. Prevalence of vitamin D deficiency [25(OH)D <25 nmol/l] in people aged ≥65 in 2005 was 13% in women and 8% in men. Nearly two thirds (57%) of women and half of men (49%) had serum 25(OH)D <50 nmol/l. Only 16% of men and 13% of women aged ≥65 years had serum 25(OH)D levels ≥75 nmol/l. There is no improvement in vitamin D status in 2005 compared to 2000 and a significant decline in vitamin D status among men in 2005 in comparison to the 1994/1995 NDNS results. The odds of hypovitaminosis D increased by age group from those aged 75–79 to aged ≥85. Season of taking a blood sample, obesity, dark skin pigmentation, not taking vitamin supplements, cigarette smoking, poor general health and longstanding illness were all significant predictors ($P < 0.05$) of serum 25(OH)D status in adjusted regression models.
Conclusions: poor vitamin D status of older people continues to be a public health problem in England. Hypovitaminosis D is associated with many risk factors and poor health outcomes. There is now an urgent need for a uniform policy on assessment and dietary supplementation of vitamin D in older people to prevent poor vitamin D status and its negative consequences.

Keywords: *vitamin D status, older people, England, population survey*

Introduction

The importance of vitamin D for bone health is well known. Prolonged vitamin D deficiency in adults clinically manifests itself as osteomalacia and osteoporosis. Adequate vitamin D status may also be protective against non-communicable diseases [1] like diabetes, cancers, cardiovascular disease, rheumatoid arthritis and autoimmune conditions like multiple sclerosis [2]. The clinical manifestation of suboptimal vitamin D levels has a significant physical, psychological and financial impact on older people and society as a whole [3].

The amount of sun exposure necessary to meet requirements depends on factors such as age, latitude, season, time of day, time of year, clothing and skin pigmentation [4]. Older people are at higher risk of poor vitamin D status due to a decline in efficiency of vitamin D synthesis and a lowered renal conversion to its active form [5]. Low endogenous production during winter months can

be compensated for by dietary intake and supplement use, but vitamin D intake among older people is presently low in the UK [6].

A high prevalence of vitamin D deficiency has been shown, particularly among older people living in institutions [7, 8]. Concerns over vitamin D deficiency worldwide have prompted the World Health Organisation (WHO) to produce guidelines on the importance of vitamin D and supplementation [9].

In the UK, there is renewed government interest in healthy lifestyles [10], the role of vitamin D in prevention of osteoporosis [11] and initiatives to achieve adequate vitamin D status in older people [12]. A recent consensus statement [13] has suggested an intake of 800–1,000 IU of vitamin D to be sufficient to achieve a serum 25(OH) D level of 75 nmol/l, considered optimal for falls and fracture prevention [14]. Vieth *et al.* [15] suggests a higher amount is required to achieve desirable 25(OH)D concentration of 75 nmol/l.

The aim of this paper is to examine serum vitamin D status among older people aged ≥65 using data from the 2005 Health Survey for England (HSE), compare results with HSE 2000 and the UK-wide National Diet and Nutrition Survey (NDNS) carried out in 1994/1995 [6]. We also investigate the associations between hypovitaminosis D and demographic, lifestyle and health risk factors.

Methods

Participants

The HSE is a continuous series of annual surveys designed to provide information on various aspects of the health of people in England. From 1991 to 2004, it was commissioned by the English Department of Health and since 2005 by the NHS Information Centre. In 2005, the HSE included nationally representative general population sample of English people aged ≥65, living in private households [16]. The sample included 4,269 residents (1,897 men and 2,372 women) who were interviewed. Like in previous years, in the HSE, the 2005 survey adopted a multi-stage stratified probability sampling design using the Postcode Address File as the primary sampling frame. It comprised the core (general population) sample and a boost sample of people aged ≥65. The overall response rate was 71% in the general population sample and 74% in the boost sample. The sampling design and methods used have been described in detail elsewhere [16].

Interviewers collected data from participants by computer-aided personal interview on socio-demographic aspects (including age, sex, ethnicity and region), health behaviours (including questions about general self-reported health, smoking etc.) and doctor diagnosed health conditions (ischaemic heart disease, stroke and diabetes). Height and weight measurements were taken in light clothing without shoes, and body mass index (BMI: weight (kg)/height $(m)^2$) was calculated.

After the interviewer visit, those who agreed had a nurse visit. Nurses collected information including current medication and vitamin supplement usage and took measurements such as blood pressure and obtained non-fasting blood samples.

Among those aged ≥65 participating in a nurse visit (2,174), a blood sample was obtained from 70% of men and 71% of women with written consent. A valid serum 25(OH)D sample was obtained from 2,070 informants, 950 men and 1,120 women. Those who gave a blood sample were representative of those interviewed (see details in Appendix 1 in the supplementary data available in *Age and Ageing* online). Blood samples were collected throughout the year from January to December 2005.

Comparisons of the vitamin D results were made with HSE 2000 [17], which included a valid serum 25(OH)D sample obtained from 1,766 informants (708 men and 1,058 women) throughout January to December 2000, analysed in the same laboratory (Royal Victoria Infirmary in Newcastle upon Tyne, UK) and used the same method as in HSE 2005.

The HSE data were compared with the NDNS [6], a nationally representative survey of people aged ≥65 living in private households in Great Britain. The NDNS sample was also selected using a multi-stage random probability design; the study designs for all three surveys were comparable [6, 16, 17]. It included analyses of serum 25(OH)D concentrations for (927 people from private households). The NDNS was carried out from October 1994 to September 1995.

The methods by which serum 25(OH)D samples were analysed (using the DiaSorin Kit, DiaSorin Inc, Stillwater, MN, USA) in all three surveys were comparable. The laboratories performing the 25(OH)D analyses took part in the Vitamin D External Quality Assessment Scheme. In these surveys, there was no significant change in the assay's performance throughout its use, as assessed from quality assurance parameters [6, 17, 18].

In this study, vitamin D deficiency was defined as serum concentrations 25(OH)D <25 nmol/l [12], while a level <50 nmol/l was defined as hypovitaminosis [19].

Statistical analysis

Analysis was carried out using SPSS v15 and STATA v9.0. The descriptive data were analysed by 5-year age bands to calculate age-specific mean, prevalence of vitamin D deficiency and hypovitaminosis. Comparisons of mean and prevalence of vitamin D status of the three surveys included age standardisation of the data using the mid 2000 population estimates. In all three surveys, informants with missing information were excluded from the analysis. Descriptive statistics were weighted to correct for the sampling probabilities in all three surveys and non-response in HSE 2005 [18]. The normality of the data was confirmed using both the Kolmogorov–Smirnov test and the 'Skewness index' which was between 0.3 and 0.7 in the three surveys.

Table 1. Mean 25(OH)D concentrations, prevalence of vitamin D deficiency (25(OH)D <25 nmol/l) and hypovitaminosis D (25(OH)D <50 nmol/l) among older people aged 65 years and over living in private households by sex and age group in HSE 2005

		Age group (HSE 2005)					
		65–69	70–74	75–79	80–84	85+	All aged 65 and over
Men	*N*	331	250	205	98	66	950
	Mean vitamin D[a] (SE)	53 (1.3)	56 (1.7)	52 (1.6)	49 (2.0)	48 (2.3)	53 (0.8)
	Vitamin D deficiency, %	8	8	12	7	8	8
	Hypovitaminosis, %	46	44	53	57	55	49
Women	*N*	349	308	221	155	87	1,120
	Mean vitamin D[a] (SE)	52 (1.4)	52 (1.3)	44 (1.4)	45 (1.6)	42 (2.6)	48 (0.7)
	Vitamin D deficiency, %	7	11	19	16	22	14
	Hypovitaminosis, %	51	50	62	66	69	58

[a]nmol/l.

Table 2. Age standardised mean 25(OH)D concentrations, prevalence of vitamin D deficiency (25(OH)D <25 nmol/l) and hypovitaminosis D (25(OH)D <50 nmol/l) among older people aged 65 years and over living in private households (NDNS 1994/1995 HSE 2000 and HSE 2005)

		NDNS 1994/1995	HSE 2000	HSE 2005	Difference in vitamin D status between years 95% CI and *P* values		
					NDNS vs HSE 2000[b]	NDNS vs HSE 2005[c]	HSE 2000 vs HSE 2005[d]
Men	*N*	476	485	950			
	Mean vitamin D[a] (SE)	59 (1.3)	60 (1.3)	53 (0.7)	1 (−2.6, 4.6, $P = 0.5$)	−6 (3.1, 8.9, $P < 0.001$)	−7 (4.0, 10.0, $P < 0.001$)
	Vitamin D deficiency, %	7	7	8	0	1 (−1.9, 3.9, $P = 0.5$)	1 (−1.9, 3.9, $P = 0.5$)
	Hypovitaminosis D, %	41	42	49	1 (−5.7, 7.2, $P = 0.75$)	8 (2.6, 13.4, $P = 0.004$)	7 (1.6, 12.4, $P = 0.01$)
Women	*N*	451	565	1,120			
	Mean vitamin D[a] (SE)	51 (1.1)	53 (1.0)	49 (0.7)	2 (−0.9, 4.9, $P = 0.18$)	−2 (−0.5, 4.5, $P = 0.12$)	−4 (1.6, 6.4, $P = 0.001$)
	Vitamin D deficiency, %	12	8	13	−4 (0.3, 7.7, $P = 0.03$)	1 (−2.7, 4.7, $P = 0.6$)	5 (1.9,8.1, $P = 0.03$)
	Hypovitaminosis D, %	55	50	57	−5 (−1.2, 11.2, $P = 0.12$)	2 (−3.4, 7.4, $P = 0.5$)	7 (2.0,12.0, $P = 0.006$)

[a]nmol/l.
[b]Compares difference between NDNS 1994/1995 and HSE 2000.
[c]Compares difference between NDNS 1994/1995 and HSE 2005.
[d]Compares difference between HSE 2000 and HSE 2005.

Differences in mean serum concentration of 25(OH)D between HSE 2005, HSE 2000 and NDNS 1994/1995 were compared using Analysis of Variance (ANOVA). The Chi square test was used to test differences in prevalence of vitamin D deficiency and hypovitaminosis D between the years. A logistic regression model was developed to examine the link between hypovitaminosis D and possible risk factors. The dependant variable was hypovitaminosis D. The independent variables were age group, BMI, cigarette smoking status, chronic diseases (including hypertension, coronary heart disease, Type 2 diabetes and stroke), ethnicity, general health, longstanding illness. current musculoskeletal condition, multivitamin supplement use, use of diuretics (thiazides), vitamin D and calcium taken for osteoporosis, region, sex, season and social class (further information can be found in Appendix 2 in the supplementary data available in *Age and Ageing* online). Analyses were conducted using forward stepwise regression in SPSS to select the variables related to hypovitaminosis D. The final model was run in STATA to enable statistical adjustment for the complex (clustered and stratified) survey design (described in detail in the report) [18]. We found no significant interactions between the variables included in the regression analysis.

Results

Table 1 in Appendix 3 (supplementary data available on *Age and Ageing* online) presents participants' characteristics. The age standardised mean serum 25(OH)D levels in HSE 2005 were significantly higher among men than women (53 nmol/l and 49 nmol/l, respectively; $P < 0.0001$). Among men, mean serum 25(OH)D levels ranged from 56 nmol/l (95% confidence interval (CI) 52.7–59.4) in those aged 70–74 to 48 nmol/l (95% CI 43.3–52.6) among those aged ≥85; in women, 52 nmol/l (95% CI 49.4–54.6) among those aged 65–69 to 42 nmol/l (95% CI 36.9–47.1) among those aged ≥85 (Table 1).

Table 1 also shows the prevalence of vitamin D status by sex and age group for HSE 2005. Prevalence of vitamin D deficiency (25(OH)D <25 nmol/l) among men and

Table 3. Estimated odds ratio for hypovitaminosis D (25(OH)D <50 nmol/l), by demographic, lifestyle and health status variables among people aged 65 years and over living in private households in England 2005

Variables	*N*	Unadjusted odds ratio and 95% CI†	*P* values	Adjusted* odds ratio and 95% CI†	*P* values
Age ($P = 0.0001$)					
65–69	680	1		1	
70–74	558	0.9 (0.76, 1.19)	0.65	0.9 (0.71, 1.17)	0.48
75–79	426	1.4 (1.12, 1.83)	0.004	1.4 (1.09, 1.88)	0.01
80–84	253	1.7 (1.29, 2.32)	<0.001	1.8 (1.26, 2.48)	0.001
85+	153	1.8 (1.27, 2.61)	0.001	1.8 (1.18, 2.60)	0.01
Sex ($P < 0.0001$)					
Male	950	1		1	
Female	1,120	1.4 (1.15, 1.63)	0.0004	1.5 (1.19, 1.78)	<0.001
Ethnicity ($P < 0.0001$)					
White	2,032	1		1	
Non-white	34	5.6 (2.15, 14.43)	0.002	7.9 (2.76, 22.6)	<0.001
Season ($P < 0.0001$)					
Spring: March–May	473	1		1	
Summer: June–August	574	0.6 (0.50, 0.82)	<0.001	0.6 (0.43, 0.74)	<0.001
Autumn: September–November	582	1.2 (0.93, 1.50)	0.18	1.1 (0.86, 1.46)	0.42
Winter: December–February	441	2.2 (1.68, 2.88)	<0.001	2.4 (1.77, 3.19)	<0.001
Region ($P = 0.02$)					
London	170	1		1	
North East	118	0.9 (0.53, 1.38)	0.53	1.2 (0.68, 1.98)	0.58
North West	314	0.7 (0.47, 1.00)	0.05	0.6 (0.42, 0.99)	0.04
Yorkshire and The Humber	226	1.0 (0.67, 1.50)	1.00	1.1 (0.71, 1.77)	0.64
East Midlands	185	0.7 (0.45, 1.03)	0.07	0.8 (0.49, 1.24)	0.30
West Midlands	208	1.0 (0.63, 1.44)	0.82	1.1 (0.71, 1.79)	0.61
East of England	231	0.7 (0.48, 1.07)	0.11	0.8 (0.51, 1.24)	0.32
South East	359	0.6 (0.42, 0.87)	0.05	0.7 (0.48, 1.10)	0.13
South West	259	0.6 (0.42, 0.91)	0.01	0.7 (0.44, 1.05)	0.08
General health ($P = 0.02$)					
Very good/good	1,311	1		1	
Fair	571	1.6 (1.29, 1.92)	<0.001	1.3 (0.99, 1.58)	0.06
Bad/very bad	188	2.7 (1.96, 3.81)	<0.001	1.6 (1.11, 2.39)	0.01
Longstanding illness ($P = 0.01$)					
No longstanding illness	646	1		1	
Limiting longstanding illness	596	1.8 (1.10, 1.72)	0.005	1.3 (1.02, 1.68)	0.03
Non-limiting longstanding illness	828	1.4 (1.48, 2.24)	<0.001	1.4 (1.09, 1.81)	0.01
Cigarette smoking ($P = 0.003$)					
Never smoked	978	1		1	
Ex smoker	873	1.0 (0.82, 1.18)	0.84	1.0 (0.84, 1.29)	0.69
Current smoker	217	1.8 (1.30, 2.39)	<0.001	1.8 (1.26, 2.46)	<0.001
Taking multivitamin supplement ($P < 0.0001$)					
Yes	929	1		1	
No	1,141	2.7 (2.23, 3.19)	<0.001	2.6 (2.17, 3.21)	<0.001
BMI status ($P = 0.0002$)					
20–24.9 kg/m^2	458	1		1	
<20 kg/m^2	41	1.0 (0.55, 1.97)	0.91	0.8 (0.40, 1.54)	0.48
25–29.9 kg/m^2	782	1.1 (0.84, 1.34)	0.60	1.1 (0.86, 1.43)	0.41
>30 kg/m^2	455	1.6 (1.21, 2.04)	0.001	1.6 (1.16, 2.10)	0.003

*Adjusted by age, sex, ethnicity, vitamin supplement use, season, BMI status, cigarette smoking status, region, general health, longstanding illness (limiting and non-limiting).

†Odds ratio and confidence interval (CI) are weighted to represent English population.

women aged ≥65 years was 8% (95% CI 6.3–9.7) and 14% (95% CI 12.0–16.0), respectively. Prevalence of hypovitaminosis D (25(OH)D <50 nmol/l) was 49% (95% CI 45.8–52.2) in men and 58% (95% CI 55.1–60.9) in women. Further analysis shows that only 16.2% (95% CI 13.9–18.5) of men and 13.2% (95% CI 11.2–15.2) of women aged ≥65 years had serum 25(OH)D levels ≥75 nmol/l (data not shown).

In NDNS and HSE 2005, vitamin D deficiency was more prevalent among women than men (12 vs 7%, $P = 0.01$ and 13 vs 8%, $P < 0.001$, respectively). Women were also significantly more likely to have hypovitaminosis D than men in 1994 (55 vs 41%, $P < 0.001$), 2000 (50 vs 42%, $P = 0.02$) and in 2005 (57 vs 49%, $P < 0.001$, Table 2).

There have been no significant improvements in vitamin D status among older people since 1994 (Table 2). In wom-

en, the prevalence of vitamin D deficiency was significantly higher in 2005 than in 2000 ($P = 0.03$). Among men, there was no significant change with time. The prevalence of hypovitaminosis D was significantly higher in 2005 than in 2000 in men ($P = 0.01$) and in women ($P = 0.006$), and in men only, the prevalence of hypovitaminosis D was also higher in 2005 than in 1994 ($P = 0.004$, Table 2).

Table 3 shows unadjusted and adjusted regression analyses. Adjusted analyses showed significant associations indicating that women were more likely to have hypovitaminosis D than men. Odds of hypovitaminosis D increased with age and were more likely in people who described their ethnicity as non-white in people who are obese, current smokers, reported poor general health, reported limiting or non-limiting longstanding illness and did not take vitamin supplements. Hypovitaminosis D was also more frequent in blood samples taken in the winter than in the spring and summer (Table 3).

Discussion

The results from HSE 2005 show a high prevalence of suboptimal serum 25(OH)D levels and a small proportion of older people with levels in line with current recommendations at ≥75 nmol/l [14]. The data also show no significant improvements since 1994/1995. It is disappointing that vitamin D deficiency continues to exist at high levels among older populations in the UK [7] and similarly in other countries [20, 21].

There is controversy regarding inadequate serum 25(OH)D values. Conventionally, vitamin D deficiency has been defined as serum concentrations 25(OH)D <25 nmol/l [12]; <50 nmol/l has been associated with mild increase of bone turnover [19]. In some studies, serum 25(OH)D concentrations <20 nmol/l have been clinically associated with rickets and osteomalacia [22]. Other studies suggest that 25(OH)D >80 nmol/l can reduce the risk of hip and other non vertebral fractures [14]. Levels above 75 nmol/l are currently considered to be desirable [14].

Our findings show that women were more likely to have hypovitaminosis D than men, consistent with other literature [23]. This may be due differences in dietary intake or in vitamin supplement use between the sexes. Information on dietary vitamin D intake on the HSE was not available, however, the NDNS [6] showed men to have higher dietary intake from vitamin D rich foods than women. In all three surveys vitamin supplement use was higher in women than men [6, 16]. Suboptimal vitamin D levels in post-menopausal women are increase risk of hip fractures [24]. In older women, calcium and vitamin D supplementation reduced the risk of hip fractures [25]. However, in other studies calcium (1,000–1,200 mg) and vitamin D (800 IU) supplementation did not reduce the incidence of fractures [26]. However, this study had a number of limitations, such as serum 25(OH)D levels not being measured at baseline and poor compliance.

Our findings also show that hypovitaminosis D is associated with poor general health and having a longstanding illness, whether limiting or non-limiting. This association was also shown for vitamin D deficiency (25(OH)D levels <25 nmol/l) in the earlier HSE 2000 results [7].

Our analysis confirms the expected seasonal differences in serum 25(OH)D levels <50 nmol/l. Informants with blood samples collected in the winter had lower serum 25(OH)D levels than those collected in the spring and in the summer (see Figure 1 in Appendix 4 in the supplementary data available in Age and Ageing online). Housebound older people are at increased risk of vitamin D deficiency and need to spend more time outdoors in all seasons. However, older people also have lowered capacity to synthesise vitamin D when exposed to sunlight, so it is difficult for them to meet their requirements via sunlight [5].

In our analysis, those with a BMI ≥30 kg/m^2 (obese) had >50% increased odds of having hypovitaminosis D in comparison with those with a normal BMI of 20–25 kg/m^2. Other studies also show this association [27], suggesting that this is due to decreased bioavailability of vitamin D due to its deposition in fat. However, other evidence shows very lean people are also prone to vitamin D deficiency [7, 28].

Our results are consistent with those of other researchers who found a greater risk of hypovitaminosis D in people who smoked cigarettes [29] and those with darker pigmented skin [30].

Recent reviews suggest suboptimal vitamin D status may play a role in the development of chronic diseases. We examined the relationship between serum 25(OH)D and various chronic diseases. In adjusted models, hypovitaminosis D did not show an association with any of the chronic diseases included in the model. Informants on medication for hypertension were less likely to have hypovitaminosis D than those that were not hypertensive, but this was no longer significant after adjustment for thiazide use, which suggests that vitamin D levels are affected by thiazide use. This has also been shown in a review by Hathcock *et al.* [31].

Our findings fail to show any improvement in vitamin D status in older people since 1994/1995. Interventions such as early detection and treatment, increasing awareness of consuming vitamin D rich foods and getting adequate sun exposure, widespread fortification of vitamin D in food and vitamin supplementation are timely to debate [32].

Our data shows that older people not taking vitamin supplements were more likely to have hypovitaminosis D. The use of vitamin D supplements (800 IU) is shown to be effective in reducing falls and fractures among older people [14], recommended in those at high risk of deficiency [12] to preserve functional ability [14]. It has also been suggested that doses of vitamin D higher than 800 IU are required to increase serum levels to the desirable levels [15], but there is little evidence on long-term compliance of vitamin D supplementation among older adults living in the community [26].

The main strengths of the study are that it provides valuable information on current prevalence of vitamin D status in older people in England and makes comparisons with the earlier HSE 2000 and NDNS [6] results. These surveys are large, national surveys designed to give a representative picture of the population groups examined. Specific statistical weighting was included in all three surveys to attempt to correct for unequal sample selection [18]. We show that poor vitamin D status is also associated with a risk of poor health outcomes. There are some limitations to our study; we had no information on dietary vitamin D intake on the HSE, about sun exposure or about the dose of vitamin D in the vitamin supplements taken by informants. We also had limited information about any medications that may affect vitamin D status. In HSE 2005, a small percentage (4.1%) of participants took calcium and vitamin D for osteoporosis, suggesting that vitamin D status has been underestimated.

Poor vitamin D status, a preventable public health problem exists at alarming levels among older people in England and is associated with many risk factors and poor health outcomes. Due to limited ability to access vitamin D due to ageing indicates a clear rationale and an urgent need for a uniform policy on the assessment and dietary supplementation of vitamin D in older people to prevent further decline in vitamin D status and its negative consequences.

Key points

- The HSE 2005 shows that mean serum 25(OH)D levels are 53 and 49 nmol/l in men and women, respectively, significantly lower than the currently recommended levels at ≥75 nmol/l.
- ge standardised prevalence of vitamin D deficiency [25(OH)D <25 nmol/l] in people aged ≥65 in 2005 was 13% in women and 8% in men, and prevalence of hypovitaminosis D [serum 25(OH)D <50 nmol/l] was higher in women (57%) than in men (49%).
- There is no improvement in vitamin D status in 2005 compared to 2000, and results show a significant decline in vitamin D status among men in 2005 in comparison to the 1994/1995 NDNS results.
- Multivariate regression analyses show that women were more likely to have hypovitaminosis D than men. Hypovitaminosis D was more likely in people who were obese, current smokers or those who did not take vitamin supplements.
- Assessment and dietary supplementation of vitamin D in older people are urgently required to prevent further decline in vitamin D status and consequent poor health outcomes.

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Conflicts of interests

None declared.

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Ethical approval

Ethical approval for the HSE was obtained from the North Thames Multi-centre Research Ethics Committee (MREC) and from relevant Local Research Ethics Committees (LRECs) in England. The NDNS survey was approved by the South Thames MREC and National Health Service LRECs. Participants providing a blood sample gave written consent.

Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

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PAPER III

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Predictors of 25-hydroxyvitamin D status among adults in two British national surveys

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Several recent reports have found a high prevalence of vitamin D deficiency in the adult British population. The present paper investigates the associations of low income/material deprivation and other predictors of serum 25-hydroxyvitamin D (25(OH)D) status in two surveys: The National Diet and Nutrition Survey (NDNS) of the population aged 19–64 years in mainland Britain and the Low Income Diet and Nutrition Survey (LIDNS) of adults aged ≥19 years in all regions of the UK who were screened to identify low-income/materially deprived households. A valid serum 25(OH)D sample was obtained in 1297 and 792 participants from the NDNS and LDNS respectively. The NDNS participants who were not receiving benefits (*n* 1054) had a mean 25(OH)D of 50·1 nmol/l, which was higher than among NDNS participants receiving benefits (*n* 243) with a mean 25(OH)D of 43·0 nmol/l ($P<0·001$) and the LIDNS sample (46·5 nmol/l; $P<0·05$). For all three samples, the season of drawing blood, skin colour, dietary intake of vitamin D, and intake of dietary supplements were significant predictors ($P<0·05$) of serum 25(OH)D status in mutually adjusted regression models. National prevention and treatments strategies of poor vitamin D status need to be targeted to include the adult population, particularly deprived populations, in addition to the elderly and ethnic minorities.

25-Hydroxyvitamin D status: Adults: Low income: Population surveys

Sufficient vitamin D is crucial for good bone health, but increasing evidence suggests that it may also play an important role in the prevention of diabetes, cancers, heart disease and other non-communicable diseases[1,2]. Vitamin D in the form of cholecalciferol is generated in the skin when exposed to daylight. The amount produced depends particularly on the wavelength and strength of the light and the individual's skin colour[2]. Low endogenous production during winter months can be compensated for by dietary intake and supplement use, but vitamin D intake is presently low in Britain[3].

Vitamin D deficiency has primarily been addressed as a problem among the elderly[2], children[4,5] and ethnic minorities[6,7]. However, two recent surveys of British adults, The National Diet and Nutrition Survey (NDNS) of adults aged 19–64 years[3] and the 1958 British birth cohort[8], both report that approximately 15 % of the population had serum 25-hydroxyvitamin D (25(OH)D) levels below 25 nmol/l (indicating deficiency)[9]. The estimated prevalence of deficiency was somewhat higher in the Low Income Diet and Nutrition Survey (LIDNS), with 23 % of adult men and 18 % of women being below the reference[10]. The aim of the present paper was to examine the influence of low income/material deprivation on vitamin D status and investigate predictors of 25(OH)D status using data from the NDNS of adults aged 19–64 years and the adult population of LIDNS (≥19 years).

Methods

Samples

The LIDNS sample selection followed a multi-staged clustered design using all regions of the UK. The target population was the 15 % most deprived households in the UK and participants were selected based on screening questions aimed at identifying low-income or materially deprived households (combination of questions regarding, for instance, type of housing, car ownership, employment status, receipt of certain benefits or pensions). Up to two respondents (one adult and one child) were selected from a household, excluding pregnant women. Data were collected during 2003–5. Participants aged ≥19 years consisted of 1048 men and 2019 women. Of these, 96 % started the individual questionnaire or the first of four dietary recalls. Ninety percent agreed to be visited by a nurse, 81 % were successfully revisited and 51 % (both sexes) provided a blood sample. A valid serum 25(OH)D sample was obtained from 246 men and 546 women[10].

The NDNS sample was selected using a multistage random probability design using all postal sectors within mainland Britain. Eligibility was defined as being aged 19–64 years and not pregnant or breast-feeding. One eligible adult per household was selected at random. Data were collected during 2000 and 2001[3]. Of the 3704 eligible respondents,

Abbreviations: LIDNS, Low Income Diet and Nutrition Survey; NDNS, National Diet and Nutrition Survey; $NDNS_B$, NDNS sample receiving benefits; $NDNS_{NB}$, NDNS sample not receiving benefits; 25(OH)D, serum 25-hydroxyvitamin D.

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61 % completed the dietary interview. Participants were asked to provide further measurements, including anthropometry, blood pressure and a urine sample. Blood samples were obtained in 61 % of men and 59 % of women in the dietary sample. A valid serum 25(OH)D sample was obtained from 592 men and 705 women[11,12].

Blood collection and analysis

Blood samples were collected non-fasted and analysed for serum 25(OH)D by the DiaSorin Kit (DiaSorin Inc., Stillwater, MN, USA) for both the NDNS and LIDNS. The laboratories performing the 25(OH)D analyses took part in the Vitamin D External Quality Assessment Scheme. In these surveys there was no significant change in the assay's performance throughout its use as assessed from quality-assurance parameters[10,11].

Anthropometry and other covariates

In both studies, interviewers collected data on sociodemographic aspects (including age, sex, ethnicity, region of residence, and season of data collection) and health behaviours (including the intake of vitamin supplements). Height and weight measurements were taken in light clothing without shoes, and BMI (kg/m^2) was calculated. Dietary vitamin D intakes were obtained from four 24 h recalls on random days (including at least one weekend day) in the LIDNS sample[10] and by 7 d weighed dietary records in the NDNS sample[11].

Statistical analyses

Simple and multiple regression analyses were used to model the relationships between serum 25(OH)D as a continuous outcome measure and covariates including age group, ethnicity, sex, region of residence, dietary intake, and dietary supplement use. For the NDNS sample, significant interactions were found for benefit status and season of data collection, BMI, ethnicity, dietary vitamin D intake, and supplement use ($P<0{\cdot}01$). Therefore the NDNS sample was divided into those receiving benefits ($NDNS_B$) and those who did not ($NDNS_{NB}$). To assess if the predictors of serum 25(OH)D in the LIDNS sample were similar to those in other low-income groups, analysis was carried out separately for the three samples, LIDNS, $NDNS_B$, and $NDNS_{NB}$. Descriptive statistics were weighted to correct for the sampling probabilities and non-response in the two surveys[10,11]. For all the three samples, the 'skewness index' for the distribution of serum 25(OH)D was between 0·5 and 0·8 samples, and hence there was no need to transform the variable before analysis.

Results

Participants in the $NDNS_{NB}$ sample had a mean 25(OH)D of 50·1 nmol/l, which was significantly higher than among the $NDNS_B$ sample (43·0 nmol/l; $P<0{\cdot}001$) and the LIDNS sample (46·5 nmol/l; $P<0{\cdot}05$). There was no significant difference between the two latter samples. The mean serum 25(OH)D concentrations were not significantly different between men and women within each of the three samples, nor across age groups. There was a marked seasonal variation in all three populations, with the mean levels being approximately 50 % higher for blood samples collected in July–September compared with January–March. Serum 25(OH)D concentrations were also strongly associated with ethnic group and supplement use in the expected manner. In all three samples dietary vitamin D intake (three levels) was associated with serum 25(OH)D levels. The proportion of individuals taking vitamin supplements was significantly higher in the $NDNS_B$ (42·1 %; $P<0{\cdot}001$) in comparison with the LIDNS (17·1 %) and $NDNS_{NB}$ sample (25·1 %; Table 1), and in all samples supplement use was strongly associated with serum 25(OH)D levels.

For all three samples, having a blood sample drawn in the summer, being light skinned, having higher dietary vitamin D intake and taking vitamin supplements were factors significantly associated with higher serum 25(OH)D levels in the fully adjusted analyses (Table 2). There was a inverse association between serum 25(OH)D status and BMI only in the LIDNS sample. Area of residence was only significant for the $NDNS_{NB}$ sample where those living in Scotland had the lowest vitamin D status. The relationship between 25(OH)D and household composition was inconsistent between the samples. Sex and age group did not show significant associations with serum 25(OH)D concentrations (data not shown), and were not presented in the final models.

Discussion

The present study shows that the low-income/materially deprived population in Britain has lower vitamin D status than the general population. Both the NDNS and the LIDNS surveys were designed to give a representative picture of the nutritional status of the population groups examined. In both surveys, the blood samples were taken after dietary assessments at a separate visit by a nurse. The participants were asked to comply with several measurements in addition to giving blood, which may have contributed to the lower response rate. However, specific statistical weighting was used to attempt to correct for the non-response in addition to unequal sample selection[10,11]. The factors shown to affect vitamin D status, i.e. season (light levels), skin type, dietary intake of vitamin D, and intake of dietary supplements, apply to all three samples independently. The question on supplement use was not specified on vitamin D content, and can to some extent reflect that supplement users have a generally healthier diet and lifestyle.

The current UK recommendation advises a daily vitamin D intake of 10 μg (400 IU) to be taken among those aged over 65 years[2]. However, the long-term compliance with intake of supplements for larger population groups can be questioned[13]. Given the emerging evidence on possible wider health benefits of good vitamin D status and the several studies indicating insufficient vitamin D status across all age groups, it is timely to have a debate on whether there should be more widespread fortification of vitamin D in food[14,15]. The national prevention and treatment strategies of vitamin D deficiency and sub-optimal status need to be targeted to include the adult population and the deprived populations particularly, as well as the elderly and ethnic minority populations.

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Table 1. Serum 25-hydroxyvitamin D concentrations (nmol/l) among individuals aged 19–64 years living in private households in the UK from two population surveys: the Low Income Diet and Nutrition Survey (LIDNS) and the National Diet and Nutrition Survey (NDNS)

(Mean values and 95% confidence intervals)

	LIDNS (*n* 792)				NDNS sample receiving benefits (*n* 243)				NDNS sample not receiving benefits (*n* 1054)			
Characteristics	*n*	Mean	95% CI	*P*†	*n*	Mean	95% CI	*P*†	*n*	Mean	95% CI	*P*†
All		46·5*	44·0, 49·0			43·0**	39·7, 46·3			50·1	48·6, 51·7	
Sex				0·4				0·7				0·3
Men	246	45·1	40·7, 49·4		84	42·3	37·1, 47·4		508	49·2	47·0, 51·4	
Women	546	47·2	44·3, 50·1		159	43·5	39·2, 47·7		546	51·1	48·8, 53·3	
Age group (years)				0·5				0·6				0·2
19–34	233	47·0	42·6, 51·3		99	42·3	37·2, 47·4		264	49·2	45·9, 52·5	
35–49	312	47·5	43·9, 51·1		105	43·0	38·2, 47·8		436	49·0	46·8, 51·1	
50–64	247	44·5	40·2, 48·8		39	44·7	36·8, 52 6		354	52·4	49·9, 54·8	
Region‡				0·3§				0·04§				0·005§
Scotland	75	44·2	35·9, 52·5		22	37·7	30·7, 44·6		73	44·4	39·3, 49·5	
Northern	220	49·3	44·6, 54·0		83	46·8	40·8, 52·8		255	53·1	49·8, 56·4	
South/Central/Wales	365	45·5	42·2, 48·8		138	41·4	37·2, 45·7		726	49·7	47·8, 51·6	
Northern Ireland	132	46·1	41·5, 50·8		–	–			–	–		
Season				<0·001				<0·001				<0·001
January–March	193	39·1	35·2, 42·9		66	31·5	28·0, 35·0		242	42·8	39·9, 45·8	
April–June	233	43·7	39·5, 47·9		72	42·5	37·0, 48·1		352	46·6	44·4, 48·9	
July–September	202	58·6	52·9, 64·4		51	60·5	51·5, 69·5		216	68·7	65·2, 72·1	
October–December	164	47·5	42·3, 52·6		54	39·9	34·9, 44·9		244	45·8	42·9, 48·7	
Ethnic group				<0·001				<0·001				<0·001
White	728	49·0	46·3, 51·6		221	44·5	41·1, 47·9		1008	51·4	49·8, 53·0	
Non-white	64	29·9	25·9, 33·9		22	27·5	21·9, 33·2		46	26·4	22·1, 30·6	
Household composition‖				<0·01				0·05				0·2
a	233	44·2	39·8, 48·6		42	37·1	31·3, 42·9		212	49·7	46·5, 52·8	
b	133	45·3	40·2, 50·4		43	39·2	32·7, 45·6		519	51·1	48·9, 53·3	
c	260	53·5	49·3, 57·8		83	48·3	43·5, 53·0		26	40·2	33·3, 47·2	
d	166	43·0	38·4, 47·6		75	44·0	38·0, 50·0		297	48·7	45·9, 51·4	
BMI (kg/m^2)				0·03				0·8				0·07
18·5–24·9	296	49·3	45·1, 53·5		108	42·0	37·5, 46·5		423	50·1	47·6, 52·6	
≥ 25–29·9	240	47·3	43·5, 51·2		92	43·6	37·8, 49·3		400	53·0	50·4, 55·7	
≥ 30–34·9	124	41·8	36·5, 47·1		23	47·6	39·8, 55·3		169	45·2	42·2, 48·2	
≥ 35	89	43·8	37·7, 49·9		20	40·4	27·2, 53·6		62	45·4	37·6, 53·1	
Vitamin D intake from food (μg/d)¶				0·0009				<0·0001				<0·0001
0·1–1·7 (Lowest)	264	40·6	36·8, 44·4		74	35·1	30·7, 39·4		336	44·9	42·0, 47·8	
1·7–2·9 (Middle)	264	49·8	45·2, 54·3		75	42·9	37·3, 48·6		336	52·9	50·1, 55·6	
2·9–32·4 (Highest)	264	49·9	45·9, 54·0		75	50·0	44·0, 56·0		336	53·5	50·9, 56·2	
Taking vitamin supplements				0·001				0·0006				0·002
Yes	154	54·5	49·3, 59·8		61	54·6	46·6, 62·7		444	53·1		
No	638	44·9	42·1, 47·6		182	39·3	36·0, 42·6		610	48·1		

Mean value was significantly different from that for the NDNS sample not receiving benefits. *P< 0 05, **P<0·001.

† Test for a linear trend.

‡ Different regional grouping in the two studies as the NDNS was carried out only in mainland Britain.

§ Test for heterogeneity.

‖ NDNS: a, living alone; b, with spouse or partner, other adults, no dependent children; c, with dependent children, no spouse; d, with dependent children, with spouse. LIDNS: a, one adult of working age or one adult of retirement age; b, two or more adults, at least one of working age or two or more adults, all of retirement age; c, one adult, one or more children; d, two or more adults, one or more children.

¶ In thirds. For the NDNS, the vitamin D intake (μg/d) range for those who received benefits is 0·18–1 67, 1·70–2 78 and 2·79–26·84 for the lowest, middle and highest thirds respectively; the vitamin D intake (μg/d) range for those not receiving benefits is 0·04–2 22, 2·22–3·73 and 3·70–22·10 for the lowest, middle and highest thirds respectively.

Table 2. Adjusted* regression coefficients (ARC) for serum 25-hydroxyvitamin concentrations (nmol/l) by associated risk factors and sex aged 19–64 years living in private households from the Low Income Diet and Nutrition Survey (LIDNS) and National Diet and Nutrition Survey (NDNS)

(Adjusted regression coefficients and 95 % confidence intervals)

	LIDNS (*n* 792)			NDNS sample receiving benefits (*n* 243)			NDNS not receiving benefits (*n* 1054)		
Risk factors	ARC	95 %CI	*P*†	ARC	95 %CI	*P*†	ARC	95 %CI	*P*†
Season			<0·001			0 001			<0 001
January–March	Reference			Reference			Reference		
April–June	6 2	0 5, 11 9		6·1	−0·3, 13 0		2 3	−1 5, 6·0	
July–September	21·4	15·3, 27·5		26·2	18·3, 34·0		25·1	20·6, 29 5	
October–December	9 6	3 5, 15 6		6·8	0 5, 13·1		3 6	−0·4, 7·6	
Region‡						0·08			0·03
Scotland	–			Reference			Reference		
Northern	–			6 9	−0·8, 14 5		5·8	0·2, 11·4	
Central/Midlands/Wales/South (London)	–			2 8	−4 4, 10 0		3·0	−1·9, 8·0	
Ethnicity			<0·001			<0·0001			<0 0001
Non-white	Reference			Reference			Reference		
White	20·1	15 2, 25·1		17·1	8·7, 25·6		21·2	16·7, 25 8	
Household composition§			0 02			0·003			0 7
a	Reference			Reference			Reference		
b	2 8	−4 0, 9 7		3 2	−3 6, 10·0		2·2	−1·3, 5·7	
c	8 5	3 0, 13 9		12·1	5·7, 18 5		−4 8	−11·3, 1·7	
d	1 8	−3 4, 7·0		7·6	0·5, 14·7		3·1	−0·7, 6 9	
BMI (kg/m²)	−0 6	−0 9, −0 2	0 009	−0·02	−0·4, 0·3	0·9	−0·1	−0·3, 0·2	0 8
Vitamin D intake from food (μg/d)‖			0 05			0 0005			0 004
0 1–1 7 (Lowest)	Reference			Reference			Reference		
1·7–2 9 (Middle)	6 7	1·4, 12·1		5·2	−0·7, 11·1		5·5	2·1, 9·0	
2·9–32·4 (Highest)	5 2	0 0, 10·3		12 8	7·0, 18 7		8 2	4 8, 11·6	
Taking vitamin supplements			0 004			0 002			<0·001
No	Reference			Reference			Reference		
Yes	8 4	2 6, 14 3		9 9	3 0, 16 9		5·6	2 6, 8 4	

* Adjusted for all factors listed above.

† Test for a linear trend.

‡ Region was not associated with vitamin D status in the LIDNS sample.

§ NDNS: a, living alone, b, with spouse or partner, other adults, no dependent children; c, with dependent children, no spouse; d, with dependent children, with spouse. LIDNS: a, one adult of working age or one adult of retirement age, b, two or more adults, at least one of working age or two or more adults, all of retirement age; c, one adult, one or more children, d, two or more adults, one or more children.

‖ In thirds. For the NDNS, the vitamin D intake (μg/d) range for those who received benefits is 0 16–1·67, 1·70–2·78 and 2 79–26 84 for the lowest, middle and highest thirds respectively; the vitamin D intake (μg/d) range for those not receiving benefits is 0 04–2 22, 2 22–3 73 and 3 70–22·10 for the lowest, middle and highest thirds respectively.

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V. H. initiated the idea of the paper, carried out the literature review, interpreted the results, and drafted the manuscript. A. H. contributed to the design of the analysis, the interpretation of results, and revised the manuscript. G. M. designed and conducted the analyses, interpreted the results, and revised the paper. G. M. had full access to the survey data and had final responsibility to submit for publication. The authors have no conflicts of interest to declare.

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PAPER IV

Relationship Between Vitamin D Levels and Depressive Symptoms in Older Residents From a National Survey Population

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Objective: To investigate the association between vitamin D deficiency and depressive symptoms in a national community sample of older people. Vitamin D deficiency is common in older people with potential effects on mood. **Methods:** Data were analyzed from 2070 participants aged ≥65 years who had participated in the 2005 Health Survey for England. Serum 25-hydroxy vitamin D (25(OH)D) levels and depressive symptoms (Geriatric Depression Scale) had been measured. Covariates included age, sex, social class, season of examination, and physical health status. **Results:** Depressive symptoms were associated with clinical vitamin D deficiency (25(OH)D levels <10 ng/mL; present in 9.8%) independent of other covariates but not with broader deficiency states. This association was not modified by season of examination. **Conclusion:** Vitamin D deficiency is associated with late-life depression in northern latitudes. **Key words:**vitamin D, depressive disorder, community sample, aging.

25(OH)D = 25-hydroxy vitamin D; **HSE** = Health Survey for England; **GDS10** = 10-item Geriatric Depression Scale; **BMI** = body mass index; **OR** = odds ratio; **CI** = confidence interval.

INTRODUCTION

Depression in older people is common and substantially disabling (1). It is almost invariably found to be associated with worse general health, probably both as a cause and consequence (1,2). Micronutrient deficiencies (whether relatively low levels or clinical deficiency states) have been found to be associated with depression (3,4) and are likely to be particularly important in older people because of higher levels of morbidity and frailty. Recent studies (5,6) have suggested that depression may be associated with vitamin D deficiency. This may reflect influences of depressive states on sunlight exposure, diet, and nutritional supplementation. However, there are also plausible biological pathways for a role of vitamin D deficiency in the pathogenesis of depression, including effects on nerve growth factor synthesis (7) and a variety of potential neurotransmitter targets (8). Regardless of the direction of causation, the relationship is potentially of high public health importance because of the adverse impact of both states on well-being. In a nationally representative British survey of health in older people, we investigated the association between 25-hydroxy vitamin D (25(OH)D) levels and depressive symptoms, as well as the extent to which these were modified by general health status and (given the known influence of sunlight exposure on 25(OH)D levels) by the time of year at which examinations had been carried out.

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METHODS

Sample

Data were analyzed from the 2005 Health Survey for England (HSE), an annual survey designed to measure health and health-related behaviors in a nationally representative sample of adults and children living in private households in England. The survey has a series of core elements that are included every year and special topics that are included in selected years. In 2005, the HSE included an additional, nationally representative general population sample of English people aged ≥65 years, living in private households (9). Like previous surveys in the HSE series, the 2005 survey adopted a multistage stratified probability sampling design, using the English Postcode Address File as the primary sampling frame. It comprised a core (general population) sample randomly selected, using 7,200 addresses in 720 postcode sectors, and a boost sample of people aged ≥65 years who were selected, using 11,520 additional addresses at the same 720 postcode sectors as the core sample. Households were screened to identify whether older people were resident and, in these cases, interviews and nurse visits were conducted. The total sample, aged ≥65 years who were interviewed, included 4,269 residents (723 men, 873 women in the general population sample and 1,174 men and 1,499 women in the boost sample). The overall response rate among men and women aged ≥65 years was 71% in the general population sample and 74% in the boost sample. The sampling design and methodology have been described elsewhere (9). Ethical approval for the survey was obtained from the North Thames Multicentre Research Ethics Committee and from relevant Local Research Ethics Committees in England.

Data were collected on two visits. Blood samples were only collected for participants who agreed to a second nurse visit. Among those aged ≥65 years who agreed to this nurse visit (n = 3145), a blood sample was obtained with written consent. A valid serum 25(OH)D sample was obtained from 2,070 participants: 950 men and 1120 women. The mean age of participants who provided a blood sample was 73.7 years compared with 74.5 years for all those interviewed. Blood samples were collected throughout the year from January to December 2005.

Measurements

The interviewers carried out a computer-aided personal interview with the sample participants. Interviewers collected data on sociodemographic aspects (including age, sex, social class), health behaviors (e.g., smoking), and self-reported general health (subjective general health and extent of limiting health conditions—for the latter, participants were asked whether they had any long-standing illness; those providing an affirmative response were asked whether this limited their daily activities in any way). Depressive symptoms were measured, using the 10-item Geriatric Depression Scale (GDS10), with a score of ≥3 defined as case level, according to usual practice (10,11).

After the interviewer visit, those who agreed had a nurse visit within 2 to 3 days. Nurses collected additional information, including information on current medication and vitamin supplement usage, and they took measurements, including body mass index (BMI, weight in kilograms divided by height in meters squared), blood pressure, and obtained nonfasting blood samples with assays on these including 25(OH)D. Vitamin D analyses were carried out at the Royal Victoria Infirmary in Newcastle on Tyne, United Kingdom, using the Diasorin Kit (DiaSorin Inc., Stillwater, Minnesota). Full

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details on blood sample collection and analysis are described elsewhere (12). The timing (month) of the interview was also treated as a covariate.

Vitamin D deficiency has been conventionally defined as serum concentrations 25(OH)D <10 ng/mL (13). Two other relative deficiency states were also defined for the following reasons: 1) a level of <20 ng/mL has been associated with slightly elevated serum parathyroid hormone concentration and mild increase of bone turnover (14); 2) optimal levels are currently considered to be ≥30 ng/mL (15). In this analysis, an a priori decision was made to consider separately these three definitions of low vitamin D status as independent variables.

Statistical Analysis

Specific statistical weighting was used to correct for nonresponse at each stage, in addition to unequal sample selection, using information available about responders and nonresponders. Following a description of the sample, associations between case-level depressive symptoms and the three 25(OH)D deficiency categories were analyzed in logistic regression models with sequential adjustments for demographic factors, season, supplement intake, and smoking status, followed by further separate adjustments for BMI, reported long-term illness, and subjective general health status. Stata 10 software was used.

RESULTS

After sampling, further confirmatory analyses showed that participants for whom vitamin D data had been obtained were representative of those interviewed. For example, mean age was 74.5 years in those interviewed and was 73.7 years in those who gave a blood sample. Furthermore, 44% of those interviewed and 46% of those providing a blood sample were male. Income, region, and social class were also similar between groups.

Characteristics of the analyzed sample are summarized in Table 1. Sixty percent were aged between 65 and 74 years and <10% described poor physical health; however, an appreciable proportion had one or more limiting long-standing illness. Examinations were evenly distributed across seasons. The prevalence of case level depressive symptoms was 25.2% in the total analyzed sample. In participants with 25(OH)D levels of <30 ng/mL (85.4%), prevalence of depressive symptoms was 22.6%; in participants with 25(OH)D levels of <20 ng/mL (51.4%), prevalence of depression was 25.8%; and in participants with 25(OH)D levels of <10 ng/mL (9.8%), prevalence of depression was 35.0%. With respect to this latter deficiency category compared with the remainder of the sample, the prevalence ratio for depressive symptoms was 1.45 and the population attributable fraction calculated from this was 4.2%. The Spearman correlation coefficient between 25(OH)D levels and the number of depressive symptoms (GDS score) was −0.14 ($p < .001$) with evidence of nonlinearity. With respect to distributions, 25(OH)D levels were normally distributed, whereas GDS score showed pronounced positive skew.

Logistic regression analyses of the associations between the three deficiency states and depressive symptoms are summarized in Table 2. All three associations were significant before adjustment. Associations with the broader two deficiency categories were no longer significant after adjustment, but those with the most severe deficiency syndrome (25(OH)D levels of <10 ng/mL) remained independent. The most marked reductions in the strength of association occurred post adjustment for general health status. Stratification by season of examination (Table 3) did not reveal any marked or consistent variation (p value for interaction term between season and 25(OH)D deficiency 0.84). Finally, the dose-response association between 25(OH)D level and depressive symptoms was investigated in a linear model and found to be strongly significant (B-value, −1.94; 95% CI, −2.67, −1.20). In a secondary analysis, further adjustment for alcohol consumption (amount consumed on heaviest day in the past week) did not change the results meaningfully (data not shown).

TABLE 1. Descriptive Characteristics of Informants With a Valid Serum 25(OH)D Included in the Analysis

Characteristic	*n*	Proportion (%)
Age, yrs		
65–74	1238	59.8
75+	832	40.2
Sex		
Male	950	45.9
Female	1,120	54.1
Social class		
Nonmanual	1119	54.1
Manual	890	43
Season		
Spring	473	22.9
Summer	574	27.7
Autumn	582	28.1
Winter	441	21.3
Taking vitamin supplements		
Yes	929	44.9
No	1141	55.1
Smoking status		
Never	978	47.3
Previous, occasional	873	42.2
Current	219	10.5
Body mass index (BMI)		
Normal: 20–25 kg/m²	458	22.1
Underweight: <20 kg/m²	41	2.0
Overweight: 25–30 kg/m²	782	37.8
Obese: >30 kg/m²	455	22.0
Long-standing		
None	646	31.2
Illnesses		
Nonlimiting	596	28.8
Limiting	828	40.0
General health		
Good/very good	1311	63.3
Fair	571	27.6
Poor/very poor	188	9.1

DISCUSSION

In an analysis of data from the 2005 HSE, we investigated the association between vitamin D deficiency and depressive symptoms. These were found to be associated but only for conventionally defined clinical vitamin D deficiency states and not for milder levels of deficiency. The association was not accounted for by physical health or other potential confounding factors and was not substantially modified by the

TABLE 2. Logistic Regression Analyses for Associations Between Vitamin D Status and Depression Before and After Adjustment for Covariates

Regression model	Associations With Depression (OR, 95% CI)		
	Serum 25(OH)D <10 ng/mL	Serum 25(OH)D <20 ng/mL	Serum 25(OH)D <30 ng/mL
1. Unadjusted	2.10 (1.53–2.87) $p < .001$	1.46 (1.17–1.82) $p < .001$	1.46 (1.04–2.04) $p = .03$
2. Adjusted for age	1.99 (1.45–2.73) $p < .001$	1.41 (1.13–1.76) $p < .001$	1.41 (1.00–1.97) $p < .001$
3. Model 2 plus sex	1.92 (1.40–2.64) $p < .001$	1.38 (1.10–1.72) $p = .005$	1.38 (0.98–1.94) $p = .06$
4. Model 3 plus social class	1.82 (1.32–2.51) $p < .001$	1.35 (1.08–1.69) $p = .01$	1.32 (0.94–1.86) $p = .11$
5. Model 4 plus season	1.88 (1.36–2.61) $p < .001$	1.39 (1.10–1.74) $p = .005$	1.36 (0.96–1.9) $p = .08$
6. Model 5 plus vitamin D supplement intake	1.79 (1.28–2.49) $p < .001$	1.33(1.05–1.68) $p = .02$	1.30(0.92–1.83) $p = .14$
7. Model 6 plus smoking status	1.80 (1.29–2.51) $p < .001$	1.31(1.04–1.66) $p = .02$	1.28(0.91–1.82) $p = .16$
8. Model 7 plus BMI	1.61 (1.14–2.28) $p < .001$	1.20(0.94–1.52) $p = .15$	1.18(0.83–1.69) $p = .35$
9. Model 6 plus long-standing limiting illness (3 groups)	1.57 (1.12–2.21) $p = .01$	1.19 (0.93–1.52) $p = .16$	1.27 (0.89–1.82) $p = .18$
10. Model 6 plus subjective general health status	1.46 (1.02–2.08) $p = .04$	1.10 (0.86–1.41) $p = .44$	1.14 (0.79–1.63) $p = .48$

OR, odds ratio; CI, confidence interval; BMI, body mass index.

TABLE 3. Logistic Regression Analyses of Associations of Depression and Vitamin D Deficiency, Stratified by Season of Examination, Before and After Adjustment

	ORs (95% CIs) for the Association Between Depression and Vitamin D Deficiency[a]			
	Winter: Dec–Feb (n = 441)	Spring: March–May (n = 473)	Summer: June–Aug (n = 574)	Autumn: Sept–Nov (n = 582)
1. Unadjusted	2.06 (1.14–4.54) $p = .02$	2.27 (1.14–4.54) $p = .02$	2.31 (1.03–5.14) $p = .04$	2.36 (1.35–4.15) $p = .003$
2. Adjusted for age and sex	1.93 (1.06–3.49) $p = .03$	1.96 (0.96–3.99) $p = .06$	2.20 (0.97–5.03) $p = .06$	2.19 (1.23–3.88) $p = .008$
3 Adjusted for age, sex, social class	1.99 (1.09–3.62) $p = .03$	1.84 (0.89–4.54) $p = .02$	1.92 (0.83–4.45) $p = .13$	2.03 (1.13–3.64) $p = .02$
4. Model 2 plus vitamin D supplement intake	1.79 (0.96–3.32) $p = .07$	1.64 (0.78–3.47) $p = .20$	2.01(0.86–4.67) $p = .11$	1.91 (1.06–3.45) $p = .03$

ORs, odds ratios; CIs, confidence intervals.
[a] 25(OH)D levels<10 ng/mL.

time of the year at which the examination was carried out. Particular advantages of this study were the presence of directly measured vitamin D levels, a widely used scale for measuring depressive symptoms in older people, and a large and nationally representative sample.

The importance of vitamin D in calcium absorption and metabolism for bone health is well known, but increasing evidence (16,17) also suggests that adequate vitamin D status may be protective against noncommunicable diseases like diabetes, cancers, cardiovascular disease, rheumatoid arthritis, and autoimmune conditions. The amount of sun exposure (a primary source of serum vitamin D) necessary to meet requirements depends on factors, such as age, latitude, season, time of day, time of year, clothing, and skin pigmentation (18). Maximum vitamin D production occurs in summer months, and above latitude 37° North, the sun is not strong enough to provide any vitamin D in winter (for example, at the latitude of London, little vitamin D is generated from sun exposure between the middle of October and the middle of April). In the absence of sunlight, 1000 IU of vitamin D is necessary to maintain a healthy level of 25-hydroxyvitamin D >30 ng/mL (19). The half-life of vitamin D has been estimated to be of the order of 3 months (20). Older people are at higher risk of poor vitamin D status due to a decline in efficiency of vitamin D synthesis and a lowered renal conversion to its active form (21). Low endogenous production can

be compensated for by dietary intake and dietary supplement use, but in the United Kingdom, dietary intake of vitamin D-containing foods (oily fish, such as herring and mackerel, fortified margarines, meat and meat products, and eggs) among older people is also poor (22). Winter vitamin D levels in older people in the United Kingdom have been found to be associated with diet and overseas holidays within the last 6 months but not with winter sun exposure (23). The importance of vitamin D deficiency and variation in levels by season have been reported previously for the sample analyzed here (24).

Although vitamin D deficiency has been investigated in relationship to mental disorders in younger adults (25,26), relatively little research has investigated this association in older people, despite the higher potential impact. In a case-control study of older people with or without mild Alzheimer's disease, lower 25(OH)D levels were associated with mood disorder as well as with cognitive impairment (5). The Longitudinal Aging Study Amsterdam also found lower 25(OH)D levels, as well as higher parathyroid hormone levels, to be associated with both major and minor depression (6). Our findings are consistent with these results, although increased depressive symptoms were only seen in the most severe deficiency state with no marked increases in association with more mild relative deficiency.

Several processes may underlie the association. Long-standing physical health problems may influence both risk of depression and a person's access to sun exposure. However, adjustment for this revealed only modest confounding effects. Direction of causation is perhaps the most important consideration and cannot be concluded from a cross-sectional design. In particular, it is possible that depressive states were a cause, rather than a consequence, of vitamin D deficiency although, if this were the case, the association with depression would be expected to be to a similar extent with any relative 25(OH)D deficiency rather than, as observed in this sample, restricted to the 10% lowest levels (i.e., show associations across the range of 25(OH)D levels). Also, if depression caused vitamin D deficiency due to lack of sunlight exposure, then the association between 25(OH)D levels and contemporaneous depressive symptoms would be expected to be stronger in the summer months when levels are most strongly influenced, which was not evident in this sample. However, ultimately prospective research is required to clarify the direction of cause and effect.

Considering methodological issues, an advantage of the study was that the sample was drawn specifically to generalize to the national population. However, it should be borne in mind that participants were all community residents who represent a relatively healthier subpopulation of older adults because those requiring institutional care were not included. However, we do not believe that this compromises the principal findings for this subpopulation—it simply restricts the generalizability to more dependent groups. Conventional confounding factors were taken into account in this analysis. Other unmeasured potential confounding factors might include general life-style (for example, the ability/willingness to travel to overseas destinations with higher sunlight exposure) and cognitive impairment (for example, causing both depressive symptoms and vitamin D deficiency), neither of which were measured in this wave of the study. However, were data to be present for cognitive function, its role would probably remain difficult to determine, as cognitive impairment could also be a consequence of both vitamin D deficiency and depression. Dietary intake of vitamin D was also not measured, and it was not possible to determine vitamin D supplementation (because of varying doses in multivitamin preparations) but these are likely to be important, particularly in people with less than adequate sun exposure/absorption. However, the role of diet, if causal, is potentially complex because of the difficulty distinguishing micronutrients of interest. For example, oily fish are key sources of vitamin D but are also of interest in depression as a source of essential fatty acids (27). The role of somatic comorbidity is another salient consideration. Long-standing illness, which was present in a large proportion and which was potentially associated with both depression and (through reduced sunlight exposure) vitamin D deficiency, did not seem to have a substantial influence on the association of interest. A limitation was that comorbidity relied on self-report information which, in addition to measurement inaccuracy, may be influenced by depression status. Its inclusion in regression models could represent overadjustment which was why it (as well as BMI for the same reasons) was adjusted for as a separate procedure. Finally, the nonfasting nature of the blood sample will not have influenced vitamin D levels meaningfully, as sunlight exposure is a much more important determinant (28).

If vitamin D deficiency is demonstrated to be a cause of depression, the calculated population attributable fraction suggests that removing vitamin D deficiency could be an effective public health measure to reduce depression prevalence in later life. As summarized earlier, it is becoming increasingly recognized that this exposure has wider adverse effects than those on bone structure and skeletal integrity. Previous trial findings have suggested positive effects of vitamin D supplementation on seasonal affective disorder and mood (29,30) and, as stated earlier, there are plausible biological pathways that might account for a causal association, including involvement in nerve growth factor synthesis (7) and a variety of potential neurotransmitter targets (8). Hoogendijk and colleagues (6) investigated a mediating role of hyperparathyroidism, but their evidence did not support this.

Regardless of the direction of causation, the higher than expected co-occurrence of vitamin D deficiency and depression is an important public health issue for older populations in northern latitudes because both are common, both have substantial adverse health consequences, and both are potentially reversible.

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PAPER V

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GENERALISED AND ABDOMINAL ADIPOSITY ARE IMPORTANT RISK FACTORS FOR CHRONIC DISEASE IN OLDER PEOPLE: RESULTS FROM A NATIONALLY REPRESENTATIVE SURVEY

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Abstract: *Objectives:* To look at the trends in prevalence of generalised (body mass index (BMI) ≥25 kg/m2) and abdominal obesity (waist circumference (WC) >102cm, men; >88cm, women) among older people from 1993 to 2008, prevalence of chronic disease by overweight/obesity and WC categories in England 2005 and evaluate the association of these measures with chronic diseases. *Design:* Analyses of nationally representative cross-sectional population surveys, the Health Survey for England (HSE). *Participants:* Non-institutionalised men and women aged ≥ 65years (in HSE 2005, 1512 men and 1747 women). *Measurements:* Height, weight, waist circumference, blood pressure measurements were taken according to standardised HSE protocols. Information collected on socio-demographic, health behaviour and doctor diagnosed health conditions. *Results:* Generalised obesity and abdominal obesity increased among men and women from 1993 to 2008. In 2005, the HSE 2005 focussed on older people. 72% of men and 68% of women aged over 65 were either overweight or obese. Prevalence of raised WC was higher in women (58%) than in men (46%). The prevalence of diabetes and arthritis was higher in people with generalised obesity in both sexes. Men were more likely to have had a joint replacement and had a higher prevalence of stroke if they were overweight only but women were more likely to have had a joint replacement only if they were obese (13%) and had a higher risk of falls with generalised obesity. The pattern was similar for the prevalence of chronic diseases by raised WC. Multivariate analysis showed that generalised and abdominal obesity was independently associated with risk of hypertension, diabetes and arthritis in both men and women. In women only, there was an association between generalised obesity and having a fall in the last year (OR: 1.5), and between abdominal obesity and having a joint replacement (OR: 1.9, p=0.01). *Conclusion:* Complications of obesity such as diabetes, hypertension and arthritis, are more common in men and women aged over 65 who are overweight or obese, as well as in those with a raised WC. These conditions impact on morbidity, mortality and have cost implications for the health service and are known to improve with weight loss even in old age. Treatment strategies to address these conditions such as weight management and prevention of overweight and obesity are important even in older people. There is a need to ensure that older people are given appropriate advice about keeping physically active and eating sensibly.

Key words: Older people, obesity, chronic diseases, population survey.

Introduction

The global prevalence of obesity is increasing rapidly in all age groups, including older people and is a cause for major concern (1). The World Health Organisation has described the situation as an epidemic and estimates that 1 billion adults worldwide are overweight, of whom at least 300 million are obese (2). Obesity is an important public health burden among older people due its association with poor health and well-being (3), reduced life expectancy, (4) and premature death (5) due to associated co-morbidities such as cardiovascular disease (CVD), diabetes, hypertension and stroke, and certain forms of cancer (6).The literature shows quite conflicting associations between obesity and mortality (7, 8). A systematic review (9) showed the overall association between body mass index (BMI) and all-cause mortality in people over 65 as a flat-bottomed U-shape curve, with increased mortality in those with BMI above 30-31 kg/m². It has also been suggested that as associations of BMI with mortality are at least in part due to confounding factors such as physical activity, diet, body composition or fat distribution so it is difficult to isolate the causal effects (10, 11).

With ageing there are changes in body composition (sarcopaenia): the age-related loss of muscle mass and increase in fat mass (12) that results in little change in BMI. There is also a change in distribution of fat with age, an increase in abdominal fat in relation to skeletal or total body fat (13). It is generally recognised that the central deposition of fat (abdominal or visceral obesity) is more closely associated with obesity-related chronic diseases (14, 15) and quality of life (16). waist circumference (WC) measurements are considered important, in the absence of body composition data. The International Obesity Task Force (IOTF) (17) has emphasised that the health burden of obesity would be more easily predicted if the hazards of accumulating intra-abdominal fat were also monitored, in addition to BMI, by measuring WC.

The aims of this paper are to look at the trends in the prevalence of overweight and obesity (body mass index (BMI) ≥25 kg/m² and ≥30kg/m²) and abdominal obesity (WC) >102cm, men; >88cm, women) among older people from 1993 to 2008, look at prevalence of chronic disease by generalised

and abdominal obesity and evaluate the association of these measures with chronic diseases in England 2005.

Methods

The HSE is a continuous series of large, cross-sectional annual surveys in a representative sample of the non-institutionalised English population designed to provide health related information on the general population in England. From 1991 to 2004, it was commissioned by the English Department of Health, and since 2005 by the NHS Information Centre. The survey has a series of core elements that are included every year and special topics that are included in selected years. The annual household response rate for adults varied between 76% (1993) and 68% (2008), depending on the survey year. The trends data is presented for people aged ≥65 with valid height, weight and WC data from the annual surveys over the period 1993 to 2008 (18). A majority of the sample (~94%) in each of these years was of self-defined 'white' ethnic group. The main focus of this paper is on chronic disease among older people. In 2005, the Health Survey for England (HSE) included an additional, nationally representative general population sample of English people aged 65 and over, living in private households. Like previous surveys in the HSE series, the 2005 survey adopted a multi-stage stratified probability sampling design using the English Postcode Address File (PAF) as the primary sampling frame. It comprised a core (general population) sample randomly selected using 7,200 addresses in 720 postcode sectors, and a boost sample of people aged 65 and over, selected using 11,520 additional addresses at the same 720 postcode sectors as the core sample. Households were screened to identify whether older people were resident and, in these cases, interviews and nurse visits were conducted. The total sample aged 65 and over who were interviewed included 4,269 residents (723 men, 873 women in the general population sample and 1,174 men and 1,499 women in the boost sample). The overall response rate among men and women aged 65 and over was 71% in the general population sample and 74% in the boost sample. The sampling design and methodology have been described in more detail elsewhere (19). Ethical approval for the survey was obtained from the North Thames Multi-centre Research Ethics Committee (MREC) and from relevant Local Research Ethics Committees (LRECs) in England.

Measurements

Interviewers collected data from participants by computer-aided personal interview (CAPI) on socio-demographic aspects (including age, sex, and region), health behaviours (including questions about general self-reported health, smoking etc) and doctor diagnosed health conditions (ischaemic heart disease, stroke and diabetes). Height and weight measurements were taken in light clothing without shoes. Height was measured using a portable stadiometer with a sliding head plate, a base plate and three connecting rods marked with a metric measuring scale with participants stretching to the maximum height and the head positioned in the Frankfort plane. The reading was recorded to the nearest millimetre. Weight was measured using Soehnle, Seca or Tanita electronic scales with a digital display. Informants were asked to remove shoes and any bulky clothing. The reading was recorded to the nearest 100g. Informants who were chairbound, or unsteady on their feet were not weighed. Height and weight measurements were used to calculate body mass index (BMI, the weight in kilograms divided by the square of the height in metres).

After the interviewer visit, those who agreed had a nurse visit. Nurses collected information including current medication and vitamin supplement usage; and took measurements such as WC and blood pressure (as well as other physical measurements) using standardised procedures (20). WC was defined as the midpoint between the lower rib and the upper margin of the iliac crest. WC was defined as the midpoint between the lower rib and the upper margin of the iliac crest. It was measured using a tape with an insertion buckle at one end. The measurement was taken twice, using the same tape, and was recorded to the nearest even millimetre. Those whose two WC differed by more than 3 cm had a third measurement taken. The mean of the two valid measurements was used in the analysis. Informants with measurements considered unreliable by the nurse, for example due to excessive clothing or movement, were excluded from the analysis. The definition of raised WC was, in accordance with the ATP (Adult Treatment Panel) III (21), >102cm in men and >88cm in women.

Valid height measurements were obtained from 81% of men and 76% of women; valid weight measurements were obtained from 84% of men and 80% of women interviewed. Weight and height measurements allowed BMI to be computed for 79% of men and 73% of women. Valid waist measurements were obtained for 96% of men and 95% of women who were visited by a nurse.

In this paper reference to generalised obesity is for BMI ≥25 kg/m² and abdominal obesity is defined as WC >102cm in men and >88cm in women.

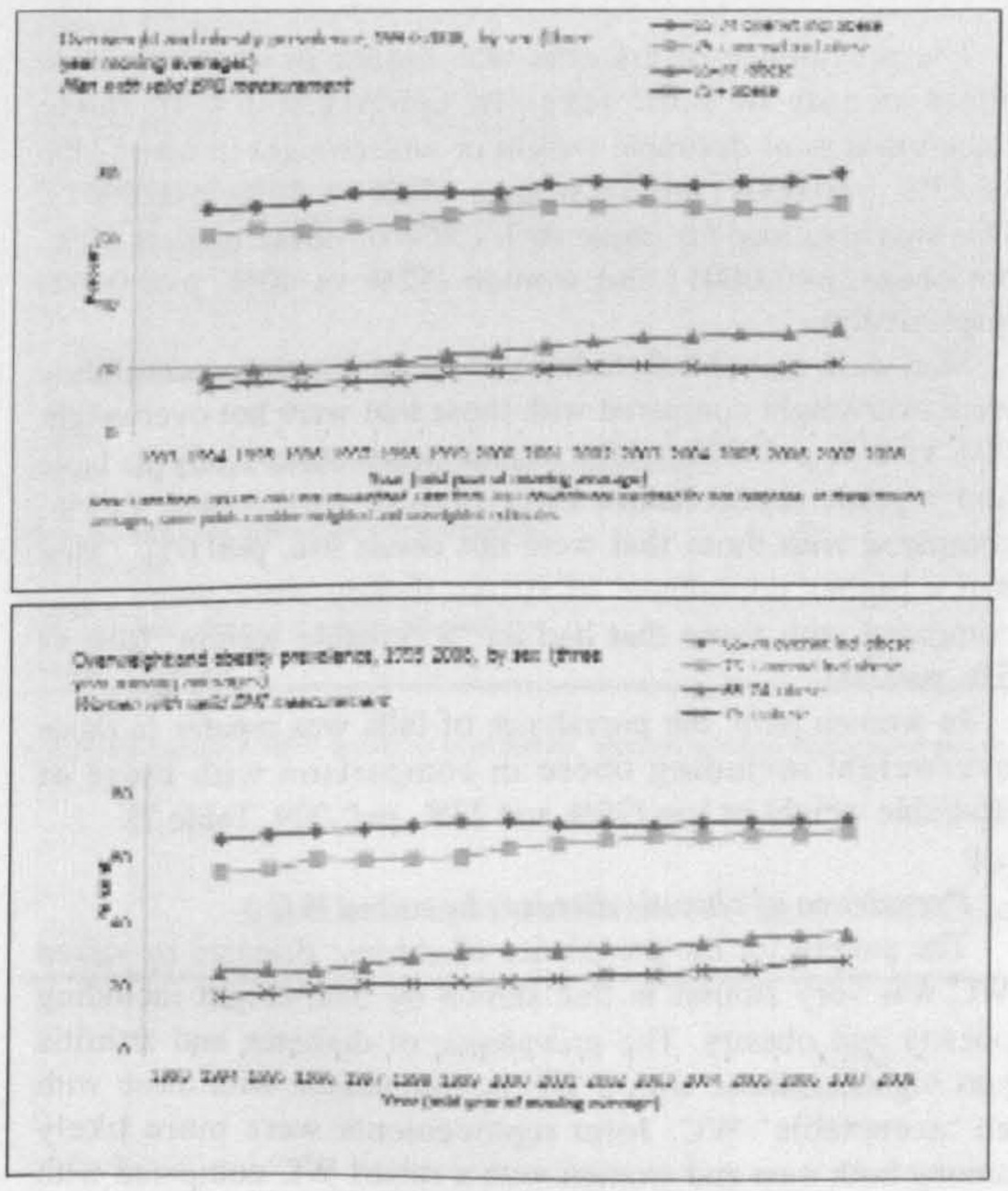
Statistical analysis

Analysis was carried out using SPSS v15 and STATA v10.0. Informants with missing information were excluded from analysis. In 2003, non-response weighting was introduced for the first time in the HSE series. Trend data presented in Figures 1 and 2 before 2003 is not weighted for non-response. Data for other analyses were weighted appropriately to take into account non-response and to correct for unequal sample selection. Data on prevalence of chronic diseases by overweight/obesity and raised WC was age- standardised to the mid-2000 population estimates and the Chi square test was used to test differences in prevalence of disease by BMI or raised WC. To further investigate the link between different fat patterns and risk of chronic disease, sex-specific logistic regression models were developed. The dependant variables in the two models were BMI ≥ 25 kg/m² and WC >102cm in men and >88cm in women which were run separately, adjusted simultaneously by the

independent variables included in the models. These were age group, smoking status, region, social class, general health, longstanding illness, hypertension, self reported chronic conditions (such as heart disease, stroke, diabetes, cancer, arthritis, osteoporosis, joint replacement, chronic lung disease) and reporting having a fall in the last year. The analysis was run in STATA to enable statistical adjustment for the complex (clustered and stratified) survey design.

Figure 1

Trends in generalised overweight and obesity (BMI≥ 25 and BMI≥ 30 kg/m²) in men and women aged 65-74 and 75 and over

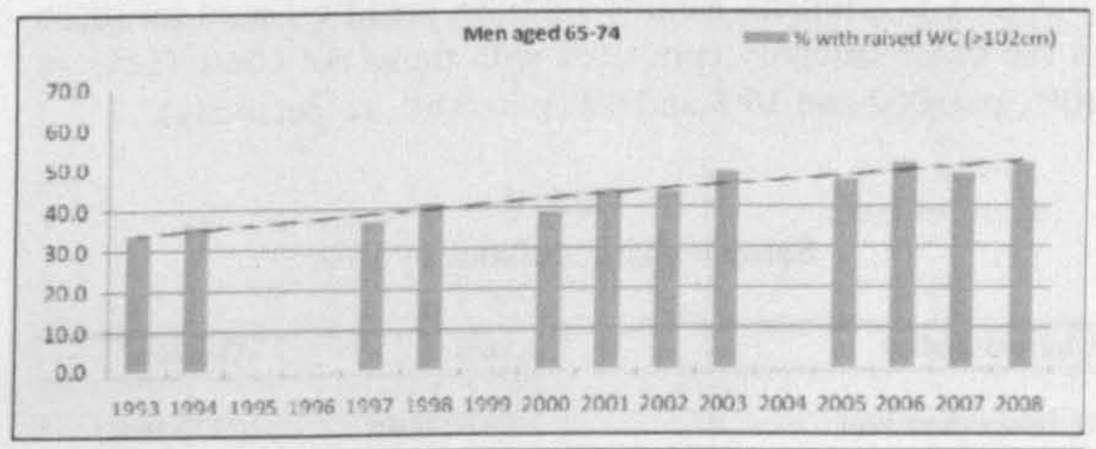


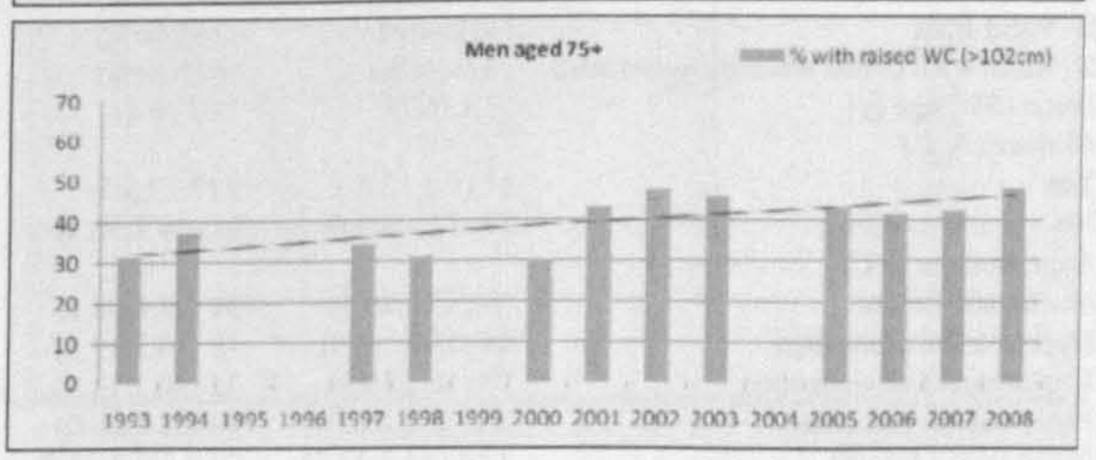
Results

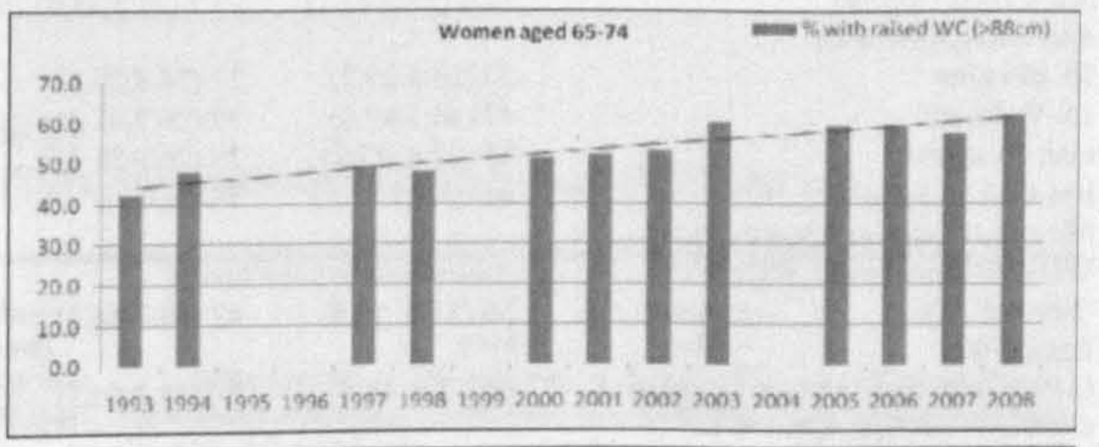
Tables 1 presents participants' characteristics. Figure 1 shows the trends in overweight including obesity (BMI ≥ 25 kg/m²) and obesity (≥ 30 kg/m²) using three year moving averages to smooth out any unusually high or low values in individual years. The prevalence of obesity increased among men aged 65-74 from 15.4% in 1993 to 34.6% in 2008 (p<0.001) and for overweight including obesity from 69.4% to 82.9 % (p<0.001). In men aged ≥75 obesity increased from 10.8% in 1993 to 23.1% in 2008 (p<0.001) and prevalence of overweight including obesity increased from 57.1% to 72.1 % (p<0.001). In women aged 65-74, prevalence of obesity increased from 22.8% in 1993 to 36.8% in 2008 (p<0.001) and prevalence of overweight including obesity from 62.9% to 71.8 % (p<0.001). In women aged ≥75, prevalence of obesity increased from 16.7% to 26.9% (p<0.001) and prevalence of overweight, including obesity increased from 58.0% to 65.7% (p<0.001). It is important to note that there were some fluctuations between these years. Abdominal obesity also increased in both men and women from 1993 to 2008, but again with fluctuations between the years (Figure 2).

Figure 2

Trends in abdominal obesity (raised waist circumference: >102cm in men and >88cm in women) in men and women aged 65-74 and 75 and over







Prevalence of overweight, obesity and raised waist circumference, by age and sex 72% of men and 68% of women were either overweight (BMI ≥ 25-30 kg/m²) or obese (BMI ≥ 30 kg/m²).A greater proportion of men than women were overweight (47% vs 39%, p<0.0001) but a greater proportion of women (28%) than men (24%) were obese (Table 1).

The proportion with a raised WC (was higher in women

(58%) than in men (46%) overall and in all age groups (p<0.0001). The largest difference between the sexes was in those aged 80-84 (60% of women, 40% of men, p<0.0001) (Table 1).

Prevalence of chronic diseases by BMI categories: overweight including obesity and obesity

Age standardised prevalence of diabetes was significantly higher in overweight including obese participants of both sexes in comparison with those who were of desirable weight or underweight (13% vs 7%, p=0.001 in men, 11% and 5%, p<0.0001 in women). Similar findings are also found for those in the obese category compared with those not obese (16% vs 10%, p=0.002 and 16% and 6%, p<0.0001, respectively).

Table 1
Sample characteristics by sex[a]

Characteristics	Men	Women
N Interviewer visit	1897(44%)	2372(56%)
N Valid BMI	1512 (46%)	1747(54%)
N Nurse visit (valid waist measurement)	1393(46%)	1617(54%)
Mean (SD) age [y]	73.1 (6.2)	73.7 (6.4)
Diabetes % CI		
Yes	11 (9.4,12.6)	9 (7.7,10.3)
No	89 (87.4, 90.6)	91 (89.7,92.3)
Hypertension % CI		
No hypertension	38 (35.6,40.5)	36 (33.8,38.3)
Hypertensive controlled	18 (16.1, 19.9)	18 (16.2,19.8)
Hypertensive uncontrolled	18 (16.1,19.9)	22 (20.1,23.9)
Hypertensive untreated	26 (23.8,28.2)	24 (22.0,26.0)
Mean BMI (kg/m²)	27.4 (27.3,27.7)	27.7 (27.5,28.0)
BMI categories % CI		
20-25 kg/m²	27 (24.8,29.2)	27 (24.9,29.1)
25-30 kg/m²	47 (44.5,49.5)	39 (36.7,41.3)
over 30 kg/m²	25 (22.8, 27.2)	29 (26.9,31.3)
less than 20 kg/m²	2 (1.3,2.7)	5 (4.0,6.0)
Mean waist circumference (cm)		
Waist circumference (WC) % CI		
'Normal' WC	54 (51.5, 56.5)	42 (39.7,44.3)
Raised WC		
(>102 cm in men, >88 cm in women)	46(43.5, 48.5)	58 (55.7,60.3)
Cigarette smoking status % CI		
Never smoked	34 (31.6,36.4)	57 (54.7,59.3)
Ex-smoker	54 (51.5,56.5)	31 (28.8,33.2)
Current smoker	12 (10.4,13.6)	11 (9.5,12.5)
Social Class % CI		
Non Manual	48 (45.5,50.5)	57 (54.7,59.3)
Manual	52 (49.5,54.5)	43(40.7,45.3)
General Health (%) CI		
Very good/good	61(58.5,63.5)	60 (57.7,62.3)
Fair	30 (27.7,32.3)	32 (29.8,34.2)
Bad/very bad	9 (7.6,10.4)	9 (7.7,10.3)
Limiting longstanding Illness (%) CI		
No longstanding illness	32 (29.7,34.4)	32 (29.8,34.2)
Limiting longstanding illness	38 (35.6,40.5)	40 (37.7,42.3)
Non limiting longstanding illness	30 (27.7,32.3)	27 (24.9,29.1)
Stroke (%) CI		
Absent	93 (91.7,94.3)	95(94.0,96.0)
Present	7 (5.7,8.3)	55 (4.0,6.0)
Heart disease (%) CI		
Absent	78 (75.9,80.1)	86 (84.4,87.6)
Present	22 (19.9,24.1)	14 (12.4,15.6)
Osteoporosis (%) CI		
Absent	98(97.3,98.7)	89 (87.5,90.5)
Present	2 (1.3,2.7)	11(9.5,12.5)
Falls in the last 12 months (%) CI		
Absent	80 (78.0,82.0)	74 (71.9,76.1)
Present	20 (18.0,22.0)	26 (23.9,28.1)
Arthritis (%) CI		
Absent	69 (66.7,71.3)	57 (54.7,59.3)
Present	31(28.7,33.3)	43(40.7,45.3)
Joint replacement (%)		
Absent	91(89.6,92.4)	88(86.5,89.5)
Present	9 (7 6,10.4)	12(10.5,13.5)

a. For partıcipants providing a valid BMI measurements(see supplementary data Appendix 2 for further information)

The prevalence of arthritis was higher in overweight or obese people of both sexes in comparison with those categorised as of desirable weight or underweight in men (34% vs 23%, p<0.0001) and in women (48% vs 35%, p<0.0001). This was also true for obese men (39% of obese men vs 29%, not obese, p<0.0001) and women (52% vs 40%, p<0.0001, respectively).

Men were more likely to have had a joint replacement if they were overweight compared with those that were not overweight (8% vs 5%, p=0.01), while women were more likely to have had a joint replacement only if they were obese (13%, compared with those that were not obese 9%, p=0.01). Men had a higher prevalence of stroke if they were overweight compared with those that had an 'acceptable weight' (8% vs 5%, p=0.04).

In women only, the prevalence of falls was greater in those overweight including obese in comparison with those of desirable weight or less (29% and 23%, p=0.009, Table 2).

Prevalence of chronic diseases by raised WC

The pattern for the prevalence of chronic diseases by raised WC was very similar to that shown by overweight including obesity and obesity. The prevalence of diabetes and arthritis was higher in those with a WC in comparison with those with an 'acceptable' WC. Joint replacements were more likely among both men and women with a raised WC compared with those with an 'acceptable' WC measurement (Table 3).

Due to these differences shown above, it was important to carry out the multivariate analysis to look at risk of chronic conditions separately for men and women and for generalised and abdominal obesity.

Multivariate regression analysis, adjusted simultaneously by the independent variables included in the models showed that for both sexes, generalised obesity declined by age group in women from age group 70-74 onwards and in men from age group 75-79 years (reference group being aged 65-69). The odds of being diabetic, having high blood pressure and arthritis were higher in people with generalised and abdominal obesity. In men only, those with generalised obesity had an increased risk of stroke (OR: 1.7, p=0.04). In women only, generalised obesity was associated with increased the risk of having a fall

Table 2

Age-standardised prevalence of chronic diseases and falls, by overweight and obesity

BMI status (%)	All ≤ 25 kg/m²	All≥25 kg/m² (overweight including obese)	Difference in prevalence of disease: (BMI≤ 25 kg/m² and≥ 25 kg/m²) Significant (p value, 95% CI) or NS	All ≤ 30 kg/m²	All ≥ 30 kg/m² (obese)	Difference in prevalence of disease: (BMI≤ 30 kg/m² and≥ 30 kg/m²) Significant (p value, 95% CI) or NS
Prevalence of disease	%	%			%	
Men[a]	*N=417*	*N=1093*		*N=1135*	*N=375*	
IHD[b]	21	22	NS	22	21	NS
Stroke	5	8	p=0.04 (0.4,5 6)	7	7	NS
Diabetes	7	13	p=0.001(2.8,9.2)	10	16	p=0 002(1.9,10.1)
Falls	22	19	NS	20	21	NS
Asthma	11	9	NS	9	13	NS
Chronic lung disease, such as chronic bronchitis or emphysema	12	7	NS	9	6	NS
Cancer or a malignant tumour (excluding minor skin cancers)	10	10	NS	10	9	NS
Arthritis (including osteoarthritis or rheumatism)	23	34	p<0 0001(6.1,15.9)	29	39	p<0.0001(4.4,15.6)
Osteoporosis	2	2	NS	2	1	
Whether ever had joint replacement(s)	5	8	p=0 04(0.4,5 6)	7	9	NS
Any emotional, nervous or psychiatric problems	6	4	NS	5	2	NS
Parkinson's disease	1	0	NS	1	0	NS
Women[a]	*N=555*	*N=1189*		*N=1229*	*N=515*	
IHD[b]	14	16	NS	13	19	NS
Stroke	7	5	NS	5	5	NS
Diabetes (excluding pregnant)	5	11	p<0.0001(3.5,8 5)	6	16	p<0.0001(6 6,13.4)
Falls	23	29	p=0.009(1.7,10.3)	26	29	NS
Asthma	10	13	NS	11	14	NS
Chronic lung disease, such as chronic bronchitis or emphysema	6	6	NS	6	7	NS
Cancer or a malignant tumour (excluding minor skin cancers)	10	9	NS	9	10	NS
Arthritis (including osteoarthritis or rheumatism)	35	48	p<0 0001(8 1,17.9)	40	52	p<0.0001(6.9,17.1)
Osteoporosis	14	10	NS	12	10	
Whether ever had joint replacement(s)	8	12	p=0.01(1.1,6 9)	9	13	p=0.01(0.7,7.3)
Any emotional, nervous or psychiatric problems	6	7	NS	6	8	NS
Parkinson's disease	0	0	NS	0	1	NS

a. N is unweighted; b IHD- Ischaemic heart disease, reported as doctor diagnosed angina or heart attack

Table 3

Age standardised prevalence of chronic diseases and falls, by raised waist circumference (WC) and sex

	Raised waist circumference (%)					
	Men[a] N=752 % with WC (<102 cm)	Men[a] N=641 % with WC (≥102 cm)	Difference in prevalence of disease: (% with WC (<102 cm) and≥ 102 cm) Significant (p value, 95% CI) or NS	Women[a] N=681 % with WC (<88 cm)	Women[a] N=936 % with WC (≥88 cm)	Difference in prevalence of disease: ((% with WC (<88 cm) and≥ 88 cm) Significant (p value, 95% CI) or NS
Prevalence of disease						
IHD[b]	22	23	NS	14	17	NS
Stroke	8	9	NS	6	6	NS
Diabetes	8	17	p<0 0001(5.5,12 5)	4	14	p<0.0001(7.3,12.7)
Falls	21	25	NS	27	30	NS
Asthma	9	11	NS	9	14	NS
Chronic lung disease, such as chronic bronchitis or emphysema	10	8	NS	6	8	NS
Cancer or a malignant tumour (excluding minor skin cancers)	10	10	NS	9	11	NS
Arthritis (including osteoarthritis or rheumatism)	27	39	p<0 0001(7.1,16 9)	40	52	p<0.0001(7.1,6.9)
Osteoporosis	2	2	NS	13	13	NS
Whether ever had joint replacement(s)	7	11	P=0.009(1.0,7.0)	9	15	p<0.0001(2.9,9.1)
Any emotional, nervous or psychiatric problems	5	3	NS	6	8	NS
Parkinson's disease	1	1	NS	0	1	NS

a. N is unweighted; b. IHD- Ischaemic heart disease, reported as doctor diagnosed angina or heart attack

Table 4

Estimated Odds Ratio for overweight including obese (BMI ≥25 kg/m²) by chronic condition status among people aged 65 years and over living in private households in England 2005

Variables	N=1512	Men Adjusted* odds ratio and 95% Confidence Interval (CI) †	P values	N=1747	Women Adjusted* odds ratio and 95% Confidence Interval (CI) †	P values
Age						
65-69	510	1		527	1	
70-74	425	0.8 (0.55,1.22)	0.3	487	0.6 (0.44,0.93)	0 02
75-79	338	0.7 (0.44,1.02)	0.06	365	0 6 (0.39,0.88)	0 01
80-84	159	0.5 (0.28,0.82)	0.008	239	0.5 (0.34,0.87)	0.01
85+	80	0.3(0 17,0.61)	0.001	129	0.4(0.20,0.67)	0 001
Diabetes						
Not diabetic	1339	1		1588	1	
Diabetic	173	1.9(1 02,3.36)	0.04	159	2.3(1.20,4.45)	0.01
Hypertension						
No hypertension	398	1		447	1	
Hypertensive controlled	187	1 9(1.17,2.98)	0.004	209	1.7(1.08,2.53)	0 02
Hypertensive uncontrolled	185	2.1(1.29,3.36)	0 003	239	1 9(1.27,2 90)	0.002
Hypertensive untreated	273	0.99(0 68,1.41)	0.95	303	1.6(1.09,2.22)	0.02
Arthritis						
Absent	1048	1		995	1	
Present	464	1.7(1.23,2.31)	0.001	752	1.5(1.04,2.07)	0.03
Stroke						
Absent	1401	1		1659	1	
Present	109	1.8(1 03,3.04)	0 04	88	0.8(0.47,1.37)	0.43
Had a fall in the last year						
No	1213	1		1292	1	
Yes	299	0 9(0 62,1 32)	0 60	455	1 5(1 05,2 01)	0 02

*Adjusted by age, cigarette smoking, social class, region, general health, long standing illness (limiting and non-limiting), presence of chronic conditions (heart disease, stroke, cancer, diabetes, hypertension, arthritis, chronic lung disease, joint replacement, osteoporosis), fall in last year; † Odds ratio and CI are weighted to represent the English population; No Hypertension: SBP <140mmHg and DBP <90mmHg and not taking medication prescribed for high blood pressure; Hypertensive controlled: SBP <140mmHg and DBP <90mmHg and taking medication prescribed for high blood pressure; Hypertensive uncontrolled: SBP ≥ 140mmHg or DBP ≥ 90mmHg and taking medication prescribed for high blood pressure; Hypertensive untreated: SBP ≥ 140mmHg or DBP ≥ 90mmHg and not taking medication prescribed for high blood pressure

Table 5

Estimated Odds Ratio for raised waist circumference (>102 cm for men and >88cm for women) by chronic condition status among people aged 65 years and over living in private households in England 2005

Variables	N=1393	Men Adjusted odds ratio and 95% Confidence Interval (CI) †	P values	N=1617	Women Adjusted* odds ratio and 95% Confidence Interval (CI) †	P values
Age						
65-69	464	1		471	1	
70-74	373	0 9 (0.63,1 19)	0.39	436	0.9 (0.63,1.16)	0.32
75-79	301	0 9 (0.66,1 25)	0.66	329	0.8 (0.57,1.13)	0 22
80-84	157	0.6 (0.38,0.91)	0 02	237	0 6 (0.45,0.98)	0 04
85+	98	0.5 (0.28,0 80)	0.005	144	0.5(0.29,0.74)	0.001
Diabetes						
Not diabetic	950	1			1	
Diabetic	1120	2.4(1.62,3.63)	<0.0001		2.8(1.70,4.76)	<0.0001
Cigarette smoking						
Never smoked	469	1		946	1	
Ex smoker	765	1.3(0 96,1.63)	0.1	504	1 4(1.07,1.80)	0.01
Current smoker	159	0.8(0.50,1.26)	0 33	167	0 8(0 52,1 21)	0.52
*Hypertension_*						
No hypertension	449	1		508	1	
Hypertensive controlled	214	2.3(1.63,3 29)	<0.0001	255	1.6(1 13,2.25)	0 007
Hypertensive uncontrolled	214	2.0(1.43,2.90)	<0.0001	304	2.0(1.01,2.09)	<0.0001
Hypertensive untreated	312	1.5(1.09,2.04)	0.01	342	1.2(0 90,1.63)	0.90
Arthritis						
Absent	948	1		867	1	
Present	445	1.6(1.18,2.09)	0 002	750	1.3(0.98,1.61)	0.08
Joint replacement						
Absent	1274	1		1425	1	
Present	119	1 3(0 83,2 07)	0 24	190	1 9(1 23,2 80)	0 003

*Adjusted by age, cigarette smoking, social class, region, general health, long standing illness (limiting and non-limiting), presence of chronic conditions (heart disease, stroke, cancer, diabetes, hypertension, arthritis, chronic lung disease, joint replacement, osteoporosis), fall in last year.; † Odds ratio and CI are weighted to represent the English population; No Hypertension: SBP <140mmHg and DBP <90mmHg and not taking medication prescribed for high blood pressure; Hypertensive controlled: SBP <140mmHg and DBP <90mmHg and taking medication prescribed for high blood pressure; Hypertensive uncontrolled: SBP ≥ 140mmHg or DBP ≥ 90mmHg and taking medication prescribed for high blood pressure; Hypertensive untreated: SBP ≥ 140mmHg or DBP ≥ 90mmHg and not taking medication prescribed for high blood pressure

in the last 12 months (OR: 1.5, p=0.02) and women with abdominal obesity were more likely to have had a joint replacement (OR: 1.9, p=0.01, Tables 4 and 5).

Discussion

This study shows obesity to be a significant problem among older people living in England 2005. This large nationally representative dataset shows that the prevalence of generalised and abdominal obesity increased among older people from 1993 to 2008, but with fluctuations in some years. Obesity represents an increasing problem worldwide (22). A disruption in energy balance, environmental and social factors have a predominant role in development of overweight and obesity throughout the life course (23). Data from another study shows the rapid rise in obesity in younger adults (24). As the ageing population is increasing and this trend is likely to continue (25), both the rise in the obesity epidemic and the increase in the ageing population predicts an unprecedented demand on social and health care systems that is likely to increase substantially in the future (26).

The data show a high prevalence of generalised and abdominal obesity in both men and women. Men had a higher prevalence of being overweight than women but a higher proportion of women were obese than men. The results are in agreement with another similar survey (27). Abdominal obesity was more prevalent in women than in men (58% and 46% respectively). Abdominal obesity in women has been found to be associated with higher levels of blood pressure and insulin resistance (28).

This is the first investigation in England using data collected in large, nationally representative samples to look at generalised and abdominal obesity and risk of chronic conditions in older people. Our data shows that both generalised and abdominal obesity are associated with increased risks of diabetes, hypertension and arthritis, in both sexes. Obesity is a well known contributing factor to the development of type 2 diabetes, which itself can increase the risk of cardiovascular disease and can lead to other complications that can affect the quality of life. The results of this study are in agreement with other studies providing evidence of both types of obesity being associated hypertension (29-31).

The data shows that arthritis was more common in those with generalised and abdominal obesity, which has also been shown in other studies (32, 33). An effective treatment for severe arthritis is joint replacement, which is found in the age adjusted prevalence analysis to be as more likely in people categorised as overweight or with raised WC. Multivariate analysis, adjusting for other factors shows that joint replacement was common only in women with abdominal obesity. Another survey has shown that overweight and obesity as well as raised WC were related to increased prevalence of cardiovascular disease, diabetes, hypertension and arthritis in men and women (34). It is surprising that our data does not show any association between abdominal or generalised adiposity and heart disease. This may be due to the nature of the survey which was cross-sectional. It is evident that overweight/obese individuals and those with diabetes have a higher incidence of, and also higher mortality from, circulatory diseases (35) and are probably less likely to survive to be included in this survey, compared with overweight and obese individuals without diabetes.

This study shows that among men, stroke was associated with generalised obesity but not with abdominal adiposity. Contrary to the findings in a prospective study that showed abdominal adiposity to be more closely associated than generalised obesity to stroke (36), although general adiposity may be more important for cardiovascular disease and mortality (37).

Women with generalised obesity are shown to have increased risk of falls, after adjusting for other factors. Muscle weakness and a poorer sense of balance are more common in those leading sedentary lives (38). Obesity is therefore an additional indirect risk factor for falls. Encouraging physical activity, such as by walking or cycling by incorporating it into daily life could help reduce risk of falls and also contribute to curbing or reversing the obesity epidemic.

The multivariate analysis shows a steady decline in BMI by age group among people aged 65 and over, seen in both sexes. This is likely to reflect age related changes in body composition i.e. a decline in lean muscle mass and increase in fat mass, the latter being lighter in weight. This has also been shown in other studies (39). Longitudinal studies confirm that after 65 years of age, the rate of weight loss occurs at an average rate of up to 0.65 kg/yr (40), although there is substantial variation between individuals. Loss of muscle mass begins from 30 to 40 years of age and continues into advanced old age (41). Ageing also influences the distribution of adipose tissue. Because fat replaces fat-free mass with increasing age, older people may have a greater proportion of fat than younger individuals with the same BMI. The change in distribution of fat with age results in an increase in abdominal fat in relation to total body fat. Thus older people are more likely to have a raised WC, a risk factor for metabolic syndrome and other adverse health outcomes (36, 37) that predicts future risk of chronic conditions such as type 2 diabetes, morbidity (14) and all-cause mortality. The data showed that abdominal obesity increased by more than 10% from 1993 to 2008 in both men and women. These results strongly suggest the need for health care professionals to incorporate WC measurements in their routine practice for early identification of abdominal obesity.

The results show a strong association between both types of obesity with hypertension, diabetes and arthritis and other chronic conditions. It is evident that unless there are effective strategies to slow the increase or reverse the direction of trends in generalised and abdominal obesity in all groups (3, 42) there may be a substantial rise in the prevalence of some of these co-morbidities in the future, increasing the burdens of disability-associated health and social care costs (43).

There is large body of evidence indicating that weight loss is an effective strategy for reducing risk for hypertension, diabetes and arthritis and other conditions and can lead to clinical benefits and improvements in health (33, 44-48) Reviews by Villareal et al (13), and Zamboni et al (49), have shown that management of obesity is important in older people (aged ≥65) and can improve obesity-related complications. Although a recent systematic review and meta- analysis showed a lack of high-quality evidence to support the efficacy of weight loss programmes in obese older people (50), it is of paramount importance to include strategies to control obesity and related co-morbidities among older people. Lifestyle modifications that include increasing physical activity to preserve muscle mass is an important component in any weight loss or weight management programme for people who are overweight to prevent them becoming obese.

Research shows that being overweight can offer some protection for older people, it reduces the loss of bone mass, and overweight elderly people are less likely to suffer hip fractures, a major cause of morbidity and mortality (13). However, the range of evidence of health risks of overweight and obesity are greater than any advantages.

Limitations of this study are that this is a cross-sectional study; therefore the directionality of the associations between chronic conditions and adiposity cannot be clearly established. However, evidence from other epidemiological studies show that obesity predicts chronic conditions to support our findings (32-34).

The most commonly used anthropometric index of obesity is the BMI. However, BMI has been questioned in the assessment of older populations as it is not a good indicator of body fat distribution. There is evidence that measures of abdominal obesity have a more important role than BMI in physical health outcomes (51).

There is controversy about the best measure in the assessment of abdominal obesity. We used WC measurements rather than waist-hip ratio (WHR) calculations in accordance with the ATP III recommendations (21), also in view of the lack of consensus about appropriate WHR levels and what thresholds should be used to define raised WHR (14).Measurements of body composition (that are not included in the HSE) are a better indictor of fat mass, important to look further at the link between fat percentage (that increases with ageing) and risk of chronic disease.

Conclusion

Both generalised and abdominal obesity rates continue to increase among older people in England. Because of this increase it can be expected that the risk of co-morbidities will also increase in the future. Our findings have shown the high prevalence of chronic diseases and problems that require healthcare among people aged 65 and over. The consequences of obesity such as diabetes, hypertension and arthritis improve with weight loss even in old age. Prevention of obesity is therefore as important as other treatment strategies for chronic diseases. There is an urgent need for improvement in treatment of obesity through effective evidence based weight management interventions aimed to include the older population.

Key points

- This nationally representative data in older people shows that generalised obesity and abdominal obesity increased in older people from 1993 to 2008 and that an impact on increased risk of associated co-morbidities.
- Generalised and abdominal obesity is shown to be independently associated with risk of hypertension, diabetes and arthritis in both older men and women.
- In older women only, there was an association between generalised obesity and having a fall in the last year and between abdominal obesity and having a joint replacement.
- Interventions to prevent obesity are therefore as important as other treatment strategies for chronic diseases in older people.

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Appendix 1

Method

Representativeness of the data included in the analysis

The participants were asked to comply with many components in the survey in addition to the nurse visit. These included giving a blood sample, which contributed to differences in response rate. However, specific statistical weighting were used to attempt to correct for the non-response at each stage, in addition to unequal sample selection, using information available about responders and non-responders. Further confirmatory analysis showed that the participants from whom a valid waist circumference (nurse visit) was obtained were representative of those interviewed. For example, mean age was 74.5(SD 6.8) years in those interviewed and 74.0 (SD 6.6) in those who had a valid waist circumference measurement; 44% of those interviewed, and 46% of those providing a valid waist circumference measurement were male. Similar comparisons for income, region, and social class all confirmed the representativeness of the data.

Appendix 2

Description of variables included in the regression analysis (Tables 4 and 5 in main paper)

Overweight, obesity and raised waist circumference was assessed in relation to the following variables:

Age: Age was grouped into five age groups: 65-69, 70-74, 75-79, 80-84 and 85+.

Sex: The analysis was adjusted to take sex differences into account.

Social class: Social class was assigned on the basis of occupation of the head of the household, with the Registrar General's standard classification*. 11 Social classes were further grouped into manual (skilled manual, partly skilled, and unskilled occupations) and non manual (professional, managerial and technical, and skilled occupations).

Cigarette smoking status: Participants were asked if they smoked or had ever smoked. The answer was categorized as never smoker, former/ex smoker, or current cigarette smoker.

Body mass index (BMI): Height and weight in the HSE were measured by a trained interviewer and those where reliable/valid measurements were taken were included in the analysis. BMI was calculated as kg/m2 and categorised as underweight (less than 20), normal weight (20-24.9), overweight (25.0–29.9), obese (30.0 or over).

Region: There are nine Government Office Regions (GOR) in England: the categories included were North East, North West, Yorkshire and the Humber, East Midlands, West Midlands, East of England, London, South East and South West.

General health: Participants were asked the question 'How is your health in general? Would you say it was 'very good', 'good', 'fair', 'bad', or 'very bad'? In the table, the five categories are combined to present as, 'very good'/ 'good'; 'fair'; 'bad'/'very bad '.

Limiting longstanding illness: Participants were asked whether they had any longstanding illness. Those who reported such an illness were asked whether the condition limited their activities in any way. Participants were categorised as 'not having a longstanding illness', 'having a limiting longstanding illness' and having a 'non-limiting longstanding illness'.

Self reported doctor diagnosed conditions:

Coronary heart disease: Participants were classified as having coronary heart disease if they reported ever having angina or a heart attack, confirmed by a doctor.

Diabetes: Participants were classified as having diabetes if they reported diabetes that was doctor diagnosed. The Health Survey for England interview makes no distinction between type 1 and type 2 diabetes. Diabetes that occurred only during pregnancy was excluded.

Stroke: Participants were classified as having a stroke if they reported ever having a stroke, diagnosed by a doctor.

Current musculoskeletal condition: Participants were classified as having a musculoskeletal condition if they reported ever having this condition, diagnosed by a doctor.

Joint replacement: Participants were classified as having a joint replacement if they reported ever having this condition, diagnosed by a doctor.

Cancer: Participants were classified as having cancer if they reported ever having this condition, diagnosed by a doctor.

Falls: Participants were classified as having a fall if they reported having a fall in the last 12 months.

Chronic lung disease: Participants were classified as having a this condition if they reported ever having chronic bronchitis, or emphysema, diagnosed by a doctor.

Blood pressure: This was measured three times after a five minute rest by a trained nurse according to standardised procedures. Informants were classified as having high blood pressure (BP) if they had a systolic blood pressure (SBP) of 140 mmHg or above, or a diastolic blood pressure (DBP) of 90 mmHg or above, or were currently taking medication specifically prescribed to treat their high blood pressure. Those with hypertension were further divided into the following categories:

Controlled	SBP below 140 mmHg/ DBP below 90 mmHg but taking medication for blood pressure
Treated but uncontrolled	SBP at or above 140 mmHg/ DBP at or above 90 mmHg and taking medication for blood pressure
Untreated	SBP at or above 140 mmHg/ DBP at or above 90 mmHg and not taking medication for blood pressure

* OPCS. Registrar General's Standard Occupational Classification: Vol 3.London, UK: HMSO; 1991.

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