Bone health of Bangladeshi mother–daughter pairs resident in the UK

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Bone Health of Bangladeshi mother-daughter pairs resident in the U.K

By

Diane Harper

A Doctoral Thesis

Submitted in partial fulfilment of the requirements for the award of Doctor of Philosophy of Loughborough University

(2018)

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I am indebted to Loughborough University for providing the funds to carry out this research and to Mark Lewis who contributed to the cost of providing study volunteers with a token of appreciation for the time and costs incurred in participating.

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Rights and Equalities Charnwood, Mrs. Minara Rahman and Mrs. Amina Wadood, who helped in the recruitment phase of the study. Other Bangladeshi women who helped included Mrs. Rosna Kalam, Mrs. Shelina Shaheduzzaman, Mrs. Jorin Bibi and many others, too numerous to name. Mrs Minara Rahman was a consistent support throughout the whole process of the PhD study.

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Finally, I would like to express my gratitude to family and friends who have given me constant support and encouragement over the past few years, especially my husband, Martin.
Abstract

Osteoporosis, characterised by low bone mineral density (BMD) and increased risk of bone fracture, constitutes a high socio-economic cost worldwide and is predicted to rise further in the future due to the ageing population. Asians are generally reported as having shorter stature, lower BMD and lower fracture risk (despite lower BMD) than people of European origin. There is evidence that lower BMD in South Asians (SA) is associated with smaller skeletal size, whilst possible explanations for their lower fracture risk include smaller body size and stronger hip structure. Migration Theory predicts that migrants from poor income countries to higher income countries increase in height over subsequent generations, as a consequence of a healthier environment in the host country. If this is the case for UK SA, then it would suggest that their BMD and some hip geometry dimensions (markers for fracture risk) would increase in parallel with increased height i.e. skeletal size. My study thus aimed to evaluate intergenerational differences in SA mother-daughter dyads, and differences related to place of birth, as well as confirming previous studies that ethnic differences between SA and Europeans could be explained by skeletal size.

My study focussed on a specific UK SA group, the Bangladeshi (BD) community. The study predictions were: 1) differences in bone mass and hip geometry dimensions between BD and indigenous British (IB) women would be associated with skeletal size, 2) BD daughters (born in UK or migrated at a younger age) would be taller, with greater bone mass and hip geometry dimensions, than their mothers (migrated at older age), and 3) BD daughters born in the UK would be taller, with greater bone mass and hip geometry dimensions, than BD daughters born in Bangladesh.

Data on these measurements, along with sociodemographic, early life environment and reproductive variables, were collected from Bangladeshi (BD) and indigenous British (IB) mother-daughter pairs. Study results confirmed previous evidence that lower BMD in Asians compared to Europeans is associated with skeletal size, but the other two predictions could not be adequately tested, due to limitations of the data set including small sample size. UK-born BD daughters appeared to have greater height, but lower BMD, than BD-born daughters, contrary to the usual association of skeletal size with BMD, and might suggest that UK-born BD daughters have a more gracile skeletal frame than BD-born daughters. This
agrees with previous reports that populations in higher income countries are becoming more gracile with increasing sedentism and lower physical activity, meriting further study. My study provides data on an under-researched area (bone status in the UK BD community) and hopefully will provide a useful platform for future research.

**Keywords**: Asian, Bangladeshi, BMD, Hip Geometry, Fracture
# List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>AHA</td>
<td>Advanced Hip Analysis</td>
</tr>
<tr>
<td>BA</td>
<td>Bone Area</td>
</tr>
<tr>
<td>BD</td>
<td>Bangladesh/Bangladeshi</td>
</tr>
<tr>
<td>BMAD</td>
<td>Bone Mineral Apparent Density</td>
</tr>
<tr>
<td>BMC</td>
<td>Bone Mineral Content</td>
</tr>
<tr>
<td>BMD</td>
<td>Bone Mineral Density</td>
</tr>
<tr>
<td>BR</td>
<td>Buckling ratio</td>
</tr>
<tr>
<td>BSA</td>
<td>Bangladeshi Social Association</td>
</tr>
<tr>
<td>BSI</td>
<td>Bending Strength Index</td>
</tr>
<tr>
<td>BUA</td>
<td>Broadband Ultrasound Attenuation</td>
</tr>
<tr>
<td>BVF</td>
<td>Bone Volume Fraction</td>
</tr>
<tr>
<td>CHD</td>
<td>Chronic Heart Disease</td>
</tr>
<tr>
<td>CSI</td>
<td>Compression Strength Index</td>
</tr>
<tr>
<td>DALY</td>
<td>Disability-adjusted life years</td>
</tr>
<tr>
<td>DOHaD</td>
<td>Developmental Origins of Health and Disease</td>
</tr>
<tr>
<td>DXA</td>
<td>Dual X-ray Absorptiometer</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>FNW</td>
<td>Femoral Neck Width</td>
</tr>
<tr>
<td>FRAX</td>
<td>Fracture Risk Assessment Tool</td>
</tr>
<tr>
<td>GH</td>
<td>Growth Hormone</td>
</tr>
<tr>
<td>GLOW</td>
<td>Global Longitudinal Study of Osteoporosis in Women</td>
</tr>
<tr>
<td>HAL</td>
<td>Hip Axis Length</td>
</tr>
<tr>
<td>HSA</td>
<td>Hip Structure Analysis</td>
</tr>
<tr>
<td>HSE</td>
<td>Health Survey for England</td>
</tr>
<tr>
<td>HSI</td>
<td>Hip Strength Index</td>
</tr>
</tbody>
</table>
List of Abbreviations (continued)

IB Indigenous British
IGF-1 insulin-like growth factor 1
ISI Impact Strength Index
LEL Lower Extremity Length
MINA Migration, Nutrition and Ageing across the Lifecourse in Bangladeshi Families
MLR Multiple Linear Regression
NHANES National Health and Nutrition Examination Survey
NIH National Institute of Health
NSA Neck shaft angle
PA Projected Area
PCOS Polycystic ovary syndrome
QUS Quantitative Ultrasound
QCT Quantitative computer tomography
RR Relative Risk
SA South Asian
SES Socioeconomic Status
SM Section Modulus
SOS Speed of Sound
SWAN The Study of Women’s Health Across the Nation
TBF Trabecular Bone Fraction
US United States
vBMD volumetric BMD
WHI Women’s Health Initiative
WHO World Health Organisation
Z Section Modulus
# List of Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asians</td>
<td>People who originate from any country in the Asian continent</td>
</tr>
<tr>
<td>Europeans</td>
<td>People who originate from Europe (includes those in US)</td>
</tr>
<tr>
<td>Generation</td>
<td>Mother or daughter, irrespective of birthplace</td>
</tr>
<tr>
<td>South Asian</td>
<td>People who originate from India, Pakistan or Bangladesh</td>
</tr>
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**Bone Health of Bangladeshi mother-daughter pairs resident in the U.K**

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1 Introduction

Osteoporosis, characterised by low bone mineral density (BMD) and bone fragility (European Foundation for Osteoporosis Conference Report, 1991), is a major risk factor for bone fracture (WHO, 1994). Bone fractures currently constitute a high socio-economic cost, predicted to rise further in the future, both in the UK and worldwide, due to the ageing population (Johnell and Kanis, 2006; Gutiérrez et al., 2012). Although both males and females, of all ethnicities, are at risk of osteoporosis with ageing, women have a higher risk of osteoporosis and fracture than men (van Staa et al. 2001), so bone research generally involves women.

The majority of research on bone status has focussed on people of European ancestry, with less literature on people from other ethnicities. In the UK, ethnic minority groups comprise a substantial proportion (14%) of the UK population (ONS, 2012) and this proportion is expected to rise over the next few decades (Coleman, 2010; Lievesley, 2010), so more information on the bone status of UK ethnic minorities is important in terms of understanding their risk of osteoporosis and fracture in the UK, and related health care requirements. A major UK ethnic minority group is the South Asian (SA) community (originating from India, Pakistan or Bangladesh) but there is very little research on bone health in this group. There are only a few UK studies reporting on bone health in UK SAs and comparative research in the US regarding ethnic differences in bone status has generally focussed on Hispanics, East Asians and people of African origin.

Published research concludes that UK SAs have lower height and lower BMD at lumbar spine, proximal femur and radius compared to indigenous British (IB) (Roy et al. 2005; Brooke-Wavell et al. 2008; Hamson et al. 2003). However, despite lower BMD, UK SA women have a lower fracture risk than indigenous British (IB) (Donaldson et al., 2008; Curtis et al., 2016). This inconsistency has been reported in other Asian groups compared to people of European origin (Marquez et al., 2001; Finkelstein et al., 2002; Barrett-Connor et al., 2010; Melamed et al., 2010; Khandewal, Chandra and Lo, 2012). Although a number of explanations for this paradox have been proffered, including smaller body size and a
stronger hip structure, further research is needed to explore bone health in Asian populations.

A disadvantage of most studies on bone status in different ethnic groups, is that the description of the ethnic group can be very broad e.g. Asians, rather than relating to a specific country of origin e.g. India or Bangladesh, thus introducing a larger range of genetic, environmental and cultural influences on the bone measurements of the study participants. Future research needs to focus on a single ethnic group. Of all the UK SA communities, Bangladesis are particularly noted for poor health (Bhopal et al., 1999; Kuppuswamy and Gupta, 2005) as well as being the most deprived of all UK ethnic minority groups (Nazroo, 1998; Kuppuswamy and Gupta, 2005; Whitley et al., 2008; Nazroo et al., 2009). Therefore, it might be expected that of all the UK ethnic minority groups, the Bangladeshi (BD) community might be particularly at risk of poor bone health, but no studies to date have focussed on bone status of the UK BD community. To fill these gaps in the research my thesis study was designed to explore bone health in a specific UK SA ethnic group, the UK BD community. An advantage of recruiting UK BD women is that they generally originate from just one district, Sylhet, (Gardner, 1995) thus reducing genetic and environmental variation, resulting in a more homogenous population.

A defining feature of any UK ethnic minority group is that they or their forebears have migrated from their land of origin. Migration Theory, in the context of international migration, predicts that the phenotype of a migrant will become similar to that of the host community, over the course of one or more generations, as a result of sharing common environmental influences. Migration Theory originated with seminal work by Boas (1912), based on the migration of European immigrants to New York, US. Boas found that the US-born children of European immigrants were taller than their parents. He suggested that this was due to improved social conditions and a healthier environment in the new country, especially at the time of birth and during the years of growth and development. Subsequent studies reported similar findings regarding height in migrants who had migrated from lower to higher income countries (Boas, 1912; Shapiro, 1939; Goldstein, 1943; Lasker, 1952; Greulich, 1957; Malina, Buschang, Aronson, 1982; Mascie-Taylor and Little, 2004).
A more recent study showed that Maya American children in Florida, US are significantly taller than their contemporaries in Guatemala, and closer in mean height to American children of European and African heritage (Bogin et al., 2002). This change in height is attributed to a healthier environment in Florida e.g. safe drinking water, better health care and nutrition during growth and development (Bogin et al., 2002). This is a similar scenario to the SA community in the UK, in that SAs are shorter than IB, and the UK provides a healthier environment than South Asia in terms of more freedom from infection, safe drinking water and better health care (Northrop-Clewes et al. 2001; Alam et al. 2006; BBS 2013; NIPORT 2013; WHO 2015). Therefore, it seems likely that UK SA women, born in the UK, or migrating to the UK during childhood, will show a similar increase in height, becoming closer to the height of IB women. This is supported by the limited research in the area which suggests that height in UK SA adults increases over generations (Shams and Williams, 1997). Later reports conclude that UK-born Pakistani women were taller than migrant Pakistani women (Pollard et al., 2008), and height significantly increased in one generation of UK BD women (Bogin et al., 2014). If generational height increase is seen in UK SA women this has implications for their bone status as BMD is linked to skeletal size (indicated by height) (Carter, Bouxsein and Marcus, 1992; Seeman, 2001). An increase in height would also be expected to be accompanied by an increase in some hip geometry dimensions. Therefore, it is possible that bone status of the UK SA community might change in the future. To summarise, Migration Theory, supported by the published literature, predicts that height in UK SAs will increase over future generations to become closer to that of IB. More research is required to confirm this prediction and to investigate the implications for bone measurements.

The main paradigm shift, resulting from the earlier migration studies, was that environment had more of a role in determining phenotype than was previously thought. With the advent of recent discoveries relating to epigenetics (the study of changes in gene expression without altering the DNA sequence itself), a mechanism was found that could explain the effect of environment on phenotype (Carey, 2012).

Migration Theory is associated with the biocultural perspective i.e. the recognition that culture is a major force in humans’ adaptation to the environment. Furthermore, culture itself can change the environment, so there is an interaction between the biological
environment and culture. The combination and interaction of these two forces, biological environment and culture, is labelled “biocultural”, and taking a biocultural perspective presupposes that this is the predominant explanation for the diversity of the human populations (Bogin, 1999). This does not refute a genetic basis and Darwinian natural selection, but asserts that “environmental forces, including the social, economic and political environment, regulate the expression of DNA, as much, or more so, than DNA regulates human biology” (Bogin, 1999). The respective roles of bioculture and genes (and their interaction) will depend very much on the topic under study, which for this thesis is bone status in a specific UK SA ethnic minority group, the BD community. As will be emphasised later, bone is very plastic, having evolved to respond efficiently and quickly to environmental influences throughout the life course, and therefore likely to change quickly in subsequent generations of the BD community.

In a new environment, migrants are exposed to different physical, biological and biocultural changes that can have positive or negative impacts on phenotype and health status over the life-course. A number of theories, discussed in more detail in the next chapter, have been developed to describe and explain environmental effects on humans. Although these theories were not developed specifically in connection with Migration Theory, they are relevant for explaining the mechanism of how a new environment might change the phenotype of migrants. An important theory, relevant to Migration Theory, is the developmental origins of health and disease (DOHaD) theory which proposes that the environmental cues of maternal nutrition, behaviour and stress cause epigenetic modifications in the foetus and thus its phenotype, which can have implications for health in later life (Barker, 2007; Gluckman & Hanson, 2005). Osteoporosis is one of the diseases which are modifiable by early life influences (Cooper et al., 2006), making the collection of data on the environment at time of birth useful in bone studies on migrants based on Migration Theory.

Life History Theory considers the impact of environment on health throughout the life course, and how an organism has evolved to ensure evolutionary survival at each stage of its life by trade-offs between growth, reproduction and maintenance of the organism (Bogin, 1999; Kuzawa, 2007). Bone development and bone loss are strongly associated with human Life History events, so the availability of energy resources at the time of the event will be
particularly important in modulating bone status (Leidy, 1996). Reproductive life events are different in SA women e.g. more children and longer periods of lactation, compared to IB women. Acculturation (the process of social, psychological and cultural change within a migrant population, rendering it more similar to the host population) may result in future generations of SA women becoming more similar to IB women in terms of reproductive variables, thus contributing to a similar bone status. Further research is needed to explore whether reproductive life events are changing in the UK SA community, and if so whether this is associated with bone status.

Intergenerational theory explains how changes in phenotype, due to environmental influences, are passed on through the generations. This theory was originally defined as “those factors, conditions, exposures, and environments experienced by one generation that relate to the health, growth, and development of the next generation” (Emanuel, 1986, pp 27), partly through epigenetic modifications on the foetus and also socio-cultural factors that continue from one generation to the next. Therefore, it is not only the current biocultural environmental conditions experienced by the immigrant, but those of their mother and grandmother (which, in turn have been influenced by their mothers and grandmothers) which impacts on the phenotype of an individual (Emanuel, Kimpo and Moceri, 2004). Because of these intergenerational effects, not to mention genetic inheritance, it can take a number of generations of exposure to the new environment before an immigrant population acquires characteristics similar to those of the host population. Studies on migrant groups that explore how diverse environments at birth and during growth and development, experienced by different generations, affect the phenotype, should control for intergenerational influences.

Current risks for bone health in UK SA women are low BMD as measured by dual x-ray absorptiometry (DXA), low vitamin D levels, poor nutrition, high visceral fat, and lack of exercise and diabetes (see Background chapter). Despite these risk factors for poor bone health in BD and other SA women resident in the UK, the fact that they, in common with other ethnic groups, have come to a country which, generally speaking, is more beneficial to health than their home country, might lead to bone health improvement in the future. Bangladesh is classified as a lower income country with lower life expectancy, higher child mortality, higher prevalence of malnutrition, poor sanitation, limited access to clean water,
limited medical care and higher exposure to infectious diseases (especially intestinal parasites) relative to wealthier countries such as the UK (Northrop-Clewes et al. 2001; Alam et al. 2006; BBS 2013; NIPORT 2013; WHO 2015). Although UK BD women mainly come from the Sylhet region of Bangladesh, where nutritional and economic stresses are not as intense as in other Bangladeshi areas (Gardner, 1995; Houghton et al., 2014) they still suffered from the other disadvantages mentioned above, such as immunological challenges, limited access to clean water and a lower quality of health and pre-natal care. The environment experienced at birth e.g. breast feeding, pre-natal care, vaccination and home births, also generally differs between low income and high income nations, so women born and brought up in Bangladesh experience a very different early biocultural environment than those born and brought up in the UK. The UK environment at birth may be better than that in Bangladesh, in terms of health care, vaccinations etc. which, in accordance with DOHaD theory may improve health and bone status in BD women born in the UK.

However, migrating to a country with a higher standard of living, such as the UK, is not always a guarantee of a healthy environment for bone status. It has been suggested that lifestyles in developed countries might contribute to hip fracture because global indicators of health, education and socioeconomic status are positively correlated with fracture rates (Cauley et al., 2014). The higher fracture risk in developed countries has also been linked to higher levels of urbanization (Ballane et al., 2014). Therefore, there are risks as well as benefits for bone health in SAs migrating to the UK.

Another potential risk for UK BD and other SA migrants is the fact that inhabitants of high-latitude countries can suffer from vitamin D deficiency due to low sunlight exposure, especially in winter months (Macdonald et al., 2008). SAs migrating to more northerly countries, suffer from less exposure to sunlight, which has been thought to decrease their serum vitamin D levels (Holvik et al., 2005; Brouwers et al., 2010). Widespread vitamin D deficiency was reported in men and women born in Turkey, Sri Lanka, Iran, Pakistan and Vietnam who were residing in Oslo (Holvik et al., 2005) whilst osteomalacia has been diagnosed in the SA community in the UK (Finch et al., 1992) and reported in SA immigrants in Northern European countries (Brouwers et al., 2010).
The balance between the benefits and disadvantages of living in the UK on bone status for UK BD women is not known, but as mentioned above there is good evidence that height and knee height is increased in the daughters of BD migrants to the UK (Bogin et al., 2014). Increased knee height is a marker of an improved environment at birth and during growth and development. Taller stature is generally linked to better health which is associated with an improved biocultural environment (Boas, 1912; Bogin, Smith, Orden, Silva, & Loucky, 2002; Silventoinen, 2003; Tanner, 1992). Increased knee height and taller stature indicates improved health in UK BD women which would suggest improved bone status. Also, as height correlates positively with skeletal size, which, in turn, correlates positively with BMD (Roy, 2005), the observed increase in height in UK BD women might be paralleled by an increase in BMD in these same women, either because of a better early environment and/or a direct consequence of an increase in skeletal size. The height and BMD of future generations of BD women might increase to become similar to those of IB women. Although greater height is linked to higher BMD measurements, which in turn is associated with reduced fracture risk (Marshall, Johnell and Wedel, 1996), greater height has also been associated with increased fracture risk, especially hip (proximal femur) fracture (Armstrong et al., 2016). Explanations for this association of height with fracture risk are discussed further in the Background chapter. One possible contribution to hip fracture risk is body size, with a greater body size resulting in increased impact on the femur in a fall and thus higher risk of fracture (Hayes et al., 1993). Another possibility is that greater skeletal size is associated with longer hip axis length (HAL) and a more protruding greater trochanter which render the femoral neck more susceptible to breakage (Faulkner et al., 1993; Gregory and Aspden, 2008).

So, for BD women, increased skeletal size (as indicated by increased height) could have benefits (higher BMD) as well as disadvantages (increased impact in a fall, longer HAL, more protruding greater trochanter) for fracture risk. The overall balance of risk is currently unknown. However, increases in height in successive generations of BD migrants suggest the possibility that there may be changes in bone health in these successive generations.

To address the limited research on bone status in UK SA groups, and the total lack of research on bone status in the UK BD community, my study focussed on the UK BD community. Unlike the majority of studies on bone status in ethnic groups, my study is
informed by Migration Theory. Migration theory, in conjunction with published evidence that the UK provides an overall healthier environment than Bangladesh, predicts that UK BD women who were born and/or spent their early years of development in the UK will grow taller than their mothers, who migrated as adults. This increase in height is predicted to occur over succeeding generations, until BD women have a similar mean height to IB women. Based on published evidence that the significant differences in BMD at various skeletal sites between SA and IB women is associated with skeletal size, it is also predicted that an increase in skeletal size in BD women will be accompanied by a corresponding increase in BMD. Another predicted consequence of increased skeletal size is a lengthening of HAL and possibly other hip geometry parameters.

My study cannot measure fracture risk (which would require epidemiological type longitudinal studies with large sample numbers), but by measuring markers of fracture risk (BMD and HAL), it aims to explore the current bone status of the UK BD community and suggest how this may change in the near future. In addition, the association between BMD and skeletal size is explored to explore the prediction that changes in BMD are associated with skeletal size.

The following research question and predictions were therefore proposed.

**Study’s research questions**

**Are improved early life environmental and cultural conditions experienced in the UK associated with higher values of height and knee height, bone mass and hip geometry dimensions in the UK Bangladeshi population?**

**Are ethnic and/or generation differences in bone status measurements associated with skeletal size?**
For my study, BD and IB mother-daughter pairs were examined and comparisons made according to ethnicity and generation. My use of the term “generation” refers to whether the participant is a mother or a daughter, irrespective of birthplace. Such a sample has four groups of women who have had different exposures to the UK environment, allowing the above predictions to be tested. The use of mother-daughter dyads controlled as far as possible for biocultural influences.

The order of magnitude of UK exposure (highest first) for the four groups is summarised below.

1) IB women
   Born in UK
   Forbears born in UK (daughters)

2) BD women
   Born in UK

3) BD women
   Born in BD
   Migrated at young age (daughters)

4) BD women
   Born in BD
   Migrated at older age (mothers)

Study’s predictions and hypotheses

IB women have greater height, knee height, bone mass and hip geometry dimensions than BD women (independent of menopausal status). Any ethnic differences found do not persist after controlling for skeletal size.

Null hypothesis: there is no difference between BD and IB women for these variables

BD daughters have greater height, knee height, bone mass and hip geometry dimensions than their BD mothers (independent of mother’s menopausal status). Any generational differences found do not persist after controlling for skeletal size.

Null hypothesis: there is no difference between BD daughters and mothers for these variables

UK-born BD daughters have greater height, knee height, bone mass and hip geometry dimensions than BD-born BD daughters.

Null hypothesis: there is no difference between UK–born BD daughters and BD-born BD daughters for these variables
To summarise, my thesis research aimed to fill a gap in the literature by focusing on bone status in the BD community, a specific UK SA community, not previously studied. Based on Migration Theory and DOHaD, it was predicted that height, knee height, bone mass and hip geometry dimensions would be higher, the greater the study participant’s exposure to the UK environment in early life.

The layout of the thesis, including the means by which the above predictions were tested, is as follows:

Chapter 2

This is general background information, describing in more detail the topics mentioned above, e.g. cost of osteoporosis and fracture in the UK, Migration Theory and related theories such as DOHaD, Intergenerational Theory and Life History Theory. A brief overview of the skeletal system is also included. This is followed by a discussion of bone status in UK SAs, along with a general description of BMD and hip geometry parameters. Factors influencing BMD and hip geometry parameters and skeletal development throughout the life course are also discussed.

Chapter 3

In addition to primary data from my own study, I initially examined secondary data to test the prediction that an increase in height was mirrored by an increase in bone status in BD daughters, who were reported as being significantly taller than their mothers (Bogin et al., 2014). These data came from a previous research study, the Migration, Nutrition and Ageing across the Life course in Bangladeshi Families (MINA) Project (Thompson et al., 2014), which recruited UK BD women from Cardiff. The MINA project also collected data on quantitative ultrasound (QUS) measurements at the calcaneous (unpublished). The QUS scores comprised broadband ultrasonic attenuation (BUA) which is influenced by BMD and speed of sound (SOS) which is influenced by various bone characteristics including elasticity. I used these data to explore whether QUS measurements paralleled the height difference between the two generations, i.e. predicting that QUS measurements in Cardiff BD daughters would be higher than their mothers. The MINA project also reported that UK-born BD daughters had greater height and knee height than BD-born daughters (Bogin et al.,
I therefore compared QUS measurements in UK BD daughters to see whether the greater height of UK-born BD daughters was reflected in greater QUS measurements, compared to BD-born daughters.

Chapter 4

This chapter covers the methods used for my Loughborough study in which UK BD and IB mother-daughter pairs were recruited from the same residential area in Loughborough. Using BD mother-daughter dyads to compare between older BD women who migrated at an older age (mothers) with younger BD women who were born in the UK or migrated at a younger age (daughters), controlling for familial influences (genetic, environmental and cultural) which contribute greatly to the variance in skeletal size and bone status. Recruiting IB women from the same location as the BD women controlling, as far as possible, for SES and local environment.

Protocols for collecting anthropometric and bone status measurements are described. Because my study was based on Migration Theory and DOHaD theory, I also collected data related to the environment at birth, to explore and document the differences between birthplace (UK or Bangladesh). Reproductive variables were also recorded to explore how life events associated with reproduction differ between BD and IB women, which according to Life History theory would impact on bone status.

Chapter 5

The results and conclusions arising from my Loughborough study are reported. The Loughborough study aimed to confirm and extend findings from the earlier report of a significant increase in height and knee height in UK BD daughters compared to their mothers (Bogin et al., 2014). The Loughborough study was designed to test the prediction that height, knee height, bone mass and hip dimensions were higher in BD daughters than their mothers, and higher in UK-born BD daughters compared to BD-born BD daughters.

From a clinical perspective, BMD, irrespective of its association with skeletal size, is the strongest predictor of the clinical end-point, fracture risk (Marshall, Johnell and Wedel, 1996). As such, BMD is the most important health measure in this research. In order to understand the mechanisms of ethnic and generational differences in BMD, if ethnic or
generational differences were found, analyses were repeated, taking into account skeletal size. Ethnic and generational differences in hip geometry parameters were also explored and the relationship with skeletal size examined.

Chapter 6 summarises the findings, and presents the conclusions of the thesis, along with suggestions for future research.
2 Background

This chapter covers the literature which provides the background information that is relevant to the study.

2.1 Sources of information

The information was obtained using a number of methods, including searches in PubMed and Google Scholar electronic databases, recommendations from supervisors and colleagues, following up citations and publications that cited key papers, and notifications from various sources (Mendeley, Google, and relevant journals).

2.2 Cost of osteoporosis

A major problem in the UK and many other countries worldwide is the increasing cost, personal and socioeconomic, of ill health associated with higher numbers of elderly people within the population (Caley and Sidhu, 2011). These spiralling costs predominately arise from the so-called diseases of ageing: dementia, type 2 diabetes, cardiovascular disease, cancer and osteoporosis. The prevalence and incidence of osteoporosis in the UK’s ageing population is high. At the turn of the millennium, 3 million (5%) UK residents suffered from osteoporosis, incurring up to 300,000 fractures a year (Burge and Worley, 2001), and in the United States (US) it has been estimated that 10 million (3%) Americans suffer osteoporosis, accounting for 1.5 to 2 million fractures annually (Burge 2007).

A British woman aged 50 years has a 1 in 2 chance of sustaining an osteoporotic fracture in her remaining lifetime; for British men it is a 1 in 5 chance (van Staa et al., 2001). The most serious osteoporotic fractures are those of the hip and vertebrae. A hip fracture involves the breaking of the proximal end of the femur. A vertebral fracture resulting from osteoporosis is generally characterised by a vertebral bone in the spine decreasing in height (Vedantam, 2009). Data from the Women’s Health Initiative (WHI) Observational Study, based on over 80,000 US women aged 50 to 79 years, reported that the age-adjusted annualized incidence rate of hip fracture was greater than breast cancer, irrespective of ethnic origin (Cauley et al., 2008). A recent study concluded that the burden of hospitalisation for US women, aged 55 years and older, was greater for osteoporotic
fractures than for myocardial infarction, stroke or breast cancer (Singer et al., 2015) as shown in Figure 2.1

**OF = osteoporotic fracture; MI = myocardial infarction**

![Figure 2.1 Unadjusted rate of total osteoporotic fracture, myocardial infarction, stroke and breast cancer hospitalisation for US women, aged 55 years and older](image)

Reproduced from Singer et al. 2015

This high incidence of osteoporotic fractures imposes a considerable economic, social and personal burden in the UK (Gutiérrez et al., 2012) and is a significant cause of morbidity and mortality worldwide, especially in developed countries (Johnell and Kanis, 2006). Because osteoporotic fracture generally occurs in older people, who may also be suffering other illnesses, it is difficult to attribute mortality directly to the fracture (Teng, Curtis and Saag, 2008). However, it is well established that risk of mortality is higher after hip or vertebral fracture (Cooper et al., 1993; Keene, Parker and Pryor, 1993; Center et al., 1999), with the highest risk occurring in the first year after fracture (Johnell et al., 2004). A recent UK study of 33,152 patients aged over 60 years with a hip fracture, reported mortality to be 31.2% a year after the fracture (Leal et al., 2016) and a systematic review of 22 studies from Europe
and the United States reported excess mortality after hip fracture to be double that of the age-matched general population (Abrahamsen et al., 2009).

In terms of morbidity, hip fractures impair the ability to walk. A recent prospective cohort one year follow-up study of 390 hip fracture patients aged 65 years and older, showed that only 48% regained their pre-fracture mobility (Vochteloo et al., 2013). The likelihood of regaining mobility varied depending on the level of pre-fracture mobility, with fully mobile patients the least likely to regain previous mobility (Vochteloo et al., 2013).

Vertebral fractures also cause considerable morbidity in terms of back pain, loss of independence and reduced quality of life (Suzuki, Ogikubo and Hansson, 2008). Although vertebral fractures are underdiagnosed (Gehlbach, Fournier and Bigelow, 2002; Delmas et al., 2005) they are still reported as being more common than hip fracture (Burge et al., 2007). The Global Longitudinal Study of Osteoporosis in Women (GLOW), which involved a sample of over 50,000 post-menopausal women from nine European countries and the United States, reported 1,822 incident fractures after one year follow up, 10% of which were vertebral fractures compared to 7% hip fractures (Roux et al., 2012).

Morbidity and mortality can be combined using Disability Adjusted Life Years (DALYs) which integrates the life-years lost due to premature mortality and the years of disabled life in survivors (Murray and Lopez, 2012). In Europe, osteoporosis accounted for 2.0 million DALYs lost (Figure 2.2), less than osteoarthritis (3.1 million) and greater than rheumatoid arthritis (1.0 million) (Johnell and Kanis, 2006).

In addition to personal suffering, there are high economic costs associated with osteoporosis in terms of treating fractures and the subsequent after care required as a consequence of disability resulting from the fracture. Dolan and Torgerson (1998) estimated that osteoporotic fractures in the UK cost 942 million pounds a year; this figure was later updated to 1500 million pounds (Johansen and Stone, 2000). A more recent UK study involving a cohort of patients aged over 60 years estimated the cost to the hospital services in the year following a hip fracture to be 1.131 billion pounds at 2012/2013 unit costs (Leal et al., 2016).
Figure 2.2 Disability-adjusted life years (DALYs) lost due to a selection of noncommunicable diseases in Europe (COPD – Chronic Obstructive Pulmonary Disease)

From Cole et al. 2008 who adapted it from Johnell and Kanis 2006

Burge et al. (2001) using previous publications (Dolan and Torgerson, 1998; Netten, Dennet and Knight, 1998) estimated that total UK costs due to osteoporotic fracture in the first year after fracture for the year 2000 were accounted for by hospitalisation (45%), nursing home residency (50%), outpatient care (5%) and drug costs (0.4%). Hip fractures explained 84% of the total costs as they accounted for 74% of the hospitalisation costs and all the nursing home costs (Burge and Worley, 2001). A similar analysis in the United States in 2005 attributed the total cost of incident osteoporotic fractures to be 57% inpatient care, 13% outpatient care and 30% to long-term care with hip fractures accounting for 72% of the total costs (Burge et al., 2007). A study in the Netherlands of a sample of 116 osteoporotic patients suggested that indirect costs such as sick leave also have a considerable impact on the total socio-economic costs related to fracture (Eekman et al., 2014).

Moreover, costs are predicted to rise as the number of elderly individuals increases in the future (Cummings and Melton, 2002). It has been estimated that the number of hip fractures worldwide was 1.26 million in 1990; this is predicted to approximately double to 2.6 million by the year 2025 and then to 4.5 million by the year 2050 (Gullberg, Johnell and
Kanis, 1997). The major reason for the increase in hip fractures is the change in the
demographic structure of the world population with higher numbers of elderly people,
especially in Asia and Latin America (Cooper, Campion and Melton, 1992).

To summarise, the costs, personal and socioeconomic, of osteoporosis are high and
predicted to rise even further in the future. As mentioned in the Introduction, ethnic
minority groups comprise a large proportion of the UK population but less is known about
their bone status and fracture risk. Therefore, further research on bone health in
understudied ethnic groups, and trends in bone health in generations following migration,
are important to anticipate future health care needs, and potentially to inform or target
preventive strategies.

2.3 Osteoporosis

In the early nineties a consensus development conference, sponsored by various
organisations involved in bone health, defined osteoporosis as follows: “a disease
characterized by low bone mass and micro-architectural deterioration of bone tissue leading
to enhanced bone fragility and a consequent increase in fracture risk” (European
Foundation for Osteoporosis Conference Report, 1991). This general definition was
endorsed by the World Health Organisation (WHO, 1994) along with recommendations for
an operational classification based on measurements of bone density (Compston, 1995).
More recent definitions recognise that there are other factors in addition to bone density
which contribute to bone strength and fracture risk. For example, the WHO recommended
that clinical risk factors such as age were included in fracture risk assessment (WHO, 2004)
and in the US the National Institute of Health (NIH) defines osteoporosis as “a skeletal
disorder characterised by compromised bone strength” (NIH, 2000).

In addition to the above definition of osteoporosis as a skeletal disorder, there is the term
“osteoporotic fracture”, also termed fragility or low trauma fracture. This is a fracture that
is caused by very little trauma or force (e.g. falling from standing height) at a site containing
a large amount of trabecular bone and commonly associated with osteoporosis i.e. proximal
femur, vertebra or wrist. For example, a low-trauma fracture at the radius is termed
“osteoporotic fracture”, whereas a high trauma fracture, which often occurs at the radius, is
not an osteoporotic fracture.
An osteoporotic fracture is not always linked with low bone density (Sanders et al., 2006). People with only moderately low (Pasco et al., 2006) or even normal bone density (Wainwright et al., 2005; Premaor et al., 2010) can still be said to suffer an osteoporotic fracture. A recent publication reported that 50% of 528 women who had suffered an osteoporotic fracture did not have osteoporosis as defined by bone density (Bluic et al., 2014). Conversely, a person with a very low measurement of BMD is diagnosed as having osteoporosis without necessarily having suffered a fracture.

As mentioned above, osteoporosis is characterised by low BMD at the femoral neck and/or lumbar spine as measured using DXA technology. The recent operational definition of osteoporosis by WHO has the femoral neck as the standard measurement site and compares the individual’s T-score with that of an international reference standard (Kanis et al., 2008), where the T-score is the number of standard deviations difference from that of a young healthy population of the same sex (Watts, 2004). The reference population used was young women from the NHANES III study (Looker et al., 1998). The operational definition of osteoporosis is defined as a BMD value which is 2.5 or more standard deviations below the mean of a young adult of the same sex in the reference population (WHO, 1994; Kanis et al., 2008).

In recognition of the fact that other factors in addition to bone density contribute to bone strength and fracture risk, WHO have now developed a software tool called Fracture Risk Assessment Tool (FRAX) https://www.shef.ac.uk/FRAX/ which combines femoral neck BMD with other clinical and lifestyle factors to estimate a patient’s 10-year fracture probability (Kanis et al., 2009). The additional factors that FRAX uses are those known to be associated with osteoporosis e.g. age, sex, weight, smoking, alcohol use, long-term use of oral glucocorticoids, rheumatoid arthritis and fracture history (Kanis et al., 2009). Femoral neck BMD is preferable to spine BMD for predicting overall risk of fracture as the femoral neck is less affected by osteoarthritis which can spuriously increase spine BMD measurements (Garg and Kharb, 2013). FRAX also takes into account nationality of the participant by obtaining the relevant information using databases from different countries to estimate the fracture risk associated with a BMD reading. Unfortunately, there is very little epidemiological information about fracture risk in the Indian subcontinent (Dhanwal et al.,
2011) and this is reflected in the fact that India, Pakistan and Bangladesh were initially not included in FRAX, although they have since been added.

Osteoporosis is a disease associated with increased age. With ageing the balance between bone resorption and formation tends to be tipped in favour of resorption, so reducing the overall bone mass and density (Walsh 2015). The main explanation for this increased resorption of bone in women, is the loss of oestrogen after the menopause, which is followed by an increase in bone turnover and accelerated bone loss (Han et al., 1997). Eventually, age related bone loss can result in osteoporosis, termed primary osteoporosis (Orimo et al., 1998). Osteoporosis associated with an underlying disease or certain medications is termed secondary osteoporosis (Orimo et al., 1998).

Osteoporosis is often referred to as the “silent disease” because its presence is not clinically manifested until a fracture occurs. In the case of vertebral fractures, the fractures themselves are not always diagnosed (Gehlbach, Fournier and Bigelow, 2002; Delmas et al., 2005).

SAs are often reported to have low BMD and osteoporosis but as SAs are also at higher risk of another skeletal disorder, osteomalacia (Finch et al., 1992), low BMD readings may indicate osteomalacia rather than osteoporosis. This is discussed later.

2.4 Brief overview of the skeletal system:

2.4.1 Description of the skeleton and its functions

The adult human skeleton occupies about 9% of the body by volume and at least 17% by weight. It provides a framework, firstly to support the body and secondly as levers against which muscles can act to move the body and its parts. Bones, being hard and strong, also serve as protection for the softer, more vulnerable organs. The human skeleton is testimony to evolutionary engineering, being strong enough to give support to the body and protect the internal organs whilst being light enough to allow movement. It carries out these functions efficiently due to its unique properties of being stronger, lighter and more flexible than cast iron (Buckwalter et al., 1995).

In addition to these essential functions the skeleton provides a reservoir for minerals e.g. calcium and phosphate, allowing them to be taken up from, or released into, the blood.
stream in their ionic form in response to the body’s requirements. The typical human body contains 1-2 kg of calcium, 99% of which is in the skeleton. The bone marrow, a spongy substance found in bone cavities, is the location of blood cell formation and a reservoir for fat. More recently it has been shown that bone cells also have important roles in metabolic regulation (Karsenty and Ferron, 2012).

2.4.2 Classification of bones and types of bone structure

The human skeleton comprises 206 bones making up the axial skeleton (skull, vertebral column and rib cage) and appendicular skeleton (upper and lower limbs plus their girdles). Generally, bones are classified by their shape as long, short, flat or irregular.

There are two types of mature bone structure, cortical and trabecular. Cortical bone, also termed compact bone, is dense and strong with cylindrical subunits, called osteons or Haversian systems (Borer, 2005). Cortical bone comprises about 80% of the total skeleton in weight and makes up the outer layer of all bones and the shafts of long bones (Borer, 2005). The high density of cortical bone makes it well suited to the supportive, protective and mechanical functions of the skeleton. Cortical bone has two types of surfaces: the inner surface that faces the bone marrow is the endosteum (often called the endosteal envelope) and the other surface, on the outer side, facing the soft tissue of the body is the periosteum (the periosteal envelope) (Borer, 2005).

Trabecular, also called spongy or cancellous, bone is lighter and more porous than cortical bone. The subunits are trabeculae which are rod shaped and form a three dimensional network of cross bridges filled with marrow, giving it a honeycombed or spongy appearance (Borer, 2005). The structure of trabecular bone makes it better suited for shock absorption: it can deform to a greater degree without cracking than cortical bone and thus can absorb energy more efficiently (Seeman, 2008). Osteoporosis is generally the result of thinning of the cortex, and thinning or loss of trabeculae (Seeman, 2002).

The ratio of trabecular bone to cortical bone by mass varies depending on skeletal site. Bones which are more exposed to shock, such as the lumbar spine, are more than 66% trabecular bone whereas bones such as the femur, which provide mechanical support, have less trabecular bone and more cortical bone (Riggs et al., 1982). The ratio of trabecular bone to cortical bone can vary within the same bone e.g. radius (Figure 2.3).
2.4.3 Architecture of long bones

Long bones generally comprise a shaft (diaphysis) and two ends (epiphyses). The diaphysis is primarily composed of cortical bone encircling trabecular bone in the centre whilst the epiphyses consist mainly of trabecular bone covered by a relatively thin shell of cortical bone. Figure 2.4 shows the femur, a typical long bone, and the relative locations of the epiphysis, metaphysis and diaphysis. The epiphyseal line was originally the growth plate when the bone was growing in length.
**2.4.4 Bone tissue and bone cells**

Bone consists of an unmineralised, organic component, termed osteoid, an inorganic component and water, which, respectively make up approximately 20%, 65% and 10% of the bone by wet weight (Buckwalter et al., 1995). The majority of the organic component is type I collagen and the inorganic component is mineral, mainly crystalline apatite composed of calcium and phosphate (Buckwalter et al., 1995).

There are three main types of bone cells in the adult mammalian skeleton. The most numerous are osteocytes (90-95% of all bone cells) then osteoblasts and osteoclasts, which
make up 4-6% and 1-2% of all bone cells respectively (Bonewald, 2009). These three cell types act together to maintain bone homeostasis and play an important role in bone modelling and remodelling.

2.4.5 Bone growth (modelling and remodelling)

An important feature of bone is that it is constantly being broken down and regenerated (Clarke, 2008). This allows it to grow longitudinally and radially throughout childhood and adolescence, a process termed modelling. Longitudinal growth occurs by interstitial growth and is characterised by the formation of new bone at the growth plates in the epiphyseal and metaphyseal areas of long bones. Cartilage has the advantageous property of being hard when squeezed rapidly but soft when deformed slowly which allows it to be strong enough to withstand stress when required e.g. high impact exercise, but soft enough to allow the chondrocytes to secrete new extracellular matrix when no stress is applied (Rauch, 2005). Longitudinal growth of bone only occurs up until early adulthood whereas radial growth of bone can take place throughout life.

Radial growth, also termed subperiosteal appositional growth, occurs by the increase of periosteal and endocortical diameters (Kaptoge et al., 2003).

Bone remodelling is a different process in which the osteoblasts and osteoclasts act in concert to change the bone in response to certain physiologic influences or mechanical forces (Martin and Seeman, 2008). If remodelling involves a specific site it is termed “targeted remodelling” e.g. to repair damaged bone (Goldring, 2015). “Non-targeted remodelling” is not site specific e.g. bone breakdown or build-up to maintain mineral homeostasis. Non-targeted remodelling is regulated by hormones like parathyroid hormone, thyroxine, growth hormone and oestrogen as well as antiresorptive drugs like bisphosphonates (Eriksen, 2010). This explains why these hormones are important when considering bone status and osteoporosis.

A major driver for bone adaptation is a theoretical construct known as Frost’s mechanostat model which proposes that bone tissue, via osteocytes, constantly monitors the deformations (strains) caused by forces applied to the bone e.g. tensile force from muscles, change of bone length during growth and weight loading (Frost, 1996, 2003). The degree of deformation is compared to a pre-set target level called ‘set-point’ and if there is a deviation
from set-point then osteocytes signal to effector cells, which alter bone strength by changing bone architecture and mass through bone formation and resorption (Frost, 2003). The mechanostat is an adaptive mechanism that optimizes bone mass and architecture, based on the usual mechanical strain to which it is exposed, and is the mechanism whereby physical activity has its impact on BMD as discussed later.

2.4.6 Bone strength

A simplistic view of bone is that the stronger the bone, the less likely it is to break. However, bones break for a variety of reasons e.g. they are too flexible, too weak or too brittle (Currey, 2001) and a characteristic that might be considered beneficial in one situation may be detrimental in another (Bouxsein, 2003). For example, increased mineralisation improves stiffness but decreases toughness (Davison et al., 2006) whereas poorly mineralised bone has a lower density, but more elasticity (Lang, 1970). This is why osteoporotic bone and osteomalacic bone, even if they have the same BMD, have different properties, a relevant issue when considering bone status and fracture risk (discussed later).

2.4.7 Evolution of the human skeleton

An important feature of human bone evolution is that recent modern humans (Holocene Homo sapiens) are reported to have a relatively gracile postcranial skeleton (Ruff et al., 1993; Nowlan, Jepsen and Morgan, 2011) and lower trabecular BMD (Chirchir et al., 2015) compared to earlier hominins. A gracile long bone is often defined as relatively long and slender compared to a robust (short and thick) long bone.

Assessment of long bone robusticity was initially carried out on specimens of long bone by comparing cross sectional dimensions of the long bone diaphyses (using linear measures of diameter or circumference) to the bone length (Trinkaus and Ruff, 2012). Further information comes from cross-sectional geometry of the long bone which gives a measure of the distribution of cortical bone as well as the cross-sectional diaphyseal shape (Trinkaus and Ruff, 2012). Less research has been carried out on trabecular BMD due to technical challenges, one being the need for high-resolution computer tomography (Chirchir et al., 2015).
Long lower limbs with large joint surfaces are found in humans, as opposed to shorter, lower limbs and smaller joint surfaces in apes (Jungers, 1988). The larger joint surfaces would be expected to lead to lower bone volume, due to the larger joint surfaces distribution of loads across a greater area (Ryan, 2015). The difference in bone morphology between modern humans and apes has led researchers to speculate that long limbs and large joint surfaces have evolved as a consequence of habitual bipedalism and larger body size, characteristic of the modern human body plan (Jungers, 1988). An alternate explanation for longer lower limbs and larger joint surfaces in humans, compared to earlier hominins, is the change in lifestyle, from early hunter-gatherers to a more sedentary existence because of technological and cultural innovations, leading to less physical activity and hence less loading on the bones (Ruff et al., 1993; Holt, 2003).

Chirchir et al. (2015) assessed trabecular bone fraction (TBF) i.e. bone volume relative to total volume, in the epiphyses of upper and lower limbs of humans, chimpanzees and early hominins. They reported that the TBF in modern humans (Holocene period) was lower than that of chimpanzees and early hominins, with the TBF of chimpanzees being similar to that of some of the early hominins (Chirchir et al., 2015). These findings confirmed their hypothesis that the decrease in trabecular density occurred relatively recently, as lifestyle became more sedentary. The fact that early modern humans (Pleistocene period) had a similar body plan to recent modern humans, but higher TBF than recent modern humans, suggested that the change to more gracile bones was not an adaptation to body plan (Chirchir et al., 2015). Further work on five Holocene population samples that had subsistence strategies, ranging from foraging through horticultural to industrial, confirmed that a decrease in activity levels as a result of agriculture and industrialization was associated with lower TBF (Chirchir et al., 2017). The lifestyle changes of food production and increased sedentism in the Holocene period would have changed the biocultural environment in a number of ways that could have changed bone morphology. The lack of physical activity is thought the most significant factor, but altered nutrition or disease prevalence may also have played a part.

Physical activity is not always associated with increased bone status in forager-horticultural populations. A recent study involving a contemporary pre-industrial population, the Bolivian Tsimane forager-horticulturalists, found reduced bone status, as measured by
calcaneal QUS, compared to more sedentary American matched controls (Stieglitz, Beheim, et al., 2015a). The authors point out that the different technique i.e. *in vivo* calcaneal QUS, may account for the different conclusions regarding physical activity and bone status (Stieglitz, Beheim, et al., 2015b). Furthermore, Tsimane are likely to have different environments e.g. diet, disease exposure, to ancestral human populations. A later study linked a high pathogen burden and greater immune activation to this reduced bone status in Tsimane (Stieglitz et al., 2016). The authors conclude that contemporary pre-industrial populations are exposed to factors detrimental to bone status such as poor nutrition, high pathogen burden, and high fertility with long lactation duration and short birth spacing, which may counteract the benefits of high physical activity on bone (Stieglitz, Madimenos, et al., 2015; Stieglitz et al., 2016).

Recent research suggests that lifestyle continues to impact on bone status with the increase in sedentism and reduction in daily physical activity in current populations, especially in higher income countries is resulting in a more gracile skeleton (Scheffler and Hermanussen, 2014). This is discussed more fully in connection with physical activity in section 2.7.7.

### 2.5 UK Bangladeshi Community and Migration Theory

#### 2.5.1 UK Bangladeshi Community

As mentioned in the Introduction, a substantial proportion (14%) of the current UK populace comprises ethnic minority groups (ONS, 2011) and this proportion is expected to rise over the next few decades (Coleman, 2010; Lievesley, 2010). The Bangladeshi community is one of the fastest growing ethnic groups within the UK. The most recent census, 2011, recorded 447,201 Bangladeshis (0.8% of the total population) resident in England and Wales, a rise of 50% from the previous census in 2001 (ONS, 2012). This increase was a result of both fertility and migration (Coleman, 2010; Coleman and Dubuc, 2010; Robards and Berrington, 2016).

This rapid increase in numbers has implications for future costs to the NHS, especially as ethnic minorities tend to suffer poorer health than the indigenous population, with especially higher risks for coronary heart disease (CHD), hypertension and diabetes (Nazroo, 1998; Kuppuswamy and Gupta, 2005; Whincup et al., 2010; Nazroo et al., 2009).
Explanations for these ethnic inequalities include genetic (Carulli et al., 2005), influences of early life environment (Huxley, Shiell and Law, 2000; Newsome et al., 2003; Barker, 2007), cultural factors (Chaturvedi, 2003; Zilanawala et al., 2014), socio-economic vulnerability (Gordon and Foundation, 2000; Sabates, Dex and Studies, 2012; Zilanawala et al., 2014) and racial discrimination (Karlsen and Nazroo, 2002).

The Bangladeshi community is particularly susceptible to self-reported and measured poor health status (Bhopal et al., 1999; Kuppuswamy and Gupta, 2005). Poor health status is indicated by higher rates of centralised obesity and chronic diseases such as type 2 diabetes, metabolic syndrome and CHD (Nazroo, 1998; Kuppuswamy and Gupta, 2005; Nazroo et al., 2009; Whincup et al., 2010; Gujral et al., 2013). The Bangladeshi community is also reported to be one of the most deprived populations in the UK, with high rates of unemployment, social deprivation, poverty (Gordon and Foundation, 2000; Sabates, Dex and Studies, 2012) and low rates of education (Alexander, Firoz and Rashid, 2005), particularly within those who migrated as adults (Brice, 2008).

If the poor health of ethnic minority groups leads to an earlier manifestation of diseases associated with ageing and/or a higher prevalence of these same diseases, then the impact and cost of ill health in ethnic minority communities becomes increasingly relevant as numbers increase.

### 2.5.2 UK Bangladeshi women and bone health

Factors influencing bone health are discussed in more detail in section 2.7 but a summary of environmental factors in relation to UK BD women is presented here to explain why UK BD women may be more at risk for poor bone status than the general UK population.

Important modifiable contributors to bone health are physical activity and nutrition, especially in the years of bone growth and development. Physical activity in the UK SA communities, including Bangladeshis, is very low. A systematic review of 12 studies reported that in all studies there was a lower rate of physical activity in SA people and, according to the Health Survey for England (HSE) 1999-2001, only 13% of UK BD women aged 16-34 met the recommended level of physical activity, compared to 25% of the IB women (Fischbacher, Hunt and Alexander, 2004). The HSE 2004 reports that UK BD women had the lowest self-reported levels of physical activity of all ethnic minority groups.
The MINA project concluded that the main barriers to physical activity for BD women resident in Cardiff, were a lack of understanding of the benefits of exercise and lack of knowledge about recommended levels of physical activity (Babakus and Thompson, 2012). Other barriers include lack of time, family responsibility, lack of facilities and cost (Health Education Authority, 2000). Cultural factors included dislike of mixed sex setting, dislike of seeing others’ bodies, lack of confidence and language difficulties (Health Education Authority, 2000). A systematic review of barriers to exercise for SA type-2 diabetics revealed that these were the lack of gender specific exercise facilities and concern that exercise might cause injury or worsen health (Sohal et al., 2015).

The MINA project also found that UK BD women were less active than BD women living in Sylhet, Bangladesh. Sedentees performed more physical activities such as walking outdoors, carrying bundles, climbing stairs and doing housework, and those of lower socioeconomic status (SES) tended fields and livestock (Bogin et al., 2014).

Regarding nutrition, most Bangladeshi migrants from Sylhet come from families who had access to good nutrition (Gardner, 1995), and it is reported that in London they tend to have a similar diet (Núñez-de La Mora et al., 2008). However, the UK BD women in Cardiff, Wales involved in the MINA project, had a high frequent consumption of energy-dense foods (Thompson et al., 2014).

The traditional diet of SAs is generally high in fibre and moderate fat, consisting of curries and cereals (chapatti, roti, paratha and/or rice) with fruit and vegetables (Wyke and Landman, 1997). In the late 1990s, the older generation of SAs were still following this diet but the younger generation were moving towards what SAs called “English” foods, such as chips, pizza, burgers (Wyke and Landman, 1997). It seems that the dietary habits of UK SAs are changing to a less healthy diet, higher in sugar and fat, which has been linked with their higher risk of obesity and diabetes type 2 (Bhopal et al., 1999; Khokhar et al., 2009; Choudhury, Furbish and Chowdhury, 2016). A study focused on UK Bangladeshi adolescents (11-14 years) in East London reported a high intake of fat, salt and carbohydrates due to being exposed to available and affordable energy rich food, plus living in an economically deprived area (Lofink, 2012; Choudhury, Furbish and Chowdhury, 2016).
Vitamin D and calcium are the most important nutrients for good bone health (see section 2.7.4) but UK SAs are widely reported as being particularly prone to low levels of vitamin D (Roy et al., 2007; Brooke-Wavell et al., 2008; Lowe et al., 2010; MacDonald et al., 2011; Darling et al., 2013). Low vitamin D status (25(OH)D < 15 ng/ml) in pre-menopausal UK Indian women was linked to lower BMD in the distal radius and hip (total and femur neck) compared to IB counterparts (Roy et al. 2007). Linked to low vitamin D levels in SAs is the problem of hyperparathyroidism (Serhan and Holland, 2002; Fraser, 2009). Vitamin D insufficiency and/or hyperparathyroidism is a condition more common in UK SA post-menopausal women than IB post-menopausal women (Roy et al., 2007; Lowe et al., 2010). UK SAs with low vitamin D levels and hyperparathyroidism were found to have lower BMD at the radius and hip compared to a similar group of UK SAs who had normal vitamin D and parathyroid hormone levels (Serhan and Holland, 2002). Another study found low vitamin D levels to be associated with lower BMD at the calcaneous (Brooke-Wavell et al., 2008). Hyperparathyroidism is linked to low mineralisation of the bone and lower BMD (Roy et al., 2007) so consequently, SA people are susceptible to osteomalacia i.e. low mineralisation of the bone (Finch et al., 1992). Hyperparathyroidism is also associated with lower BUA, but not SOS, at the calcaneous (Ingle, Thomas and Eastell, 2002). This may be because poorly mineralised bone has a lower density, but more elasticity, one of the properties reportedly measured by SOS (Lang, 1970). Vitamin D deficiency (Holick, 2007), hyperparathyroidism (Fraser, 2009) and inadequate dietary calcium intake are risk factors for low bone mass and osteoporotic fractures, so may explain lower BMD in SAs (but not their lower fracture rate). As sunshine is an important requirement for manufacture of vitamin D, the fact that lifestyle of UK SA women results in less exposure to sunlight (Kift et al., 2013) suggests UK BD women may have less exposure to sunlight, contributing to lower vitamin D levels, than IB women.

However, lower serum concentrations of 25(OH)D and higher serum levels of parathyroid hormone in UK SAs are not always associated with significantly reduced bone quality. One study comparing UK SA post-menopausal women and IB counterparts, found lower serum 25(OH)D levels and higher levels of parathyroid hormone in SA women, but this was not linked with lower bone quality at the calcaneous as measured by ultrasound, nor higher markers of bone resorption (Lowe et al., 2010). It was also reported that Pakistani women
resident in Norway, despite having lower vitamin D status, did not have lower BMD at the lumbar spine or femoral neck compared to indigenous Norwegian women (Falch and Steihaug, 2000). The explanation for these conflicting findings is the possibility that Asian women need lower levels of vitamin D than European women for bone health (Cauley et al., 2011) and this is discussed further in section 2.7.4.

Iodine is another essential requirement for good bone health as it is necessary for thyroid functioning (see section 2.7.5). Iodine deficiency has been a problem in Bangladesh (Yusuf et al., 1996) but this has been largely rectified due to the introduction of iodized salt in 1994 (Yusuf et al., 2008). Therefore, UK BD women born in Bangladesh before or soon after that year, would have been affected by this iodine deficiency at birth and/or during growth and development. There are still reports of some iodine deficiency in Bangladesh (Ara et al., 2010) and the UK is also not exempt from this problem according to some publications (Vanderpump et al., 2011).

The MINA project found that in UK BD women, the combination of lack of physical activity and a high energy diet was associated with overweight and obesity (Babakus and Thompson, 2012). SA immigrants have been reported to have small-for-gestational age babies and catch up growth (rapid gain of weight in infancy), which is linked to obesity throughout life (Fall, 2004). In addition to being at higher risk of overweight and obesity, SAs are more at risk of central obesity than the IB population (Bhopal, 1999). Visceral fat has deleterious effects on bone status (section 2.7.3) so increased visceral fat is another risk factor for bone health in the BD community. SAs are disposed to higher levels of visceral fat than Europeans (Raji, 2001), and a recent study concluded that greater central adiposity in Asian women is already present in adolescence (Morimoto et al., 2012) which suggests Asian women may be more at risk of poor bone status. Increased visceral fat is also linked to diabetes, a prevalent condition in SAs according to the HSE 2004 (Sproston, Mindell and Free, 2004). Diabetic patients also have a higher prevalence of thyroid disorders than the normal population (Wu, 2000), which in turn will affect bone health. The natural hormone, thyroxine, is involved in the control of bone remodelling so hypothyroidism and hyperthyroidism and/or associated medication have an effect on BMD, although the consequences are not consistent (Zaidi et al., 2009; Gogakos, Bassett and Williams, 2010).
Another feature of the BD community relates to reproductive variables: BD women (in Bangladesh and UK) have higher parity, shorter inter-birth intervals and an earlier age at first birth (Bogin et al., 2014). Life history theory predicts that bone, as a mineral source for both the mother and the foetus, will reflect the trade-off between reproduction and the mother’s somatic needs. Therefore, the prediction is that high parity, short inter-birth intervals, earlier age at first birth and long periods of lactation will reduce BMD in BD women. Contemporary pre-industrial populations are more akin to Bangladeshis than populations of higher income countries, the latter having lower parity, longer inter-birth intervals and older age at first birth. The few studies on contemporary pre-industrial populations do suggest that high parity, short inter-birth intervals, earlier age at first birth and long periods of lactation are associated with poorer bone status (Madimenos et al., 2012; Stieglitz et al., 2015).

Age at menarche is an important event in a woman’s life course. UK BD women who were born in the UK or migrated as children are reported to have an earlier menarche than BD sedentees or UK BD women who came to the UK as adults (Núñez-de La Mora et al., 2008). However, it is unclear how this might affect bone status, as the evidence on the association of age at menarche with bone status is equivocal (section 2.7.6).

Age at menopause is another significant factor in a woman’s life and is linked to declining BMD. As UK BD women are reported to have an earlier age of menopause (Murphy et al., 2013) this might put them at higher risk of poor bone status (section 2.7.6).

The final variable related to reproduction concerns hormonal contraception, which could affect bone health, although in what direction and to what extent is equivocal (section 2.7.6). However, it is likely that few UK BD women use hormonal contraception. It has been reported that in the UK, sexually active married Pakistani and Indian women, compared to other ethnic groups and IB women, have the lowest use of oral contraceptives (Saxena, Oakeshott and Hilton, 2002), especially in the cases of women who had migrated from their home country. Cultural barriers to using contraception included religion: Muslim women, e.g. Bangladeshis tended to describe their religion as discouraging or prohibiting contraceptive use (Hennink, Diamond and Cooper, 1999).
oral contraception on bone status give conflicting results and this is discussed further in section 2.7.6.

Another potential influence on bone status in BD women is socioeconomic status (SES). It has been mentioned above that the BD community suffer from deprivation and this might be expected to be linked with poorer bone status. However, the studies on effect of SES on bone mass and bone fracture are equivocal (section 2.7.9) and no studies exist comparing effects of different SES status within UK SA communities. Therefore it is sometimes difficult to distinguish between biocultural and SES influences on bone status.

There are many factors influencing bone status and they are described in more general detail in section 2.7. The current section has described some environmental factors which may contribute to low BMD in UK BD women compared to IB women, namely less physical activity and exposure to sunlight along with higher reproductive demands. However, this needs to be balanced with the benefits of migrating to a higher income country as described in the Introduction. The overall effect of migration to the UK on the current and future bone status of UK BD women is not known.

2.5.3 Migration Theory and DOHaD

As mentioned in the Introduction, the premise behind my study, based on Migration theory, is that over the next few generations, BD women will become more similar to IB women in terms of height and bone measurements. DOHaD theory is important in terms of explaining how the birthplace of BD women might affect their bone status. The DOHaD theory is based on increasing evidence that early life influences, especially within the womb, have a profound influence on health and disease in later adulthood. It is sometimes termed the “Barker hypothesis” after David Barker’s work in the 1980s which established a link between low birth weight and adult heart disease (Barker et al., 1989; Barker, 2007). DOHaD theory is particularly relevant in Migration theory because migrants born in the UK, in contrast to being born in Bangladesh, experience a totally new environment pre- and post-natally.

Examples of how a radically different environment whilst an individual is in utero can affect later outcome, are provided by retrospective analyses on records from the Dutch famine, a five-month period of extreme food shortage in 1944-1945 during the Second World War. It was found that women, whose mothers were nutritionally deprived during the second or
third trimester, were of low birth weight and went on to have children of their own who were low birth weight (Lumey, 1992). Furthermore, adult offspring of nutritionally deprived women were found to be at higher risk of certain diseases such as coronary heart disease, obstructive airways disease and diabetes compared with adults born before or after the famine period (Painter, Roseboom and Bleker, 2005). The time point in the pregnancy when the mothers became nutritionally deprived due to the famine was related to the type of pathology their offspring were most likely to endure in later life. Heart disease was associated with deprivation in early pregnancy, obstructive airways disease with deprivation in mid pregnancy and decreased glucose tolerance with deprivation in late pregnancy (Painter, Roseboom and Bleker, 2005). Low birth weight has also been linked to other pathologies such as diabetes (Newsome et al., 2003) and hypertension (Huxley, Shiell and Law, 2000). More recently, osteoporosis has been added to the list of diseases which are modifiable by early life influences (Cooper et al., 2006).

The observation that the relationship between birth size and later disease risk is continuous through the range of birth sizes suggests that the explanation is not simply an abnormal pregnancy causing both small birth size and pathology later in life (Gluckman and Hanson, 2005). It seems that it is not birth size per se that increases the risk of disease later in life, but rather birth size is a “marker” for the uterine environment with a low weight at birth reflecting an adverse uterine environment (Gluckman and Hanson, 2005). A feasible explanation for the DOHaD hypothesis is “programming” defined as “the process whereby a stimulus or insult during a sensitive or critical period has irreversible long-term effects on development” (de Boo and Harding, 2006). The critical period differs between organs depending on the stage of pregnancy when they are being developed.

There are many pathways through which the environment exerts its influence on the various organs of the foetus as it develops within the womb. Gene expression, cell numbers, balance of cell types, tissue sensitivity to hormones are all susceptible to intrauterine conditions. Epigenetics is increasingly seen as the means by which environmental factors such as the nutritional state of the mother affect foetal development.

Epidemiological studies have linked low weight at birth and during infancy with fracture risk later in life. For example, in the Hertfordshire Cohort study, poor growth in the womb and
first year of life was linked with lower bone mineral content and poorer bone geometry (Javaid et al., 2006; Oliver et al., 2007). Other studies indicate that a mother’s lifestyle e.g. nutrition, smoking, alcohol consumption and caffeine intake, during pregnancy influences bone size at birth (Cooper et al., 2006).

However, it needs to be noted that lower-than-average birth weight of UK SA groups does not seem to change over generations (Harding, Rosato and Cruickshank, 2004), despite an increase in height in UK SAs over generations. This lack of increase in birth weight in UK SA groups is not consistent with DOHaD theory which would predict an increase in birth weight as well as height in subsequent generations of UK SAs. This might indicate the increase in height in UK SA groups is not necessarily linked with reduced risk of disease in later life, in view of the lack of change in lower-than-average birth weight of UK SA groups.

A closely allied theory to DOHaD theory is weathering theory which invokes the same mechanism i.e. epigenetic modifications, to explain how prolonged psychosocial and physical challenges throughout life increase the risk of disease and chronic conditions in later life (Geronimus, 1992) and accelerate ageing (Geronimus et al., 2010). Again, the host country would be expected to have different psychosocial and physical challenges to those of the country of origin.

2.5.4 Migration and bone studies

There has been very little research focussed on how migration affects bone health of SA migrants in Europe, apart from some interest in how Asians fare in the Scandinavian countries. It has been reported that fracture risk is slightly less for first generation Asian immigrants (men and women) than for native Norwegians. However, this is inconclusive, due to the small number of Asians sampled, plus the fact that the native population has a very high fracture incidence, generally considered to be a consequence of low BMD (Lofthus et al., 2008) and/or greater height (Duarte Sosa et al., 2015). The low BMD in Scandinavians is linked to lower levels of vitamin D at these more northern latitudes (Johnell et al., 2007; Macdonald et al., 2008). Another study focussed on SA adolescent girls in the UK and found that body and lumbar spine BMD was higher in higher income SA and indigenous British girls, compared to lower income girls in India (Khadilkar et al., 2010).
Other publications about the effects of migration on bone health in Asians relate to migration of Chinese and Japanese to the US and Europe (Table 2.1). Although SA groups are reported to be more similar, genetically speaking, to European populations than to East Asians (Reich et al., 2009), most Asian groups are similar in terms of small skeletal size, low BMD and low fracture risk compared to Europeans.

Various methods are employed to investigate the consequences of migration:

A. The effect of birthplace of an immigrant population on bone health (denoted methodology A in Table 2.1). This has become especially relevant in the light of recent theories that place more emphasis on early life influences

B. The bone health of the immigrant population compared to counterparts still living in the native country (denoted methodology B in Table 2.1).

C. The effect of length of time in the country since migration on bone status (methodology C in Table 2.1).

The few studies where the immigrant participants had been born in their country of origin (method A) showed mixed results. Lauderdale (2003) measured BMD in the calcaneous of Chinese immigrants aged 50+ and reported that US Chinese women born in China had lower calcaneous BMD than the reference values for Americans of European origin and US born Asian-American women, whereas this difference was not observed in men until they were aged 70 years or more. Ishii (2012) studied hip BMD and composite strength indices of US-resident pre- and post- menopausal Chinese and Japanese women. There were no differences in hip BMD between the foreign-born Japanese/Chinese living in the US and the resident population (Japanese/Chinese born in the US) (Ishii et al., 2012). Regarding composite strength indices there was no difference in the Chinese samples but US-born Japanese women had poorer composite strength indices than those born in Japan (Ishii et al., 2012).

Studies comparing immigrants in their native countries with those in their new countries (method B) also gave mixed results. For example, Ross et al. (1995) showed that fracture risk was better for the spine, but not the hip, for Japanese who had emigrated to the US compared to Japanese still resident in Japan. Babar et al. (2006) reported BMD values of immigrant Chinese Americans did not differ from previously published BMD values of Chinese women in China and Hong Kong.
Studies looking at the association of time since immigration with bone parameters (method C in table 2.4) in Chinese migrants indicated that the longer the time in the new country (Europe or US) the better for bone health (Wang et al., 1996; Babbar et al., 2006).

The results described above did not always stem from the main objective of the study, but were often just one of a number of outcomes. Therefore comparisons may have been made between samples which did not comprise exactly the same ethnic group (Lauderdale et al., 2003; Khadilkar et al., 2010). Sometimes comparisons were made with previous published studies, again giving rise to disparate samples. Sometimes different types of DXA machines were used within a study so lessening the validity of the comparisons. Other studies that consider bone health in immigrant populations often use the blanket term “Asians” without specifying individual countries.

To summarise, the limited research concerns the migration of Chinese and Japanese to the US with generally no difference or improvements in BMD observed after migration. Although there are a few studies comparing SA migrants with the indigenous population of the host country (section 2.6.3), there are none to my knowledge that attempt to address how migration will affect migrants’ bone health in the future.
Table 2.1 Articles studying effects of migration on bone health (poorer, no different or better in new country) in females

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Ethnic group and age</th>
<th>Resident Country</th>
<th>Bone site</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Lauderdale et al., 2003)(^A)</td>
<td>Chinese, age 50+</td>
<td>US</td>
<td>Calcaneal</td>
<td>Chinese born had lower BMD than indigenous women and US-born Asian women. Adjustment</td>
</tr>
<tr>
<td>(S. Ishii et al., 2012)(^A)</td>
<td>Japanese, pre- and peri-menopausal</td>
<td>US</td>
<td>Hip</td>
<td>No difference in BMD, poorer measures on composite strength indices</td>
</tr>
<tr>
<td>(S. Ishii et al., 2012)(^A)</td>
<td>Chinese, pre- and peri-menopausal</td>
<td>US</td>
<td>Hip</td>
<td>No difference in BMD, no difference in composite strength indices</td>
</tr>
<tr>
<td>(Ross et al., 1995)(^B)</td>
<td>Japanese, age 50+</td>
<td>Hawaii, US</td>
<td>Hip</td>
<td>No difference in fracture risk</td>
</tr>
<tr>
<td>(Kin et al., 1993)(^B)</td>
<td>Japanese, all ages</td>
<td>California, US</td>
<td>Spine</td>
<td>Higher BMD in new country</td>
</tr>
<tr>
<td>(Ross et al., 1995)(^B)</td>
<td>Japanese, age 50+</td>
<td>Hawaii, US</td>
<td>Spine</td>
<td>Higher BMD and lower fracture risk in new country</td>
</tr>
<tr>
<td>(Huang et al., 1996)(^B)</td>
<td>Japanese, age 50+</td>
<td>Hawaii, US</td>
<td>Spine</td>
<td>Higher BMD and lower fracture risk in new country</td>
</tr>
<tr>
<td>(Babbar et al., 2006)(^B)</td>
<td>Chinese, post-menopausal</td>
<td>US</td>
<td>Spine &amp; Hip</td>
<td>No difference in BMD</td>
</tr>
<tr>
<td>(Wang et al., 1996)(^C)</td>
<td>S. Chinese, pre-menopausal</td>
<td>Denmark</td>
<td>Body, Trunk, Leg</td>
<td>Better BMD associated with longer time after immigration to Denmark</td>
</tr>
<tr>
<td>(Babbar et al., 2006)(^C)</td>
<td>Chinese, post-menopausal</td>
<td>US</td>
<td>Spine &amp; Hip</td>
<td>Better BMD associated with longer time in US But sample groups came from different parts of China</td>
</tr>
</tbody>
</table>

\(^A\) methodology A = comparison between birthplace (both samples living in immigrant country, comparison made first and second generation immigrants)

\(^B\) methodology B = comparison between place of residence (one sample living in native country, other sample in living in immigrant country)

\(^C\) methodology C = comparison between time spent living in immigrant country since migration
2.5.5 History of the UK Bangladeshi Community

Bangladesh, literally “The home of Bengal”, gained its name and independence in 1971 after the Bangladesh Liberation War. It forms the Bengal delta region in the Indian subcontinent (Figure 2.5). With over 150 million inhabitants, Bangladesh is the eighth most populous country of the world as well as being one of the most densely populated (Lewis, 2012).

Before independence, the area now called Bangladesh was a predominantly Muslim part of India known as East Bengal, in contrast to West Bengal which was mainly Hindu. In 1947 India gained independence after over 150 years of British rule, with East Bengal becoming a province of Pakistan and West Bengal becoming a province of India. West Pakistan, separated from East Pakistan by hundreds of miles of Indian territory, was politically and economically dominant over East Pakistan. This fact, plus the differences in religion and language, led to popular agitation and civil disobedience within East Pakistan and military retaliation from West Pakistan, culminating in the Bangladeshi Liberation War and the creation of a new country, Bangladesh. The new state endured poverty, famine, political turmoil and military coups until the restoration of democracy in 1991 (Lewis, 2012). Although Bangladesh has progressed in terms of human and social development since independence (Asadullah, Savoia and Mahmud, 2014) it still faces many challenges including political instability, poverty and vulnerability to climate change (Chowdhury et al., 2013).

The tradition of the Indian peasants leaving to work on foreign ships grew with increasing requirements of the various colonial powers in India in the 17th and 18th centuries. Up to 1947 Asian seamen, called lascars, would work on British ships, especially those connected with the East India Company and this continued after the demise of the company. Indian seamen also fought for Britain during the Second World War. The first migrants to Britain would jump ship at UK ports e.g. London, Cardiff, Liverpool and set up small migrant communities which acted as a nucleus of support for later migrants (Alexander, Firoz and Rashid, 2010).

In the 1950’s and 1960’s Bangladeshi men came to Britain seeking to escape the civil unrest in Bangladesh and looking for employment in the steel and textile mills in industrial cities e.g. London, Birmingham, Oldham, Manchester, Leeds, Bradford. The process of ‘chain migration’ refers to British-based Sylhetis assisting migration from Bangladesh by arranging credit, documents and places to stay (Gardner, 1995). In the 1970s Bangladeshi women
began arriving in large numbers leading to the establishment of a permanent British Bangladeshi community. In the 1970s and 1980s key changes to legislation in Britain made migration more difficult thus encouraging concerned Bangladeshis to make a concerted effort to bring their relatives over to the UK. As the manufacturing industries collapsed many found work in “Indian” restaurants most of which are owned by and employ Bangladeshis.

The UK Bangladeshi community is now a significant section of the UK population and plays a substantial role in UK culture, politics and economics. As the UK Bangladeshi community is
an ethnic minority group suffering poorer health and living conditions than the indigenous population, more research on their health and wellbeing is warranted.

2.5.6 The Bangladeshi community in Loughborough

According to the 2011 census the majority of Bangladeshis in Loughborough resides in East Loughborough, in two clearly defined and small wards, Lemyngton and Hastings, where Bangladeshis account for 13% of the Bangladeshi population in the county of Leicestershire (Jivraj and Finney, 2013). Like most UK BD communities, the majority of Bangladeshis in Loughborough originated in Sylhet. In 1990 a Bangladeshi Social Association (BSA) publication recorded 93% of families as originating from Nabiganj, Habiganj and Maulvi Bazar, all districts in Sylhet (Khan, 1990).

The centres of community and cultural life, where religious and educational activities take place, are the BSA and the mosque. Many of the “Indian” restaurants in Loughborough are owned by and employ Bangladeshis. Driving taxis is another common occupation for BD men in Loughborough.

2.6 Bone Mineral Density and Hip Geometry Parameters

2.6.1 Description of BMD

Bone density is an important property of bone, having a major impact on bone strength (Rice, Cowin and Bowman, 1988; Martin, 1991) and is therefore a crucial measurement in the current study. There are two relevant measures of bone density. One is apparent density, \( \rho_a \), which refers to the total (bulk, tissue, structural) density and so includes both the mineralised component plus the soft, non-mineralised tissue (pores). The term “pores” in the context of bone, relates to cavities in bone which are not mineralised i.e. the soft tissue components of bone. They are considered to be voids because they do not possess strength with respect to non-hydrostatic stresses (Martin, 1991). The other measure of density is real density \( \rho_m \) which is the bone solid matrix or material density i.e. the density of the mineralised component alone. Mineralised bone comprises organic matrix, water and mineral content.

Porosity is a term that distinguishes between the pores and the solid matrix which comprise bone. If a bone sample contained no pores at all, it would have a porosity of 0%. As
porosity increases, the ratio of apparent to real density will decrease. Porosity has a considerable impact on strength, the higher the porosity the weaker the bone. The relationship between strength and porosity generally fits a power law which means that small changes in porosity are associated with large changes in bone strength (Turner, 2002). Cortical bone has 5% - 30% porosity, mostly in the range 5% - 10%, and trabecular bone has 30% - 90% porosity, mostly in the range 75% - 90% (Martin, Burr and Sharkey, 1998).

Some studies refer to bone volume fraction (BVF) which is the ratio of bone material volume to total (tissue) volume (BV/TV). BVF is measured using micro computed tomography which requires skeletal bone in vitro, so it is commonly used in studies which involve skeletons from deceased people e.g. studies that compare recent human bone with that from other hominoids and extinct hominin species.

The two measures of bone density, apparent density and real density, and the definition of porosity have been described above to emphasise the important point that DXA-measured BMD is apparent density, not real density. BMD is not a measure of real bone density or porosity, but a combination of the two parameters. This is important in the context of bone studies on SAs, because SAs, for reasons described later, are reported to be at particular risk of osteomalacia, a metabolic bone disorder characterised by the decreased mineralisation of osteoid (Finch et al., 1992; Gifre et al., 2011; Thacher and Clarke, 2011). A low BMD value from a DXA scan could indicate osteoporosis (adequate bone mineralisation but many pores) or osteomalacia (low bone mineralisation but adequate porosity). This is illustrated in the figure below where two hypothetical bone samples could have the same apparent density and therefore, the same DXA-derived BMD readings, but their real density and porosity (which differs between the two samples) cannot be established.
Figure 2.6 Schematic diagrams of two hypothetical bone samples with the same apparent density (and therefore BMD) but different real density and porosity.

A low BMD reading in a woman of European origin may be due to osteoporosis, whereas a low BMD reading in a SA woman may be due to osteomalacia. Poorly mineralised bone in Asians may explain their lower fracture risk, despite their lower BMD, compared to European women. This is because osteomalacia allows the bone to deform more easily due to low stiffness. Also, it is proposed that structural changes in response to loading are overestimated by the mechanostat so causing an increase in cross section of the bone to compensate which improves the bone strength (Rauch, 2006).

The only technology that can measure real density and porosity is quantitative computer tomography (QCT).

The other important issue with bone density as measured by DXA, is that DXA only measures in two dimensions so cannot measure true volumetric density. BMD is more accurately defined as “the integral mass of bone mineral per unit projected area” (Blake and Fogelman, 1997). Therefore, BMD is reported as grams per square centimetre and sometimes termed areal BMD, because it is based on bone area rather than bone volume.
BMD is influenced by bone size as well as bone density (Carter, Bouxsein and Marcus, 1992; Seeman, 2001) and the contribution from bone size and bone density cannot be differentiated e.g. a low BMD reading could be the result of reduced density and/or smaller bone size (Seeman, 1998). This leads to BMD underestimating the apparent mineral density of short people with smaller bones, compared to tall people with larger bones and is a confounding factor when considering ethnic and gender differences in apparent BMD (Seeman, 1998).

However, as mentioned in the Introduction, although BMD is influenced by skeletal size this is of no relevance from a clinical perspective, which is concerned only with fracture risk. BMD, which is influenced by bone density and bone size, is of practical use in predicting fracture risk, because bigger bones are generally stronger. Studies suggest that BMD and true volumetric density are equally efficient as predictors of fracture risk (Cummings, 1994a; Tabensky et al., 1996). Therefore, the BMD value as measured by DXA is reported, without attempting to adjust for skeletal size. It should also be noted that the exact contribution of skeletal size to BMD is not known because the exact volumetric dimension of a bone cannot be measured by DXA. Indicators of skeletal size, such as height or weight, are only approximate markers for skeletal size. Furthermore, weight can also influence BMD through other mechanisms e.g. weight is linked to fat mass, which tends to increase BMD because of extra force on the bones and increasing levels of oestrogen. Although there is no requirement to adjust BMD for skeletal size for fracture prediction, it is useful for researchers to understand what influences BMD e.g. bone size and vitamin D (discussed later). Therefore, some researchers attempt to account for bone thickness/skeletal size by calculating a parameter based on BMD and a marker of skeletal size. I have carried out these calculations in my study and they are described in the Methods chapter.

2.6.2 BMD as a predictor of fracture risk

Marshall et al. (1996) reviewed eleven prospective cohort studies of adult women of European origin, published between 1985 and 1994 which recorded baseline BMD at various skeletal sites (distal/proximal radius, hip, lumbar spine, calcaneous) with follow up periods ranging from 1.8 to 24 years. From an overall number of 90000 person years of observation and 2000 fractures the authors concluded that for each standard deviation reduction in BMD at any site the relative risk of fracture was 1.5 (Marshall, Johnell and
Wedel, 1996). The relative risk for fractures at the spine and hip for one standard deviation decrease in BMD at the same site was 2.3 for spine and 2.6 for hip (Marshall, Johnell and Wedel, 1996). These predictive abilities are similar to a one standard deviation increase in blood pressure for stroke and better than a one standard deviation increase in serum cholesterol for cardiovascular disease (Marshall, Johnell and Wedel, 1996). A similar review concluded that BMD of the hip was a strong indicator of future risk of hip fracture, in both men and women, with the relative risk increasing to 2.9 after the age of 65 years for both sexes for each standard deviation decrease in hip BMD (Johnell et al., 2005). Similar studies on the relationship between BMD values and fracture risk in Asian populations have yet to be carried out.

Other researchers highlight the limitations of BMD as a predictor of fracture risk (Nielsen, 2000) partly because there are many additional influences on fracture risk such as muscle strength, balance and bone dimensions (Turner, 1998). Certain clinical factors e.g. age, BMI, smoking and alcohol consumption also predict fracture risk, independently of BMD, (Kanis et al., 2008). BMD, although a predictor of fracture risk, is neither sensitive nor specific enough to warrant wide-spread population screening of postmenopausal women (WHO, 1994). However using BMD in conjunction with other clinical and lifestyle factors produces a better estimation of fracture risk and is the basis of the current computer based algorithm (http://www.shef.ac.uk/FRAX) used in the clinic to estimate a patient’s 10-year fracture probability (Kanis et al., 2009).

2.6.3 Ethnicity, BMD and fracture risk

As mentioned previously there is a paucity of studies on bone status in UK Asian ethnic groups. However, it has been reported that UK SAs have lower BMD than indigenous British, at the three main skeletal sites of interest, i.e. hip and lumbar spine (Hamson et al., 2003) and distal radial diaphysis (Ward et al., 2007), as well as at the calcaneous (Brooke-Wavell et al., 2008). This is consistent with studies on ethnic immigrants to the US which report that US SAs have lower BMD than US residents of European origin (Melamed et al., 2010). US East Asians are also reported to have the lowest BMD compared to US citizens of European and African origin (Marquez et al., 2001; Finkelstein et al., 2002; Barrett-Connor et al., 2005). A study separating US Asians into those originating from China and those originating from South Asia, found the SAs had the lowest BMD (Khandewal, Chandra and Lo, 2012). US
residents of African origin have a higher BMD than people of European and East Asian origin (Siris et al., 2001; Finkelstein et al., 2002; Barrett-Connor et al., 2005; Cauley et al., 2005; Tracy et al., 2006; Travison et al., 2011). Studies of SAs in their home countries show similar results, with Indian men and women resident in India reported to have a high prevalence of osteoporosis (Malhotra and Mithal, 2008; Marwaha et al., 2011). An international study on contraceptive use in pre-menopausal women reported women residing in Asia (Bangladeshi, Chinese and Thailand) as having lower BMD than those living in Africa and Central/South America (Zimbabwe, Mexico and Brazil) (Petitti et al., 2000).

To summarise, Asians have the lowest BMD, followed by people of European origin, and Africans have the highest BMD.

As BMD varies with ethnicity it is perhaps not surprising that fracture risk also varies with ethnicity, although, for reasons as yet unknown, fracture risk in different ethnic groups does not exactly parallel the BMD differences. UK SAs, despite having a lower BMD, have a lower fracture risk than indigenous British. The 2004 HSE reported that elderly SAs resident in the UK had lower age-adjusted fracture rates than indigenous British (Donaldson et al., 2008). This contradicted an earlier study of Asians in Leicestershire which reported that elderly (over 65 years old) Asian men had significantly higher annual incidence of fractures than their indigenous counterparts, although this was not the case for women (Calder et al., 1994). A recent article on epidemiology of fractures in the United Kingdom 1988-2012, used a large sample number from health records from the Clinical Practice Research Datalink (CPRD) (Curtis et al., 2016). This study demonstrated ethnic differences in fracture risk in men and women aged over 50, with lowest rates of fracture found amongst individuals of African origin, intermediate fracture rate in the SA population and highest rates amongst individuals of European origin (Curtis et al., 2016). These relative rates of fracture by ethnic group were consistent across all three main skeletal sites for osteoporotic fracture i.e. spine, femur/hip and radius/ulna (Curtis et al., 2016).

Studies from the US also report similar findings. One such study, on US citizens who originated from three different continents, Europe, Asia and Africa, reported that Europeans have the highest fracture risk, followed by Asians, with Africans having the lowest risk (Lauderdale et al., 1997; Lau et al., 2001; Siris et al., 2001; Barrett-Connor et al.,
Asians in these US studies generally refer to those originating from East Asia i.e. China, Japan etc., as opposed to the Indian subcontinent.

The studies mentioned above indicate that BMD and fracture risk vary between three major ethnic groups, European, Asian and African. Despite BMD measurements being related to fracture risk, average BMD values for these three different ethnic groups do not exactly parallel their fracture risk differences between the ethnic groups. This implies that the relationship of BMD and fracture risk differs, depending on ethnic origin. A recent study set out to determine whether the relationship between BMD and fracture prevalence in men aged 65 years and over, varied according to several US ethnic groups (including those of European, Asian and African origins) (Shin et al., 2014). The conclusion was that, although the age-adjusted prevalence of fracture varied with ethnic group (highest prevalence in those of European origin and lowest in those of Afro-Caribbean and Asian descent), low BMD was associated with a higher prevalence of fracture in all cohorts (Shin et al., 2014). Similar conclusions have been reported for US post-menopausal women. In the Study of Osteoporotic Fracture (SOF) the relative risk of femoral neck fracture increased as BMD decreased, but to a different extent depending on ethnic origin (Cauley et al., 2005). For example, a 1.0 standard deviation decrease in BMD was associated with a relative risk of 1.42 for women of European origin but a relative risk of only 1.20 in women of African descent (Cauley et al., 2005). The relationship between BMD and fracture risk has not been established for SA, and therefore it has been suggested that reference standards established for people of European origin may not be appropriate for SAs (Melamed et al., 2010). This is because the relationship between BMD and fracture risk in SAs is not known, and is possibly different from the BMD and fracture risk relationship in Europeans. Therefore, reference standards established for people of European origin for their BMD relationship with fracture risk, are probably not appropriate for SAs.

To understand the association of skeletal size with BMD, it is useful to know that the higher BMD values in people of African descent compared to Europeans is not totally explained by bone size (Henry and Eastell, 2000; Finkelstein et al., 2002; Barrett-Connor et al., 2005). BMD values in Africans, either living in Africa or other countries, are the highest of all ethnic groups studied (Siris et al., 2001; Finkelstein et al., 2002; Barrett-Connor et al., 2005; Cauley et al., 2006; Cauley et al., 2007).
et al., 2005; Tracy et al., 2006; Travison et al., 2011) and Africans have the lowest fracture risk of all ethnic groups studied (Lauderdale et al., 1997; Lau et al., 2001; Siris et al., 2001; Barrett-Connor et al., 2005; Cauley et al., 2005, 2007; Tracy et al., 2006). Polynesian women, like Africans, also have higher BMD than individuals of Asian or European origin and again this remains the case even after accounting for skeletal size (Cundy et al., 1995). This implies that there are other factors, in addition to skeletal size, which explain the higher BMD in Africans and Polynesians.

The reasons why there are ethnic differences in BMD, fracture risk and the relationship between BMD and fracture risk, are not yet clear. Explanations for lower BMD in Asians compared to Europeans include lower skeletal size and/or lower levels of vitamin D in Asians and this is discussed later. However, irrespective of the explanation for lower BMD in Asians, this does not explain why the fracture risk in SA women is lower than that of women with European heritage. One possibility is a difference in bone geometry, especially of the hip. Hip geometry is measured in my study and discussed later. Other parameters of bone health such as cortical thickness and relative volumetric BMD (vBMD) of cortex and trabecular bone may differ between ethnic groups and may help explain the differences in bone strength. For example, it has been found that men of European origin had a significantly lower cortical vBMD at the tibial diaphysis than men of African or SA origin (Zengin et al., 2016). The same study also reported that men of African origin had thicker cortices at the tibia and radius diaphysis than men of European or SA origin (Zengin et al., 2016). However, vBMD can only be measured using QCT technology, which is expensive to use and exposes the study participant to higher doses of X-rays.

Many other variables, besides bone status, affect fracture risk and could explain why ethnic differences in fracture risk do not parallel average BMD values between ethnicities. Other possible explanations for ethnic differences in fracture risk include body composition (Osborne et al., 2012; George et al., 2014), hip geometry parameters (Cummings et al., 1994b) bone marker turnover and body proportions (Looker, 2002; Acheson, 2005).

Body composition and hip geometry factors are discussed in more detail later. One potential influence on bone that differs between ethnic groups is body proportion. For example Africans are quoted as having longer legs and shorter trunks compared to
Europeans whilst Asians have shorter legs and longer trunks than Europeans (Seeman, 1998). These measurements can be expressed as sitting/standing height ratio and this may affect loading on the hip and spine leading to differences in bone geometry at these sites. Body proportion has been offered as an explanation of why older rural Gambian women (living in England or Africa) suffer minimal osteoporotic fractures despite their low bone mineral content (Aspary, Prentice and Cole, 1995; Aspary et al., 1996). Sitting/standing height ratio was a positive predictor for bone mineral content (BMC) at the hip and spine (but not radius) in Gambian women, possibly due to a proportionally longer torso increasing load on weight bearing bones (Aspary, Prentice and Cole, 1995).

The culture in some ethnic groups is to sit near the ground, and an interesting suggestion for the paradox of low fracture risk, despite low BMD, in Iran is that habitual squatting leads to better muscle and bone strength in the hip (Moayyeri et al., 2006). The constant lowering and rising involved in squatting may lead to stronger thigh extensor muscles and potentially less fragile supralateral femoral neck cortices, which may reduce the risk of falling and hip fractures (Moayyeri et al., 2006).

Risk of falling also influences fracture risk (Dargent-Molina et al., 1996; Roy et al., 2002) and this may differ between ethnicities for various reasons such as cultural mores e.g. amount of physical activity. Although many studies associate higher physical activity with lower fracture risk there is some evidence that lower activity can reduce risk of falling in older men (Chan et al., 2007), and SAs have been reported as having lower levels of activity than the general population (Fischbacher, Hunt and Alexander, 2004).

To summarise, Asians have lower BMD than people of European origin and this is associated with skeletal size, whereas Africans have higher BMD than both Europeans and Asians, which is only partially associated with skeletal size. Although low BMD is associated with higher fracture risk in all ethnic groups, the relationship of BMD with fracture risk varies according to ethnic group, so relative fracture risk in these three main ethnic groups do not exactly reflect their relative BMD. This is probably due to other factors, in addition to BMD, influencing fracture risk in different ethnic groups, e.g. bone geometry or risk of falling.

Studies on fracture risk in different ethnicities require large sample numbers and a longitudinal design. However smaller studies, such as mine, using DXA technology, can
measure BMD and certain hip geometry parameters, which are markers for fracture risk. The next section discusses hip geometry parameters in more depth.

2.6.4 Hip Geometry Parameters and Hip Fracture Risk

Bone geometry parameters describe how bone material is distributed and how this influences bone’s resistance to the various forces that it is likely to experience. With the advent of more sophisticated measuring techniques such as QCT, and the fact that BMD on its own has limitations as a predictor for fracture risk, recent attention has turned to measures of hip strength and hip geometry parameters. Some of these parameters can augment BMD for predicting fracture risk at the hip (Faulkner et al., 1993, 2006; Dretakis et al., 1999; Bergot et al., 2002; Brownbill and Ilich, 2003; Gregory and Aspden, 2008; Kaptoge et al., 2008).

Hip geometry parameters can also be measured by DXA (Yoshikawa et al., 1994; Beck, 2007), and in my study I have measured the following: HAL, FNW, section modulus (Z), buckling ratio (BR) at the femur neck, and femoral neck shaft angle (FSA) as well as hip strength index (HSI). These are described in the Methods chapter.

Whilst only a few hip geometry parameters are considered to have only a small predictive power compared to BMD of the hip, they do appear to have an independent relationship with fracture risk and therefore when combined with BMD can improve the predictive power (Alonso et al., 2000; Faulkner et al., 2006). Hip geometry parameters such as HAL and femoral neck width (FNW) vary between ethnicities and may partially explain why different ethnicities have differing incidences of fracture. For example, the shorter HAL and FNW of African-Americans is posited as an explanation for their lower fracture risk compared to Americans of European origin (Mikhail, Vaswani and Aloia, 1996; Theobald et al., 1998).

In addition to influencing BMD, height may influence hip geometry parameters, so my study seeks to explore whether there are any ethnic differences in hip geometry parameters, and if so, whether the difference can be explained by height. Further information about how the various hip geometry parameters relate to fracture risk and how they differ between ethnic groups is considered in the section on skeletal dimensions (2.7.2).
In addition to hip geometry parameters, other bone geometry parameters e.g. cortical thickness, and other skeletal sites e.g. tibia, may also be relevant in understanding how bone geometry is linked to fracture risk and whether these bone geometry measurements vary between ethnicities and hence may explain some of the ethnic differences in fracture risk.

### 2.7 Factors influencing BMD and hip geometry parameters

#### 2.7.1 Sex

Generally speaking, regarding age-associated osteoporosis and low trauma fracture risk, after the age of 50 years, women are more at risk of fracture than men, due to their smaller bones and thinner bone cortex, and, after the menopause, considerably reduced oestrogen levels (Seeman, 2002). At younger ages (20 to 40 years) men have a higher risk of fracture than women due to a higher incidence of high trauma accidents e.g. road traffic accidents (Curtis et al., 2016).

#### 2.7.2 Skeletal Dimensions (height and hip geometry)

For reasons explained above, skeletal size is an important component of DXA measured BMD, and so skeletal size is often considered to be the mediator of the lower BMD readings in Asians compared to Europeans (Tobias et al., 1994; Alekel et al., 2002; Finkelstein et al., 2002; Mehta et al., 2004; Barrett-Connor et al., 2005; Roy et al., 2005). To explore the impact of bone size on the BMD measurement, researchers attempt to adjust for bone size. As described in the Methods chapter, this can be done by applying a formula which takes into account the skeletal size of the site of interest. Alternatively, many studies use height as an indicator of skeletal size.

Despite height being linked to higher BMD, certain studies report a positive correlation between height and fracture risk (Meyer, 1993; Cummings et al., 1995; Joakimsen et al., 1998). The rate of hip fracture in Norway is double that found in Spain and the reason is thought to be partly due to the taller height of Norwegians (Duarte Sosa et al., 2015), as well as lower exposure to sunlight (Macdonald et al., 2008). Mechanisms by which greater height may increase fracture risk include greater impact of falling (Dargent-Molina et al.,
1996) and/or the association with greater HAL, which positively correlates with fracture risk (Faulkner et al., 1993; Lee et al., 2016).

The GLOW study mentioned previously (section 2.2) reported a positive association of height with spine fracture but no association of height with hip or wrist fracture (Compston et al., 2014). However, a large study involving over 700,000 postmenopausal UK women and using Cox regression models with attained age as the underlying time variable, concluded that height was associated with increased fracture risk at the femoral neck (Armstrong et al., 2016). Height was associated with increased fracture risk at other sites but to a lesser degree (Armstrong et al., 2016). The studies cited above made adjustments for age, a confounding variable in the association of height with fracture risk. Positive association of height with fracture risk is greater in younger people than older people (Opotowsky, Su and Bilezikian, 2003). In elderly men and women recent height loss (often due to vertebral fracture, itself a symptom of declining bone health) is linked with increased risk of hip fracture (Hannan et al., 2012).

Analysis of 2,263 women aged 40-74 from the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study also reported that the positive relationship between height and hip fracture risk was stronger for younger age groups (Opotowsky, Su and Bilezikian, 2003). The same study also demonstrated that lower extremity length (LEL) (standing height – sitting height) predicted hip fracture risk equally among all age groups (Opotowsky, Su and Bilezikian, 2003). The authors therefore recommended that LEL is a better predictor of hip fracture risk than height (Opotowsky, Su and Bilezikian, 2003). This is because LEL removes the bias of smaller height due to vertebral fractures and age-induced loss of height, which generally occurs in the trunk rather than the legs (van Leer, van Noord and Seidell, 1992). However, the method of measuring LEL is biased by gluteo-femoral fat mass in that fatter people will appear to have shorter LEL than is actually the case (Bogin and Varela-Silva, 2008). Therefore, the association of short LEL with reduced fracture risk may be partially reflecting a beneficial influence of fat mass. Although BMI was not reported in this article (Opotowsky, Su and Bilezikian, 2003), I calculated a BMI for each group in the analysis from the reported average height and weight. The resulting BMIs suggest that most of the participants in this study were overweight, and therefore LEL was likely to have been affected by gluteo-femoral fat.
mass. Knee height, rather than LEL, may have been a better parameter to have measured and analysed as a predictor of hip fracture. Knee height is a good indicator of participant’s stature as it is unbiased by age (Prothro and Rosenbloom, 1993; Roubenoff and Wilson, 1993) and, unlike LEL, it is not biased by gluteo-femoral fat mass (Bogin and Varela-Silva, 2008).

Another issue with height is its association with early life environment, in that height (and knee height) is often used as a marker for the biological and social environment during growth and development, with a taller stature denoting a good, healthy development. Therefore, height might influence fracture risk in opposing ways, positively in that it reflects a better early life environment and increased BMD, and negatively due to higher impact on falling and/or greater HAL.

As height increases, certain hip geometry dimensions may also increase. HAL has already been mentioned briefly and of all the commonly used geometric measures, HAL appears to be the strongest predictor of fracture risk (Brownbill and Ilich, 2003). HAL is known to correlate with height (Flicker et al., 1996; Gnudi et al., 1999), and height has been reported as a more significant predictor of HAL than ethnicity in Pakistani and American premenopausal women (Alekel et al., 1999). A longer HAL has been linked to increased fracture risk independent of age, femoral neck BMD, height and weight (Faulkner et al., 1993). The association was not as large as that found between BMD and fracture risk, but when used in conjunction with BMD improves prediction (Faulkner et al., 2006).

Subsequent publications have confirmed this link between HAL and fracture risk (Reid, 1994; Im and Lim, 2011; Iolascon et al., 2015). However, a few studies found no significant association between HAL and fracture risk (Alonso et al., 2000) and see reviews (Brownbill and Ilich, 2003; Gregory and Aspden, 2008). The lack of association in some studies was attributed to using radiographs, using different populations or not using a Lunar Prodigy, the DXA machine approved by the Food and Drug Administration (FDA), (Brownbill and Ilich 2003). An increase in HAL in elderly, white women in New Zealand over a 35-year period was associated with a doubling of age specific rates of hip fracture over the same period (Reid, 1994). The opposite finding was reported in a sample of Cretan postmenopausal women where those women who had suffered a hip fracture had a significantly shorter HAL than the control group (Dretakis et al., 1999). The type of hip fracture may be relevant as a
study using elderly French women (from the EPIDOS prospective study) found an association between longer HAL and cervical fracture, but no such association between HAL and trochanteric fracture (Duboeuf et al., 1997).

One explanation for the increased fracture risk associated with a long HAL is that when an individual falls and hits their hip on the ground, a bending moment is applied to the femoral neck. A longer HAL may indicate a greater femoral moment arm (the perpendicular distance from an applied force to the centre of the pivot) i.e. a higher moment of force, so the femoral head is more likely to fracture (Gregory and Aspden, 2008). However, Faulkner (1993) argues that an accurate measurement of the femoral moment arm would not include pelvic bone or acetabular tissues (which are included in the HAL measurement – see Methods for a definition of HAL). Another possibility is that a longer hip axis may cause the greater trochanter to extend further beyond the pelvis thus making it a more vulnerable target in a fall (Faulkner et al., 1993). As a long HAL is linked with larger body size, which would result in a greater impact force on the hip in the case of a fall, this may also explain the link between a longer HAL and fracture risk. Hip strength index (HSI) is an attempt to combine various influences on hip strength to calculate the overall hip bone strength, taking into consideration individual’s height, weight and hip bone geometry.

HAL has been reported as being significantly shorter in Indian and Pakistani pre-menopausal women compared to those of European origin (Alekel et al., 1999). Therefore, it has been suggested that the shorter HAL of SAs can explain their lower hip fracture risk. It is expected that BD women, being of shorter stature, will have a shorter HAL than IB women.

Another hip geometry parameter that is related to skeletal size is FNW, which has been reported as correlating with height and weight (Gnudi et al., 1999), so the expectation in my study is that FNW will be lower in the BD women than IB women. Biomechanical studies measuring femoral strength in vitro have demonstrated that an increased FNW increases strength (Gregory and Aspden, 2008). However one study has reported no association between FNW and fracture risk (Faulkner et al., 1993) and a number of studies have found a higher FNW to be significantly associated with increased fracture risk (Alonso et al., 2000; El-Kaissi et al., 2005; Dinçel et al., 2008; Kaptoge et al., 2008; Im and Lim, 2011). The authors of one of these studies which involved fracture cases versus controls, in Spanish
men and women aged 60 to 90 years, suggested the femoral neck widened to increase the moment of inertia as a compensatory response to age-related bone loss (Alonso et al., 2000). Other publications have also provided evidence that in some bones e.g. femur shaft and femoral neck, as BMD decreases with age, there is widening of the bone by periosteal expansion to compensate for the loss of strength associated with a lower BMD (Beck et al., 2001). Although a wider femoral neck increases bone cross sectional area thus improving bone strength, the fact that an increase in FNW is related to age related bone loss, may explain why a wider femoral neck is actually linked with increased, not decreased, fracture risk (Alonso et al., 2000).

As skeletal size increases, the cross sectional area of bones, including the femur neck also increases. This, in addition to increasing BMD, also increases section modulus (Z). The only study, to my knowledge, that compared Z values between Asians and Europeans, took place in Australia and compared pre- and post-menopausal Chinese women with Australians of European origin (Wang et al., 2005). It was found that the Chinese women had significantly lower height, weight and Z than Australians of European origin (Wang et al., 2005).

As cross sectional area is expected to be lower in SAs (due to smaller skeletal size) it is expected that Z in BD women will be lower than IB women. Whether this difference will be removed when adjusted for height cannot be predicted because the distribution of bone mass is not known in the femur neck of SA women. There is a report that SA men have a higher cortical vBMD at the tibial diaphysis then European men (Zengin et al., 2016). However, there is also the finding that UK SA pre-menopausal women have a lower cortical thickness than IB counterparts (Ward et al., 2007).

Although a larger Z value is considered to reduce the risk of fracture, it needs to be considered in terms of cortical thickness. If Z increases due to a wider cross sectional area and the cortex does not thicken, this may increase the risk of buckling (Nelson et al., 2011). Buckling ratio (BR) may change with increased skeletal size. A high BR in femur shaft and/or intertrochanter increases fracture risk (LaCroix et al., 2010). There is limited, equivocal data on BR in the femur neck in Asian women. Chinese women had a significantly higher BR than US women of European origins, whilst Japanese women had a significantly lower BR than US European women (Danielson et al., 2013a). The differences in BR do not seem to be totally
due to skeletal size, as both Chinese and Japanese were of similar height, although both shorter than the US European women.

NSA is an interesting hip parameter in that as populations became increasingly urbanised and sedentary there was an increase in mean NSA, probably associated with lack of exercise (Anderson and Trinkaus, 1998). In babies the NSA is very large (about 145°) but decreases to about 136° by the age of 4-5 years as the child learns to walk and NSA is stable by mid adolescence (Gregory and Aspden, 2008). A lower NSA produces a more stable joint which is especially important in the first decade of life when the acetabulum is mainly cartilaginous (Anderson and Trinkaus, 1998). NSA therefore reflects load levels incurred in the hip region during development (Anderson and Trinkaus, 1998). However, NSA has also been reported as being influenced by body build, which in turn may be influenced by the climate i.e. the stocky body shape of populations living in colder climates increases loading on the femoral neck during early development, causing a lower NSA than people living in hotter climates (Gilligan, Chandraphak and Mahakkanukrauh, 2013). If this is so, then BD women may have a greater NSA than IB women. However, more physical activity is associated with lower NSA, so if BD women have had more physical activity over the generations (as might be expected with Bangladesh being a less developed country than the UK) then they might be expected to have a lower NSA than IB women. It is therefore difficult to predict how BD women will compare with IB women in terms of NSA.

Greater NSA is associated with increased fracture risk (Gnudi et al., 1999, 2002; Alonso et al., 2000; Partanen, Jämsä and Jalovaara, 2001; Kaptoge et al., 2008; Iolascon et al., 2015). It has been suggested that the inferior femoral neck cortex will attain less bending stress if the NSA is higher, and hence the inferior femoral neck cortex will remain thinner, predisposing the neck to a greater fracture risk (Rafferty, 1998). This is consistent with the finding that greater NSA was associated with risk of femoral neck fracture but not intertrochanteric fracture (Gnudi et al., 2002). Other published data showed no significant differences in NSA between control group, femoral neck fracture and intertrochanteric fracture in post-menopausal Chinese women (Li et al., 2016). Some studies report lower NSA being associated with increased fracture. Pre-menopausal Korean women who had suffered a fracture had a lower NSA than the control group (Lee et al., 2016), and American
post-menopausal women with a fracture had a lower NSA than the control group (Kaptoge et al., 2008).

The link between height, BMD and some hip geometry parameters is a major issue in my study research question. If UK SAs grow taller in subsequent generations, how will this impact on their BMD values and some hip geometry parameters, all of which have implications for their fracture risk in the future.

One of the problems with investigating the impact of skeletal size on BMD is that height, weight, skeletal size and BMD are all positively correlated so the influence of skeletal size per se on BMD, cannot be differentiated from the additional influences of weight (increased load and increased adipose tissue – see below).

2.7.3 Body Composition

It is generally recognised that body weight i.e. body mass, is positively correlated with BMD, to the extent that a high BMI is considered to be protective against fractures (De Laet et al., 2005). Later studies have gone on to show that weight is a better predictor of BMD than BMI (Sen et al., 2005; Robbins et al., 2006). It is generally agreed that the increased load on the body induced by the higher weight causes an increase in BMD, as predicted by the mechanostat hypothesis (Frost, 1996, 2003). Although body weight is positively correlated with BMD, excessive weight due to fatness, i.e. obesity, does not necessarily protect against fracture in postmenopausal women (Premaor et al., 2010; Compston et al., 2011). The GLOW study, mentioned above (section 2.2), concluded that BMI was inversely associated with hip, spine and wrist fractures, but positively associated with ankle fractures and weight showed similar, but slightly weaker, inverse associations with fracture risk at these skeletal sites (Compston et al., 2014).

Weight influences fracture risk in two opposing ways, positively via its positive association with BMD and negatively in that the impact of falling is greater in heavier people. However, the effect of weight on BMD is more complicated than simply imposing a heavier load on bones, causing them to grow stronger. Body mass includes fat (adipose) tissue and lean tissue, with lean mass having the most positive association with bone status (Travison et al., 2008; Osborne et al., 2012). Travison et al. (2011) reported lean mass was associated with higher BMD as well as higher cross sectional area and Z in the femoral neck of men.
Furthermore, lean mass alone accounted for a large proportion of differences in femoral neck BMD between ethnic groups (Americans of African and European origin and Hispanics) (Travison et al., 2011). Osborne et al. (2012) also reported that lean and fat mass were positively associated with cross sectional area and Z at the femoral neck, with lean mass being the most important contributor (Osborne et al., 2012). Lean muscle action causes mechanical stress on bones which influences BMD and structural parameters (Beck et al., 2001; Travison et al., 2008; Bailey and Brooke-Wavell, 2010a). This is consistent with the observation that during growth, peak muscle mass velocity precedes peak bone mineral accumulation, and during ageing, declining muscle function precedes bone loss (Ward, 2012).

Adipose tissue is one of the major sources of aromatase, an enzyme that synthesizes oestrogens from androgen. The production of oestrogen in adipose tissue is a possible mechanism whereby fat mass has a protective effect on bone (Reid, 2002). In men and postmenopausal women (where the ovaries no longer produce oestrogen) adipose tissue becomes the main source of oestrogen. A study from South Korea adjusted for the mechanical loading effect of body weight and found that fat mass had a negative effect on BMD in premenopausal women but no relationship with BMD in men or postmenopausal women (Yoo et al., 2012). The authors suggest that the negative effect of fat on BMD is caused by inflammatory processes which, in postmenopausal women and men, are counterbalanced by the positive effect of oestrogen from the adipose tissue (Yoo et al., 2012). However this, and similar studies, are open to criticism because in an attempt to adjust for body weight both body weight and fat mass are used as predictors although they are collinear (Reid, 2010). Other studies report the lack of positive effect of adipose tissue on BMD in American adolescents and young adults (Janicka et al., 2007) and young Mexican females (Lazcano-Ponce et al., 2003).

It has been recorded that men and oestrogen-deficient women tend to accumulate more visceral fat than premenopausal women (Lovejoy and Sainsbury, 2009). When the association of subcutaneous and visceral fat with femur bone strength of pre-menopausal women was assessed, it was reported that subcutaneous fat was beneficial to bone, whereas visceral fat was deleterious (Gilsanz et al., 2009). This may be explained by the positive correlation of visceral adiposity with promoters of bone reabsorption e.g.
parathyroid hormone (George et al., 2016) and proinflammatory cytokines (Morley, 2004), whereas subcutaneous fat is associated with higher levels of aromatase and leptin that are beneficial to bone (Gilsanz et al., 2009).

Visceral fat is also linked to insulin resistance and diabetes (Bavenholm, 2003). Both type 1 and type 2 diabetes are linked to increased risk of fracture (Janghorbani et al., 2007; Mayne, Stout and Aspray, 2010; Kurra and Siris, 2011; Leslie et al., 2012), although type 2 diabetes is not linked with a lower BMD (Vestergaard, 2007). Again, the high prevalence and incidence of type 2 diabetes in UK SAs compared to indigenous British (Barnett et al., 2006) would indicate the SAs have poorer bone status. Type 2 diabetes is the extreme form of metabolic syndrome, a common metabolic disorder generally defined as a constellation of metabolic abnormalities including glucose intolerance, insulin resistance, central obesity, high blood levels of lipids and hypertension (Eckel, Grundy and Zimmet, 2005). Metabolic syndrome in connection with BMD and fracture risk has been explored and it was found that the incidence of osteoporotic non-vertebral fractures was higher in those suffering from metabolic syndrome, despite metabolic syndrome being linked to higher BMD (Von Muhlen et al., 2007). The higher BMD found in metabolic syndrome and type 2 diabetes was attributable to the higher BMI associated with metabolic syndrome (Von Muhlen et al., 2007).

2.7.4 Vitamin D, Calcium and parathyroid hormone

Vitamin D, calcium and parathyroid hormone are very important factors influencing bone status. They are often considered together as all three act in conjunction with each other to affect bone growth and status. Calcium is the main component of bone, and bone acts as a reservoir for calcium which is necessary for many physiological processes. Therefore, it is important there is sufficient calcium available and that efficient bone metabolism maintains good bone status. The hormone, vitamin D, has a major influence on bone through its influence on calcium metabolism by a number of mechanisms: calcium transport, renal calcium reabsorption, intestinal calcium absorption and release of calcium from the bone (Holick, 2007). Vitamin D is mainly manufactured in skin exposed to ultraviolet radiation, with some contribution from diet (Holick, 2003; MacDonald et al., 2011). Parathyroid hormone also influences calcium metabolism. It acts to preserve blood levels of calcium ions via a negative feedback mechanism. Low serum levels of calcium ions stimulate the
release of parathyroid hormone, which in turn stimulates osteoclasts to resorb bone and so release calcium back into the blood restoring serum calcium ions to their correct level, generally between 1.1 and 1.3 mmol/L.

The lack of vitamin D can cause osteomalacia (Pearce and Cheetham, 2010) and short stature (Holick, 2007; Bueno, Czepielewski and Raimundo, 2010). Osteomalacia is a metabolic bone disorder characterised by the decreased mineralisation of osteoid (Gifre et al., 2011; Thacher and Clarke, 2011) and results in a softening of the bone. Insufficient levels of vitamin D can cause osteomalacia in adults and rickets in children (Holick, 2007). Symptoms of osteomalacia include generalised bone pain, muscle weakness and disturbances of gait (Thacher and Clarke, 2011). Osteomalacia and rickets used to be considered diseases of the past but there is now concern that rickets and osteomalacia are becoming more common in the UK (Pearce and Cheetham, 2010).

Osteomalacia differs from osteoporosis in being due to compromised bone mineralisation rather than reduced bone formation i.e. the laying down of osteoid by osteoblasts in bone formation is normal but the mineralisation of this osteoid is reduced (Parfitt, Qiu and Rao, 2004). As discussed earlier, osteomalacia, like osteoporosis, causes a reduction in BMD and lower bone strength. Unlike osteoporosis, osteomalacia is generally associated with pain in bones and muscles (Holick, 2003).

Dark skinned ethnic groups, such as SAs, are more susceptible to osteomalacia than paler skinned ethnic groups. This is because melanin in the skin is a natural sunscreen, absorbing harmful ultraviolet radiation and transforming it into heat. Melanin filters sunlight at similar wavelengths required for synthesis of vitamin D and therefore increases risk of low vitamin D levels (Holick, 2004). Dark skinned immigrants in high-latitude countries, including the UK, where sunlight exposure is lower, are at particular risk of low vitamin D levels. Widespread vitamin D deficiency was reported in men and women born in Turkey, Sri Lanka, Iran, Pakistan and Vietnam who were residing in Oslo (Holvik et al., 2005), whilst osteomalacia has been diagnosed in the SA community in the UK (Finch et al., 1992) and reported in SA immigrants in Northern European countries (Brouwers et al., 2010). Even the indigenous population of high-latitude countries can suffer from vitamin D deficiency due to low sunlight exposure, especially in winter months (Macdonald et al., 2008).
Although the lower blood levels of vitamin D in SA people and all ethnic groups with similarly darker skin, is generally understood to be a consequence of increased melanin reducing their ability to manufacture vitamin D in the skin (Harris and Dawson-Hughes, 1998), a recent study casts some doubt on this assertion (Hakim et al. 2015). This study reports Asian women needed a shorter exposure to UVR compared to IB women to produce the same amount of vitamin D (Hakim et al., 2015). However, this study was confounded by different initial levels of vitamin D in the two ethnic groups as well as small sample numbers (Hakim et al., 2015). Further evidence that optimum levels of vitamin D may not be the same for all ethnic groups comes from a recent report on people of African origin. Africans, although having higher BMD and lower fracture risk compared to other ethnic groups, were also found to have lower serum 25(OH)D levels, higher parathyroid hormone levels and lower calcium intake than people of European origin (Gutiérrez et al., 2011). In fact it has been suggested that higher levels of serum 25(OH)D (> 20 ng/ml) are associated with fracture risk in African women (Cauley et al., 2011). The latter study also reported levels of serum 25(OH)D > 30 ng/ml were associated with fracture risk in Asian women (Cauley et al., 2011), indicating that Asian women need lower levels of vitamin D than European women for bone health. These apparent differences in optimum vitamin D levels between ethnic groups lead some researchers to conclude that the idea of a global desirable vitamin D level is not tenable (El-Hajj Fuleihan, Rahme and Bassil, 2013).

Hyperparathyroidism is a condition in which heightened levels of parathyroid hormone stimulate more bone to be reabsorbed with deleterious consequences for BMD and bone strength (Fraser, 2009). The highest incidence of hyperparathyroidism is in postmenopausal women (Fraser, 2009), and has been linked to metabolic syndrome in older men, but not older women (Reis, Von Mühlen and Miller, 2008).

2.7.5 Nutrition and diet

Good nutrition is important for bone health, especially the ingestion of foods containing calcium, mainly found in dairy products (Rizzoli, 2008). The main source of vitamin D is the action of sunlight on the skin, as mentioned above, so if sunlight is in poor supply, e.g. in countries at higher latitudes and/or during the winter, foods rich in vitamin D, such as oily fish, are beneficial to bones (MacDonald et al., 2011). A good diet for bones should include appropriate intake of iodine which is a component of thyroid hormone, an important
regulator of bone maintenance and repair (Waung, Bassett and Williams, 2012). Appropriate intake of Iodine (found in dairy products and seafood) is essential for healthy thyroid gland functioning, and extreme iodine deficiency can lead to goitre and stunting, and even borderline iodine deficiency can cause thyroid dysfunction and increased risk of osteoporosis (Knudsen et al., 1999). Consequences on bone status of a poor diet have been discussed above in relation to the UK BD community (section 2.5.2).

2.7.6 Reproductive variables (menarche, parity, lactation and menopause)

Bone metabolism is strongly influenced by oestrogen so factors and events associated with female reproduction are important in connection with BMD, osteoporosis and fracture risk in women. Oestrogen is an especially important hormone connected with good bone health due to its protection against bone loss (Khosla, 2010), the probable mechanism being the prevention of apoptosis in osteoblasts (Bradford et al., 2010) and stimulation of osteoblast function (Tobias and Compston, 1999). Another benefit of oestrogen is that it increases mechanosensitivity, the ability of bone cells to respond to strain, leading to greater osteogenic responses to mechanical loading (Devlin, 2011). There has also been recent interest in the role of progesterone in maintaining women’s bone health and preventing osteoporosis (Seifert-Klauss and Prior, 2010).

Duration of fertility, i.e. years of menstruation, the time between menarche and menopause, is linked with exposure to oestrogen, so the duration time of fertility might be expected to correlate positively with BMD and protect against fracture. Duration of fertility longer than 33 years has been reported to protect against postmenopausal osteoporosis (Cavkaytar et al., 2015). Menarche is an important event of adolescence in girls, generally occurring 9-12 months after the peak of the adolescent growth spurt in height. Age at menarche is linked to bone health, but research studies give conflicting results. An earlier menarche has been associated with lower risk of osteoporosis, as a consequence of being exposed to oestrogens for a longer period of time (Parker et al., 2014). A study involving Shuar women of Amazonian Ecuador, a subsistence-based, natural fertility group, reported that early menarche and greater stature were significantly associated with higher BMD of the calcaneous in post-menopausal women (Madimenos et al., 2012). This is consistent with the finding that later age at menarche is associated with poor BMD and increased fracture risk in later life (Chevalley et al., 2009; Bonjour and Chevalley, 2014). However, other
researchers state that the impact of menarche on later fracture risk is inconclusive (Rauch et al., 1999). Later age at menarche gives the bones a longer time for growth and development and has been cited as the reason that women living a lifestyle classed as hunter-forager have a stronger skeleton than women in developed countries, who have an earlier menarche (Devlin, 2011). Indeed, the later age of onset of puberty for boys (14 years compared to 12 years for girls) is cited as one of the reasons that boys have greater peak bone mass than girls as they have an extra couple of years of prepubertal growth (Gilsanz et al., 1997). Another possible reason that boys have greater peak bone mass than girls is because boys’ pubertal growth spurt lasts 4 years rather than the 3 years for girls (Gilsanz et al., 1997). Early menarche is also linked with increased BMI in girls, and this weight increase has been associated with increased BMD at the femoral neck and increased cortical thickness and volumetric trabecular density of the distal tibia in women (Chevalley et al., 2011). These results complement a study indicating BMI gain in girls from the age of one to twelve years was associated with a reduced risk of hip fracture in later life (Javaid et al., 2011).

Menopause is another important event in a woman’s life due to cessation of ovarian output and decline in oestrogen (Riggs, Khosla and Melton, 2002). The reduction in BMD is especially marked after the menopause, with losses of 20-30% trabecular bone and 5-10% cortical bone over the first decade after menopause (Riggs et al., 1982). Bone loss is greater in the first decade after menopause, after which bone loss continues at a slower rate. There have been few studies on whether menopausal BMD loss differed between ethnic groups. Finkelstein (2008) looked at bone loss in lumbar spine and total hip over the menopause period using The Study of Women’s Health Across the Nation (SWAN) which included Americans of African, European and East Asian origin. In general, lumbar spine BMD loss was most rapid in East Asian women, intermediate in European women and slowest in African women (Finkelstein et al., 2008). However these apparent ethnic differences in rates of bone loss were largely explained by differences in body weight, higher weight being associated with lower rates of BMD loss (Finkelstein et al., 2008). Early menopause reduces a woman’s exposure to oestrogen and similarly has been reported as an indicator of fracture risk especially at older age (van Der Voort, van Der Weijer and Barentsen, 2003). However, when subjects are age 75 or older, then age at menarche and menopause seemed of limited or no importance as a risk factor for osteoporosis (Gerdhem and Obrant, 2004).
Between menarche and menopause, lie a woman’s reproductive years in which parity, inter-birth interval and lactation all play a part in affecting bone status. Life History theory predicts that bone, as a mineral source for both the mother and the foetus, will reflect the trade-off between reproduction and the mother’s somatic needs. Therefore, parity, inter-birth intervals, age at first birth and period of lactation will affect BMD in women. BMD is reported to decrease during lactation (Laskey et al., 2011) because providing calcium in the mother’s milk for the baby draws on the mothers’ reserves of calcium from the bone. Women who are exclusively breast feeding lose an average of 210 mg calcium each day (Kovacs, 2016). Although breast feeding has been reported to decrease BMD, it is regained after breastfeeding has ceased (Ensom, Liu and Stephenson, 2002; Laskey et al., 2011; Kovacs, 2016). Extended lactation period and/or multiple pregnancies were not a factor in fracture risk (Karlsson, Ahlborg and Karlsson, 2005). This review concluded that pregnancy and lactation lead to a BMD loss of up to 5%, but it is reversed after weaning (Karlsson, Ahlborg and Karlsson, 2005). The same review also concluded multiparous women had a similar or higher BMD than women with no history of pregnancy (Karlsson, Ahlborg and Karlsson, 2005). A more recent review concluded that, despite conflicting results from published studies, generally pregnancy has a protective effect on bone, especially if followed by lactation (Salari and Abdollahi, 2014). High parity has been reported as associated with increased hip BMD, higher BMI and later age at menopause but the benefit of high parity on BMD was lost after menopause (Streeten et al., 2005). A different conclusion was reported in a large study of almost 10,000 postmenopausal women in the WHI Observational Study which reported that parity and lactation history were generally unrelated to BMD or fracture risk (Crandall et al., 2017). A longitudinal study following over 6000 Canadian women over 15 years, also reported that parity and lactation had no long-term association with BMD or fracture in older women (Cooke-Hubley et al., 2017). These results are contrary to Life History theory which predicts that the demands of reproduction depletes resources from the body. However, the publications cited above are generally based on women from higher income countries who have low parity, reduced lactation duration, energy-rich diets, sedentary lifestyle and reduced pathogen burden. A more recent study on women who breastfed for longer periods showed that Swedish women with long lactation (9 months or longer) had not regained BMD at the ultradistal tibia at 18 months postpartum (Brembeck et al., 2015). This led the authors to conclude that longer
follow-up periods are required to explore whether long periods of lactation could potentially lead to an increased risk of fracture in later life (Brembeck et al., 2015). More relevant to the BD community are studies on populations who tend to have higher parity, shorter inter birth intervals and higher lactation duration but such studies are very few.

The aforementioned study on Shuar women of Amazonian origin (who have high parity, shorter inter birth intervals and higher lactation duration) found no long lasting effects of lactation and inter birth interval on calcaneal BMD in premenopausal women (Madimenos et al., 2012). However, a study on another contemporary pre-industrial population, Tsimane women, who by the time of menopause had had an average of 9.7±3.7 births, with a mean inter birth interval of 30.4±9.9 months and an average age at first birth of 18.5±3.1 years reported the opposite finding (Stieglitz et al., 2015). They concluded that greater reproductive effort (greater parity, shorter inter birth interval and early age at first birth) was associated with reduced calcaneal BMD. This is in accordance with life history theory which posits a trade-off between fertility and somatic condition (Stieglitz et al., 2015).

Oestrogen and progesterone levels in the body are also affected by contraception and HRT. The literature on the effects of oral contraception on bone status gives conflicting results, as individual studies demonstrate a positive (Recker et al., 1992) and a negative (Shoepe and Snow, 2005) effect of oral contraception on BMD. A systematic review on hormonal contraception and bone metabolism concluded that combined oral contraceptives and progestogen-only contraceptives did not appear to have a significant effect on BMD in the general population (Nappi et al., 2012). Another study looking at young adult women living in Africa, Asia and Latin America concluded that hormonal contraception use was associated with small changes in BMD (increases in the case of combined oral contraceptives and decreases in the case of progestogen-only implants) that are reversible (Petitti et al., 2000). However, a recent study on over 12000 UK women concluded that a lower risk of fracture was associated with use of oral contraception, especially when the duration was at least five years (Dombrowski et al., 2017).

There is good evidence that HRT enhances bone status (Torgerson and Bell-Syer, 2001). The Endocrine Society set up a committee to establish the benefits and risks of taking hormonal therapy (Santen et al., 2010). The committee concluded that oestrogen, with or without
progestogen, protected against some of the bone loss experienced after menopause as well as preventing hip and vertebral fractures (Santen et al., 2010). Prevalence of oestrogen usage in the form of HRT is higher in US women of European origin compared to US women of other ethnic origins and may contribute to the differences in BMD between different US ethnic groups (Nam et al., 2013).

2.7.7 Physical Activity

There is considerable evidence that physical exercise, especially weight bearing activity, strengthens bone, via the mechanostat, by increasing BMD (Nurmi-Lawton et al., 2004; Engelke et al., 2006; Beck et al., 2011) and improving bone geometry. Exercise leads to thickening of the femoral neck cortex (Mayhew et al., 2005) and recent studies using QCT have shown that exercise beneficially alters the geometric properties of the proximal femur in men (Allison et al., 2015), premenopausal women (Bailey and Brooke-Wavell, 2010b) and postmenopausal women (Hamilton, Swan and Jamal, 2010). Results from the WHI observational study led the researchers to conclude that exercise improved the strength of the femur, mainly by adding bone to the outer cortical surface which improves resistance to bending (Beck et al., 2011). Exercise, especially regular exercise, during skeletal development i.e. in children and adolescents, is most effective in promoting BMD (MacKelvie et al., 2002; Zanker et al., 2003) and helps prevent osteoporosis in later life (Chan, Anderson and Lau, 2003). However, other researchers conclude that if exercise is not maintained throughout life, then the benefits of exercise during growth will not protect against bone loss in later life (Ducher and Bass, 2007). The period during growth during which physical activity occurs can be important. Increased loading during the peri-pubertal period is most effective in enhancing cross-sectional bone geometry in the tibia (Rantalainen et al., 2015), and a study on females, playing tennis and squash, demonstrated that there was a twofold increase in BMD in women who started playing before or at menarche, compared to those who started playing later (Kannus et al., 1995).

Similar results on the benefits of exercise are reported when QUS measurements are used. A study of young Chinese male students showed that those who took part in a sporting activity had higher QUS parameters than those who did not exercise (Yung et al., 2005). Interestingly, swimming, a non-impact sport which is reported to have negligible effect on BMD (Gómez-Bruton et al., 2013) also significantly improved QUS scores, but not to such an
extent as dancing and soccer, which suggests swimming may affect other bone properties such as elasticity and microstructure which are only detectable in QUS (Yung et al., 2005). The importance of physical activity on bone status has been discussed in the context of evolution of the post-cranial skeleton, where it was postulated that modern humans have a more gracile skeleton than earlier hominins due to increased sedentism (section 2.4.7). This plasticity of the skeletal system (as evidenced in the evolution of more gracile bones in modern humans) has also been demonstrated over more recent times i.e. the last few decades. In the US, it has been observed that the femur diaphysis over the last few decades has been increasing in length whilst decreasing in width (mediolateral breadth), possibly a result of decreased physical activity (Trotter, Peterson and Wett, 1968; Harrington and Wescott, 2015; Wescott and Zepho, 2016). However, the very recent increase in obesity may reverse this trend, as the extra loading due to weight leads to an increase in width of the femur diaphysis (Agostini and Ross, 2011; Harrington and Wescott, 2015).

The last decade in particular has shown a substantial decrease in daily physical activity in all age groups, especially children, reviewed in Dollman, Norton and Norton (2005). This has been linked to an ever more gracile skeleton in an analysis of data from over 50,000 females and males aged 3 to 18 years collected from cross sectional anthropological surveys in Germany (Scheffler and Hermanussen, 2014). The researchers measured skeletal robustness in terms of relative elbow breadth (to height) and relative pelvic breadth, and found that both measures decreased significantly in both sexes from the time period “1991 to 2004” to “2005 to 2012” (Scheffler and Hermanussen, 2014). They also analysed comparable thoracic parameters which did not change over these two time periods, and so concluded the changes in measures of robustness in elbow and pelvis were the consequences of decreased loading as result of sedentism (Scheffler and Hermanussen, 2014). This highlights the phenotypic plasticity of humans in response to environmental conditions, and raises concerns of how these changes in skeletal robustness will impact on bone status in later life.

### 2.7.8 Familial Influences

BMD and other markers of fracture risk e.g. QUS, bone geometry and bone turnover, as well as osteoporotic fracture are all reported to have a high heritability component (Ralston and Uitterlinden, 2010). Twin and family studies show that, depending on the skeletal site,
between 50% and 85% of BMD variance is genetically determined (Ralston, 2002). It has been reported that a maternal history of hip fracture doubled an individual’s risk of hip fracture (Cummings et al., 1995). A large meta-analysis, using 34928 men and women combined from several prospectively studied cohorts, concluded that a family history of fracture was associated with a significant risk of all osteoporotic fracture, Relative Risk (RR) = 1.54 and an even higher risk of hip fracture, RR = 2.27 (Kanis et al., 2004). It also concluded that parental history of fracture association with an individual’s fracture risk was independent of individual’s BMD (Kanis et al., 2004).

Familial influences on BMD have been investigated using mother-daughter pairs where a significant correlation between BMDs of mother and daughter, or the fact that mother’s BMD was a significant predictor of daughter’s BMD, suggested a strong familial impact (Lutz and Tesar, 1990; Picard et al., 2001; Shetty et al., 2016). Other studies which investigated inter-generational effects on QUS scores in mothers and daughters showed links between mothers and daughters QUS score for women in the US (Danielson et al., 1999), Poland (Drozdzowska and Pluskiewicz, 2001) and Japan (Yoneyama, Shimizu and Beppu, 2008).

Up until recently, the strong association of daughter’s BMD and QUS measurements have been mainly attributed to genetic variation, with evolution and natural selection driving the changes in an individual’s genetic make-up. However, as mentioned earlier in connection with Life History theory and the bio-cultural perspective, there is substantial plasticity in many phenotypic traits, especially bone which can change characteristics within a lifetime in response to nutrition and physical activity, allowing the bio-cultural environment, over the course of an individual’s lifespan, to shape traits to a greater degree than previously thought. Some researchers argue that heritability has been overestimated in many so called “Life History” traits such as birth weight, age at menarche, adult height, BMD and age at menopause (Wells and Stock, 2011). They cite various papers to support their argument, pointing out that monozygotic twins used in twin studies not only share the same genetic make-up, but are also exposed to the same epigenetic influences (Kaminsky et al., 2009). Wells and Stock (2011) also point out that the Life History traits mentioned above, despite being reported as having high heritability, have few significant individual genetic markers, and display secular trends, suggesting the environment and its interaction with genetics plays a larger role than previously thought.
Irrespective of whether the familial influence on a person’s bone status is driven by genetics, environment or the interaction between the two, these studies indicate that familial factors strongly influence BMD, QUS measurements and fracture risk. Therefore familial influences need to be controlled for as far as possible in any study which aims to compare bone status measurements between two generations of women.

There is also a strong familial influence on leg length, again probably due to an interaction between genetics and environment. A good example comes from a study of three generations of women of Maya ethnicity living in Merida, Mexico, which showed significant correlations in leg length between mother-to-child and grandmother-to-mother (Azcorra et al., 2015), demonstrating the importance of considering mothers’ measurements of height and leg length in assessing influences on an individual’s height and leg length.

2.7.9 Socioeconomic Status

It would be expected that low socioeconomic status (SES) and social inequality would have an adverse impact on bone health, especially if the DOHaD hypothesis holds true. Few good-quality studies have been carried out on the impact of an individual’s SES on his/her bone health and fracture risk (Brennan et al., 2009). A recent study demonstrated no relationship between SES and fracture type, or diagnosis of osteoporosis in those adults who presented to a fracture clinic in the UK (Ong et al., 2015), whilst a large UK study reported a positive correlation with deprivation and higher fracture risk in men, but not women where the reverse trend was found (Curtis et al., 2016). Socioeconomic factors have been reported to play a part in the causation of fracture in younger adults but not in elderly people in the UK (Jones et al., 2004). A recent large UK population-based study of incident hip fracture admissions assessed by levels of deprivation in men and women for over 14 years, concluded that deprivation predicted hip fracture incidence, especially in men, although the impact was greater among women due to the overall higher hip fracture incidence in women (Bhimjiyani et al., 2018).

In other countries, there are also conflicting reports e.g. no link was found between osteoporosis or osteoporotic fracture, with social inequality in Europe and the US (Syddall, Evandrou and Dennison, 2012) whilst a large retrospective cohort study in Spain reported a 30% increased incidence of hip fracture among the wealthiest population compared to the most deprived but this was mainly explained by age-sex differences between the two
groups (Reyes et al., 2015). It is possible that SES interacts with other factors which influence bone status so it is recommended that studies comparing bone status in different ethnic groups control for SES.

2.7.10 Generation/secular trends

The incidence of low trauma/osteoporotic fracture risk has been subject to secular trends. Generally speaking, in Western nations (North America, Europe, Australia and New Zealand) there was a big rise in age-adjusted fractures throughout the second half of the last century but this is now plateauing or even decreasing (Cooper et al., 2011). For example, in Finland the age-standardized incidence of low-trauma fractures in people over 50 years of age showed an increase from 1970 to 1997 (Kannus et al., 2002) but from 1997 to 2010 it was shown to be declining (Korhonen et al., 2013). The reasons for initial increases in age-adjusted fractures are not clear, but possible explanations include lower BMD or increased risk of falling (Kannus et al., 2002). Reasons for the more recent decrease in age-adjusted fractures may involve lifestyle interventions such as osteoporosis medication, smoking cessation, improvement in nutritional status and fall prevention programmes (Ballane et al., 2014). By contrast, in some East Asian countries, such as China, the age-adjusted incidence rates of hip fracture still appear to be rising, possibly due to the lifestyle and environmental factors associated with highly urbanized or industrialized cities such as Hong Kong and Singapore (Koh et al., 2001; Lau et al., 2001; Cooper et al., 2011; Xia et al., 2012). Whether SA immigrants to Western nations, will benefit from the lifestyle interventions mentioned above, needs to be investigated. It needs to be remembered that even if the incidence of age-adjusted fractures is plateauing or declining, the overall numbers of fractures will increase due to higher numbers of elderly people within the population (Caley and Sidhu, 2011).

2.8 Skeletal health and development through the life cycle

This section briefly outlines how the human skeleton grows and develops throughout the various stages of the life cycle from conception to death and Table 2.2 summarises the life stages.
Pre-natal

Up until 8 weeks, the skeleton of an embryo consists of fibrous membranes and hyaline cartilage. At about 8 weeks the bony skeleton begins to form by ossification with the majority of bone being formed in the third trimester of pregnancy (Namgung and Tsang, 2003). There are two types of ossification, intramembranous and endochondral. Intramembranous ossification develops within the membranes of connective tissue and produces bones such as the skull, mandible and collar bone whereas endochondral ossification replaces existing cartilage and is the basis of most skeletal bones including those of the arms and legs. Throughout pregnancy, the bone of the foetus is immature (woven) bone characterised by the random arrangement of collagen fibres: it consists of both cortical and trabecular bone. After birth and up to the age of about 4 years the immature bone is gradually replaced by mature (lamellar) bone.
Table 2.2 Stages of the human life cycle, based on Bogin and Smith 2012, with modifications

<table>
<thead>
<tr>
<th>Stage</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>First trimester of pregnancy</td>
<td>Fertilization to week 12</td>
<td>Embryogenesis (embryo until week 8, foetus thereafter)</td>
</tr>
<tr>
<td>Second trimester of pregnancy</td>
<td>Months 4 to 6</td>
<td>Rapid growth in length</td>
</tr>
<tr>
<td>Third trimester of pregnancy</td>
<td>Months 7 to birth</td>
<td>Rapid growth in weight and organ maturation</td>
</tr>
<tr>
<td>Neonatal period</td>
<td>Birth to 28 days</td>
<td>Extrauterine adaptation, most rapid rate of postnatal growth (total body length and maturation)</td>
</tr>
<tr>
<td>Infancy</td>
<td>Second month to end of lactation (usually by 36 months)</td>
<td>Initial rapid growth velocity with steep deceleration in velocity with time</td>
</tr>
<tr>
<td>Childhood</td>
<td>3 to 6.9 years</td>
<td>Moderate growth rate, mid-growth spurt</td>
</tr>
<tr>
<td>Juvenile</td>
<td>7 to 10 years (girls), 7 to 12 years (boys)</td>
<td>Slower growth rate</td>
</tr>
<tr>
<td>Puberty</td>
<td>Starts in brain at 9-10 years. starts in body at approx.10 years (girls) and approx.12 years (boys)</td>
<td>Short event in which there is reactivation of hypothalamic gonad releasing hormone (GnRH) pulse generator leading to a massive increase in sex hormone secretion</td>
</tr>
<tr>
<td>Adolescence</td>
<td>Girls: 10 to 18 years  Boy: 12 to 21 years</td>
<td>Adolescent growth spurt in height and weight.  Menarche in girls ~ 12-13</td>
</tr>
<tr>
<td>Adulthood</td>
<td>Women: 18-20 years to menopause  Men: 21-25 years to about 55 years</td>
<td>Completion of skeletal growth.  Menopause for European women average age 50</td>
</tr>
<tr>
<td>Old age and senescence</td>
<td>From end of adulthood to death</td>
<td>Decline in the function and repair ability of many body tissues/systems</td>
</tr>
</tbody>
</table>
From birth to puberty

During infancy and youth, long bones lengthen (by a process called interstitial growth, which occurs at the epiphyseal plate) and widen (by a process called appositional growth, which adds layers of bone to the bone already there, usually at the periosteal surface). Infancy starts with a rapid growth velocity followed by a steep deceleration in velocity (Figure 2.7).

From 12 months to puberty, the appendicular skeleton grows twice as fast as the axial skeleton (Bogin & Varela-Silva, 2010). This is the reason why leg length, particularly knee height, is often used as a biomarker of the nutritional and health conditions during the first decade of post-natal life (Leitch, 1951; Frisancho, 2008; Whitley et al., 2008; Padez, Varela-Silva and Bogin, 2009; Bogin and Varela-Silva, 2010). By the age of puberty, knee height is growing less rapidly and adult knee height is virtually established (Bogin and Varela-Silva, 2010).

Up until puberty, growth hormone (GH) and insulin-like growth factor 1 (IGF-1) are the most important hormones that control growth. GH is released by the anterior pituitary gland in a pulsatile fashion and is regulated by two hypothalamic peptides, growth-hormone-releasing hormone and somatostatin (Hindmarsh, 1998). Activation of the GH receptor generally results in the generation of IGF-1 which, in the growth plate, leads to stimulation of the chondrocytes and hence growth in length of the long bones (Hindmarsh, 1998; Walsh, 2015). Thyroid hormone is also implicated in linear growth by interacting with GH and IGF-1 to control the pace of growth plate chondrocyte differentiation (Robson et al., 2002). It has been noted that fracture risk is high during childhood while the skeleton is growing and developing (Curtis et al., 2016). Fractures in childhood tend to occur in the ankle, hand and foot as opposed to the the main type of fracture in people aged over 50 which are hip, spine, upper arm and pelvis (Johansen et al., 1997).

At puberty the male and female sex hormones, testosterone and oestrogen, increase the GH pulse amplitude which promotes the growth spurt (Hindmarsh, 1998).
Adolescence

The period of life for most rapid bone mass accrual is adolescence (Katzman et al., 1991; Bailey et al., 1999).

Between the onset of puberty and young adulthood i.e. adolescence, considerable bone mass is gained, 30%-40% of total bone mass according to Ward et al. (2014). The adolescent growth spurt in height and weight is most marked in the first phase of adolescence (Figure 2.7) when bone growth exceeds mineralisation. The velocity of bone mineral accrual lags behind skeletal growth velocity by about 5 to 7 months (Figure 2.8) depending on site. This dissociation between bone growth and mineralisation suggests a transient period of relative weakness which may explain the increase in fractures around the time of peak linear growth (Bailey et al., 1999). Growth rates decline during the second phase of adolescence (Figure 2.7).

Oestrogen is an important hormone for bone maturation in both boys and girls (Seeman, 2002). Oestrogen stimulates the acquisition of bone on the endocortical surface i.e. increasing cortical width, but also inhibits periosteal apposition i.e. widening of the bone. After puberty when oestrogen levels are higher there is less widening of the bone which explains the report that tennis playing before puberty increased the width of the mid and distal sites of the humerus to a greater degree than the same loading after puberty (Bass et al., 2002). Bone area increases up to 4 years after peak height velocity, and BMC increases for up to 6 years after peak height velocity (Baxter-Jones et al., 2011), the exact timing of these events being site dependent.

After puberty it is the length of the axial skeleton that accelerates as appendicular length growth slows down. One important event of adolescence in girls is menarche, which usually occurs 9-12 months after the peak of the adolescent growth spurt in height. The age at menarche has an impact on skeletal development as described above (section 2.7.6). When the long bones of the skeleton cannot increase in length then there is no further growth in height. Cessation of growth in length of long bones is caused by cartilage and bone cells in the growth plate losing their hyperplastic growth potential (Bogin, 1999). At the time of sexual maturity, the epiphysis and diaphysis fuse. Oestrogen has a key role in this process in both men and women (Weise et al., 2001). Because long bone growth ceases due to
increased oestrogen, the age of menarche is associated with height. It has been reported that women with a later age at menarche grow taller than women having an early menarche and this difference in height is due totally to leg length increase (Onland-Moret et al., 2005).

After long bone growth ceases, bone accrual continues, by appositional growth and increase in bone density, until bone mass reaches a maximum or plateau (often termed peak bone mass) (Figure 2.8). Peak bone mass is by definition the product of vBMD and volume (Ward et al., 2014). Peak bone mass is usually reached at an age of between 25 and 30 years, depending on skeletal region measured and measurement technique used (Johnston, 1993; Heaney and Abrams, 2000). As measured by DXA, peak bone mass of the proximal femur is achieved earliest (at about 18 years) with total skeletal peak bone mass occurring 6 to 10 years later (Matkovic et al. 1994, Heaney and Abrams 2000).

![Figure 2.7 Height and velocity curves of growth for healthy, well-nourished human beings](image-url)

Boys solid line: girls, dashed line. These are model curves based on height data for Western Europe and North America populations. The stages of postnatal growth are abbreviated as follows: I, Infancy; C, Childhood; J, Juvenile; A, Adolescence; M, Mature adult. Modified from (Bogin 1999)
Old age and senescence

Finally, in old age and senescence there is a decline in the function and ability to repair many of the body tissues, including bone (Seeman, 1997, 2002). With increasing age over 50 years, BMD decreases (Riggs et al., 1982; Melton et al., 2000; J. Kanis et al., 2008) (Figure 2.9) and fracture risk increases (Ensrud, 2013; Curtis et al., 2016) especially of the hip, spine, upper arm and pelvis (Johansen et al., 1997). An additional problem for older people is that fractures heal more slowly (Gruber et al., 2006). The loss of bone as a consequence of normal aging in both men and women is due to quantitative and qualitative changes. These include alterations in bone cell populations resulting in an imbalance between bone resorption and formation, variations in calcium-regulating hormones, changes in bone architecture, accumulation of microfractures and decreased blood flow (Kiebzak, 1991). In men the reduction of oestrogen levels with age is also thought to play a significant role in bone loss and fracture incidence (Gennari et al., 2003). There are methods of compensating for age induced bone loss, such as widening of the bone (Section 2.7.2) or confining the increased porosity to be near the neutral axis of the bone where the adverse effects on strength are minimal (Martin, 1991).
Bone geometry also changes with age. For example, in the hip the cortex become thinner in the inferior sector of the femoral head so elastic instability and buckling can occur (Mayhew et al., 2005).

![Graph showing changes in bone mass over life](image)

Note that men have only one phase of continuous bone loss but women have two — an early accelerated phase and a late slow phase. Note also that the accelerated phase, but not the slow phase, involves disproportionate loss of trabecular bone, reproduced from Riggs et al. (1998)

*Figure 2.9 Schematic representation of changes in bone mass over life in trabecular (broken line) and cortical (solid line) in women (left panel) and men (right panel) from age 50 onwards*

**Environmental influences throughout life cycle**

Throughout the life course the environment has a strong influence on skeletal development and maintenance. Factors such as nutrition, physical activity, maintenance of healthy weight, normal muscle mass and function and hormone status play a role in skeletal health and fracture risk (Ward et al., 2014). Most of these factors have been discussed in section 2.7, and Figure 2.10 below illustrates how environment can influence bone mass throughout the life course and fracture risk in later life.
Optimal conditions (solid line) and the effects of adverse environmental conditions (broken line) (reproduced from Heaney, 2000).

Bone density has been reported to show a high degree of tracking over the years in children and adolescents (Kalkwarf et al., 2010) and there is evidence that this tracking continues throughout life. Peak bone mass tracks throughout life (Ferrari et al., 1998) so an individual at the high end of the population at age 30 years is likely to be at this end aged 70 years. Because of this tracking it is generally accepted that peak bone mass is a good indicator of bone mass in later life (Heaney and Abrams, 2000) which is consistent with the DOHaD hypothesis (Cooper et al., 2006). However, Gafni and Baron (2007) refute the idea that peak bone mass is a determinant of bone mass in late adulthood, citing animal and human studies which show that alterations in bone mass acquisition in childhood may not have persistent effects (Gafni and Baron, 2007). The authors point out that as the skeleton is replaced in toto throughout life, the association between bone mass in early and late life is more likely to be attributed to common genetic and environmental factors (Gafni and Baron, 2007).
2.9 Summary

This chapter has briefly reviewed how bone status, which is linked to fracture risk, is affected by numerous environmental factors and Life History events. It has also described how these influences might differ, according to ethnicity and country of birth. The environmental conditions experienced in the UK are very different to those in Bangladesh so it is predicted that, consistent with Migration theory and previous research on SA women, BD women will have lower values than IB women in terms of skeletal size and bone status. Furthermore, BD women born and/or raised in the UK i.e. experiencing a different environment in utero and/or during growth and development, will have higher values of skeletal size and bone status from their mothers, and be closer to IB daughters. The figure below shows a simplified theoretical framework for the study.

![Figure 2.11 Simplified diagram showing theoretical framework used to explain a UK BD woman’s bone status](image)

The next chapter will present the results from the Cardiff study which compares height and bone status in UK BD women according to generation and birthplace.
3 Cardiff Study: Comparison of height and bone status in UK BD women according to generation and birthplace

3.1 Background

This chapter reports on the analyses of secondary data collected as part of the MINA Project, a large, cross-sectional, ERSC funded multidisciplinary project which aimed to study the effects of migration on the health and nutrition of two generations of UK BD women (Thompson et al., 2017). UK BD mother-daughter pairs, resident in Cardiff, were used to study how health and nutrition varied between the two generations, mothers and daughters. The sample comprised older women who had migrated from Bangladesh and their adult daughters, who were either UK-born or had emigrated to the UK in childhood. Mother-daughter dyads resident in Sylhet, Bangladesh were also recruited.

Many variables were collected, including anthropometric and QUS measurements at the calcaneous. As discussed in the Introduction chapter, two findings from the UK sample of BD mother-daughter pairs were of particular interest. Firstly, the mean height of UK-resident daughters was higher than the mean height of mothers (Bogin et al., 2014). Secondly, the mean height of UK resident daughters born in the UK was higher than that of daughters who had been born in Bangladesh (Bogin et al., 2014). The implication of these findings is that skeletal size is increasing in BD women who spend some, or all, of their childhood in the UK environment, especially if they were born in the UK. A change in skeletal size may affect bone status in UK resident BD women. As mentioned in the Introduction, QUS parameters are a measure of bone status. BUA is associated with BMD (Waud, Lew and Baran, 1992; Brooke-Wavell et al., 2008) and is a predictor of fracture risk (Marín et al., 2006; Moayyeri et al., 2012).

This chapter presents the results of testing the predictions that QUS measurements would be higher in BD daughters than their mothers, and higher in UK-born daughters than BD-born daughters (reflecting the taller heights of BD daughters compared to mothers and taller heights of UK-born daughters than BD-born daughters).
3.2 Methods

3.2.1 Methods used in Cardiff study (MINA project)

Methods employed in project MINA have been described previously (Bogin et al., 2014) and a short summary of these methods is provided below.

The MINA sample included a cross section of BD older women, aged 40-70 years, who had migrated from Bangladesh to the UK and their daughters, aged 17-36 years, who were either UK-born or had emigrated to the UK. A target of 40 mother-daughter pairs was set but three daughters did not attend the data collection sessions leaving 37 complete mother-daughter dyads.

The MINA research team provided expertise in public health nutrition and exercise, biological anthropology, health psychology, public health nursing, ethnobotany, environmental and media design, social gerontology and social anthropology. A considerable amount of data were generated relating to these various disciplines, including anthropometric data and bone health measurements in the form of QUS parameters, BUA and SOS. I was a research assistant on the MINA team and measured the QUS parameters as described in Chapter 4, Methods chapter (see 4.8, 4.8.5 and 4.8.6), using the same equipment as I subsequently used in the Loughborough study. The anthropometric measurements (height, knee height and weight) collected for the MINA project, followed the same protocol and used the same equipment as described in the Methods chapter (section 4.7.2) and were carried out by an experienced researcher. MINA BD research assistants completed questionnaires, covering topics such as migratory history, health status, education and general lifestyle factors, based on interviews with the study participants.

MINA researchers adopted a participatory approach, involving community members and leaders at all stages of the project. This was achieved by employing BD community members as co-researchers (two research assistants, one postdoctoral fellow) and training 11 community researchers from the Cardiff and Swansea area. These co-researchers and community researchers were fluent in Bangla and Sylheti and assisted the MINA researchers with participant recruitment, data collection, language translation, interpretation of findings
and dissemination of results. Sampling was purposive in that it depended on the contacts of the community researchers as well as the limitations of the research budget. Recruitment was through snowball sampling. All mothers were born in the Sylhet District of Bangladesh, and daughters were born in either the UK or Sylhet. All were living in or near Cardiff, Wales. Data were collected by project researchers, via community events which, in addition to the measurement and interview session, included lunch, physical activities, massage and stations providing information on health and social care services. These community events took place in Cardiff in November 2009, March 2010 and June 2010.

The MINA project was not designed to specifically study bone status in the participants, so data were not collected on diseases or medication that might have affected bone metabolism. However, each participant was asked if she suffered any other illnesses or conditions, in addition to the specific ones mentioned in the questionnaire (cancer, hypertension, stroke, diabetes, angina and heart attack). No participant mentioned thyroid problems, osteoporosis or any other condition that might have affected bone metabolism.

3.2.2 Data analysis and statistics

Statistics (means and standard deviations or medians and ranges, depending on distribution of the variable) were generated from the total sample for the following descriptive variables:

1. Migration - year and age at migration plus number of years resident in the UK
2. Reproduction - age at marriage, birth of first child and number of children, recalled age at menarche
3. Education - lack of formal education and age at which education finished
4. Health - suffering from a self-reported longstanding illness, disability or infirmity, where longstanding means anything that has troubled the participant over a period of time or that is likely to affect them over a period of time, illnesses for which the participant was taking medication.

Statistics (means and standard deviations or counts) were collected for the following variables:

5. Anthropometry - height, knee height and weight, short-stature, defined as < 150 cm
6. Bone status - QUS measurements - raw and Z-scores (i.e. scores normalised for age) for BUA and SOS at the calcaneus.

**Correlation between mother and daughter**

Pearson’s correlation coefficients between mother and daughter were calculated for anthropometric and QUS measurements to indicate how much the daughter’s measurement was related to the mother’s measurement.

**Testing normality for independent and paired t-tests**

The independent t-test assumes the observations within each group are normally distributed and the variances are equal, whereas the paired t-test assumes it is the differences between pairs that are normally distributed. Normality was tested using the Shapiro-Wilk test and if the assumption of normality was violated then the equivalent non-parametric test was used (Mann-Whitney U test instead of independent t-test and Wilcoxon signed-rank test instead of the paired t-test). When running an independent t-test, Levene’s test for equal variance was used and if variances were unequal, the probability for unequal variances was reported.

**Comparison of mothers and daughters**

As mothers and daughters are related, the paired t-test was used to compare mothers with daughters for variables with continuous data. Occasionally the paired t-test was not appropriate, for example for variables such as “age at migration” when some mothers did not have a value for their UK-born daughters, in which case an independent t-test was used. Unless otherwise stated, all t-tests were two-tailed, with statistical significance set at p value of < 0.05. If assumptions of normality were not met then the appropriate non-parametric test was used as described above. A chi-squared test was employed for discrete, non-normally distributed data.

**Comparison of daughters, based on daughter’s birthplace and migratory status**

Comparisons of height, knee height and QUS measurements between daughters, depending on daughter’s birthplace (Bangladesh or the UK) were also made. Further comparisons were then made on the sub-group of mother-daughter pairs, where only BD-born daughters and their mothers were analysed. These latter comparisons were based on whether the
daughter was an “early migrator”, defined as being less than eight years old at the time of migration, or a “late migrator”, defined as being aged eight years or older at time of migration. The cut-off point of eight years was chosen, as it is generally the point at which an endocrine event called adrenarche occurs. Adrenarche refers to the maturation of the zona reticularis of the adrenal gland and the subsequent production of dehydroepiandrosterone (DHEA). Adrenarche is associated with a change from moderate height growth velocity of childhood to the slower growth velocity of the juvenile phase (Bogin, 1999; Campbell, 2011). These two groups would therefore differ in their exposure to the UK environment at the most significant period of their bone growth. The statistical tests described above were used to explore how daughter’s anthropometric and QUS measurements varied according to the daughter’s status as either an early or a late migrator. However the small sample numbers involved caused the statistical tests to be underpowered (Table 3.1) so effect sizes of differences are reported.

A comparison of knee height between early migrator daughters, late migrator daughters and daughters born in the UK was made using ANOVA with Tukey post-hoc tests.

**Power calculations**

My analysis of the MINA data was *post hoc*, so power calculations were carried out to establish the likely accuracy of the statistical tests employed on the various data sets. Power calculations were made using G*Power version 3.1.3 ([http://www.gpower.hhu.de/](http://www.gpower.hhu.de/)). (Faul *et al.*, 2007). The basis behind the power calculation was that an independent two tailed t-test was used with level of significance, $P = 0.05$ ($\alpha = 0.05$) and a large effect size (Cohen’s $d = 0.8$). The powers of statistical tests, according to the sample sizes used, are presented below (Table 3.1).
Table 3.1 Power calculations for main comparisons using t-tests

Three comparisons were made (mother vs. daughter, UK vs. BD birthplace of daughter and early vs. late migration status of daughter) using independent two tailed t-test and large effect size (Cohen’s d = 0.8)

<table>
<thead>
<tr>
<th>Sample Numbers for different comparisons</th>
<th>Generation (Mother vs. daughter)</th>
<th>Daughter’s Birthplace (BD vs. UK)</th>
<th>Daughter’s migratory status (early vs. late)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=36 and N=36</td>
<td>100%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>64%</td>
<td>33%</td>
</tr>
</tbody>
</table>

<sup>a</sup> If effect size set to moderate (Cohen’s d = 0.4) then power is 64%  

### 3.3 Results

#### 3.3.1 Sample Number and missing data

The final sample number used in my analysis was 36 mother-daughter pairs. For QUS Z score analyses, 33 mother-daughter pairs were used. The reasons for exclusion of some of the MINA participants were:

1. As total bone mass increases with age until peak bone mass is achieved bone measurements of very young women may be lower than the rest of the daughter sample. Therefore, as one daughter was 17 years old, this Cardiff mother-daughter pair was excluded from the original data set of 37 pairs, leaving a sample of 36 mother-daughter pairs.

2. Three Cardiff mothers had their age estimated, so their Z scores were not used. This left a sample of 33 mother-daughter pairs for QUS Z score analyses.

Menopausal status was missing for one 50-year-old mother so she was classified as post-menopausal, as the average age at menopause in BD women has been reported as 45 years, compared to an average age of menopause for European women of 50 years (Murphy et al., 2013).

The sample used for the secondary analysis was kept as close as possible to that used in the publication (Bogin et al., 2014) for consistency. However, two daughters had migrated over
the age of 18 which meant they had not been exposed to the UK environment during their years of growth and development. As the results of my analyses were interpreted in view of the different environmental exposure (Bangladesh or UK) during birth, growth and development, the analyses were repeated omitting these two daughters. The main comparisons exploring generational differences in height, knee height and QUS parameters were re-run, without these two mother-daughter pairs with the same outcomes. The comparisons involving daughter’s birthplace were also re-run without these two daughters, again with the same outcomes.

3.3.2 General description of sample

All 36 mothers were born in Bangladesh, emigrating to the UK at a median age of 28.5 years, whereas about half (47%) of the daughters had been born in Bangladesh and emigrated to the UK, generally with their mothers, at a median age of eight years (Table 3.3). The 1980s was the decade of most migration (Table 3.3). All women born in Bangladesh i.e. all mothers and 47% daughters, came from the Sylhet region. All daughters were pre-menopausal and the majority (78%) of mothers were post-menopausal (Table 3.3).

3.3.3 Correlation of mother and daughter’s experimental variable measurements

Anthropometric variables, height, knee height and weight were significantly correlated between mother and daughter (Table 3.2). Regarding QUS measurements, there was a significant correlation between mother and daughter for SOS, but not BUA. This demonstrates that variance of BD pre-menopausal women’s measurements of height, knee height and SOS were partially accounted for by their mother’s measurements.
Table 3.2 Correlation coefficients between Cardiff BD mothers and daughters for height, knee height, weight and QUS measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Correlation coefficient (r) for mother-daughter pairs N=36</th>
<th>Variance of daughter’s measurement predicted by mother’s measurement (R^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>0.665 (p&lt;0.001)***</td>
<td>0.44</td>
</tr>
<tr>
<td>Knee Height (cm)</td>
<td>0.498 (p=0.002)***</td>
<td>0.25</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.383 (p=0.023)b*</td>
<td>0.05</td>
</tr>
<tr>
<td>BUA Raw Score (dB MHz^-1)</td>
<td>0.080 (p=0.641)</td>
<td>0.01</td>
</tr>
<tr>
<td>SOS Raw Score (m s^-1)</td>
<td>0.522 (p=0.001)***</td>
<td>0.27</td>
</tr>
<tr>
<td>BUA Z score&quot;</td>
<td>0.274 (p=0.123)</td>
<td>0.08</td>
</tr>
<tr>
<td>SOS Z score&quot;</td>
<td>0.456 (p=0.008)**</td>
<td>0.21</td>
</tr>
</tbody>
</table>

*p <= .05, **p <= .01, ***p <= .001 level of significance
'n=35 for (1 daughter missing weight value)
"n=33 (3 mothers estimated age so no Z scores available)

3.3.4 Comparisons of mothers and daughters

The range of ages at migration for the mothers was large, with the youngest age at migration being 23 years and the oldest age being 55 years (Table 3.3). For daughters born in Bangladesh (n=17), ages at migration ranged from 0 to 23 years. The median year of migration for all mothers was 1982 and for BD-born daughters it was 1988 (Table 3.3). More details about migration follow in later sub-sections.

Mothers married significantly earlier (16.2±2.8 years) compared to daughters who married on average a couple of years later at a mean age of just under 19 years (18.7±2.3 years), based on a Mann-Whitney U test (p = 0.002) (Table 3.3). Statistical comparisons on marriage need to be treated with caution, due to the exclusion of 12 daughters who were unmarried. Although mothers married earlier than married daughters, the mean age at birth of first child was similar for both mothers and married daughters i.e. about 21 years of age (Table 3.3). Two mothers had their first child at 13 years old and one mother had her
first child when she was 15 years old. Apart from these three exceptions, the rest of the mothers and all daughters had their first child at age 17 years or older.

Regarding educational attainment, mothers clearly had a poorer education compared to their daughters. Twelve (33%) mothers had had no formal education at all, whereas all daughters had received formal education (Table 3.3). The mothers that did undergo formal education, finished their education on average about four years earlier than their daughters (Table 3.3). One daughter was an outlier in that she finished her education at age 30 years. However, omitting this value from the comparisons reported in Table 3.3 did not change any of the outcomes.

A higher proportion of mothers (78%) had a longstanding illness compared to daughters (25%): age would have been a major factor contributing to poor health in the mothers (Table 3.3).

Regarding anthropometric measurements, it was found that daughters were significantly taller than their mothers by about 4% based on a paired t-test (t=7.04, df=35, p < 0.001) (Table 3.3). Average knee height in daughters was also significantly greater by about 3% than their mothers based on a paired t-test (t=4.01, df=35, p < 0.001) (Figure 3.1 and Table 3.3). Average weight was similar for mothers and daughters, being around 65-66 kg. However, the mean BMI value in daughters was significantly lower than their mothers based on a paired t-test (t=2.25, df=34, p=0.031), due to the daughters being significantly taller than their mothers (Table 3.3).

Regarding QUS measurements, BUA Z scores and SOS Z scores were not different between mothers and daughters (Figure 3.2 and Table 3.3), suggesting that the significant differences in QUS raw scores between mothers and daughters were explained by age and mother’s menopausal status.

Two mothers and two daughters had low SOS measurements but average BUA measurements, and one mother had a high SOS measurement but an average BUA measurement. There was no reason to drop these women though it was noticed that four out of the five were obese. Reanalysis of QUS data, after omitting these five women, did not affect the outcome.
It was noted that BUA Z score was less than zero for both mothers and daughters, suggesting that BUA raw score in Bangladeshi women was not as high as the age-matched manufacturer’s European reference population. In contrast, SOS Z score was close to zero suggesting that SOS raw score in Bangladeshi women was similar to the aged-matched manufacturer’s European reference population.
Table 3.3 Comparisons of Cardiff mothers with daughters (n=36 pairs)

Mean values ± standard deviations, medians (ranges) or numbers (percentages)
All values are as measured with no statistical adjustment for age difference.

<table>
<thead>
<tr>
<th></th>
<th>BD Mothers (n=36)</th>
<th>BD Daughters (n=36)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.0 ± 7.4</td>
<td>27.7 ± 5.3</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td></td>
<td>56.5 (40 to 69)</td>
<td>27.0 (20 to 30)</td>
<td></td>
</tr>
<tr>
<td>Year of birth</td>
<td>1952.8 ± 7.8</td>
<td>1981.7 ± 5.2</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>No. pre-menopausal (%)</td>
<td>8 (22%)</td>
<td>36 (100%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>No. born in BD (%)</td>
<td>36 (100%)</td>
<td>17 (47%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Age at migration a</td>
<td>30.7 ± 9.4</td>
<td>8.2 ± 6.8</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td></td>
<td>28.5 (18 to 55)</td>
<td>8.0 (0 to 23)</td>
<td></td>
</tr>
<tr>
<td>Year of migration a</td>
<td>1983.9 ± 8.5</td>
<td>1989.7 ± 7.3</td>
<td>0.007**</td>
</tr>
<tr>
<td>Years resident in UK a</td>
<td>25.3 ± 8.6</td>
<td>19.8 ± 7.3</td>
<td>0.012*</td>
</tr>
<tr>
<td></td>
<td>27.0 (4 to 39)</td>
<td>21.0 (4 to 30)</td>
<td></td>
</tr>
<tr>
<td>Age at marriage b</td>
<td>16.2 ± 2.8</td>
<td>18.72 ± 2.3</td>
<td>0.002**</td>
</tr>
<tr>
<td>Number of children b</td>
<td>6 (2 to 10)</td>
<td>2 (0 to 4)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Age at birth of 1st child c</td>
<td>20.8 ± 4.3</td>
<td>21.3 ± 2.2</td>
<td>0.290</td>
</tr>
<tr>
<td></td>
<td>20 (13 – 29)</td>
<td>21 (17 -25)</td>
<td></td>
</tr>
<tr>
<td>Age finished education d</td>
<td>13.6 ± 2.7</td>
<td>18.0 ± 2.9</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td></td>
<td>13 (8 to 20)</td>
<td>18 (14 to 31)</td>
<td></td>
</tr>
<tr>
<td>Number lacking formal education</td>
<td>12 (33%)</td>
<td>0 (0%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Number with longstanding illness</td>
<td>28 (78%)</td>
<td>9 (25%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Number (%) of short-stature (&lt;= 150 cm)</td>
<td>23 (64%)</td>
<td>9 (25%)</td>
<td>0.001***</td>
</tr>
<tr>
<td>Weight (kg) e</td>
<td>65.6 ± 13.7</td>
<td>65.0 ± 14.5</td>
<td>0.794</td>
</tr>
<tr>
<td></td>
<td>64.4 (41 to 100)</td>
<td>61.6 (42 to 107)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²) f</td>
<td>30.1 ± 5.2</td>
<td>27.6 ± 5.7</td>
<td>0.794</td>
</tr>
<tr>
<td></td>
<td>29.0 (22 to 44)</td>
<td>27.4 (20 to 43)</td>
<td></td>
</tr>
<tr>
<td>Experimental Variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>147.4 ± 6.3</td>
<td>153.2 ± 5.8</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Knee Height (cm)</td>
<td>45.3 ± 2.5</td>
<td>46.7 ± 2.4</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td></td>
<td>45.9 (40 to 49)</td>
<td>47.3 (40 to 51)</td>
<td></td>
</tr>
<tr>
<td>BUA Raw Score (dB MHz⁻¹)</td>
<td>42.4 ± 7.4</td>
<td>46.5 ± 6.8</td>
<td>0.017*</td>
</tr>
<tr>
<td>SOS Raw Score (m s⁻¹)</td>
<td>1549 ± 13</td>
<td>1558 ± 11</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td></td>
<td>1553 (1508 to 1582)</td>
<td>1559 (1529 to 1591)</td>
<td></td>
</tr>
<tr>
<td>BUA Z score f</td>
<td>-0.69 ± 0.78</td>
<td>-0.76 ± 1.05</td>
<td>0.469</td>
</tr>
<tr>
<td>SOS Z score f</td>
<td>0.30 ± 1.27</td>
<td>0.29 ± 1.07</td>
<td>0.136</td>
</tr>
<tr>
<td></td>
<td>0.51 (-3.37 to 2.92)</td>
<td>0.28 (-2.53 to 3.46)</td>
<td></td>
</tr>
</tbody>
</table>

*p <= .05, **p <= .01, ***p <= .001 sig difference between mothers and daughters (see appendix I for tests used)

a n=36 for mothers (all born in Bangladesh) and n=17 for daughters (born in Bangladesh)
b n=24 for daughters (12 not married)
c n=32 for mothers (4 missing values) n=20 for daughters (who had children)
Figure 3.1 Bar charts showing height and knee height as means and st.dev. for Cardiff BD mothers and daughters

*"p<0.05, ***"p<0.001 sig difference between mothers and daughters using paired t-test
Figure 3.2 Bar charts showing BUA and SOS (raw and Z scores) as means and st.dev for Cardiff BD mothers and daughters.

* p <= .05, ** p <= .01 sig difference between mothers and daughters using t-test
### 3.3.5 Comparisons based on birthplace of daughters

The median year of migration for daughters born in Bangladesh (n=17) was 1988 (Table 3.4) and the median age of their mothers was the same i.e. 1988, which is consistent with both mother and daughter emigrating to the UK together. However, five mother-daughter pairs did not migrate to the UK at the same time. Three daughters migrated before their mothers, and two daughters were reported as having migrated after their mothers. The mother of one of these latter daughters was reported to have migrated to the UK in 1971, aged 30, but her daughter was born in Bangladesh in 1986 and came over to the UK in 1988, aged two years. Presumably, the mother returned to Bangladesh to have her child and brought her back two years after her birth. In this case, although the daughter was born in Bangladesh, her mother had experienced fifteen years in the UK prior to giving birth to the daughter. Apart from this one exception, all the mothers of daughters born in Bangladesh had lived in Bangladesh prior to the birth.

The daughters, irrespective of birthplace (UK or Bangladesh), were similar in terms of age (and therefore year of birth), education, number of longstanding illnesses and birth order (Table 3.4). The only significant differences associated with daughter’s birthplace were height and knee height (Figure 3.3 and Table 3.4). UK-born daughters were significantly taller with a height of 155.2±4.8 cms compared to 151.0±6.1 cms for BD-born daughters (t=2.30, df=34, p=0.028) with a moderate effect size (Cohen’s d = 0.77). This was consistent with a higher proportion (47%) of short-BD-born daughters compared to UK-born daughters (5%) (Table 3.4). The difference was more marked in a mean knee height which was greater (47.8±1.6 cm) in UK-born daughters than BD-born daughters (45.6±2.7 cm), with a large effect size (Cohen’s d = 0.99) and greater statistically significance (t=3.10, df=34, p=0.004). Weight was higher, though not significantly so, in UK-born daughters compared to BD-born daughters (Table 3.4). The higher height, as well as weight, in UK-born daughters resulted in a similar BMI value for both sets of daughters (Table 3.4).

There were no differences in QUS measurements, BUA and SOS (raw and Z scores), between the two sets of daughters (Table 3.4) although this cannot be considered reliable as the tests were under-powered due to low sample numbers (estimated power was 64% to pick up a large effect size, see Table 3.1).
Similar statistical comparisons were carried out on mothers, based on daughter’s birthplace, to explore whether familial influences could explain the differences in height and knee height found between the two sets of daughters (Table 3.4). Both sets of mothers (differentiated by daughter’s birthplace) on average were born in the early 1950s, reporting a mean age of 56 years old at time of data collection (Table 3.4). Mothers of UK-born daughters migrated in the 1970s and early 1980s, at a mean age close to 25 years old, whereas mothers of daughters born in Bangladesh tended to migrate, on average, ten years later, in the 1980s and 1990s, at a mean age of 36 years old (Table 3.4). Apart from different years of migration and age at migration, the mothers, irrespective of daughter’s birthplace, were very similar in terms of: age, menopausal status, age at birth of daughter in study, number of children and number of self-reported long-standing illnesses (Table 3.4). One difference found between mothers was that mothers of BD-born daughters had a higher percentage (53%) lacking formal education compared to mothers of UK-born daughters (16%) (Table 3.4).

Regarding anthropometric measurements (Table 3.4), mothers of UK-born daughters had higher, though not significantly so, values for height and knee height than mothers of BD-born daughters (Figure 3.3). It was noted that a higher percentage of mothers of BD-born daughters (84%) were of short stature compared to percentage of short-statured mothers of UK-born daughters (47%) (Table 3.4).

QUS measurements in mothers did not differ according to daughter’s birthplace, which was the same outcome found for daughters i.e. no differences in QUS measurements according to daughter’s birthplace (Table 3.4).
Figure 3.3 Bar charts showing height and knee height in Cardiff BD mothers and daughters, according to daughter’s birthplace.
### Table 3.4 Descriptive data for Cardiff daughters and their mothers, according to daughter’s birthplace

Mean ± standard deviations, medians (ranges) or numbers (percentages). Short stature defined as height <= 150 cm. Birth order defined as number of older siblings + 1

<table>
<thead>
<tr>
<th></th>
<th>UK-born Daughters (n=19)</th>
<th>BD-born Daughters (n=17)</th>
<th>P value</th>
<th>Mothers of UK-born daughters (n=19)</th>
<th>Mothers of BD-born daughters (n=17)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27.4 ± 5.2 (20 to 36)</td>
<td>27.9 ± 5.4 (20 to 36)</td>
<td>0.754</td>
<td>55.7 ± 7.5 (156 to 75)</td>
<td>56.3 ± 7.6 (156 to 75)</td>
<td>0.826</td>
</tr>
<tr>
<td>Year of birth</td>
<td>1982.0 ± 5.1 (1973 to 1989)</td>
<td>1981.5 ± 5.5 (1973 to 1990)</td>
<td>0.754</td>
<td>1952.7 ± 8.1 (1936 to 1966)</td>
<td>1952.8 ± 7.7 (1941 to 1969)</td>
<td>0.826</td>
</tr>
<tr>
<td>Number of pre-menopausal (%)</td>
<td>19 (100%)</td>
<td>17 (100%)</td>
<td>-</td>
<td>5 (26%)</td>
<td>3 (18%)</td>
<td>0.695</td>
</tr>
<tr>
<td>Age at migration</td>
<td>Not applicable</td>
<td>8.2 ± 6.8 (0 to 23)</td>
<td>-</td>
<td>25.7 ± 6.0 (18 to 42)</td>
<td>36.1 ± 9.6 (20 to 55)</td>
<td>&lt;0.001 ***</td>
</tr>
<tr>
<td>Year of migration</td>
<td>Not applicable</td>
<td>1990 ± 7.3 (1980 to 2006)</td>
<td>-</td>
<td>1979.3 ± 4.8 (1971 to 1987)</td>
<td>1989.2 ± 8.7 (1971 to 2005)</td>
<td>&lt;0.001 ***</td>
</tr>
<tr>
<td>Years resident in UK</td>
<td>Not applicable</td>
<td>19.8 ± 7.3</td>
<td>-</td>
<td>30.0 ± 5.0</td>
<td>20.12 ± 8.8</td>
<td>&lt;0.001 ***</td>
</tr>
<tr>
<td>Age finished education</td>
<td>17.7 ± 2.1 (14 to 24)</td>
<td>18.3 ± 3.7 (15 to 31)</td>
<td>0.925</td>
<td>13.9 ± 2.9 (8 to 20)</td>
<td>13.1 ± 2.4 (8 to 20)</td>
<td>0.417</td>
</tr>
<tr>
<td>No. (%) lacking formal education</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>-</td>
<td>3 (16%)</td>
<td>9 (53%)</td>
<td>0.033*</td>
</tr>
<tr>
<td>Birth order of daughter</td>
<td>3.8 ± 2.0</td>
<td>3.2 ± 1.6</td>
<td>0.318</td>
<td>See daughter</td>
<td>See daughter</td>
<td>-</td>
</tr>
<tr>
<td>Mother’s age at birth of daughter</td>
<td>28.32 ± 6.5</td>
<td>28.35 ± 8.2</td>
<td>0.988</td>
<td>See daughter</td>
<td>See daughter</td>
<td>-</td>
</tr>
<tr>
<td>Number (%) of short-stature</td>
<td>1 (5%)</td>
<td>8 (47%)</td>
<td>0.006**</td>
<td>9 (47%)</td>
<td>14 (82%)</td>
<td>0.029*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.6 ± 14.3 (14.5)</td>
<td>61.9 ± 14.5 (14.5)</td>
<td>0.243</td>
<td>67.8 ± 16.0 (16.5)</td>
<td>63.1 ± 10.4 (10.4)</td>
<td>0.307</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.0 ± 5.6</td>
<td>27.1 ± 6.0</td>
<td>0.385</td>
<td>30.2 ± 5.4</td>
<td>29.9 ± 5.1</td>
<td>0.867</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155.2 ± 4.8</td>
<td>151.0 ± 6.1</td>
<td>0.028*</td>
<td>149.1 ± 6.6</td>
<td>145.4 ± 5.6</td>
<td>0.082</td>
</tr>
<tr>
<td>Knee Height (cm)</td>
<td>47.8 ± 1.6</td>
<td>45.6 ± 2.7</td>
<td>0.004**</td>
<td>45.9 ± 2.3</td>
<td>44.7 ± 2.6</td>
<td>0.149</td>
</tr>
<tr>
<td>BUA Raw Score (dB MHz⁻¹)</td>
<td>46.0 ± 6.6</td>
<td>47.0 ± 7.3</td>
<td>0.664</td>
<td>42.8 ± 7.3</td>
<td>41.9 ± 7.8</td>
<td>0.728</td>
</tr>
<tr>
<td>SOS Raw Score (m s⁻¹)</td>
<td>1559 ± 12</td>
<td>1558 ± 10</td>
<td>0.731</td>
<td>1547 ± 15</td>
<td>1551 ± 10</td>
<td>0.925</td>
</tr>
<tr>
<td>BUA Z score</td>
<td>-0.83 ± 1.0</td>
<td>-0.67 ± 1.1</td>
<td>0.667</td>
<td>-0.71 ± 0.82</td>
<td>-0.66 ± 0.76</td>
<td>0.866</td>
</tr>
<tr>
<td>SOS Z score</td>
<td>0.28 ± 1.16</td>
<td>0.29 ± 1.00</td>
<td>0.510</td>
<td>0.30 ± 1.27</td>
<td>0.29 ± 1.07</td>
<td>0.817</td>
</tr>
</tbody>
</table>

*p <= .05, **p <= .01, ***p <= .001 level of significance (see appendix I for tests used)

a n =16 for mothers of daughters born in UK, n=8 for mothers of daughters born in Bangladesh (women who had received formal education)
b n =16 for daughters born in Bangladesh (1 missing value)
c n =17 for mothers of UK-born daughters, n=16 for mothers of BD-born daughters (3 mothers had estimated age, so no Z scores)
3.3.6 Comparisons based on migratory age of daughters

When migratory status was taken into account, the difference in mean knee height of UK-born and BD-born daughters was most marked between UK-born daughters and early migrator BD-born daughters (migrating at age < 8 years old) (Figure 3.4).

Of the 17 daughters who were born in Bangladesh, eight were early migrators (migrating at age less than eight years) and nine were late migrators (migrating at age eight years or older). Mother-daughter pairs, in which the daughter was an early migrator, tended to migrate earlier, mainly in the 1980’s whereas mother-daughter pairs, in which the daughter was a late migrator, migrated several years later, mainly in the 1990’s (Table 3.5).

Age, education, number of longstanding illness, birth order, anthropometric measurements, including knee height (Figure 3.4), and QUS measurements, in the daughter samples did not differ according to daughter’s migratory status, early or late (Table 3.5).

The same outcome was observed in the mother samples. For all variables, including knee height (Figure 3.4), there were no significant differences found between mothers, according to their daughter’s migratory status (Table 3.5).
Figure 3.4 Bar charts showing knee height in Cardiff BD mothers and daughters, according to daughter’s birthplace and migratory status.

Migratory status = UK-born, early migration age < 8 years or late migration age >= 8 years.

*p < 0.05 from ANOVA, Tukey post-hoc test, showing UK-born daughters had significantly greater knee height than BD-born daughters who migrated early (< 8 years old).
### Table 3.5 Descriptive data for Cardiff BD-born daughters and their mothers, according to daughter’s migratory status

Mean values ± standard deviations or medians, (ranges) or numbers (percentages).

Early migrator (migrated to the UK at age < 8 years) or late migrator (migrated to the UK at age >= 8 years). Birth order defined as number of older siblings +1

<table>
<thead>
<tr>
<th></th>
<th>Early Migrator Daughters (n=8)</th>
<th>Late Migrator Daughters (n=9)</th>
<th>P value</th>
<th>Mothers of early Migrator Daughters (n=8)</th>
<th>Mothers of late Migrator Daughters (n=9)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.3 ± 5.6</td>
<td>29.4 ± 5.1</td>
<td>0.277</td>
<td>56.8 ± 9.7</td>
<td>55.9 ± 5.7</td>
<td>0.824</td>
</tr>
<tr>
<td>Year of birth</td>
<td>1983.3 ± 5.4</td>
<td>1979.9 ± 5.4</td>
<td>0.277</td>
<td>1952.3 ± 9.8</td>
<td>1952.3 ± 5.9</td>
<td>0.824</td>
</tr>
<tr>
<td>No. Pre-menopausal (%)</td>
<td>8 (100%)</td>
<td>9 (100%)</td>
<td></td>
<td>2 (25%)</td>
<td>1 (11%)</td>
<td>0.576</td>
</tr>
<tr>
<td>Age at migration (years)</td>
<td>1.63 ± 2.0</td>
<td>13.11 ± 5.6</td>
<td>&lt;0.001 ***</td>
<td>31.6 ± 9.7</td>
<td>40.2 ± 8.0</td>
<td>0.046 *</td>
</tr>
<tr>
<td>Year of migration</td>
<td>1985.9 ± 4.0</td>
<td>1993 ± 8.1</td>
<td>0.114</td>
<td>1984.4 ± 7.3</td>
<td>1993.4 ± 7.9</td>
<td>0.059</td>
</tr>
<tr>
<td>Years resident in UK</td>
<td>22 (19 to 30)</td>
<td>21 (4 to 25)</td>
<td>0.114</td>
<td>25.1 ± 7.3</td>
<td>15.7 ± 7.8</td>
<td>0.059</td>
</tr>
<tr>
<td>Number lacking formal education</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
<td>3.0 (16%)</td>
<td>6.5 (53%)</td>
<td>0.347</td>
</tr>
<tr>
<td>Age finished education</td>
<td>17.9 ± 2.0</td>
<td>18.7 ± 4.8</td>
<td>0.888</td>
<td>13.2 ± 2.6</td>
<td>13.0 ± 2.6</td>
<td>1.000</td>
</tr>
<tr>
<td>Number with longstanding illness</td>
<td>3 (38%)</td>
<td>3 (33%)</td>
<td>1.000</td>
<td>7 (88%)</td>
<td>6 (67%)</td>
<td>0.312</td>
</tr>
<tr>
<td>Birth Order of daughter</td>
<td>3.4 ± 1.8 (1 to 6)</td>
<td>3.1 ± 0.5 (1 to 5)</td>
<td>0.746</td>
<td>See daughter</td>
<td>See daughter</td>
<td></td>
</tr>
<tr>
<td>Age of mother at birth of daughter</td>
<td>30.5 ± 10.5</td>
<td>26.4 ± 5.4</td>
<td>0.673</td>
<td>See daughter</td>
<td>See daughter</td>
<td></td>
</tr>
<tr>
<td>Number (%) of short-stature (&lt; 150 cm)</td>
<td>4 (50%)</td>
<td>4 (44%)</td>
<td>1.000</td>
<td>7 (88%)</td>
<td>7 (78%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>61.7 ± 17.5</td>
<td>62.0 ± 12.9</td>
<td>0.956</td>
<td>65.9 ± 13.1</td>
<td>60.6 ± 7.1</td>
<td>0.310</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.9 ± 7.1</td>
<td>26.4 ± 5.4</td>
<td>0.639</td>
<td>31.8 ± 5.4</td>
<td>28.1 ± 5.1</td>
<td>0.146</td>
</tr>
<tr>
<td>Knee Height (cm)</td>
<td>45.0 ± 3.2</td>
<td>46.1 ± 2.2</td>
<td>0.442</td>
<td>44.2 ± 2.7</td>
<td>45.1 ± 2.6</td>
<td>0.505</td>
</tr>
<tr>
<td>Number (%) of short-stature (&lt; 150 cm)</td>
<td>4 (50%)</td>
<td>4 (44%)</td>
<td>1.000</td>
<td>7 (88%)</td>
<td>7 (78%)</td>
<td>1.000</td>
</tr>
<tr>
<td>BUA Raw Score (dB MHz⁻¹)</td>
<td>47.1 ± 6.2</td>
<td>46.9 ± 8.5</td>
<td>0.944</td>
<td>42.9 ± 7.9</td>
<td>41.1 ± 8.2</td>
<td>0.658</td>
</tr>
<tr>
<td>SOS Raw Score (m s⁻¹)</td>
<td>1560 ± 8</td>
<td>1556 ± 11</td>
<td>0.321</td>
<td>1548 ± 7</td>
<td>1554 ± 12</td>
<td>0.233</td>
</tr>
<tr>
<td>BUA Z score</td>
<td>-0.65 ± 0.94</td>
<td>-0.70 ± 1.32</td>
<td>0.925</td>
<td>-0.39 ± 0.68</td>
<td>-0.87 ± 0.80</td>
<td>0.223</td>
</tr>
<tr>
<td>SOS Z score</td>
<td>0.49 ± 0.84</td>
<td>0.12 ± 1.14</td>
<td>0.481</td>
<td>0.31 ± 0.67</td>
<td>0.76 ± 1.07</td>
<td>0.349</td>
</tr>
</tbody>
</table>

*p <= .05, **p <= .01, ***p <= .001 level of significance (see appendix I for tests used)  
daughter in study  
n=5 for mothers of early migrator daughters and n=3 for mothers of late migrator daughters (women who had received formal education)  
n=7 for early migrator daughters and mothers (1 daughter missing value for weight)  
n=7 for early migrator daughters and mothers (1 mother missing Z score because her age was estimated
3.3.7 Knee height and height differences in mother-daughter pairs according to daughter’s birthplace and migratory status

As reported earlier, mothers of BD-born daughters were more likely to be classified as being of short stature and receiving no formal education, compared to mothers of UK-born daughters. Short stature and lacking formal education are both markers of low SES. This could imply that UK-born daughters’ larger mean knee height than BD-born daughters was due to a better familial environment for UK-born daughters rather than birthplace per se. Figure 3.5 illustrates that most of the UK-born daughters increase their knee height compared to their mothers, whereas fewer BD-born daughters increased their knee height compared to their mothers.

To explore the influences on knee height further, daughter’s knee height was compared with her mother’s knee height depending on daughter’s migratory status (UK-born, BD-born-early-migrator and BD-born-late-migrator). The results, in terms of effect size and p values from paired t-test are shown below (Table 3.6 and Table 3.7) and demonstrate that UK-born daughters had a significantly greater knee height than their mothers, whereas BD-born daughters, irrespective of whether they were early or late migrants, also had a greater, but not significantly so, knee height than their mothers. When the same analysis was repeated for height, it was found that daughters, irrespective of birthplace or migratory status, had a significant increase in mean height compared to their mothers (Table 3.7).
Figure 3.5 Scatter graph showing individual knee heights of Cardiff BD mothers and daughters, according to daughter’s migratory status

Migratory status = UK-born, early migration age < 8 years or late migration age >= 8 years
### Table 3.6 Knee height differences between Cardiff BD mother and daughter, according to daughter’s migratory status

Mean values ± standard deviations, p values and effect sizes reported

<table>
<thead>
<tr>
<th></th>
<th>Early Migrator daughter (n=8)</th>
<th>Late Migrator daughter (n=9)</th>
<th>UK-born daughter (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mother</td>
<td>Daughter</td>
<td>Mother</td>
</tr>
<tr>
<td>Knee Height (cm)</td>
<td>44.2 ± 2.7</td>
<td>45.0 ± 3.2</td>
<td>45.1 ± 2.6</td>
</tr>
<tr>
<td>Knee height difference t-test outcome</td>
<td>t=1.05 (df=7)</td>
<td>p=0.330</td>
<td>t=1.15 (df=8)</td>
</tr>
<tr>
<td>Statistical Power</td>
<td>56%</td>
<td>50%</td>
<td>91%</td>
</tr>
<tr>
<td>Knee height difference effect size (Cohen’s d)</td>
<td>0.27</td>
<td>0.42</td>
<td>0.96</td>
</tr>
</tbody>
</table>

***p <=0.001 sig. difference between mothers and daughters using paired t-test
Effect size (Cohen’s d) refers to knee height difference between mothers and daughters

### Table 3.7 Height differences between Cardiff BD mother and daughter, according to daughter’s migratory status

Mean values ± standard deviations, p values and effect sizes reported

<table>
<thead>
<tr>
<th></th>
<th>Early Migrator daughter (n=8)</th>
<th>Late Migrator daughter (n=9)</th>
<th>UK-born daughter (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mother</td>
<td>Daughter</td>
<td>Mother</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>143.9 ± 5.4</td>
<td>148.6 ± 6.4</td>
<td>146.7 ± 5.7</td>
</tr>
<tr>
<td>Height difference t-test outcome</td>
<td>t=2.83 (df=7)</td>
<td>p=0.026*</td>
<td>t=6.71 (df=8)</td>
</tr>
<tr>
<td>Height difference effect size (Cohen’s d)</td>
<td>0.79</td>
<td>1.18</td>
<td>1.08</td>
</tr>
</tbody>
</table>

*p <=0.05, ***p <=0.001 sig. difference between mothers and daughters using paired t-test
Effect size (Cohen’s d) refers to height difference between mothers and daughters
3.4 Discussion

3.4.1 Summary of main findings

Height and knee height were significantly greater in BD daughters than BD mothers, especially for UK-born BD daughters. UK-born BD daughters also had significantly greater height and knee height than BD-born daughters. These findings have already been published (Bogin et al., 2014) and provided the stimulus for my study. The lack of significant differences in QUS measurements between mothers vs daughters (after accounting for age and menopausal status by using Z scores) has not been reported before. There were also no significant differences in QUS measurements between UK-born daughters vs BD-born BD daughters.

My study's prediction that greater height and knee height would be paralleled by higher QUS measurements in daughters, compared to their mothers, was rejected. My study’s prediction that QUS measurements in daughters would be higher in UK-born daughters compared to BD-born daughters was also rejected.

3.4.2 Generational differences in height, knee height and QUS measurements

Daughters were significantly taller with greater knee height than mothers. The effect size was large (Cohen’s d = 0.96) for the generational difference in height, and moderate (Cohen’s d = 0.57) for the generational difference in knee height. The greater effect size in height perhaps reflects generational differences i.e. trends over time, as well as differences in early life environment. The lower effect size in knee height may be because in about half the sample, a similar early life environment in Bangladesh at birth was experienced by both mother and BD-born daughter, (47% of the total BD sample),so it would be expected that knee height might not be so different between these mothers and daughters.

The significant generational difference in height may reflect the different environment experienced by mothers compared to daughters, along with any generational secular changes in the UK. These two influences could not be differentiated because the Cardiff study did not take into account general secular changes in height and knee height in the UK.
This highlights the need for a control sample in future studies looking at generational changes in migrants.

All mothers and almost half of the daughters had the same birthplace, Bangladesh, but early life environment is not only influenced by country of birth, but by historical events in Bangladesh over the period of conception and early life growth and development. Figure 3.6 over the page displays knee height of study participants, born in Bangladesh, plotted against their year of birth, along with major events, such as flood, famine and iodine supplementation that occurred over the time line. Mothers would have spent all their growing years in Bangladesh, but the length of time daughters would have spent in Bangladesh was variable, as daughters migrated to the UK at various ages, some at a very young age (as shown in Figure 3.6). From observation, it appears that in this small sample, there was no marked association with year of birth and knee height in BD women, born in Bangladesh. There was a similar lack of association with height and year of birth (from observation, data not shown). Although various events around the time of a BD woman’s birth in Bangladesh may have influenced her adult knee height, there does not appear to be a consistent relationship with knee height and year of birthplace in the current sample, possibly due to the small sample size and confounding effect of age at migration for the BD daughters.

The fact that QUS parameters did not differ between mothers and daughters was contrary to the study prediction that the QUS parameters would parallel height differences. QUS parameters are influenced by BMD: Pearson’s correlation coefficient between BUA and BMD is 0.76, whereas for SOS and BMD it is 0.5 (Brooke-Wavell et al., 2008) and the study prediction was based on the fact that the BMD difference between BD and IB women was associated with skeletal size (indicated by height), along with the fact that taller height in migrants is often associated with improved health. The lack of QUS differences does not support the prediction of association of BMD with skeletal size and highlights the fact that DXA-measured BMD would allow for a more effective testing of study predictions.
Figure 3.6 Scatter graph showing year of birth and knee height of Cardiff BD women born in Bangladesh (all mothers and BD-born daughters) along with daughter’s age at migration
N=33 for mothers (3 omitted because age estimated) N= 17 for daughters (BD-born).
Age of migration for daughters shown in brackets. $R^2$ indicates the amount of variation in knee height associated with year born.

3.4.3 Generational differences in knee height differ depending on daughter’s birthplace
The results show that daughters had a greater knee height than their mothers. It was noticed that when daughters were differentiated according to birthplace, the biggest effect size was seen in mother-daughter dyads with UK-born daughters (Table 3.6). The publication that used the same set of data that I analysed here, reported a similar outcome, but in a different way, stating that 53% of BD-born daughters had a greater knee height than
their mothers, compared to 80% of UK-born daughters having a greater knee height than their mothers, a significant difference (p=0.04) (Bogin et al., 2014).

Therefore, it could be speculated that, even if UK-born daughters came from a better familial environment, being born in the UK conferred additional advantages (as evidenced by the significantly improved knee height over their mothers). A counter argument could be that the BD-born daughters experienced stress associated with migration which diminished the increase in knee height of the daughter compared to her mother. In other words, BD-born daughters would have had even greater knee height than their mothers had it not been for the adverse effects connected with migrating from Bangladesh.

### 3.4.4 Daughter’s birthplace and association with height, knee height and QUS measurements

UK-born daughters had a significantly greater height and knee height than BD-born daughters (Figure 3.3 and Table 3.4), already published previously as a finding of the MINA project (Bogin et al., 2014). This finding suggests that UK-born daughters had greater skeletal size (height) and better early life environments (knee height) than BD-born daughters. Although UK-born daughters had greater height and knee height than BD-born daughters, this was not mirrored in QUS scores. BUA and SOS (raw scores and Z scores) did not differ between daughters, according to daughter’s birthplace (Table 3.4). It seems that, in the case of QUS measurements there appears to be no association with skeletal size or different early life environments (UK or Bangladesh).

One of the study predictions, that UK-born daughters would have greater height and knee height than BD-born daughters, was accepted, but the accompanying prediction that this would be paralleled by greater QUS measurements in UK-born daughters than BD-born daughters was rejected.

The effect sizes for the differences in height and knee height between daughters, according to birthplace, were Cohen’s d of 0.77 and 0.99 respectively. A more marked effect of knee height, compared to effect of height, according to daughter’s birthplace suggests early life environment (UK or Bangladesh) was a major influence on daughters’ growth.
Figure 3.7 reproduces Figure 3.6 with the addition of UK-born daughters, illustrating the relationship of participant’s knee height with their generation (mother vs daughter), birthplace (Bangladesh vs UK) and year of birth.

The significantly higher height and knee height in UK-born daughters may be due to advantages of being born in the UK such as better pre- and post-natal care as well as a better environment in which to grow and develop during childhood. UK-born daughters, in contrast to BD-born daughters, would not have had to live through times of famine and flood. UK-born daughters may have also benefitted from more iodine in their diets than BD daughters. All BD daughters were born between 1973 and 1990 which was before 1994, the year that Bangladesh introduced a universal salt iodination programme (Yusuf et al., 2008). Therefore, BD-born daughters would not have benefited at birth from this initiative, although younger daughters born between 1985 and 1990 may have had gained some advantage of salt iodination during their later years of growth and development. Generally speaking, all BD-born daughters, especially older ones, would most likely have been iodine deficient (Yusuf et al., 1996). However, in the UK from the 1930s onwards there was a marked rise in the iodine content of milk due to iodine enriched cattle feed (Phillips, 1997). If UK-born daughters drank milk they would have had a greater intake of iodine than BD-born daughters, which may explain why they had greater mean knee height compared to BD-born daughters. The MINA project found that 97% of the daughters currently drank milk, although the majority (69%) reported drinking less than a quarter of a pint (unpublished). Of course, this does not indicate how much milk they consumed during childhood, during those critical first ten years of life when knee height is determined.

Another advantage for UK-born daughters was that their mothers might have benefitted in terms of mental and physical health as a consequence of living in the UK prior to the birth of the daughter, which would have had a positive effect on their daughter’s health.

An alternative or additional explanation for greater mean knee height in UK-born daughters is that they came from families with better SES than did the BD-born daughters. There is some evidence for this idea: mothers of BD-born daughters contained a higher proportion of short-statured women and women lacking formal education, compared to mothers of UK-born daughters. Height and knee height were lower, though not significantly so, in mothers
of BD-born daughters than mothers of UK-born daughters. Mother’s knee height and SES might affect daughter’s knee height via familial mechanisms and intergenerational theory.

The MINA project collected data from sedentees and reported that daughters still resident in Sylhet, Bangladesh had significantly greater knee heights than BD-born daughters living in Cardiff (Bogin et al., 2014). Therefore, the greater knee height in UK-born daughters living in Cardiff, compared to BD-born daughters living in Cardiff, may simply reflect adverse conditions associated with the migratory journey of BD-born daughters, rather than a more favourable environment in the UK. Indeed, preliminary analysis of the migration history questionnaires and interviews with participants during the MINA project, indicated various social stress related to the process of migration (Bogin et al., 2014). Childhood migration can be associated with family separation e.g. fathers migrating first, leaving wives and children in Bangladesh and separation of mothers and children (Bogin et al., 2014). As described earlier, five mothers in the study sample did not come to the UK in the same year as their BD-born daughter. These types of stresses would not have been suffered by UK-born daughters.
3.4.5 Daughter’s age at time of migration and association with height, knee height and QUS measurements

There appeared to be no marked difference in knee height associated with age at migration of BD-born daughters (Table 3.5, Figure 3.4 and Figure 3.6), but the sample sizes were very small (n=8 for early migrators, n=9 for late migrators). Similarly, the mothers, based on their daughter’s migratory status, did not appear to differ in height or knee height, nor any other variable (Table 3.5). Therefore, from this very limited sample, no major differences were observed in height and knee height between early and late migrating daughters but further studies with much larger sample numbers would be required to explore this issue further.
QUS measurements were also similar between both sets of daughters, irrespective of migratory status (Table 3.5).

### 3.4.6 Strengths and Limitations of the Cardiff study

The main strength of the study was the recruitment of mother-daughter pairs, allowing to control, as far as possible, for familial (genetic and environmental) influences in making comparisons between the two generations.

A further strength of the study was the recruitment of participants from the Bangladeshi community, considered “hard to reach” and less studied than other ethnic minority groups (Grace, 2011). The majority of UK Bangladeshis originate from just one part of Bangladesh, Sylhet, (Gardner, 1995), making the study sample a homogenous group with less biocultural variance compared to other ethnic groups. However, considerable resources were required in the hiring and training of Bangladesh community research assistants, as well as the expense of providing three day-long community events.

Limitations include a possible recruitment bias because of snowball sampling and using members of the community to recruit study participants. For example, a participant with a particular SES, may have encouraged her friends and neighbours from a similar background to participate in the study which would have biased the sample towards participants with a similar SES. Because the MINA project did not focus on bone status, information regarding HRT and contraception use was lacking. However, in the subsequent Loughborough study, no BD women reported using HRT. Also, HRT use is reported as being very low in the Bangladeshi community (Harris et al., 1999). Therefore, probably very few, if any, Cardiff BD women would have taken HRT.

Statistical limitations involve insufficient powering of statistical tests. The tests comparing variables between mother and daughter were sufficiently powered (estimated power was 100%) (Table 3.1) to detect large differences (Cohen’s d = 0.8) between mothers and daughters in height and knee height. However, comparisons between daughters, based on their birthplace, involved lower sample numbers and hence a lower power (64%) for detecting large differences (Table 3.1). The sample numbers associated with comparisons involving daughter’s migratory status (early or late) were seriously underpowered for
detecting even large differences (Table 3.1), and should be regarded as simply an indication of possible trend.

A criticism of my statistical analyses of the Cardiff data is that multiple testing was employed, so raising the probability of producing a significant outcome. The results were re-visited, using the Bonferroni correction as follows. To address the study predictions, only two comparisons are required (mother vs. daughter, UK-born daughter vs BD-born daughter), each involving six experimental variables (height, knee height and four QUS measurements). Applying Bonferroni correction by dividing the initial level of significance (p=0.05) by total number of tests (12) would give a final acceptable level of significance of p=0.004. This would not affect the acceptance of the prediction that BD daughters had greater height and knee height than their mothers. However, the conclusion regarding birthplace of daughters would have to be changed to the conclusion that UK-born daughters had greater height, but not knee height, than BD-born daughters.

The other statistical comparisons carried out in the analyses were not connected with testing study predictions, but simply to confirm that results were consistent, as well as to consider possible reasons for any significant findings.

Another limitation to the Cardiff study is the lack of a control group of IB women to indicate the generational change in height, knee height and QUS parameters found in a sample of the general UK population. Although daughters were, on average, significantly taller with larger knee height than mothers, this could have been connected with better environmental conditions in the UK over time rather than different degree of exposure to the UK environment in early life. My Loughborough study included a control group of IB women to counter this limitation.

Additional limitations of the Cardiff study are that the results only refer to one measurement of bone status and only one example of a BD community in the UK. Other measurements of bone status might give different results, as might a similar study using another BD community in the UK. Again this was addressed by my Loughborough study which had additional DXA measurements of bone status, and used another BD community in a different location.
3.5 Conclusions of analysis of Cardiff data and basis for Loughborough study

Analysing the data from BD women living in Cardiff, Wales, collected as part of the MINA project, allowed testing of some of the predictions arising from my study’s main research questions. The first finding was BD daughters had greater height and knee height measurements, but not QUS scores (after accounting for age and menopausal status), than their BD mothers. The second finding was that UK-born BD daughters had greater height and knee height measurement, but not QUS scores, than BD-born BD daughters. This suggests an association of early life environment with height and knee height, but no association of early life environment and/or skeletal size with QUS scores, a measurement of bone status.

The next chapter describes the methods employed in the Loughborough study.
4 Methods: Comparison of height and bone status in UK BD and IB women according to ethnicity, generation and birthplace (Loughborough Study)

To confirm the findings from the Cardiff data, and to explore my thesis research questions, as well as attempt to address the limitations of the Cardiff data, another study was organised. This was the Loughborough study, which forms the basic data set for this PhD thesis. The Loughborough study was designed as a cross-sectional observation study of BD mother-daughter pairs, like the MINA project, with the addition of a control group of IB mother-daughter pairs. Data was to be collected from study participants in a different location to Cardiff, and to include additional measurements of bone status, including BMD, using DXA technology. This would allow testing of the study prediction that the difference in BMD between BD and IB women was associated with skeletal size, as well as the predictions that taller height in BD daughters compared to BD mothers, and taller height in UK-born BD daughters compared to BD-born BD daughters, would be paralleled by increases in measures of BMD and some hip geometry parameters.

This chapter reports on how the data for the Loughborough study were collected, including study design, the recruitment process, protocols followed for taking measurements and the statistical tests used to analyse the data.

4.1 Background

Descriptive variables included basic demographic variables, health characteristics and features of early life environment, collected using questionnaires, and DXA-derived body composition measurements. Experimental variables i.e. those used to test out study predictions included height, knee height, DXA BMD measurements at three skeletal sites, DXA-derived hip geometry measurements, as well as QUS measurements. Statistical tests were carried out to explore ethnic and mother-daughter differences on height, knee height and bone status variables. The association of BD daughter’s birthplace with knee height and bone measurements was also analysed. The study and procedures will now be described in more detail.
4.2 Study Design

The study design was cross sectional, involving BD and IB mother-daughter dyads.

4.3 Study Setting

The study setting was based at Loughborough University and in participants’ homes.

4.4 Recruitment area

The majority of Bangladeshis in Loughborough reside in two wards, Lemyngton and Hastings, so this was designated the recruitment area. IB women were recruited from the same two wards to control, as far as possible, for SES and current environment. At the time of the 2011 census the total resident population of Lemyngton and Hastings was 12,508 whilst the Bangladeshi population was 1,601 (12.8% of the total resident population).

These two wards are defined as being in the top 10% most deprived areas in Charnwood (Leicestershire County Council, 2005) and contain a large number of socially disadvantaged people in socioeconomic classes, C1, D and E according to geodemographic data base providers e.g. http://www.checkmyfile.com/postcode-check/LE11-1SD.htm.

4.5 Recruitment process

It took a number of years and careful work to build up a rapport with the local Bangladeshi community prior to undertaking the current research. The centres of community and cultural life, where religious and educational activities take place, are the BSA and the mosque, so Professor Bogin and I first attempted to make contact with the BSA committee. Cultural differences in the BD community meant that initial contact with the BSA committee (all males) was more successful when made by Professor Bogin rather than myself. However, once my main BD female helper was enlisted, the fact that I was female and of a similar age to the mothers was beneficial in encouraging BD women to take part in the study.

Recruitment of Bangladeshi volunteers was carried out with the support of the BSA and key members of the Bangladeshi community. The MINA project as well as other studies (Grace, 2011) employed bilingual female BD members of the community as researchers, and a community orientated, personal approach for recruiting SA ethnic minority populations was
found to be successful in both the UK (Douglas et al., 2011) and the US (Lauderdale and Rathouz, 2003). These strategies were followed as far as possible for the current study. Lack of resources did not permit employment of BD researchers but some BD women volunteered to help and they were given a small sum of money as a token of appreciation. Snowballing was also used: this is a purposive sampling technique often employed to recruit “hard to reach” populations where an individual passes on the information to their family and peer group to encourage further volunteering (Sadler et al., 2010).

Events were organised at the BSA and local community centres to publicise the study to both BD and IB residents in Loughborough. I gave a presentation at the BSA to a group of older BD mothers, and took part in various health events attended by BD women. Leaflets publicising the study and asking for volunteers were distributed to virtually every household in the two wards as well as schools and local welfare/job centres. Leaflets were also handed out at a local bingo hall to recruit IB volunteers.

Sylheti is a commonly used dialect spoken by many Bangladeshis and as it has no written format this encourages the strong oral tradition of the BD community. This was a consideration during recruitment of study volunteers. Leaflets were put through doors to recruit IB women but this was not expected to be as successful in the recruitment of BD women, who needed to be informed about the study by word of mouth. However, leaflets were useful in reinforcing the oral message as younger members of a BD family were able to read the leaflets. I was advised not to spend money on translating the leaflet into Bengali as many of the older women could not read at all.

Recruitment from both ethnic groups was challenging which was expected as the Bangladeshi community are reported as being a “hard to reach” group i.e. a community that is not easily accessible to researchers (Grace, 2011).

In my study, the barriers to recruiting older BD women were language and their initial wariness. Barriers to recruiting from the IB population were mainly due to socio-economic status: some IB women or their husbands were shift workers or worked long hours so did not have time to come to the university. IB women also had more problems with finding childcare than did BD women, the latter having larger families living locally who often acted as child minders.
There were probably fewer IB mother-daughter pairs than BD mother-daughter pairs, resident in the local community, due to IB families having fewer children and more likelihood of IB mothers and daughters not living in the same local area. For the majority of BD women and many of the IB women from lower socio-economic groups, this was their first experience of university research which may have been daunting, especially for the older mothers. It was helpful having BD mother-daughter pairs as the daughters encouraged and helped their older mothers, who otherwise would probably not have participated. Inducements were necessary to encourage participation from both ethnic communities, including a small sum of money for inconvenience, as well as providing transport to and from the university.

In addition to scientific impact, research studies can also have an impact on the community. One of the aims of my study was to improve awareness of health issues related to bone in both BD and IB women from a lower SES class in Loughborough. It also helped with the integration of the local BD community. In addition, the study introduced members of the public to university research, and hopefully the experience will encourage them to volunteer for future studies at Loughborough University. Volunteers who were ineligible for the study were offered a QUS scan to assess their bone status to increase awareness of bone health and to provide good publicity for research at Loughborough University.

### 4.6 Inclusion and exclusion criteria

The number of prospective volunteers was unknown, so the inclusion criteria were as wide as possible in an effort to reach the target sample number. Also, as “word of mouth” recommendation was particularly important in recruiting BD women, I did not want to discourage women from taking part in the study by rejecting volunteers who may also have then gone on to discourage others from volunteering. All study volunteers were required to have been born in Bangladesh or the UK, and be of BD or IB origin according to their self-definition. They also had to be one of a mother-daughter pair and aged 18 years or above. At age 18, peak bone mass has generally been attained for the three skeletal sites used in my study (Henry, 2004). There was no upper age limit in an attempt to recruit as many study participants as possible.
Exclusion criteria were any condition that may affect bone measurements or contravene guidance to avoid X-ray exposure in those to whom it may be particularly harmful i.e. prescribed medication that influences bone metabolism; joint replacement or prostheses; medical conditions adversely affected by exposure to ionising radiation; history of high levels of ionising radiation exposure e.g. medical treatment; regular contact with ionising radiation e.g. work environment; pregnancy; breast feeding; cardiac pacemaker or bone surgery in the past 12 months.

The usual medication influencing bone metabolism tends to be thyroxine, steroids and medicines to treat osteoporosis or osteomalacia. No other exclusions on the basis of illness or medication taken, were made. BD women often have poor health as described in the Background chapter, so to exclude those with illnesses that may have an impact on bone health e.g. diabetes, low vitamin D levels, would have resulted in a very small sample of uncharacteristically healthy BD women, that was not representative of the general BD community. Women who had been on long term HRT were excluded, as this would have affected bone metabolism. However, current short term (less than one year) HRT users, women who had used HRT for less than one year in the past, and women using oral contraception were included for the reasons just mentioned above i.e. to obtain a representative sample and increase sample number. The evidence that oral contraception affects bone status is equivocal (see Background chapter) and the data of all participants taking HRT or using oral contraception were checked for any differences from the rest of the sample. However, for the main statistical analysis, women who had ever used HRT or were currently using oral contraceptives were dropped from the sample as advised by reviewers.

Another exclusion criterion was pregnancy, which may have affected bone status and/or given the participant concerns over safety. Even though the radiation risk to an embryo or foetus is extremely low (Damilakis et al., 2002) considerable care was taken to ensure a woman was not pregnant before accepting her on the study. Cultural sensitivities prohibited offering pregnancy tests to BD women, so all pre-menopausal women were required to have had a period within the past 28 days. As a further precaution any woman expressing doubt would be asked to return for a scan at a later date when they were confident that they were not pregnant. However, no woman expressed any doubt.
4.7 Data collection

Data were collected between April 2013 and February 2015 from BD and IB mother-daughter dyads resident in Loughborough. No measurements were taken from BD volunteers during the month of Ramadan because fasting may have decreased parathyroid hormone secretion which could affect bone metabolism (Bahijri et al., 2015), and also to avoid extra demands on BD women whilst fasting. Each participant was given money (ten pounds) to compensate for inconvenience and any expense incurred for child care, transport, loss of wages etc.

Interviews were conducted either at the university, the participant’s home (for some BD participants) or by phone (for some IB participants). Anthropometric and bone status measurements took place at Loughborough University. With a couple of exceptions, I completed all questionnaires and took all measurements, including the DXA scans, with the exception of those taken during my training period. For two elderly (over 70 years) BD mothers, data collection was slower, so I had some assistance from a Bangladeshi colleague. Transport (in my car) was offered and translation (usually by the daughters but occasionally by a Bangladeshi colleague) was provided as required.

4.7.1 Study Questionnaire

The questionnaire (see appendix II) was a shortened version of the one used in the MINA project, plus an extra section to cover early life influences. The Loughborough University standard health questionnaire (appendix III) was used to satisfy university requirements and to provide relevant data for the research.

Questions regarding menstruation were included to establish recalled age at menarche and to define menopausal status of the participant. Women who considered themselves as having normal and/or regular periods were classified as pre-menopausal, women who had irregular periods but at least one in the last year were also classified as pre-menopausal, and women who had not had a period within the last year were recorded as post-menopausal.
The questions related to early life environment were taken from prior surveys, using large samples which are designed to look at health in developing countries e.g. the Monitoring and Evaluation to Assess and Use Results Demographic Health Surveys (The World Bank, 2017). The aim of these questions was to establish the overall quality of the environment in terms of socio-economic background and health when the participant was a baby.

4.7.2 Anthropometric Measurements

The anthropometric measures taken were height, knee height, weight and heel width. DXA measured body composition parameters i.e mass and percentage of total mass for fat, lean and bone tissue, were also recorded.

Knee height is a very important measurement in my study as it is used as a marker for early life environment. As birth weight is a marker for environmental conditions in the womb, so leg length is a marker for the additional environmental impacts in early life. Leg length (femur + tibia) and knee height (tibia) are often used as biomarkers for nutritional status and health between birth and age 10 years (Leitch, 1951; Bailey et al., 2007; Whitley et al., 2008; Padez, Varela-Silva and Bogin, 2009; Bogin and Varela-Silva, 2010). This is due to the cephalo-caudal gradient in growth, whereby the relative rates of growth differ between body segments. At birth, the head and trunk tend to be closer to their adult size than the extremities, so from birth to puberty the legs grow relatively faster than the upper body. The tibia, being more distal than the femur, is the last segment to grow rapidly and is, therefore, relatively more impacted by environmental quality from birth to age 10 than are other body segments, including the femur (Jantz and Jantz, 1999).

This is particularly pertinent to migration studies where different generations may experience very different environments in the first decade of their life. Therefore, knee height was used in my study to indicate the different environmental conditions associated with birthplace and country of residence (Bangladesh or UK) in the first ten years of life of study participants.

A related measurement to leg length is relative leg length which is the proportion of the total height that is taken up by the leg length. This is often expressed as sitting height ratio which is sitting height/stature where sitting height is trunk length + head length. A high
value for sitting height ratio indicates relatively short legs compared to the trunk. A high sitting height ratio is generally considered a marker of an adverse environment (Bogin and Varela-Silva, 2010). I chose to use knee height which, unlike total leg length and relative leg length, is not biased by gluteo-femoral fat mass (Bogin and Varela-Silva, 2008).

The protocols followed for height, knee height and weight were as recommended in the literature and described more fully there (Cameron, 2013). The protocols in my study for anthropometric measurements are described below.

Height (cm)

The participant was asked to remove shoes, as much clothing as possible and any hair ornaments that may have contributed to height. She was instructed to stand upright against a Harpenden Portable stadiometer with her heels, buttocks and scapulae in contact with the stadiometer. Her head was positioned in the Frankfurt Plane and she was asked to inhale. At full inhalation the headboard of the instrument was brought down gently to make contact with the vertex of the skull, and height was recorded to the nearest mm.

A note was made if a participant was of short stature, often defined as height < 150 cm (López-Alvarenga et al., 2003; Varela-Silva et al., 2009). Short stature is an indicator of a particularly adverse early environment (Song, 2008) and often a result of vitamin D deficiency (Holick, 2007; Bueno, Czepielewski and Raimundo, 2010).

Weight (kg)

The participant had already removed shoes and outer layers of clothing. She was asked to step onto digital scales (Seca 770 model) and stand still with her weight equally distributed on both feet. When the reading had stabilised the weight was recorded to the nearest 100g.

BMI

BMI was calculated using the formula weight/height$^2$ (kg/m$^2$). BMI categories were defined using the cut-off points recommended for international classification (WHO, 1995) as shown in Table 4.1 below. These cut-off points were used for both ethnic groups to simplify comparisons although it has been recommended that Asians should have different BMI cut-
off points because there are different associations between BMI and health risks for Asians compared to those of European heritage (WHO, 2004).

Table 4.1 BMI cut off points for classification of weight (WHO, 1995)

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.50</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.50 – 24.99</td>
<td>Normal weight</td>
</tr>
<tr>
<td>25.00 – 29.99</td>
<td>Overweight</td>
</tr>
<tr>
<td>&gt;= 30.00</td>
<td>Obesity</td>
</tr>
<tr>
<td>&gt;=40.0 or</td>
<td>Morbid obesity</td>
</tr>
<tr>
<td>&gt;=35.0 + comorbidity</td>
<td></td>
</tr>
</tbody>
</table>

Knee Height (cm)

Two procedures for measuring the lower leg were used (Figure 4.1). The first method measured lower leg length (cm) in the standard manner as described in the NHANES III data collection manual (National Center for Health Statistics, 1998). The second method measured knee height (cm) using the protocol used in the MINA project (Bogin et al., 2014).

Both procedures involved the participant removing their shoes and sitting on a low stool with their bare or stockinged feet placed squarely on the floor and the knee flexed at 90°. The condyles of the femur were located by touch and then removable, adhesive marking tape was placed on the skin of the thigh directly above the condyles. Depending on the participant’s wishes, the tape was placed on the skin or fabric (some participants could not roll up their trousers to above the knee). The superior border of patella was then located by palpation and marked in the same way. A Harpenden anthropometer was used to measure lower leg length by sliding the fixed calliper under the heel, between the heel and the floor in line with the lateral malleolus. The moving calliper was then moved to rest on top of the leg on the first position marked by tape i.e. directly above the condyles. The reading on the
anthropometer was read off to the nearest mm (first method). The sliding calliper was then slightly adjusted to rest on the second tape mark i.e. the superior border of the patella and this reading was also recorded to the nearest mm. This second method excludes some of the soft tissue, especially the fat superior to the condyles of the femur which has been shown to artificially inflate other skeletal measurements (Bogen and Varela-Silva, 2008). Knee height measurements (to top of patella) were used in all subsequent reporting in this thesis. The other method (knee height to leg above condyles) was also measured so that both measurements could be compared (data not reported here).

Figure 4.1 Two methods of measuring knee height, adapted from NHANES anthropometric manual (National Center for Health Statistics, 1998)

Heel Width (cm)

The participant was asked to stand squarely with their feet apart and their back to the researcher. The medial to lateral aspect of the calcaneal region at the widest part of the right heel was measured to the nearest mm using sliding callipers.
4.8 Measurements of bone properties

The two technologies used in my study were DXA and QUS. DXA technology was used because DXA-derived BMD is the gold standard, clinical measure for the diagnosis of osteoporosis and prediction of fracture risk. DXA technology can also measure hip geometry parameters some of which are associated with hip fracture risk. DXA BMD raw scores at femur neck, lumbar spine and proximal radius were used in the study. Although BMD Z scores were available, these take into account both age and body weight, which would have compromised my investigation of the link with skeletal size and BMD, so BMD Z scores were recorded but not used in the statistical analysis.

QUS technology at the calcaneus was used because QUS parameters, BUA and SOS, reflect BMD plus other bone characteristics. QUS technology is often used in research because meta-analyses indicate that BUA at the calcaneus is as good a predictor for fracture as DXA BMD scores (Marín et al., 2006; Moayyeri et al., 2012). It has many practical advantages: QUS uses sound waves, rather than X-rays, so poses no risk to the participant in terms of ionising radiation exposure. The machine used for measuring QUS is also practical to use, being smaller (making it portable), cheaper and easier to operate than DXA.

QUS technology provides age-matched QUS Z scores, which I used in preference to raw scores, because QUS Z scores adjusted for age and menopausal status. Ethnic specific Z scores were not available with the software: the reference database was based on a sample of European women and men. This was not a problem, as the aim of my study was to compare ethnicities so Z scores needed to relate to the same reference population.

QCT is another technology used in research on bone geometry parameters. It produces high resolution three-dimensional images thus allowing more accurate values of bone mass and density to be obtained (Goldman, 2007) as well as more accurate values for hip geometry parameters. A further advantage of using QCT is its ability to distinguish cortical from trabecular bone as well as localised effects on bone e.g. a recent study reported on the effects of exercise on cortical surface density and endocortical trabecular density in the proximal femur (Allison et al., 2015). However, QCT uses X-rays at a much higher dose than DXA and is very expensive and less accessible than DXA technology which is the reason I used DXA technology. A benefit of using DXA-derived measurements allowed comparison
with previous findings from the majority of studies on bone health which also used DXA technology.

4.8.1 Mechanism of DXA

DXA uses X-rays of a very low dose to assess BMD and bone mineral content (BMC) of bones. The whole body can also be scanned to measure body composition in terms of the amount of bone, lean mass and fat mass in the participant’s body. Bones usually scanned are the hip, lumbar spine and forearm, all common sites for osteoporotic fracture. DXA involves passing low energy X-ray through the human body. Some of the radiation is absorbed by the bone and soft tissue that make up the body, the degree of attenuation depending on the thickness and density of the material. To avoid the confounding effect of soft tissue also absorbing the energy, two X-rays of differing energy levels are used (Berger, 2002). Because the different energies are absorbed differently by bone and soft tissue, the reduction due to soft tissue can be calculated and subtracted from total attenuation, thus leaving only the attenuation due to bone material (Berger, 2002). The amount of X-ray attenuation measured for each pixel within the total projected area of bone is summed and then divided by number of pixels to give the mean BMD over all the pixels identified as bone (Blake and Fogelman, 1997; Beck, 2007). BMC is given by multiplying BMD by projected area (Blake and Fogelman, 1997).

Positioning of the individual to be scanned is important as incorrect positioning can affect BMD measurements (Watts, 2004; El Maghraoui and Roux, 2008) and particularly HSA measurements (Michelotti and Clark, 1999; Beck, 2003; Khoo et al., 2005). Procedure and positioning of the participant when performing a DXA scan are discussed later in this chapter.

BMD measurements are also affected by the soft tissue in the DXA scan region of interest (ROI) although this does not necessarily compromise the clinical interpretation of DXA scans (Blake and Fogelman, 2008). Soft tissue comprises disparate components i.e. extra-osseous fat, extra-osseous lean tissue and intra-osseous marrow which lead to inaccuracies in BMD measurement (Bolotin and Sievänen, 2001). The extent and direction of the error tends to depend on the interaction between the true BMD, the ratio of fat to lean tissue and the ratio of yellow marrow to red marrow (Bolotin, 2007). A study simulated the effects of
increasing body fat on DXA measurements by layering fat on a spine phantom model and normal-weight adult volunteers (Yu et al., 2012). The researchers reported that adding fat layers increased the DXA spine BMD scores for the spine phantom and decreased DXA spine BMD scores in human volunteers (Yu et al., 2012).

Furthermore, measurements of BMD vary according to DXA machine used (Faulkner, Roberts and McClung, 1996; Tothill and Hannan, 2000; Fan et al., 2010). For example the GE-Lunar (machine used in the current study) reports lumbar spine BMD readings 11.7% higher than the Hologic machine (Fan et al., 2010). Equations are available which help to standardise between DXA machines (Lu et al., 2001).

BMD measurement can also be given as a Z-score i.e. the number of standard deviations differences from an age-matched, gender-matched and ethnic-matched mean of a reference population (Blake and Fogelman, 2007). Z-scores also normalise to body size using height and weight.

4.8.2 Protocols for DXA use

DXA scans were taken using the Lunar Prodigy Advance (GE Lunar) DXA machine (GE Healthcare, Madison, WI, US A. version encore 2008 version 12.30) which uses narrow angle fan-beam technology. Calibrations and participant positioning for scans were performed according to the manufacturer’s protocols, described in more detail below. Four scans were taken: total body, lumbar spine, right proximal femur and right radius. The effective doses for this study were 0.5 µSv per whole body scan, 0.7 µSv per lumbar spine scan, 0.7 µSv per proximal femur scan and 0.01 µSv per radius. The dose constraint for this study was 6 µSv.

On the day that a participant was booked in for a scan, a quality control (QC) assessment was carried out to correct for instrumental drift. This was also done each day on the two days preceding the DXA scan. On the day of the scan an additional calibration check was carried out using the manufacturer’s lumbar spine phantom.

Participants had previously been asked not to wear any metal or bone materials e.g. jewellery, studs, zips, hair clips etc. as these may affect the measurements. The participant removed outer clothing and shoes. A check was made that there was nothing in pockets and that the participant had indeed removed all metal items. If a metal item e.g. nose stud,
could not be removed the scan was still performed and a note made of any artefacts. The four scans were carried out using the manufacture’s protocol and summarised as follows, in the order in which they were generally performed.
Total Body Scan

The participant was asked to lie on the DXA scanning bed within the rectangle marked on the bed. A couple of participants were too wide to fit in the scanning area. In these cases it was ensured that the right side of her body lay within the marked area. The software could then make an estimate of the total body based on the measurements for the right side of the body.

The participant was required to lie straight and still, with feet relaxing outwards whilst the scan was taken. Numerous data were generated on the bone, fat and lean tissue quantities and percentages in the various body parts as shown in the output examples below. The variables used included total body mass (kg), total body fat (g), total body lean tissue (g), bone tissue (g), along with % fat, % lean and % bone of total body mass.

![Example Output for Total Body Scan](image)

**Figure 4.2 Example Output for Total Body Scan**
Lumbar Spine (L1-L4)

This scan usually took place after the whole body scan so the participant was already in a good starting position. She was asked to lift her lower legs onto a block so that there was a 90° angle at her hips and knees which ensured her lower back was flat on the scanning bed. BMD (g/cm²), area (cm²) and BMC (g) of the total region (L₁-L₄) were recorded. The region (L₂-L₄) was also recorded for reasons described in section 4.8.3.

![Figure 4.3 Example Output for Lumbar Spine]
**Proximal femur scan**

For this scan the participant lay on the DXA bed with their legs apart and a positioning block was put between the feet. The participant was requested to rotate both legs inwards to ensure that the femoral neck was in plane with the scan and a scan was taken of the right hip. BMD (g/cm$^2$), area (cm$^2$) and BMC (g) of the proximal femoral neck were the parameters recorded.

Positioning of the leg when taking the DXA scan is important as hip abductions shortens the apparent HAL (Michelotti and Clark, 1999).

Hip strength analysis allows certain hip structural parameters to be calculated from DXA images (Bonnick, 2007). The GE-Lunar Prodigy has additional software, Advanced Hip Analysis (AHA) which records measurements of variables relating to the bone geometry at the hip. The variables that were recorded were HAL, FNW, Z, BR at the femur neck, NSA and HSI.

![Example Output for Right Femur](image)

**Figure 4.4 Example Output for Right Femur**
Proximal Radius

The participant was seated on a chair next to the DXA machine and her right forearm was placed on the DXA bed on top of a positioner with the elbow at right angles to the positioner and the forearm aligned between the two guide lines on the positioner. BMD (g/cm²), area (cm²) and BMC (g) of the part of the radius labelled 33% were the parameters used in my study.

Figure 4.5 Example Output for Right Radius
4.8.3 Bone Mineral Apparent Density

A further parameter, Bone Mineral Apparent Density (BMAD), was calculated for each skeletal site to account for the influence of bone size on BMD (Katzman et al., 1991; Carter, Bouxsein and Marcus, 1992).

BMAD was a parameter proposed by Katzman et al. (1991) to reflect vBMD as opposed to areal BMD. As bones differ in size and geometry, the marker of skeletal size used to calculate BMAD will depend on the shape of the bone under investigation e.g. a vertebra is considered to be similar to a cube. In Table 4.2 below, the equations used by Katzman et al. (1991) are given for various skeletal sites commonly measured by DXA. Other researchers calculated vBMD for lumbar spine, using a slightly different equation to Katzman et al. (1991) but based on the same principles, and reported a good correlation with vBMD calculated using MRI technology (Kröger et al., 1995).

For reasons explained earlier, BMAD does not predict fracture risk as well as BMD (Cundy et al., 1995).

Table 4.2 Equations to calculate BMAD (g/cm³) for spine, mid-radius, femoral neck and whole body skeleton (Katzman et al., 1991)

<table>
<thead>
<tr>
<th>Skeletal Site</th>
<th>BMAD (g/cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine (L₂ - L₄)</td>
<td>BMC ÷ Ap^{3/2}</td>
</tr>
<tr>
<td>Mid-radius</td>
<td>BMC ÷ Ap²</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>BMC ÷ Ap²</td>
</tr>
<tr>
<td>Whole skeleton</td>
<td>BMC ÷ [Ap²×height]</td>
</tr>
</tbody>
</table>

(Ap = projected area of bone)

Other variables related to body size such as weight (Reid, 2008), height, BMI (Robbins et al., 2006) and body surface area (Nielsen, 2000) also correlate with skeletal size and have been used as markers for skeletal size. In many studies, if a significant difference in BMD is found between groups, then the statistical analysis is repeated, using weight or height as a
covariate, to investigate whether skeletal size might explain the difference (Kin et al., 1993; Russell-Aulet et al., 1993; Ross et al., 1996; Finkelstein et al., 2002; Alver et al., 2005; Roy et al., 2005; Ward et al., 2007).

In my study, I calculated BMAD for spine, radius and femoral neck using the equations above (Table 4.2) to investigate whether skeletal size might be the explanation for any ethnic differences found in BMD.

Lumbar spine BMD measurements are generally reported for four vertebrae, L₁ to L₄, but BMAD has only been validated for three vertebrae L₂ to L₄. This was because the dimensions (length, width and height) of these three vertebrae have been measured using cadavers (Kelly et al., 1990). This allowed area and volume for vertebrae L₂ to L₄ to be measured accurately, leading to the opportunity to compare the measured (true) volume of the these three vertebrae with their estimated volume (BMAD = area$^{3/2}$) (Katzman et al., 1991). It was found that there was a very high correlation (r=0.99) between measured and estimated volume thus validating the formula for lumbar spine L₂ to L₄ (Katzman et al., 1991).

One final point regarding the issue of BMD and skeletal size concerns the calculation of BMAD, which is sometimes more simply calculated as BMAD = BMD/body height for any skeletal site of interest. Roy et al. (2005) used both equations for lumbar spine BMAD. One was the same as I used i.e. BMAD = lumbar spine BMD/BA$^{1.5}$, and the other was BMAD = lumbar spine BMD/body height. Using both equations resulted in the same overall conclusion (Roy et al., 2005). I repeated my analysis for all three skeletal sites using BMAD = BMD/body height and, likewise, there was no change in the overall conclusion for all three skeletal sites (data not shown). It would appear that using height in the equation for BMAD might be the easier option. Cundy et al (1995) also used both equations for calculating BMAD at various skeletal sites, including lumbar spine and femoral neck, in four different ethnic groups. They found virtually identical outcomes for both equations, with no indication that one equation was superior to the other.

4.8.4 Hip Geometry parameter measurements

More recently, DXA scan images have been used to measure bone geometry of the proximal femur (Beck, 2007; Yoshikawa et al., 1994). Software can be installed on the DXA scanner to
measure or calculate some of these geometric parameters. This software is generally referred to as Hip Structure Analysis (HSA) or, if a GE Lunar DXA scanner is used, Advanced Hip Analysis (AHA). However, because DXA scan images are two-dimensional and DXA scanners were not designed for geometric measurement, the values obtained are relatively imprecise (Beck, 2007) and more accurate measurements are made using QCT (Adams, 2013).

Some of the hip geometry parameters recorded in my study are illustrated in the figure below and defined in the following text.

![Figure 4.6 Geometrical measurements related to the proximal femur (Gregory, 2008)](image)

**Hip axis length (HAL)**

HAL (mm) is the distance along the femoral neck axis from the inner pelvic brim to the lateral aspect of the greater trochanter.

**Femoral neck width (FNW)**

FNW (mm) is defined as the narrowest distance across the femoral neck, perpendicular to the neck axis.
Cross sectional area (CSA) and section modulus (Z) at femur neck

The larger the CSA ($mm^2$) of a bone, the greater is its resistance to loading, because the load is spread over a bigger area (Faulkner et al., 2006), so a large CSA of bone decreases fracture risk (Ahlborg et al., 2005). Another parameter, linked to CSA, commonly reported for bone geometry, is Z ($mm^3$), sometimes referred to as bending strength (Beck, 2007), which is the polar moment of inertia divided by the maximum distance of any of voxels from the centre of gravity (Schoenau et al., 2001). If the long bone were a perfect cylinder then the maximum distance of any pixel area from the centre would be synonymous with the outer radius. Mass distributed at this maximum distance i.e. at the perimeter, has maximum effectiveness in resisting force. Therefore, Z gives an indication of how effective the distribution of mass is compared to its optimal distribution, the higher the Z the stronger the bone, and reduced fracture risk (Kaptoge et al., 2008).

Figure 4.7 below illustrates how widening the diameter of a bone increases the bending strength i.e. Z.

![Diagram showing the effect of increasing bone diameter on SM (Schoenau et al., 2001)](image)

**Figure 4.7 The effect of increasing bone diameter on SM (Schoenau et al., 2001)**

### Buckling Ratio (BR)

If the bone mass is concentrated too much at the perimeter i.e. a thin cortex width (thus increasing the value of Z, and hence, ostensibly, strength) there is a risk of buckling. If a long bone is thought of as a hollow tube (like a straw) then it is only as strong as the wall thickness i.e. cortical bone. If the ratio of the outer radius of the bone (tube) to the cortex...
(wall) thickness is high, i.e. thin cortex, then the bone (tube) is more liable to bend i.e. “buckle”. So if a bone increases in diameter without a commensurate increase in cortex width, the ratio of the outer radius to the cortex/wall thickness (BR) increases, and if it exceeds a factor of about 10, there is a susceptibility to buckling (Beck, 2007). It seems that BR measurements using DXA may not be accurate, as a low level of precision has been reported for BR when using DXA technology (Hind et al., 2012).

**Neck Shaft Angle (NSA)**

NSA (°) is the angle between the femoral neck axis and femur shaft (Brownbill et al., 2003).

**Hip Strength Index (HSI)**

The GE-Lunar DXA software, AHA, calculates HSI as described in Figure 4.8 (from GE-Lunar software documentation, based on Yoshikawa et al., 1994).

HSI is the ratio of the estimated compressive yield strength of the femoral neck to the expected compressive stress of a fall on the greater trochanter (Yoshikawa et al., 1994; Faulkner et al., 2006). Increased values of HSI are associated with reduced fracture risk (Faulkner et al., 2006). As height and HAL in SAs are lower than Europeans, HSI will help compare the overall balance for fracture risk between BD and IB women in my study.

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*Force from falling (F) causes a compressive force (Fc) and a bending moment (M) on the femoral neck. The stress at point P can be estimated using the bending moment, compressive force, cross section area (CSA), cross sectional moment of inertia (CSMI), distance from the centre of the femoral head to the section of minimum CSMI along the neck axis (d1) and distance from the centre of mass to the upper neck margin for the minimum CSMI (y) (Yoshikawa et al., 1994).*

**Hip Strength Index = strength/stress where,**

\[
\text{Strength} = 185 - 0.34 \times \text{age} - 45 ; \quad \text{Age} > 45
\]

\[
\text{Stress} = \frac{\text{Moment} \times y}{\text{CSMI} + \text{force} \times \text{CSA}}
\]

\[
\text{Moment} = d1 \times 8.25 \times \text{weight in Newtons} \times 9.8 \text{(height in cm / 170)}^{0.5} \times \cos(180° - \theta)
\]

\[
\text{Force} = 8.25 \times \text{weight in Newtons} \times 5.8 \text{(height in cm / 170)}^{0.5} \times \sin(180° - \theta)
\]

\[
d1 = \text{distance along the neck axis from the centre of the femoral head to the section of minimum CSMI}
\]

\[
y = \text{distance from centre of mass to the upper neck margin, along the section of minimum CSMI}
\]

\[
\theta(\theta) = \text{angle of the intersection of the neck and shaft axes}
\]

**Figure 4.8 Calculation of HSI (GE-Lunar software documentation, based on Yoshikawa et al., 1994).**
In my study, I used HSI as a mean index of hip strength but other researchers have used alternative composite indices for femoral neck strength. Karlamangla et al. (2004) suggested that the ability of the femoral neck to withstand the compressive and bending forces induced by an individual’s body weight can be approximated by indices which combine BMD of the femoral neck, body weight and hip geometry parameters, FNW and HAL. They are termed the Compression Strength Index (CSI) and Bending Strength Index (BSI) respectively and the equations for these two indices are:

\[
\text{CSI} = \frac{\text{BMD} \times \text{FNW}}{\text{Weight}} \quad \text{BSI} = \frac{\text{BMD} \times \text{FNW}^2}{\text{HAL} \times \text{Weight}}
\]

Another index calculated is impact strength index (ISI) which is suggested to be the ability of the femoral neck to absorb the energy of impact in a fall from standing height, the equation being:

\[
\text{ISI} = \frac{\text{BMD} \times \text{FNW} \times \text{HAL}}{\text{Height} \times \text{Weight}}
\]

Derivations of these equations are given by Karlamangla et al. (2004) who suggest that composite indices for femoral neck strength may improve hip fracture risk assessment (Karlamangla et al., 2004). A comparison of composite indices calculated from CT scans with those obtained from DXA scans showed good correlation (Danielson et al., 2013b). I did not use these indices in my study because they had to be adjusted for age, BMI and menopausal status using multiple regression analysis, necessitating large sample numbers, before they reflected ethnic differences (Ishii et al., 2012).

### 4.8.5 Mechanism of QUS

Another means of measuring bone strength is to use QUS. Ultrasound is electromagnetic energy with a wavelength of over 20 kHz i.e. above 20,000 cycles per second, a frequency above the threshold of audibility of the human ear (Guglielmi and de Terlizzi, 2009). Medical ultrasonography uses high frequencies (over 2 MHz) to reconstruct an image of the inner human body whereas QUS uses a range between 0.2 and 1.5 MHz to assess tissue properties (Guglielmi and de Terlizzi, 2009).
Although QUS can be used at other sites, the calcaneous has the advantage of being similar to the proximal femur and spine in that it is subject to weight bearing forces. Furthermore, being 90% trabecular bone, the calcaneous is the same bone type predominant in the vertebrae.

The methodology for measuring QUS parameters in the calcaneous was originally developed by Langton (Langton, Palmer and Porter, 1984). A transducer on one side of the water bath transmits an ultrasound pulse to the other side of the bath where it is picked up by the receiving transducer. Different wavelengths i.e. frequencies, will be attenuated to a greater or lesser degree, depending on the medium through which it passes, allowing a frequency spectrum to be generated. The frequency spectrum of the ultrasound pulse is measured in the water bath, firstly with water only in the bath, and then with the participant’s foot immersed and positioned so the ultrasound pulse goes through the heel. The comparison between the frequency spectra (obtained in water alone versus water plus heel) will produce the ultrasound attenuation spectrum for the heel. Two parameters are commonly reported, BUA and SOS. BUA is the slope of the linear part of the attenuation spectra i.e. change of attenuation (dB) with frequency (MHz), a higher value denoting better bone quality. A high value for SOS indicates a dense material as sound waves travel faster through a denser medium. SOS also measures the elasticity of a material, and in 1970 Lang was the first to demonstrate the use of ultrasound for measuring elasticity in bone (Lang, 1970). Microarchitecture and structural properties of the bone are also involved in QUS (Njeh et al., 2001), although there is still not a clear understanding of BUA dependence upon the material and structural parameters of bone (Langton, 2011).

There are a variety of QUS devices on the market for measuring the calcaneous, using either water or gel as the medium through which the ultrasound waves pass. A comparison of six devices concluded that absolute BUA and SOS values varied between the devices although they gave a similar fracture prediction (Njeh, Hans, et al., 2000). The lack of standardisation of results between different devices and manufacturers (Njeh, Hans, et al., 2000; Stewart and Reid, 2000) and the lack of enough databases to allow specific diagnostic thresholds has led to QUS not being used so much in the clinic as it is in research.
A measure of heel width has been recommended when measuring QUS, as the size of the calcaneous and amount of overlying soft tissue can affect the BUA and SOS values (Hans et al., 1995). Also oedema is reported to reduce BUA, but not SOS (Johansen et al., 1997).

4.8.6 Protocol for QUS

The DTU-one (Osteometer MediTech Inc. Denmark) water-based ultrasound scanner was used to measure QUS parameters, BUA and SOS, at the calcaneous. This imaging device has the advantage of measuring the QUS parameters in a region of bone chosen by bone properties and therefore independent of foot size and positioning (Njeh, Fuerst, et al., 2000), which removes the potential bias of skeletal size, a characteristic that may differ between ethnic groups. The software manufacturers include a reference population of healthy indigenous European people for calculating the participant’s age-adjusted Z score. The machine was used according to the manufacturer’s instructions. Calibration with a phantom was carried out every time the machine was set up. The participant had gel applied to the right heel to lessen the possibility of air bubbles forming which interferes with the measurement. A background reading was taken first and then the participant put her foot in the water bath for the scan which took about 10 minutes. The machine used and scan obtained plus examples of the graphs displayed by the software are shown in the figures 4.9 and 4.10.

![Figure 4.9 The DTU-one ultrasound scanner and image obtained of the calcaneous](image-url)
4.9 Statistical Analysis

Data were recorded and analysed using SPSS version 23 (IBM Corporation, New York). The small sample numbers plus wide ranges of potential confounders such as age, menopausal status and BD daughters’ birthplace, limits multivariate or mixed-models statistical analysis. These limitations are described further in the Results chapter. Therefore, statistics are mainly descriptive, with effect sizes and trends reported to give a general idea of the characteristics of each ethnic group. To test study predictions, reviewers’ recommendations were followed, which involved pooling mothers and daughters together, and excluding some of the study sample. The various statistical tests and related samples are summarised below and described more fully in the rest of this chapter. Differences were considered statistically significant at the 5% probability level (p=0.05).

4.9.1 Summary of statistical methodology

Means and standard deviations, medians and ranges, or numbers and percentages were reported for all variables, using the total study sample (22 BD dyads and 26 IB dyads). Due to limitations of the study data set in terms of sample size and age distributions (see Results), very few statistical tests were carried out on descriptive variables. Where used,
the independent t-test (for continuous, normally distributed data), Mann-Whitney test (for continuous, non-normally distributed data) or chi-squared test (for discrete, non-normally distributed data) were employed to compare results of certain descriptive variables between ethnic groups. These were only carried out on important variables to the study hypotheses where appropriate and relevant, and are reported in the Results chapter when used. Effect size was also reported to give an indication of trends, using Cohen’s d (where 0.2 to < 5.0, 0.5 to < 0.8 and >0.8 were small, moderate and large effect size respectively) (Cohen, 1988).

To test the first two predictable hypotheses (see over page), the reviewers advised pooling the mother-daughter data from both ethnic groups to increase the sample number, thus allowing standard multiple linear regression (MLR) models to be run. This resulted in a sample number of 96 women. The reviewers also advised excluding certain women to remove the confounding effects of HRT, oral contraception and BD daughters who were born in the UK.

To test the third study prediction (see over page), only BD daughters were used. Data from six other BD daughters (whose measurements had been recorded, despite their not having a mother in the study) were added to increase the sample number to 28 daughters (13 BD daughters born in BD and 15 BD daughters born in the UK). The mean age of the BD daughters differed significantly, according to birthplace, (section 5.1.5). This could have influenced the outcome of any statistical test, and as the sample number was small, only effect sizes and trends were considered, although probabilities from t-tests were reported for interest.
**4.9.2 Power Calculations**

As recommended, standard MLR was used for testing the study predictions, so post hoc power calculations were made using G*Power version 3.1.3. ([http://www.gpower.hhu.de/](http://www.gpower.hhu.de/)). (Faul *et al.*, 2007). Following the equation for recommended sample size in MLR, \( N = 50 + 8 \times \text{number of predictor variables} \) (Tabachnick and Fidell, 2001), and knowing the sample number equalled 68 women, suggested two predictor variables could be used. However, three to four predictor variables were of interest: - ethnic group, generation (mother/daughter), menopausal status and, potentially height, if any ethnic difference was found. Using G*Power 3.1.9.2 and specifying a medium effect size \( (f^2 = 0.15) \) and three predictors gave a power of 74%. Using two predictors gave a power of 80% (see Appendix IV for G*power output). An inspection of the data indicated that it would not be necessary to use four predictors because menopausal status and generation were not both significant predictors in any of the models.
4.9.3 Testing assumptions and controlling for confounders

One basic assumption underlying statistical analysis is that study participants are selected at random. This assumption was not fully met as there were certain unavoidable biases due to snowball and purposive sampling in the recruitment process of BD women and to a lesser extent, IB women. One feature of the Bangladeshi community, having strong family ties, is the possibility of participants (in addition to mothers and daughters) being genetically related to each other, although no such cases were apparent.

For comparisons between variables which used the independent t-test the assumption of normality was tested for dependent variables using Kolmogorov-Smirnov and Shapiro-Wilk tests of normality. If a paired t-test was used, the distribution of the differences was tested for normality. Stem-and-leaf plots also helped test for normality as well as identifying outliers. Outlying data points were checked for possible transcription errors or artefact, but if there was no good reason to drop the outlier, they were kept in the analysis. Only one outlier was found with greater than or less than 3 standard deviations from the mean of one of the variables: this was a 30-year old IB daughter who was morbidly obese with a weight of 143.5 kg (3.2 standard deviations from IB daughters mean weight of 75.88 kg). However, there was no reason to exclude this woman, as I personally remember her being very heavy, and all her other measurements were consistent with a high weight. She was taking medication for lung problems and depression. Fat tissue can compromise BMD readings (Bolotin and Sievänen, 2001) so the analyses involving BMD and BMAD were run again, excluding this participant, with the same outcomes.

Statistical analysis was carried out on very few variables for previously mentioned reasons, so testing for normality was not required for all the variables. MLRs do not require that the dependent variable is normally distributed.

For each MLR that was run, the usual assumptions were tested for i.e. multicollinearity, singularity, outliers, normality, linearity, homoscedasticity and independence of residuals. These are considered further in the next section.

Age, especially age since menopause, is a known influence on many of the bone health variables measured in the current study. If possible, this needed to be controlled for in the
MLRs. Therefore, correlations were carried out between age and experimental variables to see if age could be accounted for in the statistical analysis. These correlations were carried out on the sample that was used for MLRs i.e. the reduced study sample, with all UK-born BD daughters and HRT or contraception users excluded.

Table 4.3 below shows the correlation coefficients between age and each experimental variable, for each ethnic group, divided into pre- and post-menopausal women. The samples were divided into pre- and post-menopausal status because it is known that the relationship between age and bone status measurements differs depending on menopausal status. The pre-menopausal samples included some (pre-menopausal) mothers as well as all the daughters, so some of the cases may be related i.e. not independent. Scatter graphs shown below (Figure 4.11) illustrate the relationship between age and the following variables: - femur neck BMD, lumbar spine BMD, 33% radius BMD, height, knee height, BUA raw score and SOS raw score.

From the correlation coefficients and scatter graphs, it was concluded that the relationship between age and the experimental variables in pre- and post-menopausal women was not sufficiently clear to be able to control for age in the study data set. However, the scatter graphs which have a mixture of pre-and post-menopausal women do show a general trend for lower DXA BMD and QUS raw scores in post-menopausal women compared to pre-menopausal women. It was therefore decided that menopausal status should be taken into account in the statistical analysis. Using Z-scores allows age and menopause to be taken into account but as explained in the Methods chapter BMD Z scores could not be used. Instead BMD raw scores were used, with menopausal status as one of the predictor variables in the MLR analysis. QUS Z scores are only adjusted for age so QUS Z scores were used in the MLR analysis (although raw scores are also presented in tables for comparison with previous publications).
Table 4.3 Correlation coefficients for age and experimental variable, according to ethnicity and menopausal status, for the sample used in MLR analyses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Correlation coefficient (r) with age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BD post-men. women (n=12)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.05 (p=0.888)</td>
</tr>
<tr>
<td>Knee Height (cm)</td>
<td>-0.02 (p=0.940)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>-0.48 (p=0.118)</td>
</tr>
<tr>
<td>BUA Raw Score (dB MHz⁻¹)</td>
<td>0.05 (p=0.88)</td>
</tr>
<tr>
<td>SOS Raw Score (m⁻¹)</td>
<td>0.08 (p=0.811)</td>
</tr>
<tr>
<td>DXA Femur Neck BMD (g/cm²)</td>
<td>-0.15 (0.647)</td>
</tr>
<tr>
<td>DXA Spine L₂ to L₄ BMD (g/cm²)</td>
<td>0.13 (0.681)</td>
</tr>
<tr>
<td>DXA proximal radius BMD (g/cm²)</td>
<td>0.07 (0.817)</td>
</tr>
</tbody>
</table>

*significant correlation at <0.05
Figure 4.11 Scatter graphs showing the relationship of BMD, height and knee height with age.
4.9.4 Ethnic and generational differences in anthropometric and bone measurements

In view of limitations of the data set, described later, and upon advice from the thesis reviewers, a retrospective statistical analysis was carried out. The sample number was increased by pooling the mothers and daughters together, which allowed standard MLR analysis to be used. BD daughters born in the UK were excluded to avoid confounding of BD daughter’s birthplace, so all BD women in the resulting sample were born in Bangladesh. Other exclusions included women who had ever used HRT and women who were taking oral contraceptives, as these were confounding factors for bone status. The resulting sample comprised 68 women.

Three to four predictor variables were of interest: - ethnic group, generation (mother/daughter), menopausal status and, potentially height if an ethnic difference was found. A number of women (mainly BD mothers) in the sample reported taking vitamin D medication for vitamin D deficiency which could affect their bone mass measurements. Therefore, a final model was run, comprising predictor variables previously found to be significant plus vitamin D as an extra predictor to see if this produced a different outcome.

The models for each experimental variable (height, knee height and bone measurements) were as follows: -

Model One: One predictor variable: ethnicity (one dummy variable - BD ethnic group and a IB ethnic group, as the reference).

Model Two: Two predictor variables: ethnicity, as above, and menopause (dummy variable - pre-menopausal status and post-menopausal status, as the reference).

Model Three: Three predictor variables: ethnicity and menopause as above, and generation (dummy variable – mother with daughter as the reference).

Model Four: Two predictor variables: ethnicity and menopause as above, and height as a continuous variable. An initial inspection of the data indicated that generation would not be a significant predictor so did not need to be included in this model.
Model Five: The best of the models above (as determined by adjusted $R^2$ and effect size) plus predictor variable vitamin D medication (one dummy variable - no report of vit. D medication and a second one - self-reported vitamin D medication) as the reference. This model was only run for dependent variables related to bone mass because a change from previous vitamin D levels in an individual would not have been expected to have affected hip geometry bone measurements such as HAL.

The effect size for each predictor variable was indicated by standardised beta coefficients or Cohen’s r (Durlak, 2009). The equation for Cohen’s r is:

$$r = \sqrt{\frac{t^2}{t^2 + df}}$$

Cohen’s r of 0.10, 0.30 and 0.50 were interpreted as small, medium and large effect sizes respectively.

The dependent (experimental) variables were: - height, knee height, BMD and BMAD (femur neck, lumbar spine and 33% radius), BUA Z and SOS Z score and hip parameters (HSI, HAL, BR, FNW, Z, NSA).

In model four, the prediction was that height, but not ethnicity, would make a significant contribution to variance of the bone measurement. The fourth model was not used for BMD measurements. If ethnicity was a significant contributor to the variance in a BMD measurement, then models one to three were run on BMAD (which takes into account skeletal size) to see if ethnicity contributed to the variance, once skeletal size had been taken into account. Model four was run if an ethnic influence was found for any of the hip geometry parameters or QUS scores.

The assumptions of MLR were tested. Singularity was not a problem as none of the predictor variables were a combination of any of the other predictor variables. Multicollinearity, denoted by a variance inflation factor > 10 (Field, 2013) was not flagged up as an issue. However, ethnicity and height were significantly correlated ($r = 0.79, p<0.001$) and the variance inflation factor was 2.52, indicating that in models containing ethnicity and height as predictor variables, the outcome may be biased (Field, 2013).
The other assumptions regarding the residuals (normality, linearity, homoscedasticity and independence) were also met according to the SPSS output.

Some of the women in the data set were related to each other by virtue of being a mother and daughter. However, to account for this lack of independence, a mixed model approach would have been required, which was not possible due to the small sample number involved.

### 4.9.5 Birthplace of BD daughters: differences in anthropometric and bone measurements

The sample numbers for this comparison were very small (13 BD-born daughters and 15 UK-born daughters) and the BD-born daughters were significantly older than UK-born daughters (see section 5.1.5). Because of these facts, statistical analysis was considered inappropriate so effect sizes and graphs were used to report the results. However, probability estimates from independent t-tests were reported to help interpret trends. Knee heights in mothers were also recorded to explore familial influences on daughters’ knee heights. However, some daughters did not have mothers in the study, limiting the validity of checking familial influence.

### 4.10 Ethics

Ethical approval for the study was obtained from Loughborough University Ethics Approval Committee (LUEAC) in 2012 (Study Number: Ref No: R12-P96). As participants were required to undergo a DXA scan, ethical approval was also granted by the National Research Ethics Service (NRES) (ref: 12/EM/0223). All participants were given an information sheet and asked to give written informed consent. For BD women who could not understand English, translation was provided by their daughter or another member of the BD community and verbal consent was obtained from the study participant via her representative. Consent forms were not translated into Bengali as many of the older women, even if they could speak some English, could not read at all. To ensure anonymity for participants, each study volunteer was given an identity number.
5 Results: Comparison of height and bone status in UK BD and IB women according to ethnicity, generation and birthplace (Loughborough Study)

This chapter reports on data collected from BD and IB mother-daughter pairs resident in Loughborough. This study forms the basis of my thesis and was designed to help answer the research question described in the Introduction chapter. The methods used for the Loughborough study are described in Chapter 4.

5.1 Results

5.1.1 Sample number and missing data

The final complete sample size was 22 BD and 26 IB complete mother-daughter pairs (Figure 5.1).

Initially, 34 BD mother-daughter pairs were interested in the study but the final sample size was 22 BD mother-daughter pairs because 12 pairs were excluded, or did not complete the study, for the following reasons:

a. Four mothers taking medication affecting bone metabolism (n=3 thyroxine and n=1 steroids)

b. Two daughters not interested

c. Four pairs dropped out of the study

d. One mother born in the UK

e. One mother who emigrated to the UK as a child (10 years old)

In addition to 22 complete BD mother-daughter pairs (44 individuals), data were collected from six daughters whose mothers were excluded. This resulted in a sample number of 28 BD daughters, which was the data set used to explore the association of BD daughter’s birthplace with anthropometric and bone status measurements (section 5.1.5).
Initially, 52 IB potential mother-daughter pairs were interested in the study but 26 pairs were excluded or did not complete the study, for the following reasons:

a. Two pairs declined to take part, after hearing more details about the study
b. One daughter dropped out of the study
c. Two volunteers did not have a mother or daughter
d. One pair dropped out of the study
e. Five pairs did not meet the ethnicity requirements
f. One pair was not resident in Loughborough
g. One daughter was ineligible due to previous high medical X-ray exposure
h. Four mothers were taking medication for osteoporosis
i. Six mothers were taking medication affecting bone metabolism (n=5 thyroxine, n=1 steroids)
j. Three mothers had had an early hysterectomy and were on long term HRT

For DXA and QUS measurements, the following points refer to sample size (Table 5.1). One IB mother had fused vertebrae so could provide no data for BMD lumbar spine. For three women (one BD daughter, one IB daughter and one IB mother) it was difficult to interpret the scan regarding vertebra L₄, so the average BMD for vertebrae L₁ to L₃ was used (instead of average BMD for L₁ to L₄) for lumbar spine BMD. However, for these three women, BMAD could not be calculated because BMD results for L₂ to L₄ vertebrae are required.

There were also no BMD Z-scores and QUS Z scores for one young BD daughter (aged 19 years) because she was below the software manufacturer’s reference age range of 20 to 80 years. Similarly, there were no BMD Z scores and QUS Z scores recorded for one BD mother who, aged 82 years, was above the DXA and QUS software manufacturer’s reference age range.
Figure 5.1 Flow diagram showing recruitment and sample numbers for Loughborough BD and IB mother-daughter pairs
Table 5.1 Sample numbers: BMD and QUS measurements for which there are reduced sample numbers

<table>
<thead>
<tr>
<th>Variable</th>
<th>BD mothers (n=22)</th>
<th>BD daughters (n=22)</th>
<th>IB mothers (n=26)</th>
<th>IB daughters (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine L₁–L₄ BMD (g/cm²)</td>
<td></td>
<td></td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Spine L₂–L₄ BMD (g/cm²)</td>
<td>21</td>
<td>24</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Femur Neck BMD Z score</td>
<td>21</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spine L₁ – L₄ BMD Z score</td>
<td>21</td>
<td>21</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>33% Radius BMD Z score</td>
<td>21</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spine L₂ – L₄ BMAD (g/cm³)</td>
<td>21</td>
<td>21</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>BUA Z score</td>
<td>21</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOS Z score</td>
<td>21</td>
<td>21</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.1.2 HRT and contraceptive use

No BD mother used HRT, whereas three IB mothers had taken it (two were current users in their first year of HRT use, and one had taken HRT in the past). These three IB women who had had exposure to HRT use were included in the sample, as only long-term HRT users were excluded from the study. All the anthropometric and bone status measurements of these three IB women were consistent with the rest of their group. Their descriptive statistics were reported but, based on the thesis reviewers’ recommendations, these participants were omitted from the statistical analyses comparing bone status measurements between ethnic group and generation (see Methods chapter).

One BD mother and three BD daughters (all born in Bangladesh) used oral contraception. None of the IB mothers took oral contraceptives, whereas ten IB daughters used oral contraception. The research on benefits or adverse effects of contraceptives on bone tends to be equivocal, although a recent study suggested they benefitted bone status (see Background chapter). Women using contraception were included in my study to reflect the characteristics of each ethnic group and are reported in descriptive statistics. The anthropometric and bone status measurements of women using contraception were consistent with the rest of their group. However, for statistical analyses exploring bone
status measurements according to ethnic group and generation, women using oral contraception were excluded as described in the Methods chapter.

5.1.3 General description of study sample

Demographic and reproductive variables

All 22 BD mothers were born in Sylhet, NE Bangladesh. The sample of BD daughters happened to be equally divided between birthplace, with 11 daughters born in Sylhet, Bangladesh and 11 daughters born in the UK. All 26 IB mothers and 26 IB daughters had been born in the UK.

BD mothers and IB mothers were of a similar average age, 57.1 ± 14.7 years and 57.8 ± 8.1 years respectively (Table 5.2). However, the BD mothers had a greater range of ages, 38 to 82 years, compared to the age range of IB mothers, 48 to 74 years (Table 5.2). BD daughters were on average younger than IB daughters, by about 4 years, (Table 5.2).

The ages of BD women (both mother and daughter samples) did not follow a normal distribution: instead, they tended to a bimodal distribution (Figure 5.2), with two distinct age profiles of BD mother-daughter pairs:- 1) older post-menopausal BD mothers with older daughters, and 2) younger, premenopausal BD mothers with younger daughters.

It was further observed that the older, post-menopausal BD mothers tended to have BD-born daughters, whereas the younger pre-menopausal BD mothers tended to have UK-born daughters. This caused problems when comparing associations of experimental variables with daughter’s birthplace as discussed later in the chapter (section 5.1.5).

IB mothers and daughters also had an age distribution that was not normally distributed (Figure 5.2). Furthermore, the distribution of menopausal status was different between the two ethnicities (Table 5.2), with IB mothers comprising a greater ($\chi^2$ test, $\chi^2 = 3.814$, df=1, p=0.051) number of post-menopausal women (81%) compared to the BD mother (55% post-menopausal women).

BD mothers tended to marry on average at a young age, close to 17 years, whereas IB mothers married about four years later, at an average age of 21 years (Table 5.2). BD mothers generally started a family sooner than IB mothers, and had more children (Table
This may explain the greater range of age in BD mothers, and their higher percentage of pre-menopausal women, compared to the IB mothers.

The average recalled age at menarche for BD daughters (11.6 ± 1.4 years) was younger than the other three groups whose recalled age at menarche was closer to 13 years (Table 5.2). This resulted in significantly higher recalled age at menarche in BD mothers compared to their daughters (paired t-test, t=2.602, df=17, p=0.019), as well as significantly higher recalled age at menarche in IB daughters compared to BD daughters (t-test, t=3.284, df=42, p=0.002).

Figure 5.2 Frequency distributions showing bimodal age distributions for Loughborough BD women and non-normal distributions for IB women.
Table 5.2 Demographic and reproductive variables for Loughborough BD and IB mother-daughter pairs

Reported as mean ± st.dev, median (range) or number (%).

<table>
<thead>
<tr>
<th>Variable</th>
<th>BD Mothers (n=22)</th>
<th>BD Daughters (n=22)</th>
<th>IB Mothers (n=26)</th>
<th>IB Daughters (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.4 ± 14.7</td>
<td>29.1 ± 8.9</td>
<td>57.8 ± 8.1</td>
<td>32.4 ± 7.8</td>
</tr>
<tr>
<td></td>
<td>58.5 (39 to 82)</td>
<td>24.5 (19 to 44)</td>
<td>56.0 (48 to 74)</td>
<td>30.5 (20 to 46)</td>
</tr>
<tr>
<td>Year of birth</td>
<td>1955.6 ± 14.7</td>
<td>1984.1 ± 9.0</td>
<td>1955.6 ± 7.9</td>
<td>1980.0 ± 7.8</td>
</tr>
<tr>
<td>No. (%) born in BD</td>
<td>22 (100%)</td>
<td>11 (50%)</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>No. (%) post-menopausal</td>
<td>12 (55%)</td>
<td>0 (0%)</td>
<td>21 (81%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>No. (%) HRT</td>
<td>0 (0%)</td>
<td>Not Applicable</td>
<td>3 (12%)</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>No (%) oral contraceptive</td>
<td>1 (5%)</td>
<td>3 (14%)</td>
<td>0 (0%)</td>
<td>10 (38%)</td>
</tr>
<tr>
<td>Recalled age at menarche†</td>
<td>12.9 ± 1.4</td>
<td>11.6 ± 1.4</td>
<td>13.4 ± 1.3</td>
<td>12.9 ± 1.3</td>
</tr>
<tr>
<td></td>
<td>13.0 (11 to 15)</td>
<td>12.0 (9 to 14)</td>
<td>13.0 (11 to 16)</td>
<td>13.0 (11 to 16)</td>
</tr>
<tr>
<td>Marital status</td>
<td>15 married,</td>
<td>13 single,</td>
<td>18 married,</td>
<td>10 single,</td>
</tr>
<tr>
<td></td>
<td>7 widowed</td>
<td>8 married,</td>
<td>1 co-habiting</td>
<td>11 married,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 divorced</td>
<td>6 divorced,</td>
<td>1 cohabiting,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 civil partnership,</td>
<td>2 divorced,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 separated,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 widowed</td>
</tr>
<tr>
<td>Age at marriage ‡</td>
<td>17.2 ± 1.8</td>
<td>21.0 ± 3.1</td>
<td>20.3 ± 2.1</td>
<td>25.2 ± 4.4</td>
</tr>
<tr>
<td></td>
<td>17.0 (14 to 22)</td>
<td>21.0 (17 to 26)</td>
<td>20.0 (16 to 25)</td>
<td>24.0 (20 to 38)</td>
</tr>
<tr>
<td>Number of children §</td>
<td>5.6 ± 1.6</td>
<td>3.3 ± 1.0</td>
<td>2.5 ± 0.6</td>
<td>1.3 ± 1.2</td>
</tr>
<tr>
<td></td>
<td>5.5 (3 to 9)</td>
<td>3.0 (2 to 5)</td>
<td>2.0 (2 to 4)</td>
<td>1.0 (0 to 4)</td>
</tr>
<tr>
<td>Age at birth of 1st child †</td>
<td>21.6 ± 2.8</td>
<td>23.0 ± 3.2</td>
<td>23.5 ± 4.1</td>
<td>26.6 ± 6.0</td>
</tr>
<tr>
<td></td>
<td>21.5 (17 to 29)</td>
<td>23.0 (19 to 29)</td>
<td>23.0 (14 to 22)</td>
<td>27.0 (17 to 37)</td>
</tr>
<tr>
<td>Number lacking formal education</td>
<td>3 (14%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

† 1 current HRT user for past 2 months, 1 current HRT user for 1 year, 1 woman on HRT in past
‡ n=18 for BD mothers, n=21 for BD daughters, n=23 for IB daughters (women unable to recall age at menarche excluded)
§ n=9 for BD daughters, n=16 for IB daughters (unmarried daughters excluded)
Migration history of BD women and early life environment of BD and IB women

As discussed above, the BD mother-daughter pairs containing UK-born daughters were younger (both mother and daughter) than their counterparts in BD mother-daughter pairs containing BD-born daughters (Table 5.3). UK-born daughters, whose average age was mid-twenties, were younger, by about ten years, than BD-born daughters, whose mean age was mid-thirties. Similarly, the mothers of the UK-born daughters had an average age of late forties, which was younger, by about 16 years, than mothers of the BD-born daughters, mean age mid-fifties (Table 5.3). This age difference was paralleled by a difference in the menopausal status of the BD mothers, according to daughter’s birthplace, with only 27% of the mothers of UK-born daughters being post-menopausal as opposed to 82% of mothers of BD-born daughters who were post-menopausal (Table 5.3).

Current ages of participants and their ages at migration differed between the two groups of BD mother-daughter pairs, but the average year of migration was similar, the mid 1980s.

Table 5.3 Migration data for Loughborough BD mother-daughter pairs, according to daughter’s birthplace

Reported as mean ± st.dev, median (range) or count (%).

<table>
<thead>
<tr>
<th></th>
<th>BD mothers of BD-born daughters (n=11)</th>
<th>BD-born daughters (n=11)</th>
<th>BD mothers of UK-born daughters (n=11)</th>
<th>UK-born daughters (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.6 ± 14.3</td>
<td>34.3 ± 8.2</td>
<td>49.2 ± 10.2</td>
<td>23.9 ± 6.4</td>
</tr>
<tr>
<td></td>
<td>71.0 (39 to 82)</td>
<td>36.0 (20 to 44)</td>
<td>45.0 (40 to 66)</td>
<td>22.0 (19 to 39)</td>
</tr>
<tr>
<td>Year of birth</td>
<td>1947.4 ± 14.2</td>
<td>1978.8 ± 8.1</td>
<td>1963.9 ± 10.2</td>
<td>1989.3 ± 6.8</td>
</tr>
<tr>
<td>No. (%) Post-menopausal status</td>
<td>9 (82%)</td>
<td>0 (0%)</td>
<td>3 (27%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Age at migration</td>
<td>37.9 ± 11.3</td>
<td>8.3 ± 8.3</td>
<td>21.1 ± 5.2</td>
<td>Not applicable</td>
</tr>
<tr>
<td></td>
<td>40.0 (19 to 57)</td>
<td>7.0 (0 to 21)</td>
<td>19.0 (18 to 36)</td>
<td></td>
</tr>
<tr>
<td>Year of migration</td>
<td>1985.4 ± 6.8</td>
<td>1987 ± 6.9</td>
<td>1985.1 ± 9.1</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

The age at migration of the BD-born daughters is of interest because it reflects the years of exposure to the Bangladeshi environment during early life. Sample numbers were too small
to analyse, but individual daughters’ age at migration are displayed later in this chapter (Figure 5.4 in section 5.1.5). Variables relating to the environment at birth of study participants are reported in Table 5.4 and illustrated in Figure 5.5. Generally, the majority of women born in Bangladesh (all BD mothers and 50% BD daughters) had been breast-fed, born at home, had not been vaccinated and their mothers had not received pre-natal care. The opposite outcome was found for women born in the UK (all IB women and 50% BD daughters) who were more likely to have not been breast-fed, been born in a medical facility, been vaccinated and had mothers who received pre-natal care (Table 5.4). In this study sample UK-born BD daughters born in the UK had experienced an early environment that was closer to that experienced by IB daughters.

Figure 5.3 Bar chart showing how indicators of pre- and post-natal environment differed according to ethnicity and birthplace in Loughborough BD and IB mother-daughter pairs
Table 5.4 Variables denoting environment at birth for Loughborough BD and IB mother-daughter pairs
Reported as counts (%)

<table>
<thead>
<tr>
<th>Variables denoting environment at birth</th>
<th>BD Mothers (n=22)</th>
<th>BD Daughters born in BD (n=11)</th>
<th>BD Daughters born in UK (n=11)</th>
<th>IB Mothers (n=26)</th>
<th>IB Daughters (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast-feeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>5 (46%)</td>
<td>15 (58%)</td>
<td>15 (58%)</td>
</tr>
<tr>
<td>Up to 6 months</td>
<td>1 (5%)</td>
<td>3 (27%)</td>
<td>4 (36%)</td>
<td>4 (15%)</td>
<td>10 (38%)</td>
</tr>
<tr>
<td>6 months and over</td>
<td>21 (95%)</td>
<td>8 (73%)</td>
<td>2 (18%)</td>
<td>4 (15%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Not remembered</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>3 (12%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Pre-natal care of participant’s mother</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received</td>
<td>1 (5%)</td>
<td>2 (18%)</td>
<td>7 (64%)</td>
<td>15 (58%)</td>
<td>25 (96%)</td>
</tr>
<tr>
<td>Not received</td>
<td>19 (86%)</td>
<td>9 (82%)</td>
<td>4 (36%)</td>
<td>3 (12%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Not known</td>
<td>2 (9%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>8 (31%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Born in own home or medical facility</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home birth</td>
<td>22 (100%)</td>
<td>11 (100%)</td>
<td>1 (9%)</td>
<td>16 (62%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Medical facility birth</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>10 (91%)</td>
<td>10 (38%)</td>
<td>23 (88%)</td>
</tr>
<tr>
<td><strong>Vaccination</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccinated</td>
<td>4 (18%)</td>
<td>4 (36%)</td>
<td>10 (91%)</td>
<td>18 (69%)</td>
<td>26 (100%)</td>
</tr>
<tr>
<td>Not vaccinated</td>
<td>16 (73%)</td>
<td>4 (36%)</td>
<td>1 (9%)</td>
<td>2 (8%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Not known</td>
<td>2 (9%)</td>
<td>3 (27%)</td>
<td>0 (0%)</td>
<td>6 (23%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Cared for by mother</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>17 (77%)</td>
<td>10 (91%)</td>
<td>10 (91%)</td>
<td>24 (92%)</td>
<td>24 (92%)</td>
</tr>
<tr>
<td>Mother &amp; family</td>
<td>5 (23%)</td>
<td>1 (9%)</td>
<td>1 (9%)</td>
<td>1 (4%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Adult carer</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Water supply</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural-surface/river</td>
<td>10 (45%)</td>
<td>1 (9%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Well</td>
<td>11 (50%)</td>
<td>3 (27%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pump/piped/tap</td>
<td>1 (5%)</td>
<td>6 (55%)</td>
<td>11 (100%)</td>
<td>26 (100%)</td>
<td>26 (100%)</td>
</tr>
<tr>
<td>Not remembered</td>
<td>0 (0%)</td>
<td>1 (9%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Toilet Facilities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural (river/bushes)</td>
<td>3 (14%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Latrines(^a)</td>
<td>19 (86%)</td>
<td>9 (82%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Flush</td>
<td>0 (0%)</td>
<td>2 (18%)</td>
<td>11 (100%)</td>
<td>26 (100%)</td>
<td>26 (100%)</td>
</tr>
</tbody>
</table>

\(^a\)Latrines include hole in ground, bucket or pit
Socioeconomic status and health

SES indicators include council tax band of house, number of occupants in the house and the employment status of the participant. However, these variables in the UK BD community could reflect culture instead of, or in addition to, SES. Some mothers and daughters, especially in the BD sample, lived in the same household which introduced some bias to the numbers reported.

As both ethnic samples were drawn from the same two Loughborough wards it was expected that the council tax band of the house would not differ greatly between the two ethnic groups (Table 5.5). Over 50% of both ethnic groups lived in houses with council tax bands of A and B i.e. those requiring the lowest payment of council tax, suggesting a low SES. The number of adults, living in the participant’s house differed between BD and IB women, with more adults and children living in a Bangladeshi household (Table 5.5). However, this probably reflects culture rather than SES. Employment status is also influenced by ethnic culture. The employment status of the women varied significantly between mothers in the two ethnic groups, with the majority (82%) of BD mothers looking after family home and dependents, or retired from this occupation, whilst the majority (85%) of IB mothers were in employment or retired from paid work (Table 5.5). Although being in employment is usually associated with higher SES, the higher number of IB mothers compared to BD mothers in employment probably reflects ethnic culture rather than SES. Of the BD daughters, 36% were in employment and 38% were students, the remaining daughters generally looking after the home and dependents. The majority of IB daughters (89%) were in employment.

BD daughters were quite similar to IB daughters in either being in employment, or, as current students, planning employment in the future.

The general health of the study sample can be gauged by describing the various illnesses, requiring medication, currently suffered by participants (Table 5.5). A higher number of BD mothers, compared to IB mothers, reported taking medication for diabetes, vitamin D deficiency, high blood pressure, iron deficiency/anaemia and/or high cholesterol (Table 5.5). Long-standing illnesses or disabilities were self-reported by 54% BD mothers compared to only 18% IB mothers. There were very few illnesses or disabilities in the daughters of both ethnic groups. Medications taken by both BD and IB daughters tended to be for lung problems and depression/anxiety.
**Table 5.5 Socio-economic status variables and self-reported health problems requiring medication for study sample**

Reported as count (%) or median (range)

<table>
<thead>
<tr>
<th></th>
<th>BD Mothers (n=22)</th>
<th>BD Daughters (n=22)</th>
<th>IB Mothers (n=26)</th>
<th>IB Daughters (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Council Tax Band</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>8 (36%)</td>
<td>8 (36%)</td>
<td>7 (28%)</td>
<td>7 (27%)</td>
</tr>
<tr>
<td>B</td>
<td>6 (27%)</td>
<td>7 (32%)</td>
<td>6 (24%)</td>
<td>9 (35%)</td>
</tr>
<tr>
<td>C</td>
<td>4 (18%)</td>
<td>4 (18%)</td>
<td>6 (24%)</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>D</td>
<td>2 (9%)</td>
<td>2 (9%)</td>
<td>3 (12%)</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>E</td>
<td>2 (9%)</td>
<td>1 (5%)</td>
<td>3 (12%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td><strong>No. of persons in household</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults (1 – 6)</td>
<td>3.0</td>
<td>3.0</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Adults (2 – 6)</td>
<td>3.0</td>
<td>3.0</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Adults (1 – 3)</td>
<td>3.0</td>
<td>3.0</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Adults (1 – 3)</td>
<td>3.0</td>
<td>3.0</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Adults (0 – 2)</td>
<td>3.0</td>
<td>3.0</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Adults (0 – 3)</td>
<td>3.0</td>
<td>3.0</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children (0 – 5)</td>
<td>2.0</td>
<td>3.0</td>
<td>0.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Children (0 – 2)</td>
<td>2.0</td>
<td>3.0</td>
<td>0.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Children (0 – 3)</td>
<td>2.0</td>
<td>3.0</td>
<td>0.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Children (0 – 3)</td>
<td>2.0</td>
<td>3.0</td>
<td>0.0</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Employment Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full employment</td>
<td>1 (5%)</td>
<td>8 (36%)</td>
<td>16 (62%)</td>
<td>23 (89%)</td>
</tr>
<tr>
<td>Full employment</td>
<td>1 (5%)</td>
<td>8 (36%)</td>
<td>16 (62%)</td>
<td>23 (89%)</td>
</tr>
<tr>
<td>Part time employment</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Unemployed/looking after family</td>
<td>11 (50%)</td>
<td>7 (4%)</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Unemployed/looking after family</td>
<td>11 (50%)</td>
<td>7 (4%)</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Unemployed/looking after family</td>
<td>11 (50%)</td>
<td>7 (4%)</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Unable to work due to ill health/disability</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Unable to work due to ill health/disability</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Retired (from work)</td>
<td>2 (9%)</td>
<td>0 (0%)</td>
<td>6 (23%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Retired (from work)</td>
<td>2 (9%)</td>
<td>0 (0%)</td>
<td>6 (23%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Retired (from looking after family)</td>
<td>7 (32%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Retired (from looking after family)</td>
<td>7 (32%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Student/Training</td>
<td>0 (0%)</td>
<td>7 (38%)</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Student/Training</td>
<td>0 (0%)</td>
<td>7 (38%)</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td><strong>Self-reported medical problems</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (45%)</td>
<td>1 (5%)</td>
<td>4 (16%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (45%)</td>
<td>1 (5%)</td>
<td>4 (16%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>8 (36%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>8 (36%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Angina</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Angina</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Heart Attack/problems</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Heart Attack/problems</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Joint or bone problemsa</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Joint or bone problemsa</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Lung problems</td>
<td>2 (9%)</td>
<td>2 (9%)</td>
<td>3 (12%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Lung problems</td>
<td>2 (9%)</td>
<td>2 (9%)</td>
<td>3 (12%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Depression/Anxiety</td>
<td>3 (14%)</td>
<td>2 (9%)</td>
<td>3 (12%)</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>Depression/Anxiety</td>
<td>3 (14%)</td>
<td>2 (9%)</td>
<td>3 (12%)</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td>7 (32%)</td>
<td>1 (5%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td>7 (32%)</td>
<td>1 (5%)</td>
<td>1 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>High Cholesterol</td>
<td>8 (36%)</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>High Cholesterol</td>
<td>8 (36%)</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Gastric problems</td>
<td>8 (36%)</td>
<td>2 (9%)</td>
<td>3 (12%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Gastric problems</td>
<td>8 (36%)</td>
<td>2 (9%)</td>
<td>3 (12%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Iron deficiency/anaemia</td>
<td>3 (14%)</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Iron deficiency/anaemia</td>
<td>3 (14%)</td>
<td>1 (5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*a tennis elbow, requiring pain killers
5.1.4 Ethnic and generational differences in anthropometric and bone status measurements

As explained in the Methods chapter, both ethnic groups in the initial sample were pooled together, and a number of women were excluded, before statistical analysis was attempted. However, to give an indication of the profile of the total sample before women were excluded, a table of data for the experimental variables for the total study sample is given in Table 5.6.

The numbers of women excluded to provide the sample for the multiple regression analyses were as follows: - UK-born BD daughters (n=11), women who had used HRT (n=3 IB mothers) and women using oral contraceptives (n=1 BD mother, 3 BD daughters and 10 IB daughters. This resulted in a total sample of 68 women (29 BD women born in Bangladesh and 39 IB women). The sample of 29 BD women born in Bangladesh comprised 12 post-menopausal mothers, 9 pre-menopausal mothers and 8 daughters. The sample of 39 IB women comprised 19 post-menopausal mothers, 4 pre-menopausal mothers and 16 daughters. The data for the experimental variables for this reduced sample are shown in Table 5.7.

It can be seen from both tables that the general trend is that IB women have larger measurements in height, knee height, weight, BMD, HAL, FNW, Z and BUA (raw and Z score) scores than BD women.

Daughters in both ethnic groups tend to be taller, with higher BMD of femur neck and lumbar spine raw than their mothers. It is noteworthy that whilst IB daughters are heavier in body mass than their mothers, the opposite is true for BD daughters, who are lighter than their mothers. It is also interesting to note that in the case of some bone measurement Z scores (BMD proximal radius, BUA and SOS) daughters, in both ethnic groups, have lower values than mothers.
Table 5.6 Anthropometric and bone measurements for BD and IB women, mothers and daughters for total sample (mean ± sd)

<table>
<thead>
<tr>
<th></th>
<th>BD Mothers (n=22)</th>
<th>BD Daughters (n=22)</th>
<th>IB Mothers (n=26)</th>
<th>IB Daughters (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.4 ± 14.7</td>
<td>29.1 ± 8.9</td>
<td>57.8 ± 8.1</td>
<td>32.4 ± 7.8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>151.6 ± 4.4</td>
<td>153.4 ± 4.6</td>
<td>163.1 ± 6.3</td>
<td>166.3 ± 6.2</td>
</tr>
<tr>
<td>No. (%) short-stature</td>
<td>8 (36%)</td>
<td>3 (14%)</td>
<td>2 (8%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Knee ht. (cm)</td>
<td>45.9 ± 1.7</td>
<td>46.1 ± 1.8</td>
<td>49.8 ± 2.7</td>
<td>49.9 ± 2.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>65.4 ± 12.4</td>
<td>57.3 ± 11.3</td>
<td>72.5 ± 16.9</td>
<td>75.9 ± 21.4</td>
</tr>
<tr>
<td>BMI</td>
<td>28.4 ± 4.9</td>
<td>24.4 ± 4.6</td>
<td>27.2 ± 5.9</td>
<td>27.4 ± 7.4</td>
</tr>
<tr>
<td>Fem. neck BMD (g/cm$^2$)</td>
<td>0.873±0.151</td>
<td>0.978±0.143</td>
<td>0.948±0.156</td>
<td>1.082±0.136</td>
</tr>
<tr>
<td>Spine L1–L4 BMD (g/cm$^2$)$^a$</td>
<td>1.017±0.166</td>
<td>1.157±0.138</td>
<td>1.092±0.162</td>
<td>1.245±0.131</td>
</tr>
<tr>
<td>Spine L3–L4 BMD (g/cm$^2$)$^b$</td>
<td>1.033±0.174</td>
<td>1.178±0.135</td>
<td>1.124±0.178</td>
<td>1.272±0.138</td>
</tr>
<tr>
<td>33%. Radius BMD (g/cm$^2$)</td>
<td>0.747±0.092</td>
<td>0.802±0.075</td>
<td>0.822±0.103</td>
<td>0.857±0.060</td>
</tr>
<tr>
<td>Fem. neck BMD Z score$^c$</td>
<td>0.03 ± 0.93</td>
<td>0.13 ± 1.13</td>
<td>0.56 ± 1.01</td>
<td>0.70 ± 1.13</td>
</tr>
<tr>
<td>Spine L1–L4 BMD Z score$^{cd}$</td>
<td>-0.54 ± 1.0</td>
<td>0.04 ± 1.05</td>
<td>0.04 ± 1.33</td>
<td>0.30 ± 1.11</td>
</tr>
<tr>
<td>33%. Radius BMD Z score$^c$</td>
<td>-0.66 ± 1.07</td>
<td>-1.00 ± 0.84</td>
<td>0.04 ± 1.00</td>
<td>-0.35 ± 0.68</td>
</tr>
<tr>
<td>Fem. neck BMAD (g/cm$^3$)</td>
<td>0.198±0.036</td>
<td>0.223±0.033</td>
<td>0.197±0.041</td>
<td>0.232±0.035</td>
</tr>
<tr>
<td>Spine L3–L4 BMAD (g/cm$^3$)$^b$</td>
<td>0.172±0.025</td>
<td>0.195±0.020</td>
<td>0.172±0.027</td>
<td>0.194±0.023</td>
</tr>
<tr>
<td>33%. Radius BMAD (g/cm$^3$)</td>
<td>0.330±0.053</td>
<td>0.358±0.046</td>
<td>0.333±0.058</td>
<td>0.342±0.053</td>
</tr>
<tr>
<td>HSI</td>
<td>1.56±0.39</td>
<td>1.70±0.37</td>
<td>1.63±0.40</td>
<td>1.56±0.47</td>
</tr>
<tr>
<td>BR</td>
<td>2.82±0.78</td>
<td>3.00±1.15</td>
<td>2.97±1.04</td>
<td>2.76±1.13</td>
</tr>
<tr>
<td>FNW (mm)</td>
<td>27.4±2.0</td>
<td>27.2±1.8</td>
<td>29.9±2.7</td>
<td>28.9±1.9</td>
</tr>
<tr>
<td>Z (mm$^{3}$)</td>
<td>477±97</td>
<td>517±108</td>
<td>584±101</td>
<td>660±115</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>93.1±4.2</td>
<td>95.3±4.9</td>
<td>104±5.6</td>
<td>103±5.9</td>
</tr>
<tr>
<td>NSA ($^{d}$)</td>
<td>125±3</td>
<td>126±3</td>
<td>124±4</td>
<td>125±4</td>
</tr>
<tr>
<td>BUA Raw Score (dB MHz$^{-1}$)</td>
<td>43.1±9.1</td>
<td>47.6±6.2</td>
<td>46.5±8.5</td>
<td>48.3±7.2</td>
</tr>
<tr>
<td>SOS Raw Score (ms$^{-1}$)</td>
<td>1548±11</td>
<td>1555±15</td>
<td>1551±20</td>
<td>1556±10</td>
</tr>
<tr>
<td>BUA Z Score$^c$</td>
<td>-0.48 ± 1.12</td>
<td>-0.57 ± 0.96</td>
<td>-0.15 ± 1.02</td>
<td>-0.46 ± 1.12</td>
</tr>
<tr>
<td>SOS Z Score$^c$</td>
<td>0.40 ± 0.94</td>
<td>0.01 ± 1.43</td>
<td>0.57 ± 0.85</td>
<td>0.14 ± 1.03</td>
</tr>
<tr>
<td>Heel Width (cm)</td>
<td>6.54±0.41</td>
<td>6.26±0.49</td>
<td>6.40±0.41</td>
<td>6.38±0.42</td>
</tr>
</tbody>
</table>

$^a$ n=25 IB mothers (1 fused vertebrae)
$^b$ n=24 IB mothers (1 fused vertebrae, 1 no reading for L$_4$), n=26 IB daughters (no reading for L$_4$), n=21 for BD daughters (no reading for L$_4$)
$^c$ n=21 BD mothers (1 out of age range), n=21 BD daughters (1 out of age range)
$^d$ n=25 IB mothers (1 fused vertebrae)
Table 5.7 Anthropometric and bone measurements and DXA body composition measurements for BD and IB women as used for linear multiple regression analysis

Reported as mean ± st.dev. Short-stature defined as height <= 150 cm.

<table>
<thead>
<tr>
<th></th>
<th>BD Women (n=29)</th>
<th>IB Women (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.7 ± 16.9</td>
<td>48.6 ± 13.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>151.2 ± 4.2</td>
<td>164.3 ± 6.0</td>
</tr>
<tr>
<td>No. (%) short-stature</td>
<td>10 (35%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Knee ht. (cm)</td>
<td>45.6 ± 1.6</td>
<td>49.8 ± 2.4</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.2 ± 11.6</td>
<td>75.5 ± 21.3</td>
</tr>
<tr>
<td>BMI</td>
<td>27.1 ± 4.7</td>
<td>27.9 ± 7.1</td>
</tr>
<tr>
<td>Fem. neck BMD (g/cm²)</td>
<td>0.905 ± 0.147</td>
<td>1.008 ± 0.162</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMD (g/cm²)</td>
<td>1.057 ± 0.170</td>
<td>1.170 ± 0.179</td>
</tr>
<tr>
<td>³Spine L₁–L₄ BMD (g/cm²)</td>
<td>1.072 ± 0.176</td>
<td>1.202 ± 0.188</td>
</tr>
<tr>
<td>33%. Radius BMD (g/cm²)</td>
<td>0.759 ± 0.088</td>
<td>0.832 ± 0.091</td>
</tr>
<tr>
<td>²Femoral neck BMD Z score</td>
<td>0.175 ± 0.874</td>
<td>0.656 ± 1.021</td>
</tr>
<tr>
<td>⁵Spine L₁–L₄ BMD Z score</td>
<td>-0.296 ± 1.054</td>
<td>0.226 ± 1.261</td>
</tr>
<tr>
<td>³33%. Radius BMD Z score</td>
<td>-0.750 ± 0.997</td>
<td>-0.154 ± 0.875</td>
</tr>
<tr>
<td>Fem. neck BMAD (g/cm³)</td>
<td>0.207 ± 0.037</td>
<td>0.211 ± 0.042</td>
</tr>
<tr>
<td>⁵Spine L₁–L₄ BMAD (g/cm³)</td>
<td>0.178 ± 0.027</td>
<td>0.184 ± 0.029</td>
</tr>
<tr>
<td>33%. Radius BMAD (g/cm³)</td>
<td>0.339 ± 0.051</td>
<td>0.337 ± 0.051</td>
</tr>
<tr>
<td>HSI</td>
<td>1.6 ± 0.4</td>
<td>1.6 ± 0.4</td>
</tr>
<tr>
<td>BR</td>
<td>2.9 ± 0.8</td>
<td>2.8 ± 1.1</td>
</tr>
<tr>
<td>FNW (mm)</td>
<td>27.2 ± 2.0</td>
<td>29.7 ± 2.5</td>
</tr>
<tr>
<td>Z (mm³)</td>
<td>485 ± 95</td>
<td>626 ± 109</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>93.4 ± 4.5</td>
<td>103.3 ± 5.8</td>
</tr>
<tr>
<td>NSA (°)</td>
<td>125 ± 3</td>
<td>124 ± 5</td>
</tr>
<tr>
<td>BUA Raw Score dB MHz⁻¹</td>
<td>44.7 ± 8.6</td>
<td>48.0 ± 8.3</td>
</tr>
<tr>
<td>SOS Raw Score ms⁻¹</td>
<td>1552 ± 11</td>
<td>1554 ± 11</td>
</tr>
<tr>
<td>⁵²BUA Z Score</td>
<td>-0.42 ± 1.04</td>
<td>-0.14 ± 1.06</td>
</tr>
<tr>
<td>⁵⁵SOS Z Score</td>
<td>0.46 ± 0.85</td>
<td>-0.96 ± 0.15</td>
</tr>
<tr>
<td>Fat (kg)</td>
<td>25.5 ± 7.8</td>
<td>30.5 ± 15.4</td>
</tr>
<tr>
<td>Lean (kg)</td>
<td>33.8 ± 4.5</td>
<td>42.0 ± 7.7</td>
</tr>
<tr>
<td>Bone (kg)</td>
<td>2.1 ± 0.4</td>
<td>2.6 ± 0.4</td>
</tr>
<tr>
<td>% Fat</td>
<td>40.7 ± 6.0</td>
<td>38.5 ± 10.3</td>
</tr>
<tr>
<td>% Lean</td>
<td>55.9 ± 5.9</td>
<td>57.9 ± 9.9</td>
</tr>
<tr>
<td>% Bone</td>
<td>3.4 ± 0.6</td>
<td>3.6 ± 0.6</td>
</tr>
</tbody>
</table>

¹n=37 IB women (no scan of L₄) ²n=28 BD women (no age reference value)
Participants at increased fracture risk

More BD women were identified as being at increased fracture risk i.e. 13 BD women (nine mothers and four daughters) as opposed to four IB women (two mothers and two daughters). As explained in the Background chapter, BMD is the clinical measure of bone status linked to fracture risk, so participants were deemed as being at increased fracture risk if their DXA scans showed any of the following results:

- Osteopenia (T-score =< -1 and > -2.5) and a mother/daughter also showing osteopenia/osteoporosis.
- Osteopenia in all three regions scanned
- Osteopenia in hip or spine, plus a Z-score < -2.0 which would indicate a particular low BMD for her age group

The oldest of the BD mothers at increased fracture risk were aged 78 and 82 years old, and the youngest were 42 and 48 years old. The two IB mothers at increased fracture risk were aged 53 and 56 years.

Three of the four BD daughters who were at increased fracture risk were only aged 20 or 21 years old, the remaining BD daughter being 44 years old. The two IB daughters at increased fracture risk were 36 and 37 years old.

Results of standard MLR analyses

Standard MLR was employed to explore the contribution of menopause, generation (mother/daughter status) and ethnicity to the experimental variable of interest. If ethnicity was found to be a significant predictor to the variance of BMD at one of the three skeletal sites, the same model was run, substituting BMAD for BMD. If ethnicity was found to be a significant predictor to the variance of any of the other experimental variables, a further model was run, including height as a predictor, as described in the Methods chapter.

The results of the multiple regression analyses are summarised in the two summary tables (Table 5.8 and Table 5.9), followed by the tables showing full outputs from the analyses (Table 5.10 to Table 5.17). The summary tables show the relative contribution of the predictor variable to the dependent variable e.g. IB > BD for height, means IB women were taller than BD women.
Table 5.8 Linear Regression Models: Summary of outcome of fitting models 1 to 3:
The best model for each dependent variable is displayed, showing adjusted \( R^2 \) and predictor variables.

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Best Model</th>
<th>Adj. ( R^2 )</th>
<th>Ethnicity</th>
<th>Menopause</th>
<th>Generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>2</td>
<td>0.61</td>
<td>IB &gt; BD p&lt;0.001</td>
<td>Pre &gt; Post p=0.093(^a)</td>
<td>Not used</td>
</tr>
<tr>
<td>Knee Height (cm)</td>
<td>1</td>
<td>0.48</td>
<td>IB &gt; BD p&lt;0.001</td>
<td></td>
<td>Not used</td>
</tr>
<tr>
<td>BMD Femur Neck (g/cm(^2))</td>
<td>2</td>
<td>0.40</td>
<td>IB &gt; BD p&lt;0.001</td>
<td>Pre &gt; Post p&lt;0.001</td>
<td>Not used</td>
</tr>
<tr>
<td>BMD Spine L(_2)-L(_4) (g/cm(^2))</td>
<td>3</td>
<td>0.44</td>
<td>IB &gt; BD p&lt;0.001</td>
<td>Pre &gt; Post p=0.001</td>
<td>Daughter &gt; Mother p=0.179(^a)</td>
</tr>
<tr>
<td>BMD Radius (g/cm(^2))</td>
<td>2</td>
<td>0.28</td>
<td>IB &gt; BD p&lt;0.001</td>
<td>Pre &gt; Post p&lt;0.001</td>
<td>Not used</td>
</tr>
<tr>
<td>BMAD Femur Neck (g/cm(^3))</td>
<td>2</td>
<td>0.32</td>
<td>IB &gt; BD p=0.544</td>
<td>Pre &gt; Post p=0.002</td>
<td>Not used</td>
</tr>
<tr>
<td>BMAD Spine L(_2)-L(_4) (g/cm(^3))</td>
<td>3</td>
<td>0.34</td>
<td>IB &gt; BD p=0.361</td>
<td>Pre &gt; Post p=0.005</td>
<td>Daughter &gt; Mother p=0.086(^a)</td>
</tr>
<tr>
<td>BMAD 33% Radius (g/cm(^3))</td>
<td>2</td>
<td>0.13</td>
<td>BD &gt; IB p=0.913</td>
<td>Pre &gt; Post p=0.001</td>
<td>Not used</td>
</tr>
<tr>
<td>BUA Z score</td>
<td>Not Sig</td>
<td>0.01</td>
<td>No significant contribution</td>
<td>No contribution</td>
<td>No significant contribution</td>
</tr>
<tr>
<td>SOS Z score</td>
<td>Not Sig</td>
<td>0.03</td>
<td>No significant contribution</td>
<td>No contribution</td>
<td>No significant contribution</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>1</td>
<td>0.46</td>
<td>IB &gt; BD p&lt;0.001</td>
<td>Not used</td>
<td>Not used</td>
</tr>
<tr>
<td>FNW (mm)</td>
<td>1</td>
<td>0.23</td>
<td>IB &gt; BD p&lt;0.001</td>
<td>Not used</td>
<td>Not used</td>
</tr>
<tr>
<td>HSI</td>
<td>Not Sig</td>
<td>0.02</td>
<td>No significant contribution</td>
<td>No contribution</td>
<td>No significant contribution</td>
</tr>
<tr>
<td>Z (mm(^3))</td>
<td>2</td>
<td>0.46</td>
<td>IB &gt; BD p&lt;0.001</td>
<td>Pre &gt; Post p&lt;0.001</td>
<td>Not used</td>
</tr>
<tr>
<td>BR</td>
<td>Not Sig</td>
<td>-0.04</td>
<td>No significant contribution</td>
<td>No contribution</td>
<td>No significant contribution</td>
</tr>
<tr>
<td>NSA ((^o))</td>
<td>Not Sig</td>
<td>-0.92</td>
<td>No significant contribution</td>
<td>No contribution</td>
<td>No significant contribution</td>
</tr>
</tbody>
</table>

\(^a\)Predictor variables used for models:-
Model 1 (Ethnicity) Model 2 (Ethnicity and Menopausal status) Model 3 (Ethnicity, Menopausal status and generation)
“Not used” means the predictor variable was not used in the model and had no meaningful contribution in other models
although not a significant probability, a possibly meaningful result.
Table 5.9 Linear Regression Models: Summary outcome of fitting model 4, showing dependent variables in which ethnicity had previously been a significant predictor variable.

For each dependent variable, the adjusted $R^2$ is shown and probability values for contribution of each predictor variable to variance

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adj. $R^2$</th>
<th>Ethnicity</th>
<th>Menopause</th>
<th>Height</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAL (mm)</td>
<td>0.63</td>
<td>IB &gt; BD $p=0.144$</td>
<td>Not used</td>
<td>$p&lt;0.001$</td>
</tr>
<tr>
<td>FNW (mm)</td>
<td>0.39</td>
<td>BD &gt; IB $p=0.957$</td>
<td>Not used</td>
<td>$p&lt;0.001$</td>
</tr>
<tr>
<td>Z</td>
<td>0.60</td>
<td>IB &gt; BD $p=0.398$</td>
<td>Pre &gt; Post $p&lt;0.001$</td>
<td>$p&lt;0.001$</td>
</tr>
</tbody>
</table>

"Not used" means the predictor variable was not used in the model due to having no meaningful contribution in other models.
Table 5.10 Linear Regression Models: Height and Knee Height

Output from standard multiple regression analysis, showing standardized beta coefficient ($\beta$), unstandardized beta coefficient (B) with standard error, 95% confidence interval (CI), t value, Cohen’s r and P value for significance of variable

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>Height (cm)</th>
<th></th>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th></th>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
<td>t</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Constant</td>
<td>151.25</td>
<td>0.99</td>
<td>149.3 to 153.2</td>
<td>153.4</td>
<td>1.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnicity$^a$</td>
<td>0.78</td>
<td>13.02</td>
<td>1.30</td>
<td>10.4.2</td>
<td>0.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Menopause$^b$</td>
<td>-0.13</td>
<td>-2.18</td>
<td>1.28</td>
<td>-4.7 to 0.37</td>
<td>-1.71</td>
<td>0.21</td>
</tr>
</tbody>
</table>

N = 68, R = 0.78, R$^2$ = 0.61, Adj. R$^2$ = 0.58, F (1,66) = 100.1, P <0.001

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>Knee Height (cm)</th>
<th></th>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th></th>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
<td>t</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Constant</td>
<td>45.64</td>
<td>0.40</td>
<td>44.8 to 46.4</td>
<td>115.57</td>
<td>1.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnicity$^a$</td>
<td>0.70</td>
<td>4.12</td>
<td>0.52</td>
<td>3.1 to 5.2</td>
<td>7.90</td>
<td>0.70</td>
</tr>
<tr>
<td>Menopause$^b$</td>
<td>0.05</td>
<td>0.29</td>
<td>0.52</td>
<td>-0.75 to 1.33</td>
<td>0.56</td>
<td>0.07</td>
</tr>
</tbody>
</table>

N = 68, R = 0.70, R$^2$ = 0.49, Adj. R$^2$ = 0.48, F (1,66) = 62.35, P <0.001

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>Knee Height (cm)</th>
<th></th>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th></th>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
<td>t</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Constant</td>
<td>45.52</td>
<td>0.45</td>
<td>44.6 to 46.4</td>
<td>100.72</td>
<td>1.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnicity$^a$</td>
<td>0.69</td>
<td>4.10</td>
<td>0.53</td>
<td>3.01 to 5.14</td>
<td>7.70</td>
<td>0.69</td>
</tr>
<tr>
<td>Menopause$^b$</td>
<td>0.05</td>
<td>0.29</td>
<td>0.52</td>
<td>-0.75 to 1.33</td>
<td>0.56</td>
<td>0.07</td>
</tr>
</tbody>
</table>

N = 68, R = 0.70, R$^2$ = 0.49, Adj. R$^2$ = 0.47, F (2,65) = 31.01, P <0.001

| Model 3 (Ethnicity, Menopausal status and Generation) | |
|-----------------------------------------------------|-----------------------|-------------------|---------------|------------------|------------------|
| $\beta$                                             | B                     | SE                | 95% CI        | t          | r        | P          | $\beta$        | B           | SE                    | 95% CI            | t          | r        | P          |
| Constant                                            | 45.36                  | 0.57              | 44.2 to 46.5   | 79.47      | 1.00    | <0.001    | Constant         | 45.36        | 0.57                  | 44.2 to 46.5    | 79.47      | 1.00    | <0.001    | Constant         | 45.36        | 0.57                  | 44.2 to 46.5    | 79.47      | 1.00    | <0.001    |
| Ethnicity$^a$                                       | 0.71                   | 4.16              | 0.55            | 3.1 to 5.3  | 7.61    | 0.69    | <0.001    | Ethnicity$^a$    | 0.05         | 0.29                  | 0.52            | -0.75 to 1.33 | 0.56    | 0.07    | 0.579     | Ethnicity$^a$    | 0.05         | 0.29                  | 0.52            | -0.75 to 1.33 | 0.56    | 0.07    | 0.579     |
| Menopause$^b$                                       | 0.01                   | 0.05              | 0.73            | -1.4 to 1.5 | 0.07    | 0.01    | 0.943     | Menopause$^b$    | 0.05         | 0.36                  | 0.77            | -1.2 to 1.9  | 0.47    | 0.06    | 0.639     |

N = 68, R = 0.70, R$^2$ = 0.49, Adj. R$^2$ = 0.47, F (3,64) = 20.50, P <0.001

$^a$Reference: BD women  
$^b$Reference: premenopausal  
$^c$Reference: daughter  
$\beta$ = standardised coefficient  
B = unstandardized coefficient
Table 5.11 Linear Regression Models: Femur Neck BMD and BMAD
Output from standard multiple regression analysis, showing standardized beta coefficient ($\beta$), unstandardized beta coefficient (B) with standard error, 95% confidence interval (CI), t value, Cohen’s r and P value for significance of variable

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>Femur Neck BMD (g/cm$^2$)</th>
<th>Model 1 (Ethnicity)</th>
<th>Femur Neck BMAD (g/cm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
</tr>
<tr>
<td>Constant</td>
<td>0.91</td>
<td>0.03</td>
<td>0.85 to 0.96</td>
</tr>
<tr>
<td>Ethnicity$^a$</td>
<td>0.32</td>
<td>0.10</td>
<td>0.04</td>
</tr>
<tr>
<td>N = 68, R = 0.32, R$^2$ = 0.10, Adj. R$^2$ = 0.09, F (1,66) = 7.30, P &lt;0.001</td>
<td>N = 68, R = 0.54, R$^2$ = 0.003, Adj. R$^2$ = -0.01, F (1,66) = 0.195, P =0.660</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>Constant</th>
<th>0.98</th>
<th>0.03</th>
<th>0.93 to 1.03</th>
<th>36.80</th>
<th>1.00</th>
<th>0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity$^a$</td>
<td>0.36</td>
<td>0.12</td>
<td>0.03</td>
<td>0.06 to 0.12</td>
<td>3.76</td>
<td>0.42</td>
<td>0.001</td>
</tr>
<tr>
<td>Menopause$^b$</td>
<td>-0.57</td>
<td>-0.18</td>
<td>0.03</td>
<td>-0.25 to 0.12</td>
<td>-5.96</td>
<td>0.59</td>
<td>0.001</td>
</tr>
<tr>
<td>N = 68, R = 0.65, R$^2$ = 0.42, Adj. R$^2$ = 0.40, F (2,65) = 23.32, P &lt;0.001</td>
<td>N = 68, R = 0.58, R$^2$ = 0.33, Adj. R$^2$ = 0.31, F (2,65) = 16.19, P &lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>Constant</th>
<th>1.00</th>
<th>0.03</th>
<th>0.94 to 1.07</th>
<th>29.99</th>
<th>1.00</th>
<th>0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity$^a$</td>
<td>0.33</td>
<td>0.11</td>
<td>0.03</td>
<td>10.7 to 16.1</td>
<td>3.37</td>
<td>0.39</td>
<td>0.001</td>
</tr>
<tr>
<td>Menopause$^b$</td>
<td>-0.47</td>
<td>0.04</td>
<td>0.47</td>
<td>-6.4 to -0.72</td>
<td>-3.55</td>
<td>0.41</td>
<td>0.001</td>
</tr>
<tr>
<td>Generation$^c$</td>
<td>-0.14</td>
<td>0.05</td>
<td>0.05</td>
<td>-2.7 to 4.8</td>
<td>-0.29</td>
<td>0.04</td>
<td>0.292</td>
</tr>
<tr>
<td>N = 68, R = 0.65, R$^2$ = 0.43, Adj. R$^2$ = 0.40, F (3,64) = 15.95, P &lt;0.001</td>
<td>N = 68, R = 0.59, R$^2$ = 0.35, Adj. R$^2$ = 0.32, F (3,64) = 11.35, P &lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$Reference: BD women  
$^b$Reference: premenopausal  
$^c$Reference: daughter
Table 5.12 Linear Regression Models: Lumbar Spine (L2-L4) BMD and BMAD

Output from standard multiple regression analysis, showing standardized beta coefficient (\( \beta \)), unstandardized beta coefficient (B) with standard error, 95% confidence interval (CI), t value, Cohen’s r and P value for significance of variable.

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>Lumbar Spine (L2-L4) BMD (g/cm(^2))</th>
<th>Model 1 (Ethnicity)</th>
<th>Lumbar Spine (L2-L4) BMAD (g/cm(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \beta )</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
</tr>
<tr>
<td>Constant</td>
<td>1.07</td>
<td>0.03</td>
<td>1.00 to 1.14</td>
</tr>
<tr>
<td>Ethnicity(^a)</td>
<td>0.34</td>
<td>0.13</td>
<td>0.04 to 0.22</td>
</tr>
</tbody>
</table>

N = 66\(^1\), R = 0.34, \( R^2 = 0.11 \), Adj. \( R^2 = 0.10 \), F (1,64) = 8.30, \( P < 0.001 \)

<table>
<thead>
<tr>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>Lumbar Spine (L2-L4) BMD (g/cm(^2))</th>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>Lumbar Spine (L2-L4) BMAD (g/cm(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \beta )</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
</tr>
<tr>
<td>Constant</td>
<td>1.16</td>
<td>0.03</td>
<td>1.10 to 1.11</td>
</tr>
<tr>
<td>Ethnicity(^a)</td>
<td>0.38</td>
<td>0.15</td>
<td>0.08 to 0.22</td>
</tr>
<tr>
<td>Menopause(^b)</td>
<td>-0.58</td>
<td>-0.22</td>
<td>-0.30 to -0.15</td>
</tr>
</tbody>
</table>

N = 66\(^1\), R = 0.67, \( R^2 = 0.45 \), Adj. \( R^2 = 0.43 \), F (2,63) = 25.62, \( P < 0.001 \)

<table>
<thead>
<tr>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>Lumbar Spine (L2-L4) BMD (g/cm(^2))</th>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>Lumbar Spine (L2-L4) BMAD (g/cm(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \beta )</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
</tr>
<tr>
<td>Constant</td>
<td>1.19</td>
<td>0.04</td>
<td>1.12 to 1.27</td>
</tr>
<tr>
<td>Ethnicity(^a)</td>
<td>0.35</td>
<td>0.13</td>
<td>0.06 to 0.21</td>
</tr>
<tr>
<td>Menopause(^b)</td>
<td>-0.46</td>
<td>0.18</td>
<td>-0.23 to -0.08</td>
</tr>
<tr>
<td>Generation(^c)</td>
<td>-0.18</td>
<td>-0.07</td>
<td>-0.18 to 0.03</td>
</tr>
</tbody>
</table>

N = 66\(^1\), R = 0.66, \( R^2 = 0.46 \), Adj. \( R^2 = 0.44 \), F (3,62) = 17.90, \( P < 0.001 \)

\(^a\)Reference: BD women \(^b\)Reference: premenopausal \(^c\)Reference: daughter \(^1\)2 women did not have results for Lumbar Spine (L2-L4)
Table 5.13 Linear Regression Models: Proximal (33%) Radius BMD and BMAD

Output from standard multiple regression analysis, showing standardized beta coefficient ($\beta$), unstandardized beta coefficient (B) with standard error, 95% confidence interval (CI), t value, Cohen’s $r$ and $P$ value for significance of variable

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>33% Radius BMD (g/cm$^2$)</th>
<th>Model 1 (Ethnicity)</th>
<th>33% Radius BMAD (g/cm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
</tr>
<tr>
<td>Constant</td>
<td>0.76</td>
<td>0.02</td>
<td>0.73 to 0.79</td>
</tr>
<tr>
<td>Ethnicity$^a$</td>
<td>0.38</td>
<td>0.07</td>
<td>0.03 to 0.12</td>
</tr>
</tbody>
</table>

N = 68, $R = 0.38$, $R^2 = 0.14$, Adj. $R^2 =$ 0.13, $F (1,66) = 11.06$, $P =$0.001

<table>
<thead>
<tr>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>33% Radius BMD (g/cm$^2$)</th>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>33% Radius BMAD (g/cm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>0.98</td>
<td>0.02</td>
<td>0.76 to 0.83</td>
</tr>
<tr>
<td>Ethnicity$^a$</td>
<td>0.41</td>
<td>0.08</td>
<td>0.04 to 0.12</td>
</tr>
<tr>
<td>Menopause$^b$</td>
<td>-0.40</td>
<td>-0.08</td>
<td>0.2 to -0.4</td>
</tr>
</tbody>
</table>

N = 68, $R = 0.55$, $R^2 = 0.30$, Adj. $R^2 =$ 0.28, $F (2,65) = 79.17$, $P <0.001$

<table>
<thead>
<tr>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>33% Radius BMD (g/cm$^2$)</th>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>33% Radius BMAD (g/cm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>0.78</td>
<td>0.02</td>
<td>0.74 to 0.83</td>
</tr>
<tr>
<td>Ethnicity$^a$</td>
<td>0.43</td>
<td>0.08</td>
<td>0.04 to 0.12</td>
</tr>
<tr>
<td>Menopause$^b$</td>
<td>-0.46</td>
<td>-0.09</td>
<td>0.03</td>
</tr>
<tr>
<td>Generation$^c$</td>
<td>0.09</td>
<td>0.02</td>
<td>0.03</td>
</tr>
</tbody>
</table>

N = 68, $R = 0.56$, $R^2 = 0.31$ Adj. $R^2 =$ 0.28, $F (3,64) = 9.49$, $P <0.001$

$^a$Reference: BD women  $^b$Reference: premenopausal  $^c$Reference: daughter
### Table 5.14 Linear Regression Models: BUA Z score and SOS Z score

Output from standard multiple regression analysis, showing standardized beta coefficient (\(\beta\)), unstandardized beta coefficient (B) with standard error, 95% confidence interval (CI), t value, Cohen’s \(r\) and P value for significance of variable

| Model 1 (Ethnicity) | BUA Z Score | | | | | Model 1 (Ethnicity) | SOS Z Score | | | |
|---------------------|-------------|---------------|-----------------|---------------|-----------------|-------------|---------------|-----------------|---------------|-----------------|---------------|
| \(\beta\)          | B           | SE            | 95% CI          | t   | r   | P   | \(\beta\) | B           | SE            | 95% CI          | t   | r   | P   |
| Constant            | -0.42       | 0.20          | -0.82 to -0.03  | -2.13 | 1.00 | 0.04 | Constant | 0.46         | 0.17          | 0.12 to 0.80   | 2.70 | 1.00 | 0.01 |
| Ethnicity\(^a\)     | 0.13        | 0.29          | 0.26            | -0.24 to 0.81 | 1.09 | 0.13 | 0.28 | Ethnicity\(^a\) | 0.05        | 0.09          | 0.23          | -0.36 to 0.54  | 0.40 | 0.05 | 0.69 |

N = 67\(^r\), \(R = 0.13, R^2 = 0.02, \text{ Adj. } R^2 = 0.00, F (1,65) = 1.20, P = 0.278\)

N = 67\(^r\), \(R = 0.05, R^2 = 0.00, \text{ Adj. } R^2 = -0.01, F (1,65) = 0.16, P = 0.694\)

| Model 2 (Ethnicity and Menopausal status) | BUA Z Score | | | | | Model 2 (Ethnicity and Menopausal status) | SOS Z Score | | | |
|-----------------------------------------|-------------|---------------|-----------------|---------------|-----------------|-------------|---------------|-----------------|---------------|-----------------|---------------|
| Constant                                | -0.50       | 0.23          | -0.95 to -0.05  | -2.12 | 1.00 | 0.03 | Constant | 0.43         | 0.20          | 0.04 to 0.82   | -2.20 | 1.00 | 0.03 |
| Ethnicity\(^a\)                         | 0.13        | 0.27          | 0.26            | -0.25 to 0.80 | 1.03 | 0.13 | 0.31 | Ethnicity\(^a\) | 0.05        | 0.08          | 0.23          | -0.37 to 0.54  | 0.37 | 0.05 | 0.71 |
| Menopause\(^b\)                         | 0.09        | 0.20          | 0.26            | -0.32 to 0.72 | 0.75 | 0.09 | 0.46 | Menopause\(^b\) | 0.04        | 0.07          | 0.23          | -0.38 to 0.53  | 0.32 | 0.04 | 0.75 |

N = 67\(^r\), \(R = 0.516, R^2 = 0.03, \text{ Adj. } R^2 = -0.00, F (2,64) = 0.88, P = 0.421\)

N = 67\(^r\), \(R = 0.06, R^2 = 0.00, \text{ Adj. } R^2 = -0.03, F (2,64) = 0.13, P = 0.879\)

| Model 3 (Ethnicity, Menopausal status and Generation) | BUA Z Score | | | | | Model 3 (Ethnicity, Menopausal status and Generation) | SOS Z Score | | | |
|-----------------------------------------------------|-------------|---------------|-----------------|---------------|-----------------|-------------|---------------|-----------------|---------------|-----------------|---------------|
| Constant                                             | -0.27       | 0.28          | -0.83 to -0.30  | -0.94         | 1.00 | 0.35 | Constant | 0.57         | 0.25          | 0.08 to 1.07   | 2.32 | 1.00 | 0.02 |
| Ethnicity\(^a\)                                      | 0.08        | 0.17          | 0.27            | -0.36 to 0.71 | 0.65 | 0.08 | 0.52 | Ethnicity\(^a\) | 0.02        | 0.03          | 0.24          | -0.45 to 0.45  | 0.11 | 0.01 | 0.91 |
| Menopause\(^b\)                                      | 0.26        | 0.54          | 0.36            | -0.17 to 1.26 | 1.51 | 0.19 | 0.14 | Menopause\(^b\) | 0.16        | 0.28          | 0.31          | -0.35 to 0.91  | 0.89 | 0.11 | 0.38 |
| Generation\(^c\)                                     | -0.24       | -0.53         | 0.38            | -1.28 to 0.23 | -1.39 | 0.17 | 0.17 | Generation\(^c\) | -0.17       | -0.31         | 0.33          | -0.98 to 0.35  | -0.95 | 0.12 | 0.35 |

N = 67\(^r\), \(R = 0.24, R^2 = 0.06 \text{ Adj. } R^2 = 0.01, F (3,63) = 1.24, P = 0.303\)

N = 67\(^r\), \(R = 0.13, R^2 = 0.02, \text{ Adj. } R^2 = -0.03, F (3,63) = 0.38, P = 0.765\)

\(^a\)Reference: BD women \(^b\)Reference: premenopausal \(^c\)Reference: daughter \(^r\)1 women did not have results for Z scores


Table 5.15 Linear Regression Models: HAL and FNW measurements

Output from standard multiple regression analysis, showing standardized beta coefficient ($\beta$), unstandardized beta coefficient (B) with standard error, 95% confidence interval (CI), t value, Cohen's $r$ and P value for significance of variable

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>HAL (mm)</th>
<th></th>
<th>Model 1 (Ethnicity)</th>
<th>FNW (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
</tr>
<tr>
<td></td>
<td>93.38</td>
<td>0.99</td>
<td>91.4 to 95.3</td>
<td>94.8</td>
</tr>
<tr>
<td>Ethnicity&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.68</td>
<td>9.90</td>
<td>1.30</td>
<td>7.3 to 12.4</td>
</tr>
</tbody>
</table>

N = 68, R = 0.68, R$^2$ = 0.47, Adj. R$^2$ = 0.46, F (1,66) = 57.9, P $<$ 0.001

<table>
<thead>
<tr>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>HAL (mm)</th>
<th></th>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>FNW (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
</tr>
<tr>
<td></td>
<td>93.18</td>
<td>1.13</td>
<td>90.9 to 95.4</td>
<td>98.5</td>
</tr>
<tr>
<td>Ethnicity&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.68</td>
<td>9.87</td>
<td>1.31</td>
<td>7.2 to 12.5</td>
</tr>
<tr>
<td>Menopause&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.03</td>
<td>0.47</td>
<td>1.30</td>
<td>-2.11 to 3.07</td>
</tr>
</tbody>
</table>

N = 68, R = 0.68, R$^2$ = 0.47, Adj. R$^2$ = 0.45, F (2,65) = 28.65, P $<$ 0.001

<table>
<thead>
<tr>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>HAL (mm)</th>
<th></th>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>FNW (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
</tr>
<tr>
<td></td>
<td>92.39</td>
<td>1.42</td>
<td>89.6 to 95.2</td>
<td>65.1</td>
</tr>
<tr>
<td>Ethnicity&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.70</td>
<td>10.23</td>
<td>1.36</td>
<td>7.5 to 12.9</td>
</tr>
<tr>
<td>Menopause&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-0.05</td>
<td>-0.69</td>
<td>1.82</td>
<td>-4.3 to 2.90</td>
</tr>
<tr>
<td>Generation&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.12</td>
<td>1.91</td>
<td>1.91</td>
<td>-2.06 to 5.55</td>
</tr>
</tbody>
</table>

N = 68, R = 0.69, R$^2$ = 0.48 Adj. R$^2$ = 0.45, F (3,64) = 19.33, P $<$ 0.001

<table>
<thead>
<tr>
<th>Model 4 (Ethnicity and Height)</th>
<th>HAL (mm)</th>
<th></th>
<th>Model 4 (Ethnicity and Height)</th>
<th>FNW (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>$\beta$</td>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
</tr>
<tr>
<td></td>
<td>7.79</td>
<td>15.48</td>
<td>-23.12 to 38.70</td>
<td>0.50</td>
</tr>
<tr>
<td>Ethnicity&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.18</td>
<td>2.53</td>
<td>1.71</td>
<td>-0.89 to 5.96</td>
</tr>
<tr>
<td>Height</td>
<td>0.66</td>
<td>0.57</td>
<td>0.10</td>
<td>0.36 to 0.77</td>
</tr>
</tbody>
</table>

N = 68, R = 0.80, R$^2$ = 0.64 Adj. R$^2$ = 0.63, F (2,65) = 57.32, P $<$ 0.001

N = 68, R = 0.64, R$^2$ = 0.41 Adj. R$^2$ = 0.39, F (2,65) = 22.36, P $<$ 0.001

<sup>a</sup>Reference: BD women  <sup>b</sup>Reference: premenopausal  <sup>c</sup>Reference: daughter
Table 5.16 Linear Regression Models: HSI and Z measurements
Output from standard multiple regression analysis, showing standardized beta coefficient (β), unstandardized beta coefficient (B) with standard error, 95% confidence interval (CI), t value, Cohen’s r and P value for significance of variable

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>HSI</th>
<th>Model 1 (Ethnicity)</th>
<th>Z (mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
<td>t</td>
</tr>
<tr>
<td>Constant</td>
<td>1.60</td>
<td>0.07</td>
<td>1.46 to 1.74</td>
</tr>
<tr>
<td>Ethnicity a</td>
<td>0.00</td>
<td>0.00</td>
<td>-0.19 to 0.19</td>
</tr>
<tr>
<td>N = 68, R = 0.00, R² = 0.00, Adj. R² = 0.02, F (1,66) = 0.00, P=0.979</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>HSI</th>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>Z (mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
<td>t</td>
</tr>
<tr>
<td>Constant</td>
<td>1.62</td>
<td>0.08</td>
<td>1.46 to 1.74</td>
</tr>
<tr>
<td>Ethnicity a</td>
<td>0.00</td>
<td>0.00</td>
<td>-0.19 to 0.19</td>
</tr>
<tr>
<td>Menopause b</td>
<td>-0.07</td>
<td>-0.05</td>
<td>-0.24 to -0.67</td>
</tr>
<tr>
<td>N = 68, R = 0.07, R² = 0.00, Adj. R² = 0.03, F (2,65) = 0.141 P=0.869</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>HSI</th>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>Z (mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
<td>t</td>
</tr>
<tr>
<td>Constant</td>
<td>1.60</td>
<td>0.10</td>
<td>1.39 to 1.81</td>
</tr>
<tr>
<td>Ethnicity a</td>
<td>0.00</td>
<td>0.01</td>
<td>-0.19 to 0.21</td>
</tr>
<tr>
<td>Menopause b</td>
<td>-0.10</td>
<td>-0.08</td>
<td>-0.35 to -0.19</td>
</tr>
<tr>
<td>Generation c</td>
<td>0.05</td>
<td>0.04</td>
<td>-0.24 to 0.32</td>
</tr>
<tr>
<td>N = 68, R = 0.08, R² = 0.06, Adj. R² = 0.04, F (3,64) = 0.121 P=0.948</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 4 (Ethnicity, Menopausal status and Height)</th>
<th>HSI</th>
<th></th>
<th>Z (mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>SE</td>
<td>95% CI</td>
<td>t</td>
</tr>
<tr>
<td>Constant</td>
<td>-867.8</td>
<td>281.8</td>
<td>-1430.8 to -304.9</td>
</tr>
<tr>
<td>Ethnicity a</td>
<td>0.11</td>
<td>26.4</td>
<td>31.0</td>
</tr>
<tr>
<td>Menopause b</td>
<td>-0.32</td>
<td>-78.9</td>
<td>19.5</td>
</tr>
<tr>
<td>Height</td>
<td>0.62</td>
<td>9.17</td>
<td>1.85</td>
</tr>
<tr>
<td>N = 68, R = 0.79, R² = 0.62, Adj. R² = 0.60, F (3,64) = 35.02, P&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Reference: BD women  bReference: premenopausal  cReference: daughter
### Table 5.17 Linear Regression Models: BR and NSA measurements
Output from standard multiple regression analysis, showing standardized beta coefficient (β), unstandardized beta coefficient (B) with standard error, 95% confidence interval (CI), t value, Cohen’s r and P value for significance of variable

<table>
<thead>
<tr>
<th>Model 1 (Ethnicity)</th>
<th>BR</th>
<th>NSA (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>B</td>
</tr>
<tr>
<td>Constant</td>
<td>2.87</td>
<td>0.18</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>-0.04</td>
<td>-0.08</td>
</tr>
</tbody>
</table>

N = 68, R = 0.04, R² = 0.02, **Adj. R² = -0.01**, F (1,66) =0.118, P=0.732

<table>
<thead>
<tr>
<th>Model 2 (Ethnicity and Menopausal status)</th>
<th>BR</th>
<th>NSA (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>B</td>
</tr>
<tr>
<td>Constant</td>
<td>2.79</td>
<td>0.21</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>-0.05</td>
<td>-0.10</td>
</tr>
<tr>
<td>Menopause</td>
<td>0.09</td>
<td>0.18</td>
</tr>
</tbody>
</table>

N = 68, R = 0.10, R² = 0.01, **Adj. R² = -0.02**, F (2,65) = 0.341 P=0.712

<table>
<thead>
<tr>
<th>Model 3 (Ethnicity, Menopausal status and Generation)</th>
<th>BR</th>
<th>NSA (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>B</td>
</tr>
<tr>
<td>Constant</td>
<td>2.83</td>
<td>0.27</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>-0.06</td>
<td>-0.11</td>
</tr>
<tr>
<td>Menopause</td>
<td>0.12</td>
<td>0.24</td>
</tr>
<tr>
<td>Generation</td>
<td>-0.04</td>
<td>-0.09</td>
</tr>
</tbody>
</table>

N = 68, R = 0.11, R² = 0.01, **Adj. R² = -0.04**, F (3,64) = 0.244 P=0.865

---

*aReference: BD women  
*bReference: premenopausal  
*cReference: daughter
It can be seen from Summary Table 5.8 that IB women had significantly greater height, knee height, BMD at all three skeletal sites, and hip geometry parameters, HAL, FNW and Z, compared to BD women. In the case of height and knee height, ethnicity had a large effect size (Cohen’s r of nearly 0.8 for height and 0.7 for knee height). Ethnicity also made a significant, though smaller contribution to BMD variance, with a moderate effect size ranging from Cohen’s r of 0.42 for BMD at femur neck to 0.45 for lumbar spine. Regarding hip dimensions, HAL and FNW, ethnicity made a significant contribution to model variation, especially for Z and HAL, where effect size was large (Cohen’s r = 0.63 and 0.68 respectively).

When skeletal size was taken into account for BMD, by using BMAD, the ethnic contribution to the variance of BMAD was not significant (Table 5.11 to Table 5.13). When skeletal size was taken into account for hip geometry parameters, HAL, FNW and Z, by using a model including height as a predictor, the ethnic contribution again became non significant (Table 5.15 and Table 5.16). Post-menopausal status significantly reduced measurements of BMD and BMAD at all three skeletal sites, as well as hip geometry parameter, Z. Other dependent variables (QUS Z scores and hip geometry parameters, HAL, FNW, HSI, BR and NSA) were not influenced by menopausal status.

The contribution of generation (mother or daughter) was negligible or small in all of the models for all of the dependent variables. However, the analysis was not powered sufficiently to detect small effect sizes, so the small effect size (Cohen’s r = 0.17 and 0.22) for generation in lumbar spine Lumbar Spine (L2-L4) BMD and BMAD respectively (Table 5.12) may have been significant had there been a larger sample size.

To summarise, the prediction that IB women have greater height, knee height, BMD and hip geometry parameters (Z, FNW and HAL) than BD women was accepted. There was no effect of ethnicity on HSI, BR and NSA. The prediction that IB women had higher QUS measurements than BD women was also rejected.

The prediction that ethnic differences in BMD did not persist after controlling for skeletal size, as measured by BMAD calculations, was accepted. The prediction that the higher score of HAL, FNW and Z of IB women compared to BD women was associated with skeletal size was also accepted.
Regarding generation differences, although daughters in both ethnic groups showed a trend towards greater height, knee height, bone mass and some hip geometry values (HSI and Z), than mothers, this was not significant according to MLR, which took ethnic status and menopausal status into account. However, as the sample number was not large enough to detect an interaction between generation and ethnicity, and the statistical test did not have sufficient power to detect medium or small effects, it is probably better to conclude that this prediction regarding generation difference could not be adequately tested for.

5.1.5 Birthplace of BD daughters: differences in anthropometric and bone status measurements

Data shown in Table 5.18 suggest that BD-born daughters were significantly older and shorter with slightly better bone status than UK-born BD daughters. BD-born daughters were significantly older (34.4±7.5 years) than UK-born daughters (23.5±6.1 years), based on independent t-test (t=4.25, df=26, p < 0.001).

Mean BMD, at all three skeletal sites, was higher in the BD-born daughters, with small effect sizes, ranging from Cohen’s d=0.14 for lumbar spine to 0.44 for proximal radius. These differences, according to birth place, were more pronounced in the BMD Z scores, where larger effect sizes were seen at the femur neck (Cohen’s d=0.95) and 33% radius (Cohen’s d=0.95) (Table 5.18). As DXA software adjusts for body size in BMD Z scores, and the effect sizes for BMAD birth place differences were greater than those for BMD, the implication is, that when adjusted for body size the differences in bone measurements according to BD daughter’s birthplace are even greater.

BUA raw and BUA Z scores, were also slightly higher, with only small effect sizes, in BD-born daughters compared to UK-born, whilst there was little difference according to daughter’s birthplace in SOS raw and SOS Z scores (Table 5.18).

Contrary to expectation, not only were higher bone measurements found in BD-born daughters, compared to UK-born daughters, but these higher bone measurements were not reflected in height and knee height, which were both lower in the BD-born daughters (Table
5.18). Mean knee height in particular was lower in BD-born daughters (45.6±1.8 cms) than UK-born daughters (47.4±2.3 cms), with a large effect size (Cohen’s $d = -0.87$) (Table 5.18).

There seemed little association of BD daughter’s birthplace with hip geometry parameters, except BR which was higher in BD-born daughters, with a moderate effect size (Table 5.18).

Figure 5.4 on the next page comprises three scatter-graphs involving BD daughters according to birthplace. They clearly show that UK-born BD daughters were younger than BD-born BD daughters. One scatter graph displays participants’ individual knee heights, demonstrating that UK-born BD daughters have greater knee heights than BD-born daughters. The other two scatter graphs illustrate how femur neck BMD Z score and lumbar spine BMD Z score tend to be lower in UK-born BD daughters. BMD Z scores were used in preference to BMD raw scores as they take body weight into account as well as age, and illustrate the birthplace differences clearly.
Figure 5.4 Scatter graphs of Loughborough BD daughters, showing how knee height, femur neck Z scores and lumbar spine Z scores vary according to birthplace
Table 5.18 Birthplace of BD daughters: comparison of anthropometric and bone status variables for BD daughters based on birthplace (UK or BD)  
Reported as mean ± st.dev. P values from independent t-test. Effect size is Cohen’s d

<table>
<thead>
<tr>
<th></th>
<th>Born in UK (n=15)</th>
<th>Born in BD (n=13)</th>
<th>P value</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.5±6.1</td>
<td>34.4±7.5</td>
<td>&lt;0.001***</td>
<td>2.48</td>
</tr>
<tr>
<td>Recalled age at menarche§</td>
<td>11.6±1.5</td>
<td>11.6±1.3</td>
<td>0.086</td>
<td>-0.69</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.2±5.7</td>
<td>152.5±5.0</td>
<td>0.086</td>
<td>-0.69</td>
</tr>
<tr>
<td>Knee ht. (cm)</td>
<td>47.4±2.3</td>
<td>45.6±1.8</td>
<td>0.028*</td>
<td>-0.87</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.2±14.8</td>
<td>59.5±10.7</td>
<td>0.898</td>
<td>-0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>24.7±5.7</td>
<td>25.4±4.3</td>
<td>0.664</td>
<td>0.15</td>
</tr>
<tr>
<td>Fem. neck BMD (g/cm²)</td>
<td>0.979±0.181</td>
<td>1.02±0.116</td>
<td>0.454</td>
<td>0.29</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMD (g/cm²)</td>
<td>1.148±0.140</td>
<td>1.197±0.138</td>
<td>0.364</td>
<td>0.14</td>
</tr>
<tr>
<td>33% Radius BMD (g/cm²)</td>
<td>1.172±0.139</td>
<td>1.210±0.135</td>
<td>0.471</td>
<td>0.14</td>
</tr>
<tr>
<td>33% Radius BMD Z score</td>
<td>-1.300±0.586</td>
<td>-0.615±0.839</td>
<td>0.028*</td>
<td>0.95</td>
</tr>
<tr>
<td>Fem. neck BMD Z score</td>
<td>-0.358±1.109</td>
<td>0.592±0.870</td>
<td>0.025*</td>
<td>0.95</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMD Z score</td>
<td>-0.350±0.844</td>
<td>0.323±1.101</td>
<td>0.102</td>
<td>0.69</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMD Z score</td>
<td>-0.346±0.918</td>
<td>0.254±1.056</td>
<td>0.156</td>
<td>0.60</td>
</tr>
<tr>
<td>33% Radius BMD Z score</td>
<td>-1.300±0.586</td>
<td>-0.615±0.839</td>
<td>0.028*</td>
<td>0.95</td>
</tr>
<tr>
<td>Fem. neck BMAD (g/cm³)</td>
<td>0.221±0.040</td>
<td>0.235±0.024</td>
<td>0.253</td>
<td>0.42</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMAD (g/cm³)</td>
<td>0.192±0.017</td>
<td>0.199±0.022</td>
<td>0.418</td>
<td>0.36</td>
</tr>
<tr>
<td>33% Radius BMAD (g/cm³)</td>
<td>0.354±0.044</td>
<td>0.375±0.044</td>
<td>0.203</td>
<td>0.48</td>
</tr>
<tr>
<td>HSI</td>
<td>1.7±0.4</td>
<td>1.7±0.3</td>
<td>0.911</td>
<td>0.00</td>
</tr>
<tr>
<td>BR</td>
<td>2.8±1.0</td>
<td>3.3±1.1</td>
<td>0.238</td>
<td>0.48</td>
</tr>
<tr>
<td>FNW (mm)</td>
<td>27.4±1.8</td>
<td>26.9±1.9</td>
<td>0.506</td>
<td>0.27</td>
</tr>
<tr>
<td>Z (mm³)</td>
<td>519±82</td>
<td>543±120</td>
<td>0.585</td>
<td>0.23</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>96.3±5.2</td>
<td>95.7±5.1</td>
<td>0.742</td>
<td>-0.12</td>
</tr>
<tr>
<td>NSA (°)</td>
<td>125±4</td>
<td>125±3</td>
<td>0.665</td>
<td>0.00</td>
</tr>
<tr>
<td>BUA Raw Score dB MHz⁻¹</td>
<td>46.8±7.4</td>
<td>49.2±5.8</td>
<td>0.358</td>
<td>0.36</td>
</tr>
<tr>
<td>SOS Raw Score m s⁻¹</td>
<td>1558±13</td>
<td>1554±16</td>
<td>0.513</td>
<td>-0.27</td>
</tr>
<tr>
<td>BUA Z Score</td>
<td>-0.71±1.16</td>
<td>-0.33±0.92</td>
<td>0.359</td>
<td>0.36</td>
</tr>
<tr>
<td>SOS Z Score</td>
<td>0.14±1.20</td>
<td>0.06±1.51</td>
<td>0.888</td>
<td>-0.06</td>
</tr>
<tr>
<td>Heel Width</td>
<td>6.34±0.48</td>
<td>6.23±0.46</td>
<td>0.544</td>
<td>-0.23</td>
</tr>
</tbody>
</table>

*p <= .05, **p <= .01, ***p <= .001 level of significance  § n=12 (1 BD-born daughter forgot age at menarche)  (see appendix I for tests used)
To explore whether the significant difference in knee height in BD daughters, according to birthplace, was associated with familial influences, knee height for mothers were observed. Some of the daughters in this sample set did not have mother’s knee height recorded so the sample numbers were small, n=11 mother-daughter pairs with UK-born BD daughters and n=11 for dyads with BD-born BD daughters. The mothers of UK-born daughters had lower average knee height (45.7±1.9 cm) than mothers of BD-born daughters (46.1±1.6 cm) suggesting some other factor e.g. birthplace or migratory experience, rather than familial influences may have contributed to the significantly greater knee height in UK-born BD daughters (Table 5.19).

Combining Loughborough and Cardiff data on knee height (Figure 5.5) illustrates how ethnicity, location, generation (mother/daughter), BD daughter’s birthplace and BD-born BD daughter’s age at migration relate to knee height.
Figure 5.5 Scatter graph showing individual knee heights of Loughborough and Cardiff BD mothers and daughters, according to daughter’s migratory status

**Migratory status = UK-born, early migration age < 8 years or late migration age >= 8 years**
BMD Z-scores (which takes into account age, and hence menopausal status as well as body mass) of mothers of BD-born daughters did not differ greatly from mothers of UK-born daughters, suggesting the ethnic differences in BMD Z scores between daughters, according to birthplace, were also not related to familial influences (Table 5.19). However, mothers of BD-born daughters did have a higher BUA Z score, with a small effect size, than mothers of IB-born daughters, an outcome which was consistent with the higher BUA Z scores observed in BD-born daughters compared to UK-born daughters, also with a small effect size (Table 5.19). This might suggest that BUA at the calcaneous, as opposed to BMD at the three skeletal sites used in the study, was more influenced by familial influences. However, it must be emphasised because of the small sample numbers and significantly different ages in both mothers and daughters, according to daughter’s birthplace, these conclusions are highly speculative.

The larger sample number in the Cardiff data set allowed comparisons to be made between early migrators (age < 8 years at time of migration) and late migrators (age => 8 years at time of migration) in BD daughters, but in the Loughborough data set there were only eight early migrators and five late migrators. This was too small a sample for making comparisons. Knee height measurements and age at migration are shown in Figure 5.4. Early migrators are younger and appear to have greater knee height.

Notwithstanding the caveats regarding the data, the prediction that UK-born BD daughters have greater height and knee height than BD-born BD daughters was accepted for knee height. Although the difference in height was not significant, the trend was in the direction predicted and the effect size was moderate. The prediction that UK-born BD daughters have greater bone mass and hip geometry dimensions than BD-born BD daughters was rejected.

This cannot be considered a definitive conclusion, due to the limitations of small sample size and the significant difference in age of BD daughters depending on birthplace. However, the relationship between skeletal size and bone measurements in BD daughters, according to birthplace, was opposite to the prediction that greater skeletal size would be paralleled by higher BMD in UK-born daughters.
### Table 5.19 Comparison of anthropometric and bone status variables for mothers of BD daughters, based on daughter’s birthplace (UK or BD)
Reported as mean ± st.dev.

<table>
<thead>
<tr>
<th></th>
<th>Mothers of daughters born in UK (n=11)</th>
<th>Mothers of daughters born in BD (n=11)</th>
<th>Effect size (Cohen’s d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.2±10.2</td>
<td>65.6±14.3</td>
<td>1.32</td>
</tr>
<tr>
<td>Recalled age at menarche§</td>
<td>12.8±1.5§</td>
<td>13.1±1.5§§</td>
<td>0.20</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>152.3±4.6</td>
<td>150.9±4.3</td>
<td>-0.31</td>
</tr>
<tr>
<td>Knee ht. (cm)</td>
<td>45.7±1.9</td>
<td>46.1±1.6</td>
<td>0.23</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.3±13.9</td>
<td>61.5±9.8</td>
<td>-0.65</td>
</tr>
<tr>
<td>BMI</td>
<td>29.9±5.7</td>
<td>26.9±3.7</td>
<td>-0.62</td>
</tr>
<tr>
<td>Fem. neck BMD Z scorea</td>
<td>0.00±0.83</td>
<td>0.06±1.08</td>
<td>0.06</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMD Z scorea</td>
<td>-0.45±0.82</td>
<td>-0.65±1.20</td>
<td>-0.19</td>
</tr>
<tr>
<td>33%. Radius BMD Z scorea</td>
<td>-0.91±0.89</td>
<td>-0.38±1.22</td>
<td>0.50</td>
</tr>
<tr>
<td>BUA Z Scorea</td>
<td>-0.45±1.0</td>
<td>-0.08±1.38</td>
<td>0.31</td>
</tr>
</tbody>
</table>

§n=10 for mothers of daughters born in UK (BD mother out of age range of reference group)
§§n=10 §§n=8 (4 mothers could not recall age at menarch)
5.2 Discussion

5.2.1 Summary of main findings

**Study’s predictions and hypotheses**

IB women have greater height, knee height, bone mass and hip geometry dimensions than BD women (independent of menopausal status). Any ethnic differences found do not persist after controlling for skeletal size.

Null hypothesis: there is no difference between BD and IB women for these variables

BD daughters have greater height, knee height, bone mass and hip geometry dimensions than their BD mothers (independent of mother’s menopausal status). Any generational differences found do not persist after controlling for skeletal size.

Null hypothesis: there is no difference between BD daughters and mothers for these variables

UK-born BD daughters have greater height, knee height, bone mass and hip geometry dimensions than BD-born BD daughters.

Null hypothesis: there is no difference between UK-born BD daughters and BD-born BD daughters for these variables

The prediction that IB women have greater height, knee height, BMD and hip geometry dimensions, HAL, FNW and Z than BD women (independent of menopausal status), and that any differences found in bone measurements would not persist after controlling for skeletal size, was accepted. This agrees with much of the published literature comparing BMD measurements in SA female immigrants with those of European heritage (Tobias et al., 1994; Alekel et al., 2002; Finkelstein et al., 2002; Mehta et al., 2004; Barrett-Connor et al., 2005; Roy et al., 2005). The only exceptions to the study prediction were QUS parameters which did not differ according to ethnicity.

The prediction that BD daughters would have greater skeletal size, bone mass and hip dimensions than their mothers, could not be tested adequately. The statistical analysis...
suggested there were no significant differences between mothers and daughters. However, in view of the limitations of the data set, the lack of power of the analysis to test for small effects and the lack of testing for an interaction between BD and IB mother-daughter pairs the outcome of this statistical analysis is unreliable. The trend was in the direction predicted i.e. daughters generally had larger values, for height and knee height as well as BMD, taking menopausal status into account. The prediction was accepted for height and knee height in the Cardiff sample, where greater heights and knee heights were found in the BD daughters compared to BD mothers.

The prediction that UK-born BD daughters would have greater skeletal size (height and knee height) than BD-born BD daughters was accepted. However, the prediction that UK-born daughters would have higher measurements of bone mass and some hip geometry dimensions, was rejected.

Combining Loughborough and Cardiff data on knee height showed that IB women generally have higher knee heights than BD women, and mother-daughter knee height differences are higher in BD dyads containing a UK-born BD daughter (Figure 5.4).
5.2.2 Sociodemographic characteristics of study sample

As mentioned above I found it very difficult to recruit participants from both BD and IB communities, mainly because of the ethnic and socio-economic background of the target population. A similar study to mine i.e. taking DXA BMD measurements from UK SA and IB women, reported difficulty in recruiting from the UK SA community, despite liaison with local communities and home visits (Roy et al., 2005, 2007).

Migration theory and DOHaD are very much focussed on the early life environment which is predicted to be very different in Bangladesh and the UK. The results of my study confirmed this, with variables relating to the environment experienced in early life e.g. pre-natal care, water supply etc. differing considerably depending on the participant’s birthplace, Bangladesh or the UK (Figure 5.5). The study results for early life environment variables for BD-born BD women were consistent with published statistics concerning these variables in Bangladesh (BBS, 1994; Paul and Rumsey, 2002; NIPORT, 2013). Study results also showed that UK-born BD daughters were exposed to an early environment similar to IB daughters i.e. more UK-born BD daughters, as opposed to BD-born BD daughters, were likely to have not been breast-fed, been born in a medical facility, been vaccinated and had mothers who received pre-natal care (Figure 5.5).

As migrants often live in poorer conditions than the indigenous population of the host country, often so-called “ethnic” differences are, in fact, due to SES. I tried to control as far as possible for SES by recruiting the BD and IB study participants from the same two wards of Loughborough. However, area of residence is not always a very accurate indicator of SES. Sometimes wealthier BD people prefer to live in the same area as the rest of the BD community. Also, younger, wealthier IB women rent property for a short time in these two wards. BD women, compared to their IB counterparts, had more people living in their houses and BD mothers were more likely to look after the home rather than be in employment, suggesting a lower SES by UK standards. However, in the Bangladeshi community it is difficult to separate economic and cultural drivers. It was noted that BD daughters were becoming more similar to IB daughters in terms of a higher proportion of
daughters, compared to their mothers, receiving further education and being in employment.

As described in the Background Chapter, UK SAs have poorer health than the general population and this was seen in the mothers in my study sample. BD mothers, despite a younger age profile, generally had worse health than IB mothers, with a higher proportion of BD mothers taking medication for diabetes, vitamin D deficiency, high blood pressure, iron deficiency/anaemia and high cholesterol. These findings are consistent with reports that there is a higher prevalence of diabetes (Misra et al., 2014), vitamin D deficiency (Darling et al., 2013; Gujral et al., 2013) and anaemia (Sproston and Mindell, 2006) in SA people compared to people of European origins. Eight (36% of all BD mothers) were taking medication for diabetes: half this number (four) were also taking medication for vitamin D deficiency. This agrees with literature that links vitamin D deficiency with diabetes (Alam et al., 2012). The daughters of both ethnic groups had few long-standing illnesses or disabilities according to ethnicity.

As well as more health stresses, BD mothers also had to cope with more reproductive demands. BD mothers, in my study, tended to marry at a young age, mean 17.2±1.8 years, started a family sooner at age 20.3±2.1 years and had more children, median number 5.5 children. However, the married BD daughters had similar reproductive statistics closer to IB mothers, marrying at mean age of 21 years, having their first child at age 23 years and having fewer children, median 3 children. In life history terms, the data on reproductive variables suggest more demands on a BD woman’s body and therefore a lower bone status in BD women compared to IB women. However, the BD daughters were becoming more similar to IB women in terms of later age at marriage, later age at birth of first child and fewer children, so placing less demands for resource which could protect bone status, and thus supporting the study prediction that BD daughters would have higher skeletal size and bone status than their mothers.

Menarcheal age is a useful variable to observe as it is linked with height and reproduction, which in turn are both closely associated with bone status. It was noted that BD daughters had a mean recalled age at menarche of 11.6 ± 1.4 years, which was significantly younger than BD mothers (12.9 ± 1.4 years), IB mothers (13.4 ± 1.3 years) and IB daughters (12.9 ±
1.3 years). The recalled age of menarche for BD daughters in my study agrees with published research on age at menarche of UK BD women (Núñez-de La Mora et al., 2008), who reported that pre-menopausal BD women living in London, born in the UK or emigrated to the UK as a child, had a significantly younger average age at menarche (12.3 years for those born in the UK and 12.2 years for child migrants) than their IB counterparts, whose mean age at menarche was 13.1 years. The same study reported that pre-menopausal BD women still resident in Sylhet had an average age at menarche of 13.2 years i.e. similar to the age at menarche (12.9 years) for the BD mothers in my study who had migrated to the UK as adults. Núñez-de La Mora et al. (2008) hypothesised that childhood environment influenced the timing of pubertal development amongst BD women who migrated to the UK. This was possibly due to a period of rapid catch-up growth following migration as a child (Houghton et al., 2014) though this does not explain the younger age at menarche of premenopausal BD women who were born in the UK in this same study.

It is difficult to say how this earlier recalled age at menarche in BD daughters might be associated with bone status as the evidence linking age at menarche and bone status is equivocal. Generally, at the population level, good biocultural environmental conditions during birth and childhood are linked with faster growth, taller stature and earlier age at menarche, and conversely poor biocultural environmental conditions tend to be associated with shorter height and delayed age at menarche (Tanner, 1992; Bogin, 2013). This is consistent with the results of a large study using 286,205 women from the European Prospective Investigation into Cancer and Nutrition (EPIC) which reported a secular trend to an earlier age at menarche and taller height probably due to changes in nutrition and better health in European countries (Onland-Moret et al., 2005). However, the same study found that at an individual level, women with an earlier age at menarche tended to be shorter than women who had menarche at a later age, possibly due to the earlier closure of the epiphyseal growth plate (Onland-Moret et al., 2005).

Under the current hypothesis that the UK provides a better early environment for growth and development, the finding that BD daughters had a significantly younger age at menarche, compared to their mother’s age at menarche, is consistent with this hypothesis, especially as the BD daughters are also taller than their mothers. However, IB daughters, despite being born and having ancestors in a higher income country (UK), have a
significantly later recalled age of menarche than BD daughters. Many factors are reported to influence age at menarche including migration, health history and emotional factors, so there is no single cause of age at menarche (Zacharias and Wurtman, 1969; Thomas et al., 2001; Mishra et al., 2009; Bodzsar and Zsakai, 2015).

Earlier menarche has been associated with higher BMD and lower risk of osteoporosis and fracture, as a consequence of being exposed to oestrogens for a longer period of time (Chevalley et al., 2009; Eastell, 2005; Parker et al., 2014) whereas other researchers link later menarche with better bone status, due to the increased time available for growth before epiphyseal closure (Devlin, 2011; Gilsanz et al., 1997). Early menarche is also linked with increased BMI in girls and this weight increase was associated with increased BMD at the femoral neck and increased cortical thickness and volumetric trabecular density of the distal tibia in women (Chevalley et al., 2011), a finding that complements another study which reported gain in BMI in girls from the age of one to twelve years was associated with a reduced risk of hip fracture in later life (Javaid et al., 2011). However, in my study the BD daughters, despite an earlier menarche, did not have a greater BMI than IB daughters. Due to the equivocality of studies on age at menarche and bone status, it is difficult in my study to assess how the change in recalled age at menarche between BD mothers and daughters might affect bone measurements.

To summarise, the descriptive statistics on my data set for UK BD and IB women, suggest the UK BD mothers are very similar to other SA women of similar age in the UK, in that they suffer poorer health, have a heavier reproductive load, and, if they migrated in adulthood, had a less hygienic environment at birth with scarcer resources. These factors might all contribute to a lower skeletal size and/or poorer bone status, according to Life History theory. Regarding BD daughters, data for reproductive statistics and early life environment at birth for those born in the UK, suggests acculturation is taking place in the UK BD community, which may indicate that in future generations, UK BD women become more similar to IB women in having less reproductive demands and a better early life environment. This may translate to UK BD women also becoming more similar to IB women in height and bone status.
5.2.3 Ethnic differences in anthropometric and bone measurements

The study’s prediction that BD women would have significantly lower height, knee height and BMD measurements than IB women was accepted, and is consistent with previous research showing that SA migrant women living in the US and UK, are shorter, with lower BMD measurements than the indigenous population (Tobias et al., 1994; Hamson et al., 2003; Mehta et al., 2004; Roy et al., 2005). Furthermore, the finding that BMAD did not differ between BD and IB women led to the accepting of the study prediction that ethnic differences in BMD were associated with skeletal size. This is in agreement with published studies reporting the lower BMD observed in SA women, compared to women of European descent, was attributed to their smaller bone size (Tobias et al., 1994; Mehta et al., 2004; Roy et al., 2005).
A very similar study to mine, in terms of location (Leicester, UK), DXA technology (Lunar) and migrant ethnicity (SA from Gujarat, India), measured BMD at total hip and lumbar spine of pre-menopausal women and compared measurements with a similar sample of IB women from Leicester (Hamson et al., 2003). Anthropometric and BMD values obtained in my study for BD and IB pre-menopausal women were reasonably consistent with values reported in this paper (Table 5.20) (Hamson et al., 2003). BMD values for femur neck area from my study could not be compared with those of Hamson et al. (2003) because, the area of hip used for BMD measurement was not specified in the paper (presumably it was total hip). Hamson et al., (2003) reported that SA women had significantly lower BMD measurements at lumbar spine and hip than IB women, as did my study. However, in males there was no significant difference between ethnicities (Hamson et al., 2003).

Data on a number of factors known to influence BMD were also collected in this same study (Hamson et al., 2003). In addition to significantly lower height and weight in Indian women, a significantly higher proportion of Indian women had less than four hours of sunlight exposure a day, had low serum vitamin D levels and had a vegetarian diet (Hamson et al., 2003). A higher proportion of IB women smoked and drank alcohol. All these factors were included as predictor variables in a stepwise MLR analyses, but the only significant predictors of BMD were ethnicity and weight (Hamson et al., 2003). Some of the biocultural predictor variables (sunlight exposure, serum levels of vitamin D, diet, smoking and drinking) were significantly different between the two ethnic groups and may have contributed to smaller skeletal size and BMD. Taking a bio-cultural perspective would suggest ethnicity was synonymous with these predictor variables (as well as many other factors). As ethnicity was a combination of all these influences on BMD, then that might explain why ethnicity, but not the individual predictor variables, was significant. The fact that weight, but not height, was a significant predictor of BMD is consistent with previous reports that weight is a better predictor of BMD (Sen et al., 2005; Robbins et al., 2006). Weight reflects tissue mass as well as skeletal size: tissue mass is generally beneficial to BMD, through increasing load on the bone, and other independent mechanisms of fat and lean tissue as described in the Background chapter.
Table 5.20 Age, anthropometric variables and lumbar spine BMD values of BD and IB daughters in my study compared to a similar study (Hamson et al., 2003).

Reported as means ± SD

<table>
<thead>
<tr>
<th></th>
<th>Loughborough Study</th>
<th>Leicester Study (Hamson et al., 2003)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BD Daughter (n=22)</td>
<td>IB Daughters (n=26)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>29 ± 9</td>
<td>32 ± 8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>153.4 ± 4.6***</td>
<td>166 ± 6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57.3 ± 11.3***</td>
<td>72.5 ± 16.9</td>
</tr>
<tr>
<td>Lumbar Spine L1-L4 BMD (g/cm²)</td>
<td>1.12 ± 0.14*</td>
<td>1.25 ± 0.13</td>
</tr>
</tbody>
</table>

* p <=.05, ***p <= .001 sig diff. (t-test) between BD/Indian and IB women in same study

The first study, as far as I’m aware, that considered ethnic differences in bone mass, involved 2232, mainly post-menopausal, IB women and 153 UK resident Indian women (Tobias et al., 1994). This study reported that BMC values for lumbar spine and femoral neck were lower in the UK Indians; after accounting for skeletal size, the ethnic difference in lumbar spine BMC disappeared, but persisted in femoral neck BMC (Tobias et al., 1994) (Table 5.21). A more recent study using a smaller sample of mainly peri-menopausal women reported that UK resident Indian women (n=47) had a significantly lower lumbar spine BMD than IB women (n=47), but this significant difference between ethnic groups disappeared when BMAD was used (Mehta et al., 2004). The same study also measured femoral neck BMD, and reported that, unlike the outcome reported by Tobias (2004), femoral neck BMD did not differ between the two ethnic groups, and femoral neck BMAD was significantly higher in the Indian sample (Mehta et al., 2004). Unfortunately, height and weight were not recorded in this study (the adjustments for skeletal size were made using BMAD) (Mehta et al., 2004).

The first study that recognised heterogeneity between SA groups distinguished between UK Pakistani and Indian pre-menopausal women in their sample (Roy et al., 2005). However,
only 21 Indian women were recruited so the most reliable results were from the Pakistani women, who had a significantly lower BMD, but similar BMAD, than IB women (Roy et al., 2005).

Table 5.21 Publications comparing DXA derived BMC or BMD of UK SA women with IB women and the effects of skeletal size on ethnic differences

<table>
<thead>
<tr>
<th>Reference</th>
<th>Menopause Status</th>
<th>Country of origin</th>
<th>Sample size</th>
<th>Skeletal Site</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Tobias et al., 1994)</td>
<td>Mainly Post-</td>
<td>India</td>
<td>2,232 IB 153 Indian</td>
<td>Lumbar Spine</td>
<td>Lower BMC in Indian – disappeared after adjustment for size</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Femur Neck</td>
<td>Lower BMC in Indian – persisted after adjustment for size</td>
</tr>
<tr>
<td>(Mehta et al., 2004)</td>
<td>Peri-</td>
<td>India Pakistan Bangladesh</td>
<td>47 IB 47 SA</td>
<td>Lumbar Spine</td>
<td>Lower BMD in Indian – disappeared after adjustment for size</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Femur Neck</td>
<td>Equivalent BMD in Indian – higher after adjustment for size</td>
</tr>
<tr>
<td>(Roy et al., 2005)</td>
<td>Pre-</td>
<td>Pakistan (82%)</td>
<td>119 IB 98 Pakistan</td>
<td>Lumbar Spine</td>
<td>Lower BMD in Pakistanis – disappeared after adjustment for size</td>
</tr>
</tbody>
</table>

Although the evidence from the literature outlined above and my own study seems to suggest skeletal size is the main explanation of differences in BMD between SA women and those of European origin, a few studies do contradict this.

One study found no difference in lumbar spine and femoral neck BMD between immigrant Pakistani and indigenous Norwegian pre-menopausal women (Falch and Steihaug, 2000) but caution is required when interpreting results across countries. Data from Scandinavian countries indicate the indigenous population has a lower BMD than found in people from other European countries, thus bringing the BMD of Scandinavian people closer to the low BMD values reported in Asian populations (Lunt et al., 1997). Lower BMD in Scandinavians is probably due to low vitamin D levels, because of less sunlight at higher latitudes (Johnell et al., 2007; Macdonald et al., 2008). Therefore the lack of difference in BMD values
between indigenous Norwegians and immigrant Pakistani women (Falch and Steihaug, 2000) might be because indigenous Norwegian women have a lower BMD than other Europeans. Comparisons between my data for IB and the indigenous Norwegians (Falch and Steihaug, 2000) appeared to support this explanation. Mean femoral neck BMD measurements and lumbar spine BMD from IB women in my study were higher than that of indigenous Norwegians as reported by Falch and Steihaug (2000). It therefore seems that the different results of my study compared to those reported in Norway (Falch and Steihaug, 2000) could be explained by lower BMD values in Norwegian women compared to IB women.

Another study that contradicted my findings, relates to the proximal radius (Ward et al., 2007). In my study, proximal radius BMD was significantly lower in BD women than IB women, but BMAD was similar in both ethnic groups. However, Ward et al. (2007) using peripheral QCT (pQCT), which measures vBMD accurately, reported a significantly lower true vBMD in proximal radius in SA (Pakistani and Indian) pre-menopausal women compared to IB pre-menopausal counterparts. The same study also investigated the distal radius, and reported trabecular true vBMD and total true vBMD at this site showed no difference between SA and IB women (Ward et al., 2007).

The few studies described above, which recorded BMD measures in SA women were based on a mechanistic, clinical perspective so simply focussed on bone status differences between UK ethnic communities, without recording details about migration e.g. birthplace of migrant or migration history. Only two of the studies above considered other variables e.g. vitamin D levels, in addition to ethnicity (Hamson et al., 2003; Roy et al., 2005).

BMD and skeletal size have been studied in other groups from the Asian continent. Although there is heterogeneity in the various Asian populations, most Asians tend to have lower height, lower BMD (and lower fracture risk) than people of European origin (Cundy et al., 1995; Bhudhikanok et al., 1996; Marquez et al., 2001; Finkelstein et al., 2002; Mehta et al., 2004; Roy et al., 2005; Weaver et al., 2007). Furthermore, differences in BMD between Asians, irrespective of country of origin, and Europeans generally disappear when body size is taken into account as demonstrated in the following studies on Asians, including Indian, Chinese, Japanese, Korean, Vietnamese, Cambodian and Laotian samples.
Cundy et al. (1995) studied BMD at lumbar spine and three femoral sites in a sample of 200 premenopausal women of Chinese, Indian, European and Polynesian origin, resident in New Zealand. They found that the Chinese and Indian women were significantly shorter and had significantly lower BMD than the European women, but when height was adjusted for, the differences between the Chinese and Indian women from European women almost disappeared (Cundy et al., 1995). The Chinese and Indian women were of very similar height to each other and had similar BMD measurements at all skeletal sites.

A more recent study compared US resident Chinese and Japanese late pre- and peri-menopausal women with Americans of European origin (Finkelstein et al., 2002). The heights of the Chinese and Japanese were lower than the European Americans. Lumbar spine and femoral neck BMD were also lower in the Asians, but not after adjusting for body size (Finkelstein et al., 2002). One study used US Asians who originated in China, Korea and Vietnam and compared them with European Americans. This study focussed on young men and women at varying stages of puberty and confirmed the hypothesis that ethnic differences in BMD were mainly associated with body size (Bhudhikanok et al., 1996). In another early paper, Asians from Vietnam, Cambodia and Laos, resident in the US, were compared to Americans of European origin (Marquez et al., 2001). Once again Asian men and women were reported to have lower BMD than American women of European heritage, but differences were reduced when body size was accounted for, except for bone density in the lumbar spine of postmenopausal Asian women (Marquez et al., 2001). Bone size is also suggested as an explanation for ethnic differences in BMC in early pubertal US European, East Asian (Chinese, Japanese, Hmong, Korean, Filipino) and Hispanic girls (Weaver et al., 2007).

One exception to the general finding that Asian women are generally of short stature was found in Korean pre-menopausal women (Lee et al., 2016). These women were quite tall, so I compared them with my sample of shorter BD daughters. My prediction would be that the Korean women, being taller, would have greater BMD than the BD daughters from my study, but this difference would be removed once height was taken into account. However, as can be seen from the table below, this was not the case. Despite being taller than the BD daughters, the Korean women had lower femur neck BMD. The study used the same densitometer and AHA software as used in my study. The Korean women had a significantly
lower weight and BMI than the BD women, so that may explain their lower BMD value. It does raise the question that by adjusting for skeletal size in statistical analysis, skeletal size may be acting as a marker for weight. However when I ran a standard linear regression model on my data, using BMD as the dependent variable and using ethnicity, menopause and weight as the predictor variables, ethnicity remained a significant predictor for BMD at all three skeletal sites (data not shown). This provides reassurance that the ethnic differences in BMD found in my study were wholly not associated with weight.

Table 5.22 Age, anthropometric variables and femur neck BMD values of BD daughters in my study compared to pre-menopausal women in a similar study (Lee et al. 2016)

Reported as mean ± st.dev

<table>
<thead>
<tr>
<th></th>
<th>Current Study</th>
<th>(Lee et al. 2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BD Daughter</td>
<td>Korean pre-menopausal women</td>
</tr>
<tr>
<td></td>
<td>(n=22)</td>
<td>(n=80)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>29.1 ± 8.9***</td>
<td>35.4 ± 5.8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>153.4 ± 4.6***</td>
<td>162.0 ± 0.1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57.3 ± 11.3***</td>
<td>51.2 ± 5.4</td>
</tr>
<tr>
<td>BMI</td>
<td>24.4 ± 4.6***</td>
<td>19.6 ± 2.2</td>
</tr>
<tr>
<td>Femur neck BMD (g/cm²)</td>
<td>1.12 ± 0.14***</td>
<td>0.90 ± 0.12</td>
</tr>
</tbody>
</table>

***p <= .001 level of significance between the two ethnic groups (independent t-test)

Regarding the QUS measurements, the outcome of the analyses of my Loughborough sample of BD women, suggests that there is no ethnic difference in BUA and SOS Z scores. This is in contrast to the only other publication, as far as I’m aware, that compared QUS scores between UK SA and IB women (Brooke-Wavell et al., 2008). This study concerned only post-menopausal women, also from Leicestershire and including 24% Bangladeshi women, and reported that Asian post-menopausal women had significantly lower BUA, but not SOS, raw scores than IB women, a significance that also disappeared when height was used as a covariate (Brooke-Wavell et al., 2008). As BMD is more highly positively
correlated with BUA than SOS (Waud, Lew and Baran, 1992; Brooke-Wavell et al., 2008), the authors suggested this could explain why BUA, but not SOS, differed in postmenopausal women according to their ethnicity.

The table below presents the data from the Leicestershire study (Brooke-Wavell et al., 2008) with comparable data from my study i.e. post-menopausal BD and IB women, along with data from BD post-menopausal women in the Cardiff study (MINA). In my study, the mean BUA raw score of IB women was 5.7 dB MHz⁻¹ higher than that of BD women and reported as not significant, whereas in the Leicester study it was only 4.7 dB MHz⁻¹ higher in IB women compared to SA women and reported as significant. This suggests the lack of significant ethnic difference in my study may be due to the limitations of my data set, especially the low numbers of post-menopausal women in the BD sample. Further studies need to be carried out to explore SA and IB differences in BUA raw score and the influence of menopause on any differences found.

It is interesting to note that the SA women (10 Bangladeshis and 14 Indians) in the Leicester study were taller and had higher BUA raw scores than the BD women in Cardiff which is consistent with the finding in the Leicester study of a relationship of BUA raw score with skeletal size (Brooke-Wavell et al., 2008). The slightly lower BUA raw scores for BD women in Loughborough compared to those in Cardiff may be explained by the higher age of the Loughborough BD women.
Table 5.23 Anthropometric and QUS measurements of BD and IB post-menopausal women from three studies: Leicester, Loughborough and Cardiff

Reported as mean ± st.dev

<table>
<thead>
<tr>
<th></th>
<th>Leicester (Brooke-Wavell et al., 2008)</th>
<th>Loughborough</th>
<th>Cardiff (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SA (n=24)</td>
<td>IB (n=23)</td>
<td>BD (n=12)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58.9 ± 3.3</td>
<td>58.5 ± 3.3</td>
<td>69.3 ± 8.0*</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>154 ± 6.1*</td>
<td>161 ± 5.5</td>
<td>149 ± 3.8*</td>
</tr>
<tr>
<td>Knee ht (cm)</td>
<td>47.9 ± 2.6*</td>
<td>50.2 ± 2.5</td>
<td>45.7 ± 1.6*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66.5 ± 10.2</td>
<td>68.1 ± 17.2</td>
<td>61.4 ± 12.8</td>
</tr>
<tr>
<td>BMI</td>
<td>28.2 ± 3.8</td>
<td>26.2 ± 6.5</td>
<td>27.5 ± 5.4</td>
</tr>
<tr>
<td>BUA raw score (dB MHz⁻¹)</td>
<td>44.1 ± 8.5*</td>
<td>48.8 ± 7.3</td>
<td>40.3 ± 10.7</td>
</tr>
<tr>
<td>SOS raw score (ms⁻¹)</td>
<td>1546 ± 8</td>
<td>1544 ± 10</td>
<td>1544 ± 10</td>
</tr>
</tbody>
</table>

* BD significantly different from IB: p<0.05 independent t-test

Regarding hip geometry, my study indicated that BD women had a significantly shorter HAL, narrower FNW, and lower Z compared to IB counterparts, whilst HSI, BR and NSA were similar in both ethnic groups. The differences in FNW, HAL and Z between ethnic groups did not remain when adjustment was made for height. This suggests skeletal size explains the ethnic differences in hip geometry parameters, HAL, FNW and Z.

Because the data collected in my study were relatively novel, there are few comparable studies and these studies sometimes either used a different densitometer e.g. Hologic, or if using a Lunar Prodigy (as in my study), the AHA software (Encore) was not used.

Height correlates with HAL (Flicker et al., 1996; Gnudi et al., 1999) and my finding, that a shorter HAL in BD women, compared to IB women, is explained by height confirms an earlier study, where height was reported as a more significant predictor of HAL than ethnicity in Pakistani and American premenopausal women (Alekel et al., 1999). A more
recent study also reported that mean height and HAL were significantly lower in UK SA women than IB women (Mehta et al., 2004).

A recent study, previously mentioned, used the same densitometer and AHA software as my study (Lee et al., 2016). The control group of pre-menopausal Korean women (n=80), were taller and had greater FNW and HAL than the BD daughters in my study, consistent with the expectation that greater height is linked to greater hip geometry dimensions.

The significantly lower FNW, associated with shorter height, in BD women compared to IB women in my study agrees with the fact that FNW correlates with height and weight (Gnudi et al., 1999). However, height does not always explain differences in FNW. A study compared UK Japanese and Chinese women with Americans of European origin (Ishii et al., 2012). Japanese and Chinese had similar height and weight to each other but were significantly shorter and lighter than the European Americans, yet only Chinese had a significantly shorter FNW than the European Americans (Ishii et al., 2012).

In my study, Z was lower in the BD women than IB women, as would be expected because Z is influenced by BMD and FNW. I am aware of only one study that compared Z values between Asians and Europeans: this took place in Australia, and reported pre- and post-menopausal Chinese women had significantly lower Z than Australians of European origin (Wang et al., 2005).

My study reported no difference in HSI, BR and NSA measurements between the two ethnic samples. My results, regarding BR values in BD women, did not agree with a previously mentioned study involving Asian women (Danielson et al., 2013a), which concluded that Chinese women had a significantly higher BR than US women of European origins, whilst Japanese women had a significantly lower BR than US European women.

The equation for HSI (see Methods) combines BMD, femur geometry, height and weight to give a value for femoral neck strength (Yoshikawa et al., 1994). As HSI values for BD women in my study did not differ significantly from their IB counterparts, this supports the idea that the advantages of smaller body size and shorter HAL (in terms of hip strength) of the BD women counteracts the disadvantages of lower BMD, lower FNW and lower Z values of BD women. This could imply that the hip geometry of SA women is appropriately adapted in
terms of bone strength for body size. No publications were found that explored differences in ethnic groups in terms of HSI values as calculated in my study. However, alternative measures of hip strength, composite strength indices, exist as described in the Methods chapter. A number of publications from a US research group propose that composite indices of femoral neck strength can explain the ethnic differences in fracture risk (Ishii et al., 2012). The authors also claimed that composite indices can explain the increased fracture risk in diabetic women, despite their higher BMD, than non-diabetic women (Ishii et al., 2012), as well as partially explaining the increased fracture risk associated with inflammation (Ishii et al., 2013). However, these composite strength indices had to be adjusted for age, BMI and menopausal status using multiple regression analysis, necessitating large sample numbers, before they reflected ethnic differences in fracture risk (Ishii et al., 2012). Unadjusted indices were similar in African-American and Americans of European ancestry and highest in Japanese and Chinese women (Ishii et al., 2012), probably a reflection of body size, as height and weight are a major influence in the equations.

It is worth comparing hip geometry parameters of Asians and Europeans with those recorded for Africans. Africans have the lowest fracture risk which may partially be explained by their hip geometry parameters, in addition to their relatively higher BMD. A number of studies conducted in the US have compared hip geometry parameters of African-Americans with Americans of European origin. Focussing on the hip parameters measured in my study, African pre- and post-menopausal women were similar to the BD women in my study in having a significantly narrower FNW and a shorter HAL than American women of European origins although, unlike the BD women in my study, this was not associated with height as both ethnic groups (Africans and US Europeans) were of similar heights (Mikhail, Vaswani and Aloia, 1996; Theobald et al., 1998). Unlike the BD women in my study, African post-menopausal women had a significantly bigger Z than US Europeans (Nelson et al., 2000, 2011) and African pre- and peri-menopausal women had a significantly lower BR than US Europeans (Danielson et al., 2013a). NSA was the only hip geometry parameter, of those used in my study, that was generally reported as being not significantly different in pre- and post-menopausal African women compared to US Europeans counterparts (Mikhail, Vaswani and Aloia, 1996; Theobald et al., 1998; Danielson et al., 2013a), although a large sample from the WHI reported post-menopausal US African women as having a significantly
lower i.e. more acute NSA (linked with reduced fracture risk) than US Europeans (Nelson et al., 2011).

Drawing on the publications mentioned above, plus my own study findings, ethnic groups can be compared in terms of favourable hip geometry parameters, where favourable is defined as being associated with lower fracture risk. Compared to women of European origin, African women have the lowest fracture risk (favourable HAL, FNW, BR, Z and possibly NSA), Japanese women have the next lowest fracture risk (favourable HAL, BR and NSA) followed by the BD women in my study (favourable HAL and FNW), then European women (reference group) and finally Chinese women who have the poorest hip geometry structure (no favourable hip geometry parameters). This roughly parallels the published relative fracture risks of Europeans having the highest fracture risk, Asians next and then Africans with the lowest risk (Lauderdale et al., 1997). The only anomaly was Chinese, who despite having a poor hip geometry structure according to the five parameters measured in my study, have a low fracture risk in the US second only to African-Americans (Lauderdale et al., 1997). Within countries of origin, China has a lower fracture incidence than Japan (Kanis et al., 2012).

As African women and BD women in my study both have shorter HAL and lower FNW than women of European origin, this could contribute to the lower fracture risk in Africans and Asians compared to Europeans. The fact that the difference in HAL between BD women and IB women in my study was associated with skeletal size (unlike the comparison between Africans and Europeans) suggests that if BD women become taller in the future, their HAL may also become longer, possibly predisposing them to greater fracture risk.

DXA technology, based on two dimensional scans, can only give a basic indication of hip geometry. However, other parameters of bone geometry such as cortical thickness and relative vBMD of cortex and trabecular bone may differ between ethnic groups and may help explain the differences in bone strength between ethnicities. A more appropriate technology for measuring these other parameters is QCT which can provide three dimensional scans. For example, it has been found that men of European origin had a significantly lower cortical vBMD at the tibial diaphysis than men of African or SA origin (Zengin et al., 2016). The same study also reported that men of African origin had thicker
cortices at the tibia and radius diaphysis than men of European or SA origin (Zengin et al., 2016). However, these parameters can only be measured using QCT technology and there are very few publications on bone geometry parameters as measured by QCT. Studies comparing Chinese-American women with American women of European origin, using high-resolution pQCT on the distal radius and distal tibia, reported that Chinese-American women had a thicker, denser cortex and thicker trabeculae which was postulated as the explanation of why Chinese-American women have a lower fracture risk, despite a lower BMD. The only study that I found which related to UK SA women, reported that the radius of UK SA pre-menopausal women had a lower cortical thickness but a greater cross sectional area than their IB counterparts, which overall gave similar bone strength (Ward et al., 2007). More research on bone geometry using QCT technology is needed.

To summarise, the results from my study suggest that Bangladeshi women are generally similar to SA and other Asian women, in terms of height and BMD, and confirms previous studies reporting lower height and lower BMD in Asian women compared to those of European origin. The results of my study also add further evidence for the proposition that lower BMD in all Asian populations studied is associated with skeletal size. The main conclusion from the hip geometry measurements in my study shows that UK BD women have a shorter HAL and a similar HSI compared to IB women suggesting that BD women’s smaller body size and shorter HAL compensates for their lower femur neck BMD, regarding overall hip strength.

The findings, both in my study and published literature, regarding BMD and some hip geometry parameters being associated with skeletal size provides evidence for the proposition that as UK BD women grow taller in successive generations, according to Migration theory, then their bone status will change accordingly.
5.2.4 Generational differences in anthropometric and bone measurements

Migration theory predicts that UK BD daughters become taller than their mothers, and have height and bone status measurements that become more similar to IB women. The study group of IB dyads indicates any general UK secular changes in height and bone status measurements. Although there was a trend towards BD daughters being taller than their BD mothers, MLR reported no differences in height, knee height and bone measurements between mothers and daughters. However, the power of the analysis was not sufficient for detecting small significant effects so if the difference between mothers and daughters was small it may not have been recognised. The most reasonable conclusion is that, due to the aforementioned limitations of the data set and lack of power to pick up an interaction between generation and ethnicity, the prediction that BD-born daughters have greater height, knee height, bone mass and hip geometry dimensions than their BD mothers, accounting for menopausal status, could not be accurately tested.

Height and knee height measurements from the Cardiff sample, did show Cardiff BD daughters to have a significantly greater height and knee height than their mothers (section 3.3.4). This may be because the Cardiff sample had a higher sample number (n=36 dyads).
so was a higher powered test. A larger sample number of Loughborough mother-daughter pairs would be required to reach a definite conclusion on generation comparisons in the Loughborough sample. However, an alternative or additional explanation is that the Cardiff sample of BD women may have differed from the Loughborough sample of BD women, as evidenced by the lower mean height in Cardiff BD women (153±5.8 and 148±6.2 for daughters and mothers respectively) compared to Loughborough BD women (156±5.4 and 153±4.8 for daughters and mothers respectively). Anthropometric data from the Cardiff BD women has been compared with age-matched BD women surveyed in the HSE 2004 (Bogin et al., 2014). The table from this article is reproduced below, with the addition of the data from the Loughborough BD women (Table 5.24).

The mean height of Loughborough BD women were similar to the age-matched BD sample in the HSE 2004 but the mean height of the Cardiff BD women was significantly lower than the BD women in the HSE 2004 survey (Table 5.24), suggesting the Cardiff BD women may not be representative of UK BD women. Indeed, IB Welsh women are also significantly shorter and heavier than English women (Floud, 2002) and this has been attributed to poorer living conditions, which could apply equally to IB and BD women living in Wales. The Cardiff sample appeared to be of lower SES than the Loughborough sample in terms of a higher proportion of short-statured women and lacking formal education. 44% of Cardiff BD women were of short stature and 17% of Cardiff BD women lacked a formal education, as compared to 25% and 14% respectively for Loughborough BD women. The Cardiff BD daughters’ mean height (153±5.8) was similar to the Loughborough BD daughters’ mean height (156±5.4), suggesting that the younger BD women living in Cardiff were becoming closer to that of their BD counterparts in Loughborough.

It is interesting to note from Figure 5.4 (page 200) that in the Cardiff data set of BD women there are six BD mothers of very low knee height, lower than any knee height measurement recorded in the Loughborough BD sample, consistent with the suggestion that the Cardiff sample are from a poorer background. However, normal knee height i.e. similar to knee height in BD Loughborough daughters, was regained in four of the daughters in these six dyads (Figure 5.4).
Regarding bone status, the outcome of the Loughborough study was consistent with that of the Cardiff study in that there appeared to be no significant differences in QUS raw and Z scores between BD mother and daughters, again with the caveat that this could not be adequately tested and a larger sample number of Loughborough dyads would be needed to reach a definite conclusion.

It was interesting to note that in the Loughborough study the mother-daughter comparisons for the IB women were very similar to the comparisons for the BD women, in that the trend was that daughters had higher measurements than mothers, except for 33% radius Z score, BUA Z score and SOS Z score (Table 5.6). Higher BMD values would be expected in younger women in both ethnic groups due to age. The lower values in daughters for these three Z score measurements may be an artefact connected with the reference population used by the manufacturer, or it could be an indication that at these sites, radius and calcaneous, bone status is not so good in daughters compared to mothers, irrespective of ethnicity.

It does raise the question of how bone status of the general UK population, not just that of ethnic minorities, might change in the future. There is recent concern that vitamin D deficiency and rickets are making a come-back in many countries, including the UK (Pettifor, 2004; Holick, 2006; Li, Thiruchandran and Hope, 2015). Additionally there are also reports that iodine deficiency may occur in the UK with schoolgirls (aged 14 to 15) suffering from mild iodine deficiency (Vanderpump et al., 2011). Furthermore, it is now established that the current UK population takes less exercise than previous generations (Boreham and Riddoch, 2001). All these factors may reduce bone strength and increase fracture risk in the future in both ethnic groups.
Table 5.24 Comparison of BD women from HSE 2004 compared to Cardiff study and Loughborough study

Bangladeshi mothers and daughters in the same age groups as in HSE 2004 compared to participants in Cardiff and my study, with the addition of IB mothers and daughters (within the same age grouping) from my Loughborough study.

Values for height, weight and BMI are mean±st.dev. Sample size in HSE 2004 varied depending on measurement made.

Adapted from Bogin et al. 2014

<table>
<thead>
<tr>
<th></th>
<th>Women aged over 17 to 36</th>
<th>Women aged over 40 to 70</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardiff BD daughters</td>
<td>HSE 2004 (age-matched BD women)</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>17-36</td>
<td>17-35</td>
</tr>
<tr>
<td>Sample Size</td>
<td>37</td>
<td>228-304</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>27 ± 5.5</td>
<td>26 ± 5.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>153 ± 5.8</td>
<td>156 ± 6.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64 ± 14.5</td>
<td>61 ± 12.3</td>
</tr>
<tr>
<td>BMI</td>
<td>27 ± 5.7</td>
<td>25 ± 5.2</td>
</tr>
</tbody>
</table>
5.2.5 Birthplace of BD daughters: differences in anthropometric and bone measurements

Study's predictions and hypotheses

IB women have greater height, knee height, bone mass and hip geometry dimensions than BD women (independent of menopausal status). Any ethnic differences found do not persist after controlling for skeletal size.

Null hypothesis: there is no difference between BD and IB women for these variables

BD daughters have greater height, knee height, bone mass and hip geometry dimensions than their BD mothers (independent of mother’s menopausal status). Any generational differences found do not persist after controlling for skeletal size.

Null hypothesis: there is no difference between BD daughters and mothers for these variables

UK-born BD daughters have greater height, knee height, bone mass and hip geometry dimensions than BD-born BD daughters.

Null hypothesis: there is no difference between UK–born BD daughters and BD-born BD daughters for these variables

The prediction that UK-born BD daughters have greater height and knee height than BD-born BD daughters was accepted, but the prediction that UK-born BD daughters have greater bone mass and hip geometry dimensions was rejected. However, this result needs to be treated with caution, due to low sample numbers.

UK-born BD daughters were taller, with significantly greater knee height, than BD-born BD daughters, consistent with findings of the Cardiff study as reported in chapter 3 and previously published (Bogin et al., 2014). The increase in height and knee height in UK-born BD daughers is predicted by Migration theory, based on the assumption that the UK provided a better early life environment in which to be born and spend the years of growth and development. However, there was an unexpected result in that UK-born BD daughters appeared to have poorer bone status, in terms of BMD at all three skeletal sites and QUS.
BUA, than BD-born BD daughters. This was contrary to the prediction that being born in the UK would lead to higher BMD, due to the increase in skeletal size and/or other consequences of having a better environment during birth, growth and development.

In addition to refuting the hypothesis that the improved early environment of the UK would be beneficial to BMD, these findings also suggest that bone status does not always reflect skeletal size. In this comparison of BD daughters according to birthplace, greater height was associated with lower BMD measurements. The finding that skeletal size seemed to be unrelated to BMD was further reinforced by the fact that BMAD was also higher in BD-born daughters, despite BD-born daughters being shorter than UK-born daughters (Table 5.18 and Figure 5.4).

However, the above inferences are only speculative. Firstly, the sample numbers are very small (n=15 for UK-born and n=13 for BD born daughters), allowing a few cases to have a profound influence on the outcome (Figure 5.4). Secondly, the UK-born BD daughters were significantly younger, in their early twenties, than the BD-born BD daughters, who were in their early thirties (Table 5.18 and Figure 5.4). There is no obvious reason why being younger might influence bone measurements. It could be argued that the younger UK-born daughters had not yet reached the age of peak bone mass, but peak bone mass is generally attained by 18 years for the three skeletal sites used in my study (Henry, 2004). However, the different mean ages in the two groups might reflect unknown cohort differences which influence knee height and/or bone measurements. BD daughter’s birthplace may have influenced age at menarche, which could be connected with the differences in knee height and bone measurements. However, it was found that age of menarche was similar, irrespective of birthplace (mean for UK-born daughters = 11.60±1.50 years and for BD-born daughters = 11.58±1.31 years). A previously mentioned study, involving UK BD women in London, also reported that being born in the UK or migrating from Bangladesh as children did not affect average age at menarche of BD pre-menopausal women (Núñez-de La Mora et al. 2008).

The significantly higher knee height in UK-born BD daughters may have been a result of familial influences rather than birthplace, but this did not seem to be the case because the mothers of UK-born BD daughters had lower average knee height (45.7±1.9) than the
mothers of BD-born daughters (46.1±1.6) (Table 5.19), suggesting that it was the daughter’s birthplace, rather than familial factors, which was associated with the higher knee height in UK-born BD daughters. Height in mothers of UK-born daughters was higher (152.3±4.6) than mothers of BD-born daughters (150.0±4.3), but the shorter stature in mothers of BD-born daughters may have been a consequence of their greater age (65.6±14.3) as opposed to the age of mothers of UK-born daughters (49.3±10.2) (Table 5.19).

The limitations of sample size and lack of age-matching between the two samples of BD daughters, render this finding of greater height, but lower BMD in UK-born BD pre-menopausal women, compared to BD-born women, to be merely speculative. However, it does raise the possibility that the UK-born BD daughters are more gracile than BD-born BD daughters. As described in the Background chapter, relative elbow breadth and relative pelvic breadth are decreasing significantly in young Germans (3 to 18 years) over the last few decades, and this has been attributed to increased sedentism (Scheffler and Hermanussen, 2014). In my study, no measures of bone robusticity were taken. The only bone widths recorded were FNW and heel width. FNW and heel width were similar in BD daughters, irrespective of birthplace (Table 5.18), suggesting that birthplace may not make a difference to robusticity of the skeleton.

However, heel width in BD daughters was lower than their mothers (Table 5.6) suggesting that the BD daughters might have a more gracile skeleton than BD mothers. FNW was not compared between BD mothers and daughters, as FNW tends to increase in width with age related BMD loss (Alonso et al., 2000; Beck et al., 2001).

It was also noted that heel width was similar in both ethnic groups (Table 5.18), which in view of the taller height of IB women, might suggest that BD women have a more robust skeleton than IB women.

However, this is very speculative, as my study did not set out to compare robustness of skeleton between the two ethnic groups, and heel width may not be a good indicator of robusticity of the skeleton, but it is a consideration for future work on bone status in UK SA groups, especially in light of the finding reported in the Cardiff study (MINA project) that BD women in Bangladesh had better scores on the Guralnik short physical performance battery (SPPB) compared to BD women in Cardiff (Bogin et al., 2014). This was attributed to the
fact that BD women in the UK participated in less physical activities than those in Bangladesh, due to lifestyle differences and social isolation as a result of living in the UK (Bogin et al., 2014) (see section 2.5.2).

It can be concluded that UK-born BD daughters have greater height and knee height, but lower BMD, than BD-born BD daughters, with the caveat that the statistical analysis has limitations and further studies would be required to confirm this finding.

5.3 Limitations and strengths of the Loughborough study

One very important issue in collecting the data from an ethnic minority group is the success, or otherwise, of recruiting volunteers. It was very difficult in the current study to recruit participants from BD and IB communities, mainly because of the ethnic and socio-economic background of the target population, along with the need for a mother-daughter pair which reduced the eligible population. This resulted in low sample numbers which meant that the statistical analysis was difficult. Furthermore, the need to relax inclusion criteria to facilitate recruitment resulted in non-normal age distributions and different age distributions according to ethnicity, and, within the BD sample, according to daughter’s birthplace. My difficulties in recruitment from the BD community mirrored previous publications. A similar study to mine i.e. taking DXA BMD measurements from UK SA and IB women, reported difficulty in recruiting, despite liaison with local communities and home visits (Roy et al., 2005, 2007).

The limitations of sample size necessitated combining mothers and daughters to increase power. The disadvantage of this approach was that in some cases, but not all, both mother and daughter from the same dyad were included. Migration theory would predict that the difference between BD mothers and daughters would be greater than the secular difference found between IB mothers and daughters, but sample numbers were not large enough to test for interaction between ethnicity and generation, so the regression analysis was just testing differences between mother and daughter, irrespective of ethnicity.

Data on other variables connected with bone status e.g. serum vitamin D levels, could not be collected. This was due to lack of resources, and also the wish to reduce the demand on the participants. To collect the data for the study generally required a couple of hours of the participant’s time. With the additional time for travelling a session could take a whole
morning or afternoon, so any further data collection might have reduced the cooperation and good will of participants and discouraged potential volunteers. Additional blood tests having a negative impact on response rates in SA women has been cited as a reason for not carrying out blood tests (Roy et al., 2005).

Women were excluded from the Loughborough study if they reported long term HRT use but women who had ever taken HRT for a year or less, or were using oral contraception were included in the study. This was to reflect the general characteristics of the sample study, but was a confounding variable for statistical analyses on bone status: therefore, these women had to be excluded from the statistical analysis. Furthermore, in the Cardiff (MINA) study, because the project was not specifically focused on bone status, no records were made of participants’ HRT or contraceptive use.

A strength of the Cardiff and Loughborough studies was focussing on a single Asian group. Although most Asians do seem similar in having smaller heights and lower BMD and lower fracture rates than people of European and African origin, there is still a need to focus on a relatively homogenous Asian group. Many studies do not define the ethnic group adequately and/or combine Asians from different country of origin. Such sample groups will have a wider variation in biocultural influences compared to an Asian sample originating from just one country.

Although from a practical perspective the specification of mother-daughter pairs for my study hampered participant recruitment, from a theoretical point it was necessary for testing out generational differences, to reduce the confounding effects of genetics and family environment/culture. Using a sufficient sample number of BD mother-daughter pairs in the Cardiff study showed clearly that height and knee height were significantly greater in UK BD daughters compared to their BD mothers.

Another theoretical strength of the Loughborough study was the inclusion of a control group, comprising IB mothers and daughters, to distinguish between UK secular changes and other factors influencing generational changes in the BD sample. The comparisons between ethnic groups were improved by the precaution of recruiting IB women from the same small area (just two wards in Loughborough) in which the majority of BD women resided, thus controlling as far as possible for SES and community environment.
6 Summary, future research and conclusions

Before discussing the scientific outcome of my study, it is worth mentioning that, in addition to providing useful scientific data on bone status in a UK ethnic minority group, my study had a community impact. It facilitated relationships between Loughborough University and the local BD community. Subsequent research studies have been carried out at Loughborough University which have utilised the contacts that my supervisor and I had built up with the BD community. My study also increased awareness of bone health, within the BD community and a low SES IB community. For study participants, the DXA scans either provided reassurance or initiated seeking further medical advice regarding BMD and osteoporosis.

My study provided evidence for an increase in height in a younger generation, compared to their mothers, of a migrant community, UK BD women. This is consistent with Migration theory which predicts that an ethnic group will take on the characteristics of the indigenous
population as a result of sharing the same environment. I also found a similar increase in knee height in a younger generation of UK BD women, consistent with DOHaD and published literature, as evidence that the UK has an overall healthier environment in which to be born and/or spend the years of growth and development.

The results of my study showed that ethnic differences in bone scores (BMD, and hip geometry parameters, HAL, FNW and Z) are associated with skeletal size, and could account for the significant differences in these parameters found between BD and IB women. This confirms previous reports on the association of skeletal size and ethnic differences between Asian and European women. If future generations of BD women show an increase in skeletal size, this may impact on the above bone measurements, bringing them closer to those recorded for IB women. Unfortunately, my data set had limitations so to the prediction that taller height in BD daughters was paralleled by higher BMD scores and hip geometry parameters, HAL, FNW and Z could not be adequately tested. Therefore, more research is needed to confirm that skeletal size in subsequent generations of UK BD women is increasing, as evidenced by the Cardiff and Loughborough study, and to explore whether this is accompanied by an increase in BMD, HAL and FNW.

The results of my study were equivocal in the association of QUS parameter, BUA, with skeletal size, whilst a previous study reported skeletal size to be associated with differences in BUA scores in SA and IB post-menopausal women (Brooke-Wavell et al., 2008). More studies using BUA, a measure of bone status and predictor of fracture risk, would be useful to further explore ethnic differences and the association of bone status with skeletal size.

The results of my study demonstrate that HSI is the same for both BD and IB women i.e. in terms of hip strength, the low femur neck BMD in BD women is compensated for by their smaller body size and smaller hip dimensions, HAL and FNW. Hip geometry parameters, including HAL and FNW, have been considered a possible explanation for differences in fracture risk between Asians and Europeans so future research is needed to explore this possibility by using more sophisticated technology i.e. QCT, to establish whether other bone geometry measurements, such as cortical thickness, trabecular microarchitecture and true volumetric density, not measured in my study, are protective against fracture risk in SAs.
My study suggested that birthplace of BD daughters, Bangladesh or the UK, had a
association with height and knee height in the direction predicted by Life History theory i.e.
greater in the UK-born BD daughters. However, this was not paralleled by a higher BMD
and/or hip geometry parameters, HAL, FNW and Z, in the UK-born BD daughters. Although
lower BMD in UK-born daughters was not significantly lower than BMD of BD-daughters,
possibly because of the small sample numbers, it was in the opposite direction predicted by
Migration Theory and DOHaD, which predicts that bone status measurements would be
higher in UK-born BD daughters, in line with the improved environment in the UK and
increase in skeletal size. The sample number on which this result is based is so small as to
be verging on the anecdotal, and is compromised by the different ages associated with
birthplace, but if it does reflects a true difference, then it may be further evidence that the
more sedentary environment of a developed country, compared to one of lower income, is
leading to decreased robusticity of the UK BD migrant’s skeleton. Further research, taking in
vivo measurements of skeletal robusticity, needs to be carried out to establish whether
birthplace of BD women has a significant association with skeletal size and/or bone
measurements. This would be an interesting approach in exploring the possibility that
increased sedentism, especially in developed countries, is leading to the human skeleton
becoming more gracile. There is also concern that younger generations of IB women are
becoming less robust than their mothers. More research is required in this area, as it a
particularly worrying scenario because it suggests bone health is going to worsen in the near
future in all UK groups, irrespective of ethnicity. This has implications for fracture risk,
which is already predicted to rise due to an ageing population, and which will rise even
further if bone status is deteriorating due to lack of physical activity. Such research could be
paralleled by qualitative studies, as suggested by the thesis reviewers, e.g. running focus
groups with BD women and collecting data about their physical activity during childhood in
Bangladesh. Groups could include a group of older postmenopausal women (65-80 year
olds) and a group of younger postmenopausal women (50-60 years), all born in Bangladesh,
plus a group of Bangladeshi women who were born and grew up in the UK, as well as
separate groups of IB women matched for age with the BD groups. These qualitative data
would show how childhood environment differed between Bangladesh and the UK and how
this might be affected by cultural factors for BD women born in the UK. Many of the BD-
born daughters in my study had sisters who were born in the UK, and vice versa. It would
be very interesting to return to these families and record the same measurements in a sister born in the other country to explore how their anthropometric and bone status measurements compared, as well as to collect qualitative data on the physical activity they undertook in early life and how it might have differed according to country of birth.

On the topic of follow-up studies, it would also be useful to return to the Loughborough BD and IB daughters in my study in future years and repeat the study measurements to explore how their bone status changed with age, especially after menopause. Longitudinal studies involving three generations of UK SA women, although more challenging and costly, would be particularly beneficial in exploring changes in bone status after migrating to the UK over the generations. In all future studies, it would be valuable to measure knee height in addition to height, as knee height is a good indicator of environmental conditions in the first decade of a participant’s life, and also provides a better marker for maximal long bone growth in older participants who may decline in total stature. Further studies on bone status generational change in UK ethnic groups should include a control group of IB women, to provide additional data regarding secular changes in the indigenous UK population, and to examine the possibility that IB women resident in the UK are becoming poorer in bone status which may indicate increased fracture risk later in life.

Future work studying generational changes require bigger sample sizes and more exclusion criteria to ensure better matching in terms of age and menopausal status. Generational differences are likely to be small and published literature concludes that familial influences on height and bone status are strong, so it is recommended that mother-daughter pairs are recruited to improve the power of the statistical analysis designed to detect the small effect sizes in bone measurements between mother and daughter. However, as my study demonstrated, the requirement of mother-daughter pairs makes recruitment of BD women even more difficult, but the alternative, recruiting non-related participants for a study on generational differences, would require a very high number of participants due to the lack of control for familial influences (genetic, environmental and cultural) which contribute greatly to the variance in skeletal size and bone status. My study indicated that skeletal size and BMD data for BD women were similar to that of other SA women, so it may be more efficient in future research to consider using Indian or Pakistani women, instead of BD
women, as these alternate SA groups constitute a higher proportion of the UK population and are not such a difficult-to-reach community.

Although markers of fracture risk, BMD and some hip geometry parameters, were measured in my study, fracture risk itself could not be established. Larger longitudinal studies are needed to provide further data on fracture risk, especially in the less-researched ethnicities such as Asians and Africans.

If the fracture risk of BD and other SA minority groups do rise in the future, then the health care and social costs (already predicted to be high) for coping with the results of bone fracture will further increase. Health care and social costs for the IB community are already predicted to increase, as a result of an ageing demography. If the skeleton of UK SA and/or IB people is becoming more gracile, then this will exacerbate the risk of fracture and associated costs. If these predictions are correct, then UK health policy needs to take this into account.

Means of addressing the problem of lower bone status and increased fracture risk in the future could be to disseminate more information to all ethnic groups regarding healthy lifestyles for bone health, including nutrition, diet, sunshine exposure and physical activity. Promoting health messages to the SA men and women may be more difficult due to language and cultural barriers. Furthermore, ethnic cultural differences may make it harder for BD men and women to follow the health advice. There is awareness that SAs take less exercise than other UK communities and research has been carried out on how to promote physical activity in these groups. UK health policy needs to budget for further funding to better assess those at risk, and to cope with the increased social and economic consequences of the increased fracture burden in the near future. This should be paralleled by an increase in funding to further explore the consequences of migration for UK ethnic minorities in terms of bone health and to assess the change in future bone status of all UK citizens, as a result of a rapidly changing environment which due to technology and lifestyle, is leading to less physical activity, more sedentism and, for some members of society, less exposure to sunlight, all of which are particularly detrimental to bone status. Because the skeleton displays considerable plasticity in response to the environment, deterioration in
bone status in the UK population could occur within a short time period, making it essential that the problem is dealt with using some urgency.

The results of my study strongly suggest that bone scores (BMD, BUA and hip geometry) are associated with skeletal size. If future generations of BD women show an increase in skeletal size this may eventually impact on these same bone scores. This raises the possibility that fracture risk for BD women may increase, becoming closer to the risk for IB women. If the fracture risk of BD and other Asian minority groups rise in the future, then the health care and social costs (already predicted to be high) will further increase, and UK health policy needs to take this into account.
7 References


BBS (2009) *Bangladesh Bureau of Statistics*. Available at:


Cooke-Hubley, S. *et al.* (2017) ‘Parity and Lactation Are Not Associated with BMD Loss or Incident Major Fragility Fractures Over 15 Years: Canadian Multicentre Osteoporosis Study (CaMos)’, 245


Reid, I.R. et al. (1994) ‘Relation between increase in hip axis in older women between 1950s and 1990s and increase in age specific rates of hip fracture’, *BMJ*, 309, pp 508-509


### Appendix I: Statistical Tests Used in Tables

Table 3.3 Comparisons of Cardiff mothers with daughters (n=36 pairs)

<table>
<thead>
<tr>
<th></th>
<th>BD Mothers (n=36)</th>
<th>BD Daughters (n=36)</th>
<th>Test Used</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>56.0 ± 7.4</td>
<td>27.7 ± 5.3</td>
<td>Paired t</td>
</tr>
<tr>
<td></td>
<td>56.5 (40 to 69)</td>
<td>27.0 (20 to 30)</td>
<td></td>
</tr>
<tr>
<td><strong>Year of birth</strong></td>
<td>1952.8 ± 7.8</td>
<td>1981.7 ± 5.2</td>
<td>Paired t</td>
</tr>
<tr>
<td><strong>No. pre-menopausal (%)</strong></td>
<td>8 (22%)</td>
<td>36 (100%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td><strong>No. born in BD (%)</strong></td>
<td>36 (100%)</td>
<td>17 (47%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td><strong>Age at migration</strong></td>
<td>30.7 ± 9.4</td>
<td>8.2 ± 6.8</td>
<td>Mann-Whitney U</td>
</tr>
<tr>
<td></td>
<td>28.5 (18 to 55)</td>
<td>8.0 (0 to 23)</td>
<td></td>
</tr>
<tr>
<td><strong>Year of migration</strong></td>
<td>1983.9 ± 8.5</td>
<td>1989.7 ± 7.3</td>
<td>Mann-Whitney U</td>
</tr>
<tr>
<td><strong>Years resident in UK</strong></td>
<td>25.3 ± 8.6</td>
<td>19.8 ± 7.3</td>
<td>Mann-Whitney U</td>
</tr>
<tr>
<td></td>
<td>27.0 (4 to 39)</td>
<td>21.0 (4 to 30)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at marriage</strong></td>
<td>16.2 ± 2.8</td>
<td>18.72 ± 2.3</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>Number of children</strong></td>
<td>6 (2 to 10)</td>
<td>2 (0 to 4)</td>
<td>Fishers Exact</td>
</tr>
<tr>
<td><strong>Age at birth of 1st child</strong></td>
<td>20.8 ± 4.3</td>
<td>21.3 ± 2.2</td>
<td>Mann-Whitney U</td>
</tr>
<tr>
<td></td>
<td>20 (13 – 29)</td>
<td>21 (17 -25)</td>
<td></td>
</tr>
<tr>
<td><strong>Age finished education</strong></td>
<td>13.6 ± 2.7</td>
<td>18.0 ± 2.9</td>
<td>Mann-Whitney U</td>
</tr>
<tr>
<td></td>
<td>13 (8 to 20)</td>
<td>18 (14 to 31)</td>
<td></td>
</tr>
<tr>
<td><strong>Number lacking formal education</strong></td>
<td>12 (33%)</td>
<td>0 (0%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td><strong>Number with longstanding illness</strong></td>
<td>28 (78%)</td>
<td>9 (25%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td><strong>Number (%) of short-stature (&lt;= 150 cm)</strong></td>
<td>23 (64%)</td>
<td>9 (25%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>65.6 ± 13.7</td>
<td>65.0 ± 14.5</td>
<td>Paired t</td>
</tr>
<tr>
<td></td>
<td>64.4 (41 to 100)</td>
<td>61.6 (42 to 107)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>30.1 ± 5.2</td>
<td>27.6 ± 5.7</td>
<td>Mann-Whitney U</td>
</tr>
<tr>
<td></td>
<td>29.0 (22 to 44)</td>
<td>27.4 (20 to 43)</td>
<td></td>
</tr>
<tr>
<td><strong>Experimental Variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>147.4 ± 6.3</td>
<td>153.2 ± 5.8</td>
<td>Paired t</td>
</tr>
<tr>
<td><strong>Knee Height (cm)</strong></td>
<td>45.3 ± 2.5</td>
<td>46.7 ± 2.4</td>
<td>Paired t</td>
</tr>
<tr>
<td></td>
<td>45.9 (40 to 49)</td>
<td>47.3 (40 to 51)</td>
<td></td>
</tr>
<tr>
<td><strong>BUA Raw Score (dB MHz⁻¹)</strong></td>
<td>42.4 ± 7.4</td>
<td>46.5 ± 6.8</td>
<td>Paired t</td>
</tr>
<tr>
<td><strong>SOS Raw Score (m s⁻¹)</strong></td>
<td>1549 ± 13</td>
<td>1558 ± 11</td>
<td>Wilcoxon signed rank test</td>
</tr>
<tr>
<td></td>
<td>1553 (1508 to 1582)</td>
<td>1559 (1529 to 1591)</td>
<td></td>
</tr>
<tr>
<td><strong>BUA Z score f</strong></td>
<td>-0.69 ± 0.78</td>
<td>-0.76 ± 1.05</td>
<td>Paired t</td>
</tr>
<tr>
<td><strong>SOS Z score f</strong></td>
<td>0.30 ± 1.27</td>
<td>0.29 ± 1.07</td>
<td>Wilcoxon signed rank test</td>
</tr>
<tr>
<td></td>
<td>0.51 (-3.37 to 2.92)</td>
<td>0.28 (-2.53 to 3.46)</td>
<td></td>
</tr>
</tbody>
</table>
### Appendix I (continued)

#### Statistical Tests used in Tables

Table 3.4 Descriptive data for Cardiff daughters and their mothers, according to daughter’s birthplace

<table>
<thead>
<tr>
<th></th>
<th>UK-born Daughters (n=19)</th>
<th>BD-born Daughters (n=17)</th>
<th>Test Used</th>
<th>Mothers of UK-born daughters (n=19)</th>
<th>Mothers of BD-born daughters (n=17)</th>
<th>Test Used</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>27.4 ± 5.2</td>
<td>27.9 ± 5.4</td>
<td>Mann-Whit</td>
<td>55.7 ± 7.5</td>
<td>56.3 ± 7.6</td>
<td>T-test</td>
</tr>
<tr>
<td></td>
<td>26 (20 to 36)</td>
<td>29 (20 to 36)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Year of birth</strong></td>
<td>1982.0 ± 5.1</td>
<td>1981.5 ± 5.5</td>
<td>Mann-Whit</td>
<td>1952.7 ± 8.1</td>
<td>1952.8 ± 7.7</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>Number of pre-menopausal (%)</strong></td>
<td>19 (100%)</td>
<td>17 (100%)</td>
<td></td>
<td>5 (26%)</td>
<td>3 (18%)</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>Age at migration</strong></td>
<td>Not applicable</td>
<td>8.2 ± 6.8</td>
<td></td>
<td>25.7 ± 6.0</td>
<td>36.1 ± 9.6</td>
<td>T-test</td>
</tr>
<tr>
<td></td>
<td>8.0 (0 to 23)</td>
<td>(18 to 42)</td>
<td></td>
<td></td>
<td>(20 to 55)</td>
<td></td>
</tr>
<tr>
<td><strong>Year of migration</strong></td>
<td>Not applicable</td>
<td>1990 ± 7.3</td>
<td>Mann-Whit</td>
<td>1979.3 ± 4.8</td>
<td>1989.2 ± 8.7</td>
<td></td>
</tr>
<tr>
<td><strong>Years resident in UK</strong></td>
<td>Not applicable</td>
<td>19.8 ± 7.3</td>
<td></td>
<td>30.0 ± 5.0</td>
<td>20.12 ± 8.8</td>
<td>Mann-Whit</td>
</tr>
<tr>
<td><strong>Age finished education</strong></td>
<td>17.7 ± 2.1</td>
<td>18.3 ± 3.7</td>
<td>Mann-Whit</td>
<td>13.9 ± 2.9</td>
<td>13.1 ± 2.4</td>
<td>Mann-Whit</td>
</tr>
<tr>
<td></td>
<td>18 (14 to 24)</td>
<td>18 (15 to 31)</td>
<td></td>
<td>13.5 (8 to 20)</td>
<td>12.0 (11 to 16)</td>
<td></td>
</tr>
<tr>
<td><strong>No. (%) lacking formal education</strong></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
<td>3 (16%)</td>
<td>9 (53%)</td>
<td>Fishers Exact</td>
</tr>
<tr>
<td><strong>No. (%) with longstanding illness</strong></td>
<td>3 (16%)</td>
<td>6 (35%)</td>
<td>Fishers Exact</td>
<td>15 (79%)</td>
<td>13 (76%)</td>
<td>Chi square</td>
</tr>
<tr>
<td><strong>Birth order of daughter</strong></td>
<td>3.8 ± 2.0</td>
<td>3.2 ± 1.6</td>
<td>T-test</td>
<td>See daughter</td>
<td>See daughter</td>
<td>T-test</td>
</tr>
<tr>
<td></td>
<td>6 (26%)</td>
<td>(18 to 42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mother’s age at birth of daughter</strong></td>
<td>28.32 ± 6.5</td>
<td>28.35 ± 8.2</td>
<td>T-test</td>
<td>See daughter</td>
<td>See daughter</td>
<td>T-test</td>
</tr>
<tr>
<td></td>
<td>28.35 ± 8.2</td>
<td>28.35 ± 8.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number (%) of short-stature</strong></td>
<td>1 (5%)</td>
<td>8 (47%)</td>
<td>Fishers Exact</td>
<td>9 (47%)</td>
<td>14 (82%)</td>
<td>Chi square</td>
</tr>
<tr>
<td></td>
<td>2 (13%)</td>
<td>(10 to 24)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>67.6 ± 14.3</td>
<td>61.9 ± 14.5</td>
<td>Mann-Whit</td>
<td>67.8 ± 16.0</td>
<td>63.1 ± 10.4</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td>28.0 ± 5.6</td>
<td>27.1 ± 6.0</td>
<td>Mann-Whit</td>
<td>30.2 ± 5.4</td>
<td>29.9 ± 5.1</td>
<td>T-test</td>
</tr>
<tr>
<td></td>
<td>151.3 ± 6.1</td>
<td>151.3 ± 6.1</td>
<td></td>
<td>149.1 ± 6.6</td>
<td>145.4 ± 5.6</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>47.8 ± 1.6</td>
<td>46.0 ± 6.6</td>
<td>T-test</td>
<td>42.8 ± 7.3</td>
<td>41.9 ± 7.8</td>
<td>T-test</td>
</tr>
<tr>
<td></td>
<td>45.6 ± 2.7</td>
<td>47.0 ± 7.3</td>
<td></td>
<td>44.7 ± 2.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BUA Raw Score (dB MHz^-1)</strong></td>
<td>46.0 ± 6.6</td>
<td>47.0 ± 7.3</td>
<td>T-test</td>
<td>42.8 ± 7.3</td>
<td>41.9 ± 7.8</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>SOS Raw Score (m s^-1)</strong></td>
<td>1559 ± 12</td>
<td>1558 ± 10</td>
<td>Mann-Whit</td>
<td>1547 ± 15</td>
<td>1551 ± 10</td>
<td>Mann-Whit</td>
</tr>
<tr>
<td><strong>BUA Z score</strong></td>
<td>-0.83 ± 1.0</td>
<td>-0.67 ± 1.1</td>
<td>T-test</td>
<td>-0.71 ± 0.82</td>
<td>-0.66 ± 0.76</td>
<td>T-test</td>
</tr>
<tr>
<td></td>
<td>0.28 ± 1.16</td>
<td>0.29 ± 1.00</td>
<td></td>
<td>0.30 ± 1.27</td>
<td>0.29 ± 1.07</td>
<td>Mann-Whit</td>
</tr>
<tr>
<td><strong>SOS Z score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Statistical Tests used in Tables

Table 3.5 Descriptive data for Cardiff BD-born daughters and their mothers, according to daughter’s migratory status

<table>
<thead>
<tr>
<th></th>
<th>Early Migrator Daughters (n=8)</th>
<th>Late Migrator Daughters (n=9)</th>
<th>P value</th>
<th>Mothers of early Migrator Daughters (n=8)</th>
<th>Mothers of late Migrator Daughters (n=9)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>26.3 ± 5.6</td>
<td>29.4 ± 5.1</td>
<td>Mann Wh.</td>
<td>56.8 ± 9.7</td>
<td>55.9 ± 5.7</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>Year of birth</strong></td>
<td>1983.3 ± 5.4</td>
<td>1979.9 ± 5.4</td>
<td>Mann Wh.</td>
<td>1952.3 ± 9.8</td>
<td>1953.2 ± 5.9</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>No. Pre-menopausal (%)</strong></td>
<td>8 (100%)</td>
<td>9 (100%)</td>
<td>-</td>
<td>2 (25%)</td>
<td>1 (11%)</td>
<td>Fisher</td>
</tr>
<tr>
<td><strong>Age at migration (years)</strong></td>
<td>1.63 ± 2.0</td>
<td>13.11 ± 5.6</td>
<td>T-test</td>
<td>31.6 ± 9.7</td>
<td>40.2 ± 8.0</td>
<td>Mann Wh.</td>
</tr>
<tr>
<td><strong>Year of migration</strong></td>
<td>1985.9 ± 4.0</td>
<td>1993 ± 8.1</td>
<td>T-test</td>
<td>1984.4 ± 7.3</td>
<td>1993.4 ± 7.9</td>
<td>Mann Wh.</td>
</tr>
<tr>
<td><strong>Years resident in UK</strong></td>
<td>22 (19 to 30)</td>
<td>21 (4 to 25)</td>
<td>Mann Wh.</td>
<td>25.1 ± 7.3</td>
<td>15.7 ± 7.8</td>
<td>Mann Wh.</td>
</tr>
<tr>
<td><strong>Number lacking formal education</strong></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>-</td>
<td>3 (16%)</td>
<td>6 (53%)</td>
<td>Fisher</td>
</tr>
<tr>
<td><strong>Age finished education</strong></td>
<td>17.9 ± 2.0</td>
<td>18.7 ± 4.8</td>
<td>T-test</td>
<td>13.2 ± 2.6</td>
<td>13.0 ± 2.6</td>
<td>Mann Wh.</td>
</tr>
<tr>
<td><strong>Number with longstanding illness</strong></td>
<td>3 (38%)</td>
<td>3 (33%)</td>
<td>Fisher</td>
<td>7 (88%)</td>
<td>6 (67%)</td>
<td>Fisher</td>
</tr>
<tr>
<td><strong>Birth Order of daughter</strong></td>
<td>3.4 ± 1.8 (1 to 6)</td>
<td>3.1 ± 1.5 (1 to 5)</td>
<td>T-test</td>
<td>See daughter</td>
<td>See daughter</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>Age of mother at birth of daughter</strong></td>
<td>30.5 ± 10.5</td>
<td>26.4 ± 5.4</td>
<td>Mann Wh.</td>
<td>See daughter</td>
<td>See daughter</td>
<td>Mann Wh.</td>
</tr>
<tr>
<td><strong>Number (%) of short-stature (&lt;= 150 cm)</strong></td>
<td>4 (50%)</td>
<td>4 (44%)</td>
<td>Fisher</td>
<td>7 (88%)</td>
<td>7 (78%)</td>
<td>Fisher</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>61.7 ± 17.5</td>
<td>62.0 ± 12.9</td>
<td>T-test</td>
<td>65.9 ± 13.1</td>
<td>60.6 ± 7.1</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td>27.9 ± 7.1</td>
<td>26.4 ± 5.4</td>
<td>T-test</td>
<td>31.8 ± 5.4</td>
<td>28.1 ± 5.1</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>Knee Height (cm)</strong></td>
<td>45.0 ± 3.2</td>
<td>46.1 ± 2.2</td>
<td>T-test</td>
<td>44.2 ± 2.7</td>
<td>45.1 ± 2.6</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>Number (%) of short-stature (&lt;= 150 cm)</strong></td>
<td>4 (50%)</td>
<td>4 (44%)</td>
<td>Chi-square</td>
<td>7 (88%)</td>
<td>7 (78%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td><strong>BUA Raw Score (dB MHz⁻¹)</strong></td>
<td>47.1 ± 6.2</td>
<td>46.9 ± 8.5</td>
<td>T-test</td>
<td>42.9 ± 7.9</td>
<td>41.1 ± 8.2</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>SOS Raw Score (m s⁻¹)</strong></td>
<td>1560 ± 8</td>
<td>1556 ± 11</td>
<td>Mann Wh.</td>
<td>1548 ± 7</td>
<td>1554 ± 12</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>BUA Z score</strong></td>
<td>-0.65 ± 0.94</td>
<td>-0.70 ± 1.32</td>
<td>T-test</td>
<td>-0.39 ± 0.68</td>
<td>-0.87 ± 0.80</td>
<td>T-test</td>
</tr>
<tr>
<td><strong>SOS Z score</strong></td>
<td>0.49 ± 0.84</td>
<td>0.12 ± 1.14</td>
<td>Mann Wh.</td>
<td>0.31 ± 0.67</td>
<td>0.76 ± 1.07</td>
<td>T-test</td>
</tr>
</tbody>
</table>
Table 5.18 Birthplace of BD daughters: comparison of anthropometric and bone status variables for BD daughters based on birthplace (UK or BD)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Born in UK (n=15)</th>
<th>Born in BD (n=13)</th>
<th>Test used</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.5±6.1</td>
<td>34.4±7.5</td>
<td>Mann-Wh.</td>
<td>2.48</td>
</tr>
<tr>
<td>Recalled age at menarche§</td>
<td>11.6±1.5</td>
<td>11.6±1.3§</td>
<td>Mann-Wh.</td>
<td>0.00</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.2±5.7</td>
<td>152.5±5.0</td>
<td>T-test</td>
<td>-0.69</td>
</tr>
<tr>
<td>Knee ht. (cm)</td>
<td>47.4±2.3</td>
<td>45.6±1.8</td>
<td>T-test</td>
<td>-0.87</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.2±14.8</td>
<td>59.5±10.7</td>
<td>Mann-Wh.</td>
<td>-0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>24.7±5.7</td>
<td>25.4±3.2</td>
<td>Mann-Wh.</td>
<td>0.15</td>
</tr>
<tr>
<td>Fem. neck BMD (g/cm²)</td>
<td>0.979±0.181</td>
<td>1.023±0.116</td>
<td>T-test</td>
<td>0.29</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMD (g/cm²)</td>
<td>1.148±0.140</td>
<td>1.197±0.138</td>
<td>T-test</td>
<td>0.14</td>
</tr>
<tr>
<td>Spine L₂–L₄ BMD (g/cm²)</td>
<td>1.172±0.139</td>
<td>1.210±0.135</td>
<td>T-test</td>
<td>0.14</td>
</tr>
<tr>
<td>33%. Radius BMD (g/cm²)</td>
<td>0.799±0.075</td>
<td>0.832±0.075</td>
<td>T-test</td>
<td>0.44</td>
</tr>
<tr>
<td>Femoral neck BMD Z score</td>
<td>-0.358±1.109</td>
<td>0.592±0.870</td>
<td>T-test</td>
<td>0.95</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMD Z score</td>
<td>-0.350±0.844</td>
<td>0.323±1.101</td>
<td>T-test</td>
<td>0.69</td>
</tr>
<tr>
<td>Spine L₂–L₄ BMD Z score</td>
<td>-0.346±0.918</td>
<td>0.254±1.056</td>
<td>T-test</td>
<td>0.60</td>
</tr>
<tr>
<td>33%. Radius BMD Z score</td>
<td>-1.300±0.586</td>
<td>-0.615±0.839</td>
<td>T-test</td>
<td>0.95</td>
</tr>
<tr>
<td>Fem. neck BMAD (g/cm³)</td>
<td>0.221±0.040</td>
<td>0.235±0.024</td>
<td>T-test</td>
<td>0.42</td>
</tr>
<tr>
<td>Spine L₁–L₄ BMAD (g/cm³)</td>
<td>0.192±0.017</td>
<td>0.199±0.022</td>
<td>T-test</td>
<td>0.36</td>
</tr>
<tr>
<td>33%. Radius BMAD (g/cm³)</td>
<td>0.354±0.044</td>
<td>0.375±0.044</td>
<td>T-test</td>
<td>0.48</td>
</tr>
<tr>
<td>HSI</td>
<td>1.7±0.4</td>
<td>1.7±0.3</td>
<td>T-test</td>
<td>0.00</td>
</tr>
<tr>
<td>BR</td>
<td>2.8±1.0</td>
<td>3.3±1.1</td>
<td>T-test</td>
<td>0.48</td>
</tr>
<tr>
<td>FNW (mm)</td>
<td>27.4±1.8</td>
<td>26.9±1.9</td>
<td>T-test</td>
<td>0.27</td>
</tr>
<tr>
<td>Z (mm³)</td>
<td>519±82</td>
<td>543±120</td>
<td>T-test</td>
<td>0.23</td>
</tr>
<tr>
<td>HAL (mm)</td>
<td>96.3±5.2</td>
<td>95.7±5.1</td>
<td>T-test</td>
<td>-0.12</td>
</tr>
<tr>
<td>NSA (⁰)</td>
<td>125±4</td>
<td>125±3</td>
<td>T-test</td>
<td>0.00</td>
</tr>
<tr>
<td>BUA Raw Score dB MHz⁻¹</td>
<td>46.8±7.4</td>
<td>49.2±5.8</td>
<td>T-test</td>
<td>0.36</td>
</tr>
<tr>
<td>SOS Raw Score m s⁻¹</td>
<td>1558±13</td>
<td>1554±16</td>
<td>Mann-Wh.</td>
<td>-0.27</td>
</tr>
<tr>
<td>BUA Z Score</td>
<td>-0.71±1.16</td>
<td>-0.33±0.92</td>
<td>T-test</td>
<td>0.36</td>
</tr>
<tr>
<td>SOS Z Score</td>
<td>0.14±1.20</td>
<td>0.06±1.51</td>
<td>Mann-Wh.</td>
<td>-0.06</td>
</tr>
<tr>
<td>Heel Width</td>
<td>6.34±0.48</td>
<td>6.23±0.46</td>
<td>T-test</td>
<td>-0.23</td>
</tr>
</tbody>
</table>
Appendix II: Study Questionnaire

Thank you for agreeing to complete this questionnaire. We are interested in your views. Please note there are no right or wrong answers and if there is any question you do not wish to answer then that is fine, just say that you don’t know.

All information will be anonymised and treated in the strictest confidence.

Have you read the participant information letter and do you have any questions?

Questionnaire completed by:

Date: ______________________________

Venue: ______________________________
Section A: Migration

A1 Were you born in the UK?

Yes 1 (G0 TO A5)

No 2

A2 If NO, in what year did you come to live in the UK?

Record year □□□□

A3 How old were you then?

(Interviewer: note if this is accurate or an estimate)

Record age □□

A4 Which region of Bangladesh e.g. Sylhet did you come from?

Record region/country: ______________________________

A5 Did you live in a village, city or town?

Village 1

City 2

Town 3
Section B: Education, language and literacy

B1  At what age did you finish your continuous full-time education at school or college?

Record age

☐☐

OR TICK BOX TO CODE NO FORMAL SCHOOLING  ☐

B2  What is your first language?

Bangla

English

Sylheti

Other

Please specify_______________________________

_______________________________
Section C: Demographic and Social Relations

**C1a**  Do you know your EXACT date of birth? If so, please give:

**RECORD**  Day............... Month......................Year......................

(Interviewer check, is this accurate or an estimate?)

**C1b**  If NOT, were you born before, during or after Shadinata Judu (War of Independence in 1971)?

- **Before** 1
- **The year of Shadinata Judu** 2
- **After** 3

**C1c**  If you were born BEFORE Shadinata Judu, during which of the following periods were you born?

- Great Bengal famine (1943-1944) 1
- Towards the end of British rule in India (1945-46) 2
- Partition of India (1947-1948) 3
- (Bengali) Language Movement (1948-1956) 4
- Ayub Khan era (1958-1969) 6
- Yahya Khan era (1969-1971) 7

**C1d**  If you were born AFTER Shadinata Judu, during which of the following periods were you born?

- Mujib period (1971-75, also the Famine in 1974) 1
- Zia period (1975-1981) 2
- Ershad period (1982-1990, also major floods in 1988) 3

(Interviewer confirms age in years)
C1e  So you are how old?

RECORD AGE □□

C2  Are you?

Single, no children 1 (GO TO Section D)
Single, children 1 (GO TO C4)
Married 2
Divorced 3
Separated 4
Widowed 5
Civil Partnership 6

C3  If married/divorced, how old were you when you got married?

If married more than once, first marriage

RECORD AGE □□

C4  In total how many times have you been pregnant (including miscarriages and stillbirths)?

RECORD NUMBER □□

C5  How many children do you have?

RECORD THEIR DETAILS

<table>
<thead>
<tr>
<th>Child number</th>
<th>Sex</th>
<th>Age</th>
<th>Marital status</th>
<th>Where were they born? UK/BD</th>
<th>Tick if daughter is in this study</th>
</tr>
</thead>
</table>
C6   If baby/infant recorded above, are you still breast feeding?

Yes   1
No    2

Section D: Housing

D1    What type of accommodation does your household occupy?

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>House</td>
<td>1</td>
</tr>
<tr>
<td>Flat</td>
<td>2</td>
</tr>
<tr>
<td>Bungalow</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
</tr>
</tbody>
</table>

Please specify__________________________________________________________

D2    Is it owned or rented?

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (owned)</td>
<td>1</td>
</tr>
<tr>
<td>No (rented)</td>
<td>2</td>
</tr>
</tbody>
</table>

D3    Are there any of the following in your household? (CIRCLE ALL THAT APPLY)

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refrigerator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Television</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Video Recorder or DVD Player</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Washing machine</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Computer</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
D4  How many rooms do you have?

   RECORD NUMBER □□

   [Do not count bathrooms, toilets, halls or landings, or rooms that can only be used for storage such as cupboards.]

   Do count all other rooms, for example kitchen, living rooms, bedrooms, utility rooms and study. If two rooms have been converted into one, count them as one room]

D5  How many adults (21+ years) in house including participant?

   RECORD NUMBER □□

D5  How many children (<21 years) in house?

   RECORD NUMBER □□
Section E: Employment

E1 Which of the following best describes your current work situation?

(Record code which best fits the respondent)

Looking after the family, home or dependents 1
Employed including self-employed 2
Unemployed/not working 3
Wholly retired from paid work 4
Unable to work because of long-term disability or health 5
In full-time education or training 6
Doing something else 7
Please specify______________________________

_________________________________________________
Section F: Health  (questions F1 to F7 are covered in the Health Screen Questionnaire)

F8    Do you drink 3 or more units alcohol per day?

Yes  1

No   2

F9    Do you currently smoke or chew tobacco?

Yes  1

No   2

(Interviewer note: Include chewing tobacco, tobacco paste (zarda) and paan masala (tobacco mixed with betel nut)

Also include Hukka (tobacco smoked through water using a pipe) and bidi (rolled tobacco leaf) and

Do not include paan without tobacco(plain betel leaf)
Section G: Good Beginnings

We would now like to ask you about how life was when you were a baby. No problem, if you can’t remember. For daughters, mother can be present to help answer these questions.

G1  Were you breastfed?

<table>
<thead>
<tr>
<th>Option</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>1</td>
</tr>
<tr>
<td>Up to 6 months</td>
<td>2</td>
</tr>
<tr>
<td>6 months+</td>
<td>3</td>
</tr>
</tbody>
</table>

G2  Did your mother receive prenatal care ie visits from medical people or visits to medical facilities before your birth?

<table>
<thead>
<tr>
<th>Option</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
</tr>
</tbody>
</table>

G3  Were you born in a medical facility or at home?

<table>
<thead>
<tr>
<th>Location</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Facility</td>
<td>1</td>
</tr>
<tr>
<td>Home</td>
<td>2</td>
</tr>
</tbody>
</table>

G4  Were you vaccinated in the first year of your life?

<table>
<thead>
<tr>
<th>Option</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
</tr>
</tbody>
</table>
G5  Were you looked after by your mother, adult carer or other siblings?

<table>
<thead>
<tr>
<th>Option</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother</td>
<td>1</td>
</tr>
<tr>
<td>Adult carer</td>
<td>2</td>
</tr>
<tr>
<td>Siblings</td>
<td>3</td>
</tr>
<tr>
<td>Mother + extended family</td>
<td>4</td>
</tr>
</tbody>
</table>

G6  When you were a baby/toddler did your family use water from a well/pipe/tap? Or was it from a river or other surface source?

<table>
<thead>
<tr>
<th>Option</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural (river/surface)</td>
<td>1</td>
</tr>
<tr>
<td>Well</td>
<td>2</td>
</tr>
<tr>
<td>Piped/tap water</td>
<td>3</td>
</tr>
<tr>
<td>Cannot remember</td>
<td>4</td>
</tr>
</tbody>
</table>

G7  When you were a baby/toddler what type of toilet facilities did your family use? Were they man-made (hole-in-ground, bucket, pit latrines, flush toilets) or natural (river, bushes)?

<table>
<thead>
<tr>
<th>Option</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural (river, bushes)</td>
<td>1</td>
</tr>
<tr>
<td>Latrine (hole-in-ground, bucket)</td>
<td>2</td>
</tr>
<tr>
<td>Flush toilets</td>
<td>3</td>
</tr>
<tr>
<td>Cannot remember</td>
<td>4</td>
</tr>
</tbody>
</table>
Appendix III: Health Screen Questionnaire

Health Screen Questionnaire for Study Volunteers

As a volunteer participating in a research study, it is important that you are currently in good health and have had no significant medical problems in the past. This is (i) to ensure your own continuing well-being and (ii) to avoid the possibility of individual health issues confounding study outcomes.

Please complete this brief questionnaire to confirm your fitness to participate:

1. **At present**, do you have any health problem for which you are:
   - (a) on medication, prescribed or otherwise
     - Yes [ ] No [ ]
   - (b) attending your general practitioner
     - Yes [ ] No [ ]
   - (c) on a hospital waiting list
     - Yes [ ] No [ ]

2. **In the past two years**, have you had any illness which required you to:
   - (a) consult your GP
     - Yes [ ] No [ ]
   - (b) attend a hospital outpatient department
     - Yes [ ] No [ ]
   - (c) be admitted to hospital
     - Yes [ ] No [ ]

3. **Have you ever** had any of the following:
   - (a) Convulsions/epilepsy
     - Yes [ ] No [ ]
   - (b) Breathing problems requiring an inhaler e.g. Asthma/Hayfever
     - Yes [ ] No [ ]
(c) Eczema  | Yes  | No
(d) Diabetes  | Yes  | No
(e) A blood disorder eg anaemia  | Yes  | No
(f) Head injury  | Yes  | No
(g) Digestive problems  | Yes  | No
(h) Heart problems  | Yes  | No
(i) Problems with bones or joints eg arthritis/osteoporosis  | Yes  | No
(j) Disturbance of balance/coordination  | Yes  | No
(k) Numbness in hands or feet  | Yes  | No
(l) Disturbance of vision  | Yes  | No
(m) Ear / hearing problems  | Yes  | No
(n) Thyroid problems  | Yes  | No
(o) Kidney or liver problems  | Yes  | No
(p) Allergy to nuts  | Yes  | No
(q) High Blood Pressure  | Yes  | No
(r) High Cholesterol  | Yes  | No
(s) Depression……………………………………………..  | Yes  | No
(t) Other  | Yes  | No

If Other please provide additional information

........................................................................................................

........................................................................................................
4. **Allergy Information**

(a) are you allergic to any food products?  
Yes [ ] No [ ]

(b) are you allergic to any medicines?  
Yes [ ] No [ ]

(c) are you allergic to plasters?  
Yes [ ] No [ ]

If YES to any of the above, please provide additional information on the allergy

………………………………………………………………………………………………………………………………..

5. **Questions about periods and hormones**

(a) are your periods normal/regular?  
Yes [ ] No [ ]

(b) are you on “the pill”?  
Yes [ ] No [ ]

(c) could you be pregnant?  
Yes [ ] No [ ]

(d) are you taking hormone replacement therapy (HRT)?  
Yes [ ] No [ ]

Please provide contact details of a suitable person for us to contact in the event of any incident or emergency.

Name: ……………………………………………………………………………………………………………………………

Telephone Number: …………………………………………………………………………………………………………………

Work [ ] Home [ ] Mobile [ ]
Relationship to Participant: ........................................................ ..................................................

Are you currently involved in any other research studies at the University or elsewhere?

Yes [ ] No [ ]

If yes, please provide details of the study

.................................................................................................................................................

Section F: Health

F1 Would you say that for someone of your age, your own health is generally:

<table>
<thead>
<tr>
<th>Option</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very good</td>
<td>1</td>
</tr>
<tr>
<td>Good</td>
<td>2</td>
</tr>
<tr>
<td>Neither good nor poor</td>
<td>3</td>
</tr>
<tr>
<td>Poor</td>
<td>4</td>
</tr>
<tr>
<td>Very poor</td>
<td>5</td>
</tr>
</tbody>
</table>

F2 Do you have any long-standing illness, disability or infirmity? By long-standing, I mean anything that has troubled you over a period of time or that is likely to affect you over a period of time?

Yes [ ]

No [ ] (GO TO F4)
**F3**  If YES, what is this condition?

(Interviewer guidance: please tick those mentioned by the respondent. Do **NOT** read out this list).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Had in the past</th>
<th>Have now</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High blood pressure/hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A heart attack or heart problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint/Bone diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoarthritis, Osteoporosis, Osteomalacia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchitis, Asthma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Cholesterol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other – specify</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric problems</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
F4  Do you take medication? If so, for what condition(s)

(Interviewer guidance: please tick in 3\textsuperscript{rd} column of condition for which medication is taken)

F5  How many times have you visited your GP in the past year?

(Interviewer note: ask respondent how many times in a week or a month and calculate for the whole year).

RECORD NUMBER □□

F6a  MOTHERS Only

Do you still have periods?

Yes 1

No 2

F6b  If NO can you remember when your periods stopped?

6 months ago 1

1 year ago 2

2 years or longer 3

F7  Can you remember at what age you started having periods?

RECORD AGE □□
General open-ended discussion on health:

Do you have any health worries? Do you have worries about health problems in the future? Do you worry about the health of other members of your family?

(be aware of bone/joint aches & pains but don’t prompt – if mentioned, establish site on body)

Did any of your parents/relatives have bone problems? Can you remember if any of them ever broke a bone

Is there anything that you specifically do to help your health? Eg take vitamin tablets, drink milk, exercise etc. Did that come from recommendation by doctor/family/media
Appendix IV: G*Power Output

[1] -- Tuesday, June 26, 2018 -- 10:01:33
F tests - Linear multiple regression: Fixed model, $R^2$ deviation from zero
Analysis: Post hoc: Compute achieved power
Input: Effect size $f^2 = 0.15$
$\alpha$ err prob = 0.05
Total sample size = 68
Number of predictors = 2
Output: Noncentrality parameter $\lambda = 10.200000$
Critical $F = 3.1381419$
Numerator df = 2
Denominator df = 65
Power (1-\beta err prob) = 0.8044183

[2] -- Tuesday, June 26, 2018 -- 10:02:26
F tests - Linear multiple regression: Fixed model, $R^2$ deviation from zero
Analysis: Post hoc: Compute achieved power
Input: Effect size $f^2 = 0.15$
$\alpha$ err prob = 0.05
Total sample size = 68
Number of predictors = 3
Output: Noncentrality parameter $\lambda = 10.200000$
Critical $F = 2.7481909$
Numerator df = 3
Denominator df = 64
Power (1-\beta err prob) = 0.7417710