UNIVERSITY OF SOUTHAMPTON

Human Development and Health

MRC Lifecourse Epidemiology Unit

Volume 1 of 1

A cross-cohort investigation of grip strength across the life course

by

Richard Matthew Dodds

Thesis for the degree of Doctor of Philosophy

April 2015

UNIVERSITY OF SOUTHAMPTON

ABSTRACT

FACULTY OF MEDICINE
Epidemiology
Thesis for the degree of Doctor of Philosophy

A CROSS-COHORT INVESTIGATION OF GRIP STRENGTH ACROSS THE LIFE COURSE

Richard Matthew Dodds

Introduction

Grip strength across the life course is associated with disability, morbidity and mortality, and forms a key component of the sarcopenia and frailty phenotypes in older people. However it is unclear how individual measurements of grip strength should be interpreted. My objectives were to produce centile values for grip strength across the life course in Great Britain (GB), and then to compare with those in international settings.

Methods

I combined data from 12 general population studies in GB to produce centile curves using the Box-Cox Cole and Green distribution. I estimated the prevalence of weak grip, defined as at least 2.5 SDs below the gender-specific peak mean. I then did a systematic literature search and expressed the resulting international normative data as Z-scores relative to my British centiles. I used metaregression to pool these by world region.

Results

I combined 60,803 grip strength observations from GB at ages 4 to 90. I saw an increase to a peak median in early adulthood of 51kg in males and 31kg in females, maintenance to midlife and then decline. The prevalence of weak grip increased with age, reaching 23% in males and 27% in females by age 80. My systematic literature search returned 60 papers containing 730 international normative data items. Those from developed regions were similar to my GB centiles, pooled Z-score 0.12 (95% CI: 0.07, 0.17), whereas those from developing regions were clearly lower, pooled Z-score -0.86 (95% CI: -0.95, -0.77).

Conclusion

My GB centiles are the first to cover the entire life course. Published normative data showed a similar pattern, but with clear differences in magnitude between developing and developed regions. The findings have the potential to inform the clinical assessment of grip strength, recognised as an important part of the identification of people with sarcopenia and frailty.

Executive summary

This executive summary is intended to complement the above abstract by providing additional information on the background to the work, including related projects that I completed prior to this thesis. I also summarise the strengths, limitations and implications of this work.

A life course perspective for grip strength views function in old age as a combination of both the peak obtained in early adult life and the subsequent rate of decline. From 2009 to 2012, I worked as an NIHR Academic Clinical Fellow in Geriatric Medicine. During this time, I combined clinical training with experience of research at the MRC Lifecourse Epidemiology Unit. I looked at factors across the life course which may affect grip strength including birth weight [1,2] and physical activity during adulthood [3,4]. During this time I also collaborated with researchers at the MRC Unit for Lifelong Health and Ageing at UCL and attended events on the cross-cohort research being carried out by the HALCyon (Healthy Ageing across the Life Course) collaboration.

I then started my present research fellowship funded by the Wellcome Trust. I identified the need for life course normative data for grip strength and the opportunity to establish these using both British studies and a systematic review of the international literature. The results of this work are summarised in the abstract.

The main strengths of this work are the use of 12 large British general population studies to produce, for the first time, normative data for grip strength which cover the whole life course. These data form a reference standard which I use in the second part of this thesis to investigate differences in grip strength by world region. I achieve this by undertaking a comprehensive literature search for sets of normative data, followed by data harmonisation to allow me to pool these data. Finally in both parts of this thesis, I carry out sensitivity analyses to demonstrate that the normative data are robust to differences in the dynamometer and measurement positions used to collect them.

Limitations of this work include that the normative data produced are cross-sectional in nature and hence should not be used for monitoring individual trajectories of grip

strength. The measurements used are also from a recent timeframe (1990 onwards in the case of the British centiles) and so while the resulting normative data are appropriate for current use, I cannot exclude the possibility that the relationships seen with age partly represent cohort effects.

This work has implications both for future research and clinical practice. In terms of research, this thesis confirms the pattern of grip strength across the life course. This is important for future research as it suggests we should investigate the determinants of both peak grip strength and subsequent age-related decline. The normative data could also be used to inform inclusion criteria for intervention studies in older people and to explore the possibility of screening individuals for weak grip strength. Finally in terms of research it would be possible to develop a function in statistical software so that other researchers could apply my reference values to their grip strength data.

In terms of clinical practice, I have used the life course normative data to suggest clinical cut-points for weak grip strength based on normal function in young adulthood. This is analogous to the interpretation of bone mineral density measurements in the diagnosis of osteoporosis. The normative data could further be used in the assessment of the predictive ability of grip strength, perhaps in combination with other factors such as medical history, to identify whether an individual is at risk of subsequent adverse outcomes such as hospital admission.

Contents

ABSTRACT i

Executive summary iii

Contents v

List of tables ix

List of figures xi

List of equations xiii

DECLARATION OF AUTHORSHIP xv

Acknowledgements xvi

Publications from the work in this thesis xvi

Definitions and Abbreviations xvii

1. Introduction: context for this work 1

1.1 Definition and historical perspective 1
1.2 Grip strength and its relationship with current and future health 2
1.2.1 Mortality 2
1.2.2 Disability 4
1.2.3 Morbidity and hospitalisation 5
1.2.4 Sarcopenia and age-related changes in muscle 6
1.3 A life course perspective for grip strength 7
1.4 Existing normative data for grip strength 8
1.4.1 The effect of device and position on grip strength measurement 10
1.5 Summary 13
1.6 Aims and objectives 14
1.6.1 Thesis objectives 15

2. Normative data from 12 British studies: methods 17

2.1 Objectives for this project 17
2.2 Included studies 17
2.3 Grip strength measurement 20
2.4 Data management 23

2.5 Statistical analyses 24
2.5.1 Box-Cox Cole and Green / LMS method 24
2.5.2 The GAMLSS library 27
2.5.3 Estimates of prevalence of low grip strength 30
2.5.4 Sensitivity analyses 31
3. Normative data from 12 British studies: results 33
3.1 Descriptive statistics 33
3.2 Centile curves for grip strength 37
3.2.1 Gender differences in median grip strength 41
3.2.2 Findings for the other model parameters 42
3.2.3 Z-scores for grip strength observations 43
3.3 Estimates of prevalence of low grip strength 43
3.4 Sensitivity analyses 46
4. Normative data from systematic literature review: methods 55
4.1 Objectives of this project 55
4.2 Literature search and inclusion criteria 55
4.3 Data extraction 58
4.3.1 Study level details 59
4.3.2 Details for each item of normative data 61
4.3.3 Data entry 62
4.4 Data management 62
4.5 Statistical analyses 65
4.5.1 Calculation of z-scores 66
4.5.2 Metaregression 70
5. Normative data from systematic literature review: results 73
5.1 Description of included papers 73
5.1.1 Characteristics of samples used 73
5.1.2 Protocol for grip measurement and reporting of normative data 76
5.2 Description of extracted normative data 78
5.3 Findings from metaregression analyses 83
5.3.1 Grip strength by world region 83
5.3.2 Grip strength by protocol and reporting of normative data 89
5.3.3 Grip strength by stage of the life course 90

6. Discussion: findings, strengths and limitations 93
6.1 Main findings 93
6.1.1 Normative data from 12 British studies 93
6.1.2 Normative data from systematic literature review 94
6.2 Interpretation of findings 94
6.2.1 The pattern of grip strength across the life course 94
6.2.2 Gender differences in grip strength 95
6.2.3 Comparison of my normative data to other published British norms 96
6.2.4 Differences in grip strength by country 97
6.2.5 Differences in grip strength by protocol and reporting factors 98
6.3 Strengths and limitations 100
6.3.1 Normative data from 12 British studies 100
6.3.2 Normative data from systematic literature review 101
7. Discussion: relevance and future work 103
7.1 Relevance to the life course epidemiology of grip strength 103
7.1.1 Associations during growth to peak grip strength 103
7.1.2 Associations during the decline in grip strength 105
7.1.3 The development of future interventions 105
7.2 Relevance to clinical practice 106
7.2.1 Cut-points for grip strength 106
7.2.2 Stratification of grip strength by height 107
7.3 Future work 108
7.3.1 The life course epidemiology of grip strength 108
7.3.2 Clinical practice 110
8. Conclusions 113
Appendices 115
Appendix 1. Z-scores for British grip strength observations 117
Appendix 2. Results of sensitivity analyses excluding each study in turn 127
Appendix 3. Result of further sensitivity analysis on age 131
Appendix 4. Details of extracted studies 133
Appendix 5. Copy of PLoS ONE paper 143
List of References 159

List of tables

Table 1.a Summary of results from studies comparing different dynamometers 12

Table 2.a Included studies: target populations and means of accessing data.................. 19

Table 2.b Included studies: timings and protocols of grip strength measurements 21

Table 2.c Variables extracted for each grip strength measurement 24

Table 2.d Parameters in Box-Cox Cole and Green distribution for grip strength........... 27

Table 2.e Parameters in normal distribution for grip strength 30

Table 2.f Models for grip strength including dynamometer terms 32

Table 3.a Valid measurements of grip strength from each wave of each study.............. 34

Table 3.b Normative values for grip strength 40

Table 4.a Search query used to identify articles 56

Table 4.b Study level details extracted 60

Table 4.c Variables extracted concerning each normative data item.............................. 61

Table 4.d Formulae used to produce descriptive statistics from alternatives provided .. 63

Table 4.e Factors used to convert extracted values to kilograms force 64

Table 4.f Example calculation of a pooled standard deviation....................................... 69

Table 5.a Country setting of included papers, by UN region.. 74

Table 5.b Sample and analysis characteristics of included papers, by region 76

Table 5.c Protocol and reporting characteristics of included papers, by region 78

Table 5.d Pooled Z-scores by different country classifications...................................... 84

Table 5.e Pooled Z-scores for papers based in Europe 88

Table 5.f Pooled Z-scores by protocol and reporting factors.. 90

Table 5.g Pooled Z-scores in different age groups in developing regions...................... 91

Table 5.h Pooled Z-scores in different age groups in developed regions 92

List of figures

Figure 1.a Illustration of early dynamometers 1
Figure 1.b A life course approach to sarcopenia 8
Figure 2.a Images of dynamometers used in included studies 22
Figure 2.b Illustration of the three Box-Cox Cole and Green parameters 25
Figure 2.c Median cubic splines with varying degrees of freedom 29
Figure 3.a Frequency of grip strength measurements by age 35
Figure 3.b Ages and birth years for each grip strength measurement, by study 36
Figure 3.c Cross-cohort centile curves for male grip strength 38
Figure 3.d Cross-cohort centile curves for female grip strength 39
Figure 3.e Gender differences in median grip 41
Figure 3.f Sigma and skew parameters in relation to age 42
Figure 3.g Prevalence of weak grip strength using T-scores of ≤ -2 and -2.5 45
Figure 3.h Centiles comparison: model including kurtosis 48
Figure 3.i Centiles comparison: restriction to first observation for each individual 49
Figure 3.j Centiles comparison: stratification by dynamometer type 50
Figure 3.k Centiles comparison: stratification by position of measurement 51
Figure 3.l Truncation of all participants' ages to integer values 52
Figure 4.a Flow chart showing included papers 57
Figure 4.b Screenshot of data-entry form in Microsoft Access 62
Figure 4.c Sample plot used to check data entry 65
Figure 5.a Map showing countries of included papers 75
Figure 5.b Number of observations by age and developed status 79
Figure 5.c Grip strength mean values from included papers, by region 80
Figure 5.d Grip strength Z-scores from included papers, by region 82
Figure 5.e Pooled Z-score in developing regions 85
Figure 5.f Pooled Z-score in developed regions 86
Figure 5.g Pooled Z-scores for each European country 89
Figure 6.a Pooled Z-scores for selected countries in relation to average height 97

List of equations

Equation 2.a Calculation of centiles using LMS values for a specific age 25

Equation 2.b Calculation of Z-score for an individual measurement 26

Equation 2.c Calculation of prevalence of low grip strength.. 30

Equation 4.a Calculation of standard error of the sample mean 66

Equation 4.b Formulae to calculate pooled standard deviation 68

DECLARATION OF AUTHORSHIP

I, Richard Dodds

declare that the thesis entitled

A cross-cohort investigation of grip strength across the life course

and the work presented in the thesis are both my own, and have been generated by me as the result of my own original research. I confirm that:

- this work was done wholly or mainly while in candidature for a research degree at this University;
- where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
- where I have consulted the published work of others, this is always clearly attributed;
- where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
- I have acknowledged all main sources of help;
- where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;
- the work I did on British normative data for grip strength has been published, as described overleaf.

Signed: Richard Dodds

Date: 29th April 2015

Acknowledgements

I am very grateful to my supervisors, Professor Avan Aihie Sayer, Dr Holly Syddall and Professor Diana Kuh for their support and guidance with this thesis. I am also grateful to Dr Rachel Cooper for her advice on this project.

I am grateful to the participants and data collection teams of all the included studies.

The Wellcome Trust funded my research fellowship (grant number WT099055AIA).

Professor Rose Anne Kenny and Professor Clive Osmond examined this thesis and I am very grateful for their insights and the constructive feedback they have given me on my work.

I would like to thank Karen Drake for her assistance with inter-library loans.

Finally I would like to say a massive thank-you to my partner, Chris, for supporting me as I wrote this thesis.

Publications from the work in this thesis

My work on normative data for grip strength from 12 British studies has been published in the journal PLoS ONE [5]. A copy of the paper is included in Appendix 5.

Definitions and Abbreviations

Abbreviations

ADLs	Activities of daily living
ADNFS	Allied Dunbar National Fitness Survey
ALSPAC	Avon Longitudinal Study of Parents and Children
BCCG	Box-Cox Cole and Green
BMI	Body mass index
ELSA	English Longitudinal Study of Ageing
GAMLSS	Generalised additive models for location, scale and shape
GB	Great Britain
HAS	Hertfordshire Ageing Study
HCS	Hertfordshire Cohort Study
HSE	Health Survey for England
ICC	Intraclass correlation coefficient
IQR	Interquartile range
LBC1921	Lothian Birth Cohort of 1921
LBC1936	Lothian Birth Cohort of 1936
N85	Newcastle 85+ Study
NSHD	Medical Research Council National Survey of Health and Development
SD	Standard deviation
SWS	Southampton Women’s Survey
SWSm	Referring to mothers of children in the SWS
SWSp	Referring to the partners of the mothers
T-07	West of Scotland Twenty-07 Study
UKHLS	Understanding Society: the UK Household Longitudinal Study

1. Introduction: context for this work

In this first chapter, I define grip strength and establish the historical context of its measurement. I then review evidence linking weak grip strength to subsequent adverse health outcomes before considering the reasons for using a life course perspective for grip strength. I describe existing work on normative values for grip strength, including evidence of how measurement protocol may influence the values obtained. I finish by summarising and stating the objectives of this work.

1.1 Definition and historical perspective

The action of gripping requires the contraction of the flexor muscles in the forearm and hand as well as the stabilisation of the wrist by the forearm extensors [6]. In general terms, a dynamometer is “an instrument designed to measure the torque or force exerted by a muscle or muscle group” [7]. Early versions of dynamometers for measuring grip strength, such as the Mathieu and Hammond dynamometers shown in Figure 1.a, were first used by neurologists during the second half of the 19th century [8].

Figure 1.a Illustration of early dynamometers

a. Mathieu dynamometer. b. Hammond dynamometer. Both taken from [8].

The Victorian polymath Sir Francis Galton collected grip strength measurements (the “strength of squeeze”) as part of a large battery of anthropometric tests carried out at the International Health Exhibition held in London in 1885 [9]. He published centile values using these data; the medians for the age group 23-26 were 85 and 52 pounds for men and women, respectively (around 39 and 24kg). The maximum value recorded for a woman was 86 pounds, leading Punch to print “The Squeeze of 86” shortly after Galton published his results (taken from [10]):

Maiden of the mighty muscles,
There recorded, you would be
Famous in all manly tussles,
And it’s very clear to me,
That if in the dim hereafter
Any husband should play tricks,
You would with derisive laughter,
Give a "Squeeze of 86."

Husbands be it sadly stated,
Have been known their wives to whack,
You, unless you're over-rated,
Could give such endearments back.
Yours the task to try correction,
Till your husband and your "chicks,"
Had a lively recollection
Of your "Squeeze of 86."

1.2 Grip strength and its relationship with current and future health

Grip strength is a measure of overall muscle strength and has been included as part of the assessments carried out in many cohort studies. This has allowed associations between muscle strength and health to be explored. In this section, I describe findings from systematic reviews and subsequent studies which have demonstrated how those with weak grip strength are at increased risk of mortality and disability. I also examine how grip strength has been related to morbidity and outcomes related to hospitalisation. I finish by considering the role of grip strength in the syndrome of sarcopenia and by summarising the age-related changes that occur in muscle tissue.

1.2.1 Mortality

A systematic review by Cooper et al. [11] reported results from 23 studies which had examined the relationship between grip strength and survival times. The studies spanned a range of ages, including six with a mean age below 60 at baseline. Following contact with authors, Cooper et al. were able to include 19 of these 23 studies into two meta-analyses: the first examining the effect of a 1kg increase in grip strength (13 studies) and the second comparing the lowest to the highest quarters of grip strength (14 studies), with eight studies contributing to both meta-analyses. After adjustment for age, sex and body size (height and weight or body mass index), the summary hazard ratio for a 1kg increase in grip strength was 0.97 (95% CI: 0.96, 0.98); the summary hazard ratio comparing those in the highest quarter to those in the lowest quarter of grip strength was 0.60 (95% CI: 0.52, 0.69).

The literature search by Cooper et al. covered the period from 1980 to May 2009. I therefore ran an interval literature search to look for studies published since that time which had looked at the relationship between grip strength and survival times[i]. This returned six further relevant studies.

De Buyser et al. [12] found a similar relationship to Cooper et al. between a 1kg increase in grip strength and survival in men of mean age 76 at baseline. Hamer et al. [13] examined whether a range of factors including weak grip strength might mediate the association between depression and increased all-cause mortality rates. I could only access the abstract in which they stated that weak grip strength was associated with reduced survival times.

McDermott et al. [14] looked at a group of men and women with peripheral arterial disease of mean age 75 at baseline. They found that those in the lowest tertile of grip strength were at greater risk of mortality than those in the highest, with hazard ratio of 1.71 (95% CI: 0.89, 3.32) and P-value for trend across the tertiles of 0.005, after adjustment for a range of potential confounders including physical activity.

A subsequent study by Cooper et al. [15] found a graded relationship between stronger grip at age 53 and reduced risk of death over up to 13 years of follow-up, including after adjustment for a range of potential confounders such as the presence of chronic illness. Moreover the small proportion who had been unable to complete the grip strength measurement at age 53 (approximately 2% of the sample) were found to be at the greatest risk of subsequent death.

Hirsch et al. [16] showed that weaker grip strength at mean age 79 years and a greater subsequent rate of decline over a follow-up period of up to seven years were both associated with an increased risk of mortality. In a similar fashion, Xue et al. [17] found

---

[i] Search run July 2014 using MEDLINE and the following search string:

("mortality".ti,ab. or Mortality/) and "grip".ti,ab and "strength".ti,ab.
Limits were a publication date from 2009 onwards, an available abstract and English language.

N=116 articles returned.

that both weaker grip strength at mean age 74 and greater decline over up to ten years were associated with increased risk of mortality.

In summary, there is strong evidence from a systematic review as well as subsequent studies that individuals from mid-adulthood onwards with weaker grip strength are at increased risk of death. This effect does not appear to be explained by confounding factors. There is more recent evidence that repeat measures of grip strength may provide greater predictive power than a single measure.

1.2.2 Disability

I identified two systematic reviews which were relevant to this outcome [18,19]. Both were published in 2011 and reported results of studies which had examined the relationship between grip strength and subsequent disability (either incident or progression of a disability present at baseline). The outcome measures varied but in most cases took the form of questionnaires about participants' ability to undertake activities of daily living (ADLs), such as washing or eating.

The first review, by den Ouden et al. [18], identified four studies related to grip strength whereas the second review, by Vermeulen et al. [19] reported three of these plus seven other longitudinal studies. The difference in the number of studies returned may be due to the more limited search terms used by den Ouden et al. with regard to the exposure: they state using the term "physical performance", but not terms for specific types of physical performance measures including grip strength.

In both reviews, meta-analyses were not possible but the majority of included studies did show that weak grip predicted subsequent disability. Some studies did compare grip with other physical performance measures and found that gait speed was more strongly associated with subsequent disability [20,21].

As the Vermeulen et al. review [19] searched literature to 2010 and the den Ouden et al. review [18] searched literature to early 2011, I carried out an interval literature search[ii] to identify any more recent publications on this topic. This returned three further relevant studies. In a study of middle-aged and older people (mean (SD) age 62.3 (8.9) years), a 10kg stronger baseline grip strength predicted a lower risk of ADL disability after ten years, RR 0.72 (95% CI: 0.57, 0.92) including adjustment for number of chronic diseases and educational level [22]. Two studies had examined whether repeated measurements of grip strength were more useful in predicting disability; one study found they were in terms of ADL disability [16], but another found that a single measurement was as effective as two for predicting mobility disability [23].

1.2.3 Morbidity and hospitalisation

A systematic review published in 2011 found some evidence that weaker grip strength was associated with incident fracture, cognitive decline and cardiovascular disease, although concluded that further research was needed [24]. Weak grip strength has also been associated in a cross-sectional fashion with the metabolic syndrome [25,26] and impaired glucose tolerance [27].

As part of a systematic review examining grip strength in relation to a range of health outcomes, Bohannon et al. [28] described ten studies that had shown clear associations between weak grip strength and increased length of hospital stay or complications among those undergoing surgical procedures.

One study published after the Bohannon et al. review found that older men with a weak grip strength at admission to acute care (below 21kg) had an increased likelihood of functional decline on discharge [29], although a similar relationship was not found in

---

[ii] Search run March 2014 using MEDLINE and the following search string:

("functional status" or "functional decline" or "disabil*").ti,ab. and "grip strength".ti,ab.
Limits were a publication date from 2011 onwards, an available abstract and English language.

N=234 articles returned.

women. Similarly, another subsequent study found evidence of an association between stronger grip and an increased likelihood of discharge to usual place of residence following a period of in-patient rehabilitation, again among men but not women [30].

1.2.4 Sarcopenia and age-related changes in muscle

The term sarcopenia, from the Greek meaning loss of flesh, was first suggested by Rosenberg in 1989 [31] to describe the loss of muscle mass with age. Various techniques exist to measure muscle mass including electrical bioimpedance and dual energy x-ray absorptiometry. A previous study, based on the prevalence of low muscle mass and its association with disability, estimated the healthcare costs of sarcopenia in the United States in 2000 to be $18.5 billion [32].

More recent definitions for sarcopenia have also included the loss of muscle function, such as poor muscle strength, with grip strength being recommended as the most practical method of measuring muscle strength in the clinical setting [33]. There is also evidence that muscle strength may be more predictive of the risk of subsequent disability [34] and mortality [35] than muscle mass.

While both muscle strength and muscle mass decline with age, rates of decline in muscle strength are approximately three times that of muscle mass. This has led to the idea that ageing is associated with a reduction in muscle quality: that is, the strength generated per unit of muscle mass [36].

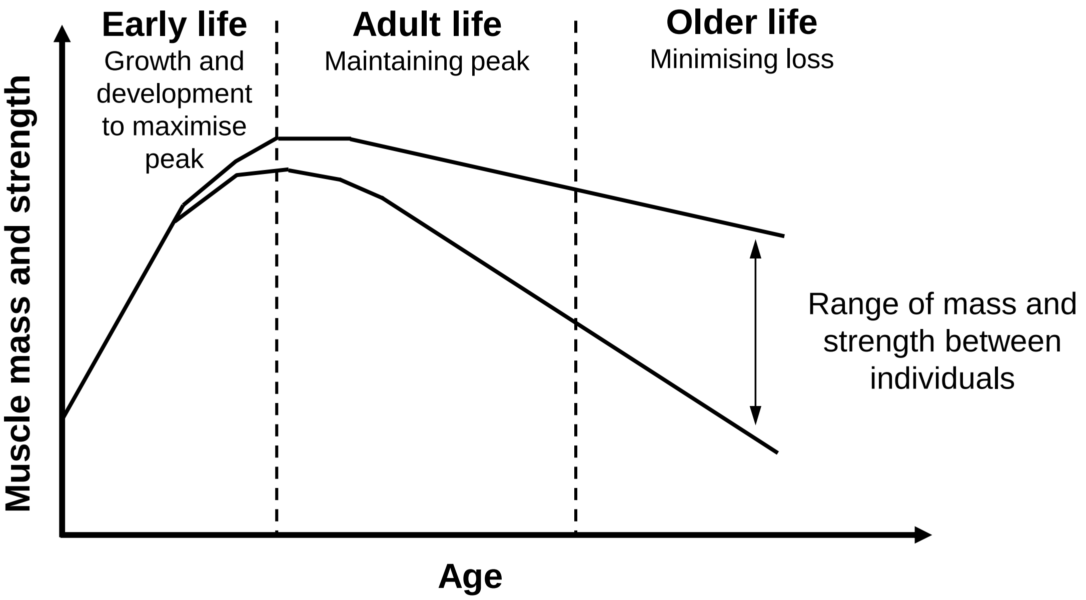
There are a range of relevant changes in skeletal muscle tissue that occur with ageing. These include a gradual loss of muscle fibres, especially type II “fast-twitch” fibres required to rapidly generate force, as well as reduced activity of muscle mitochondria [37]. Ageing is associated with reduced effectiveness of transmission from muscle excitation to contraction and also increasing infiltration of muscle by fat tissue [34]. Changes in the neuromuscular system may also play a role, with a decline in the number of spinal cord motor neurons. This leads to an increase in the number of muscle fibres innervated by a single motor neuron, through a process known as motor unit remodelling [37].

It is useful to consider the pathways by which sarcopenia may lead to the adverse outcomes described earlier in this section. For example, it seems intuitive that the age-related loss of muscle mass and function could contribute directly to the onset of disability. Muscle tissue also has a range of important metabolic functions [38] and the loss of these functions could explain the associations seen with glucose tolerance. However aspects of sarcopenia such as weak grip strength are unlikely to directly cause increased risk of death. Rather, it seems likely that grip strength is acting as a marker of frailty [39] which can be defined as a state of vulnerability to stressor events as a consequence of decline across multiple physiological systems [40]. This suggests that grip strength may also act as a marker of past exposures and hence why it is helpful to adopt a life course approach, as described in the following section.

1.3 A life course perspective for grip strength

A life course perspective for grip strength originated from the observation that grip strength in later life was positively associated with birth weight [41,42]. A conceptual framework for life course epidemiology views characteristics in later life as a combination of a peak value obtained in early adult life and a rate of decline thereafter [43], as illustrated in Figure 1.b, below [44]. There is evidence that a range of exposures across the life course may influence the peak and decline for grip strength: for example, a beneficial effect of being more physically active during childhood [45] and mid-adulthood [3,46].

Figure 1.b A life course approach to sarcopenia



Reproduced from [44], with permission. Please note that for simplicity, the figure focusses on the variation observed during older life. Variation in muscle mass and strength between individuals during early life is not shown.

A life course perspective for grip strength with the identification of normative data for grip strength across life is important for two main reasons. Firstly, individuals with weaker grip strength even in mid-adulthood are at increased risk of adverse health outcomes, as described in section 1.2. Measurement of grip strength may therefore have a future role in identifying individuals at risk of such outcomes and inform the development of interventions earlier in the life course. Secondly, one approach to identifying cut-points for weak grip strength at older ages is to use the peak values attained in young adult life as a reference. This is analogous to the interpretation of bone density measurements, where individuals are considered to have osteoporosis if their bone density is found to be two and half standard deviations or more below the young adult mean for their gender [47].

1.4 Existing normative data for grip strength

There are no existing studies of normative data for grip strength that cover the life course. Rather existing studies have often focussed on specific stages of the life course, such as childhood or older ages. This may reflect the corresponding areas of clinical practice for which the normative data are intended such as paediatrics or geriatrics.

For example, in childhood, Mathiowetz et al. [48] reported grip strength values for ages 6-19 based on a sample of 471 children from schools in the seven county Milwaukee Area in Wisconsin in the United States. The children were seated and the Jamar dynamometer was used to measure grip strength. Häger-Ross et al. [49] collected grip strength measurements at ages 4-16 from 530 children attending day care centres or schools in the municipality of Umeå in northern Sweden. They used the Grippit electronic dynamometer, again with the children seated.

Studies in older people include that by Skelton et al. [50]. They recruited 100 men and women aged 65-89 through advertisements in local and national newspapers to volunteer to undergo a day of physical performance testing. This included grip strength measured with a Takei Kiki Kogyo (TKK) mechanical dynamometer in the standing position.

There have also been multiple studies reporting normative data across adulthood. Bohannon et al. [51] carried out a meta-analysis of 12 such studies and produced normative values for ages 20 to 75. Eight of the studies were based in the United States with Canada, the United Kingdom, Sweden and Australia making up the other four. Ten of the twelve included studies were based on convenience samples. They had all used the Jamar dynamometer in the seated position.

The majority of the studies described above were based on convenience samples of participants based near the researchers, which may limit how representative they are of the general population in the country of interest. This has not been in the case in all normative data studies, however. For example, Kenny et al. [52] used random sampling from within stratified clusters across Ireland to achieve a nationally-representative sample at ages 50 and above. In total 5,819 participants had grip strength measured using a Baseline dynamometer in the standing position.

The normative data studies described above have used a variety of protocols, with differences between studies in the type of dynamometer and measurement position used. Across clinical settings there are also likely to be differences in these factors. This leads to the question of whether normative data produced from a study using one protocol, such as those using a Jamar dynamometer in the seated position, are applicable to measurements taken using a different protocol, such as a TKK dynamometer in the standing position? As far as I am aware, there have not been studies comparing sets of normative data in this regard. However, studies have examined whether grip strength measurements taken in the same individual with different protocols are comparable. In the following sub-section, I go on to review the findings from these studies.

1.4.1 The effect of device and position on grip strength measurement

I considered ten studies which had looked at the agreement between measurements taken using two or more different dynamometers [53–62], for four of which only the abstract was available [57,58,60,62].

All the studies had small samples of 100 adult individuals or fewer, except for the one by Massy-Westropp et al. [57] which had 476 participants. The majority of comparisons were made against the Jamar hydraulic dynamometer. Studies typically asked each participant to make their maximum effort with each dynamometer, with the order in which the dynamometers were tested being randomised. As shown in Table 1.a on page 12, the studies' findings varied, with the conclusion from just over half of the comparisons made (seven out of 13) being that the two dynamometers in question were exchangeable. Two studies had compared the Jamar and Grippit dynamometers and they drew differing conclusions. Svantesson et al. [62] concluded that they were exchangeable, although from the abstract this was on the basis of high correlation between the two dynamometers' values (meaning that the actual readings could still have differed). Massy-Westropp et al. [57] concluded that they were not exchangeable, due to wide limits of agreement from a Bland-Altman analysis.

As another example of a study which concluded that two dynamometers were not exchangeable, the paper by King et al. [55] compared values from a total of 80 young men and women. They had grip measured using both the Jamar electronic and hydraulic dynamometers. They found that the hydraulic dynamometer produced values on average 11% and 9% higher in men and women, respectively. The corresponding ICCs were 0.62 and 0.74, suggesting poor to moderate reliability.

One possible explanation I considered for the relatively low ICC values found by King et al. [55] is that they represent differences within individuals between each set and not the change in dynamometer type, such as fatigue or a change in motivation. However studies which have examined reliability between repeat measures of grip strength using a constant testing procedure [63–65] have shown high ICCs (0.94 or greater), making this possibility seem less likely.

Table 1.a Summary of results from studies comparing different dynamometers

Class		Hydraulic					P*	Electronic					
	Specific device	Baseline®	Jamar	Rolyan	Smedley	Takei	Rolyan	DynEx	EMG System	Grippit	Jamar	MicroFET 4	Takei
Hydraulic	Baseline®												
	Jamar	🟩 [58]											
	Rolyan		🟩 [59]										
	Smedley		🟥 [54]										
	Takei												
P*	Rolyan		🟥 [54]										
Electronic	DynEx		🟩 [61]										
	EMG System		🟥 [53]										
	Grippit		🟥 [57] 🟩 [62]										
	Jamar		🟥 [55]										
	MicroFET 4		🟩 [60]										
	Takei	🟩 [56]	🟥 [53]						🟩 [53]				

Study conclusion (ref shown):

🟩	Exchangeable	🟥	Not exchangeable

[*] P, Pneumatic.

Dynamometers are shown by class and then by usual name. Some types of dynamometer, such as the Jamar are available in more than one class (in the case of the Jamar, in both hydraulic and electronic versions).

Three studies have looked at whether being in the seated or standing position affected the measured grip strength value. Shechtman et al. [66] compared measurements in the two positions using the dynamometer function of the BTE Primus, although the sample size was only 13 people. Balogun et al. [67] (only the abstract was available to me and the dynamometer type is not specified) examined grip strength in 61 people in the seated and standing positions, with both the elbow flexed and extended; they reported that grip strength in the standing position with the elbow extended was significantly higher than seated with the elbow flexed. In a similar fashion, Liao et al. [68] reported from a sample of 249 using the Jamar dynamometer that standing with an extended elbow produced stronger grip measurements than standing or sitting with a flexed elbow. In summary, the three studies did not show a clear difference in grip strength between the seated and standing positions.

1.5 Summary

The measurement of grip strength has its origins in clinical neurology and anthropometry in the late 19th century. More recently, many studies across mid-late adulthood have suggested that weak grip appears to predict a reduced likelihood of a long and healthy old age. There is considerable interest in the related clinical condition, sarcopenia, especially in terms of how it can be assessed in the clinical setting and the development of potential treatments. In addition, it is recognised that aetiological factors for sarcopenia likely exert their effects not only in old age but across the life course. This substantially extends the window for potential interventions to prevent sarcopenia.

Existing normative data for grip strength have mainly focussed on early to mid-adulthood, with studies also considering childhood / adolescence or old age. No one study has normative data across the whole life course. Many studies have used convenience samples which limits their representativeness of the general population of interest. Existing studies for normative data have typically only used a single protocol for measurement, while at the same time smaller studies have suggested that aspects of protocol such as dynamometer type may have effects on measurement; the extent of these effects and whether they are relevant to clinical practice is unclear.

1.6 Aims and objectives

The first aim of this thesis is therefore to produce a single set of normative data for grip strength which covers all stages of the life course. Several cohort studies in Great Britain have assessed grip strength and since none cover the entire life course, it is necessary to combine data from several cohorts.

The feasibility of undertaking such work is shown by two recent British cross-cohort programmes: Healthy Ageing across the Life Course (HALCyon) [69] and the measurement and modelling of Function Across the Life Course (FALCon) [70]. Several of the general population cohorts included in these programmes contain grip strength data. These cohorts form the starting point for the first aim of this thesis.

The second aim of this thesis is to investigate whether grip strength differs by world region. There are a growing number of published studies of normative data for grip strength and yet as described in section 1.4, these are often based on samples from a single area within a country. There therefore exists the opportunity to pool results and for the first time to make comparisons by world region, using my British normative data as a reference standard.

The objectives for this thesis are shown overleaf.

1.6.1 Thesis objectives

The objectives of this thesis are:

- To produce cross-sectional normative values for grip strength across the life course by pooling data from a range of general population studies conducted in Great Britain.
    - A secondary objective is to examine the impact of aspects of measurement protocol on the normative values obtained.
- To compare the normative values produced from British studies to those in the literature, including investigation of differences in grip strength by world region
    - A secondary objective is to investigate the differences in published grip strength by aspects of measurement protocol.

2. Normative data from 12 British studies: methods

2.1 Objectives for this project

The objectives for this project are as follows:

- To produce cross-sectional normative values for grip strength across the life course by pooling data from a range of general population studies conducted in Great Britain.
    - A secondary objective is to examine the impact of aspects of measurement protocol on the normative values obtained.

In the following sections, I describe the studies with data contributing to this thesis and the methods used to measure grip strength. I then explain the data management tasks I carried out. Finally, I describe the statistical approaches that I used to model the relationship between age and grip strength, including sensitivity analyses.

2.2 Included studies

Following on from the thesis objectives, I sought to include data on grip strength from general population studies conducted in Great Britain (GB). Previous work in the Healthy Ageing across the Life Course (HALCyon) research programme had already included the assembly of data from five such studies with participants aged 50 or older [69], namely the English Longitudinal Study of Ageing [71] (ELSA), the Hertfordshire Ageing [72] and Cohort [73] Studies (HAS and HCS) , the Lothian Birth Cohort of 1921 [74] (LBC1921) and MRC National Survey of Health and Development [75,76] (NSHD). I was able to access data for these five studies.

In a similar way, I was able to access the two general population studies in the measurement and modelling of Function Across the Life Course (FALCon) [70] programme which had included grip strength. These were the Avon Longitudinal Study of Parents and Children [77] (ALSPAC) and the West of Scotland Twenty-07 Study [78] (T-07).

I identified and then gained access to the data for five related studies, including those which had measurements taken in childhood, adolescence and early adult life. These were the Allied Dunbar National Fitness Survey [79] (ADNFS), the Lothian Birth Cohort of 1936 [74] (LBC1936), the Newcastle 85+ Study [80] (N85), the Southampton Women's Survey [81] (SWS), and Understanding Society: the UK Household Panel Study [82] (UKHLS). The means by which I accessed the data for the included studies are shown in Table 2.a.

As also shown in Table 2.a, eight of the twelve studies included individuals from specific regions in Great Britain (SWS [81], ALSPAC [77], T-07 [78], HCS [72], HAS [73], LBC1936 [74], LBC1921 [74] and N85 [80]) and four drew from one (ELSA [71], ADNFS [79]) or all three countries of Great Britain (UKHLS [82], NSHD [75,76]). All included both males and females. Three studies had prospectively recruited participants at or shortly after birth (SWS, ALSPAC and NSHD) and in SWS, grip strength measurements were also available from the mother (SWSm) during her pregnancy and from her partner (SWSp). All studies had received relevant ethical approval.

Table 2.a Included studies: target populations and means of accessing data

Name of study and ref(s)	**Population**	**Data access**[*]
Southampton Women's Survey (SWS) and measurements from mother (SWSm) and her partner (SWSp) [81]	Children of women in cohort study, Southampton (as well as mother and her partner at 19 week antenatal visit)	Internal
Avon Longitudinal Study of Parents and Children (ALSPAC) [77]	Children of women attending antenatal clinics in Bristol and District Health Authority	External
Allied Dunbar National Fitness Survey (ADNFS) [79]	Random sample of English population with subsample having physical appraisal	ESDS
Understanding Society: the UK Household Longitudinal Study (UKHLS) [82,83]	Nationally representative sample of UK[†]	ESDS
West of Scotland Twenty-07 Study (T-07) [78]	Stratified sample from Central Clydeside, Greater Glasgow, Scotland	External
English Longitudinal Study of Ageing (ELSA) [71]	Participants from HSE aged 50 or older	ESDS
MRC National Survey of Health and Development (NSHD) [75,76]	Socially stratified sample of all births in England, Scotland and Wales in one week in March 1946	External
Hertfordshire Cohort Study (HCS) [72]	Those born in North, East and West Hertfordshire between 1931-9 and still resident when traced	Internal
Hertfordshire Ageing Study (HAS) [73]	Those born in North Hertfordshire between 1920-30 and still resident when traced	Internal
Lothian Birth Cohort of 1936 (LBC1936) [74]	Participants of Scottish Mental Surveys at age 11 and still resident in Lothian area of Scotland	External
Lothian Birth Cohort of 1921 (LBC1921) [74]		
Newcastle 85+ Study (N85) [80]	Those registered with a Newcastle / North Tyneside general practice	External

* Internal: internal agreement within MRC Lifecourse Epidemiology Unit. External: data sharing agreement with relevant outside university. ESDS: data freely downloadable from ESDS (Economic and Social Data Service) by researchers.

† The wave 2 nurse health assessment in which grip strength was measured was only carried out in England, Scotland and Wales.

Studies ordered by approximate age of first measurement of grip (see Table 2.b, page 21).

HSE, Health Survey for England.

2.3 Grip strength measurement

Information on the timings and protocols of grip strength measurement in the different studies is shown in Table 2.b, below. When combined, studies' grip measurements covered all the stages of the life course (from age 4 to 90+ years) with measurements occurring within a relatively recent timeframe (between 1990 and 2012). The majority (n=10) of studies had measured grip strength at one or two waves, with LBC1921 and N85 having data from three and four waves, respectively.

Seven studies used the Jamar dynamometer (including the second wave of HAS, which used the Harpenden dynamometer at the first wave), two studies (ELSA and UKHLS) used the Smedley dynamometer, two studies used the Nottingham electronic dynamometer (ADNFS and NSHD), and N85 used the Takei dynamometer. Images of the different dynamometer types are shown in Figure 2.a on page 22.

The majority (n=8) of studies measured grip in the seated position for all participants. In three of the studies using the standing position (UKHLS, T-07 and ELSA), the data files included a variable for when a participant was either unable or unwilling to stand for the measurement. In the fourth study, N85 there was not a specific variable, although for a single participant in wave 1 (who died before wave 2), the free text field noted that the measurement was performed "sitting in bed". I checked this with Karen Davies, Senior Research Nurse Manager for the study, and she confirmed that all other measurements were performed in the standing position.

All studies took measurements from both hands except ADNFS which used the dominant hand only (unless injury meant the non-dominant side had to be used), and LBC1921 which measured both hands but provided values from only the dominant hand for analyses. The majority of studies took three measurements from each hand, except for N85 and the first wave of NSHD, which took two measurements. In all cases, I used the maximum value for grip strength for my analyses.

Table 2.b Included studies: timings and protocols of grip strength measurements

Study	Year(s) of wave	Age range [y]	Device(s) used; study ref(s)	Position	Repetitions / hands used
SWS	2004 – 9	4 – 5	Jamar [2]	Seated	Six / both
	2007 – 10	6 – 7			
ALSPAC	2003 – 5	10 – 14	Jamar	Seated	Six / both
ADNFS	1990	16 – 74	Nottingham [84,85]	Seated	Three / dominant (97%)[*]
UKHLS	2010 – 12	16 – 102	Smedley	Standing (83%)	Six / both
SWSp	2002 – 5	18 – 58	Jamar [2]	Seated	Six / both
SWSm	2002 – 5	21 – 40	Jamar [2]	Seated	Six / both
T-07[†]	2007 – 8	35 – 37	Jamar [86]	Standing (99%)	Six / both
		52 – 62		Standing (99%)	
		74 – 78		Standing (97%)	
ELSA	2004 – 5	52 – 89[§]	Smedley	Standing (80%)	Six / both
	2008 – 9	50 – 89[§]	Smedley	Standing (82%)	Six / both
NSHD	1999	53	Nottingham [87]	Seated	Four / both
	2006 – 10	60 – 64			Six / both
HCS	1999 – 04	59 – 73	Jamar	Seated	Six / both
	2004 – 5	65 – 75			
HAS	1994 – 5	63 – 73	Harpenden	Seated	Six / both
	2003 – 5	72 – 83	Jamar		
LBC1936	2004 – 7	68 – 70	Jamar	Seated	Six / both
	2007 – 10	72 – 73			
LBC1921	1999 – 01	78 – 80	Jamar [88]	Seated	Six / dominant[‡]
	2003 – 5	82 – 84			
	2007 – 8	86 – 87			
N85	2006 – 7	84 – 86	Takei digital	Standing (99%)	Four / both
	2007 – 9	85 – 88			
	2009 – 10	87 – 89			
	2011 – 12	89 – 91			

Studies ordered by approximate age of first measurement of grip. For study abbreviations see Table 2.a on page 19.

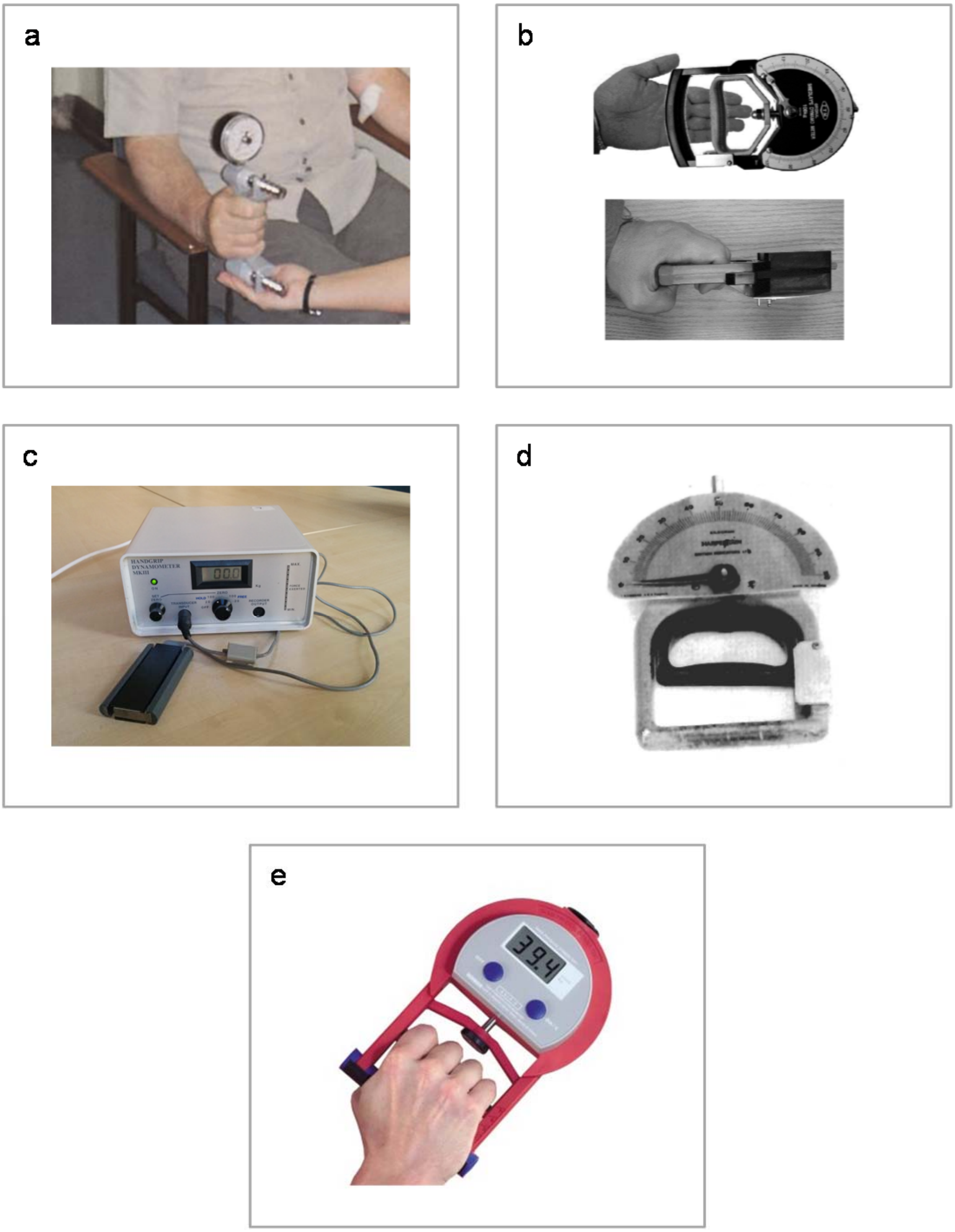
[*] A further two were taken if the third was 10% above the better of the first two. The dominant hand was used except in case of injury.

[†] The West of Scotland Twenty-07 consisted of three cohorts of different ages as shown.

[§] In the standard ELSA dataset that was used for this study, the ages of the limited number of individuals aged 90 or older are all collapsed to 90 years.

[‡] Measures taken from both hands but only those from dominant hand were available.

Figure 2.a Images of dynamometers used in included studies



Key: (a) Jamar dynamometer in the seated position with the arm supported [89]. (b) Smedley dynamometer [90]. (c) Nottingham electronic dynamometer (photo courtesy of Dr Rachel Cooper, MRC Unit for Lifelong Health and Ageing). (d) Harpenden dynamometer [91]. (e) Takei A5401 digital hand grip dynamometer; photo [92] see also [93].

2.4 Data management

I carried out data management tasks using Stata version 12.0 [94], with conversion of study data files to Stata format where needed. I reviewed each study's documentation to identify the correct variables to use and to establish where it was necessary to restrict a dataset. For example, in ELSA, some partners of study participants asked to have their grip strength measured and these values are included in the dataset. However the study documentation made clear that the partners' measures had not been part of the protocol and were not suitable for analysis [71].

As the number of observations per individual varied (between one and up to four in the case of N85), I used long format to store the data for this study, with one record per observation in the combined dataset. I extracted the variables listed in Table 2.c (below) for each observation from each study. In all cases, datasets either included the maximum grip strength value from repeated trials, or I used the maximum when individual values were provided. This is in keeping with previously published recommendations for the measurement of grip strength in clinical practice [89].

In the three studies accessed through the ESDS (Economic and Social Data Service), UKHLS, ADNFS and ELSA, only ages in years (not years and months) were available. I performed a sensitivity analysis to assess the potential impact of this on the centile curves produced (see section 2.5.4 on page 31).

Table 2.c Variables extracted for each grip strength measurement

Variable	Comments
Study	The combination of study, study ID and wave uniquely identify each observation
Unique ID number from study	
Wave of data collection (with grip)	
Sex	
Date of birth – month	
Date of birth – year	
Age at time of measurement (years)	
Type of dynamometer used	For example Jamar or Nottingham
Position of measurement	Sitting or standing
Hands used	Both, dominant or non-dominant
Trials (protocol)	Number of trials specified in protocol, e.g. six if three for each hand
Trials (actual)	Number of trials used in this instance
Grip strength (kg)	Maximum of available trials
Height (cm)	Values from same wave as grip strength measurement, where available
Weight (kg)	

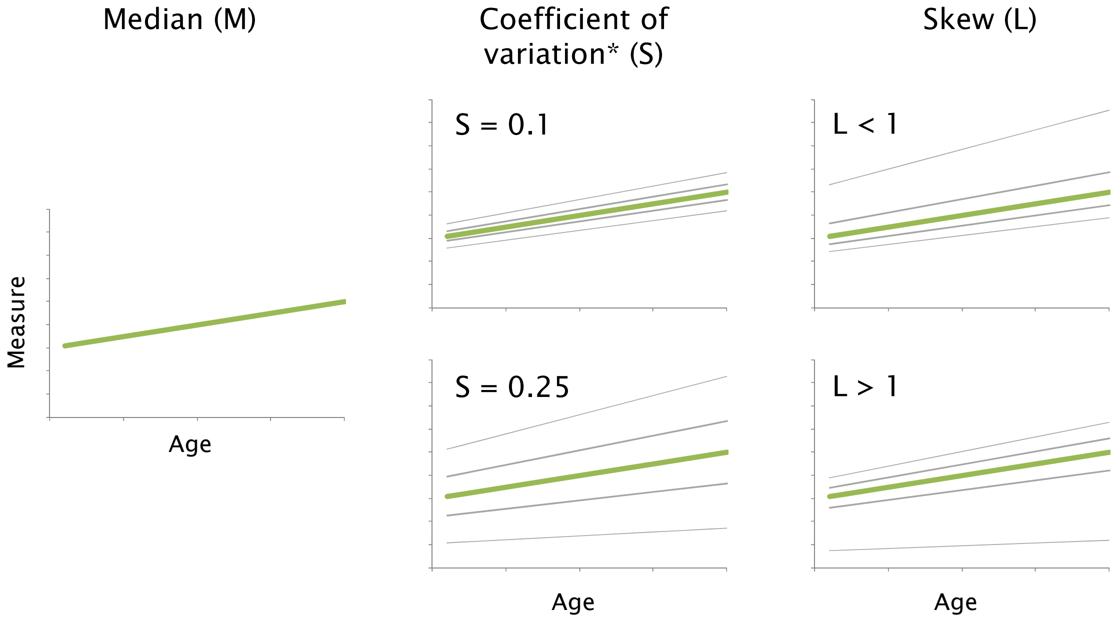
2.5 Statistical analyses

In summary, I produced gender-specific centile curves for grip strength using the Box-Cox Cole and Green (BCCG) distribution (also known as the LMS method [95], described below) implemented in the Generalised Additive Models for Location, Scale and Shape (GAMLSS) library [96] for the statistical program, R [97]. I now provide some background to this method and describe the specific models that I fitted for this thesis, including the sensitivity analyses that I undertook.

2.5.1 Box-Cox Cole and Green / LMS method

The LMS method has been widely used in the production of growth charts [98]. It models the relationship between a predictor (typically age) and three parameters describing the distribution of the outcome variable: the median value (M), an approximation to the coefficient of variation (S, sigma) and the Box-Cox power transformation to account for any skewness in the data (L, lambda). An illustration of the three parameters is shown in Figure 2.b, below.

Figure 2.b Illustration of the three Box-Cox Cole and Green parameters



The median value is represented by the green line and four sample centile lines by the grey lines.

* The S parameter is an approximation to the coefficient of variation, defined as the standard deviation / mean. (The exception is when L = 1, e.g. when the data is normally distributed, and the mean and median are equal, in which case S is equal to the coefficient of variation). As shown, as S increases, so does the spread of the data around the median.

Specific centile values for a given age can then be calculated using the L, M and S values for that age as shown in Equation 2.a. The Z-score for an individual measurement can also be calculated as shown in Equation 2.b.

Equation 2.a Calculation of centiles using LMS values for a specific age

$$C_{100\alpha}(t) = M(t)[1 + L(t)S(t)Z_{\alpha}]^{1/L(t)}$$

From Cole et al. [98]. A given centile $C_{100\alpha}$ (where $0 < \alpha < 1$) at age t can be calculated using the L, M, S values at age t and Z_{α}, the normal equivalent deviate for the required centile value. For example, for the 25th centile, $Z_{0.25}$ takes the value -0.674 since 25% of a normal distribution of mean 0 and standard deviation 1 lies below this value.

Equation 2.b Calculation of Z-score for an individual measurement

$$Z_{ind} = \frac{\left[{}^{y}/_{M(t)}\right]^{L(t)} - 1}{S(t)L(t)}$$

From Cole et al. [98]. The Z-score for an individual measurement, Z_{ind} is based on the measured value y, and the L, M and S values for the age of the individual, t.

Following from the assumption that all three parameters for the distribution of any biological variable would tend to change smoothly as a function of time, cubic splines are the technique typically used to model the relationships between age and each of L, M and S. Cubic splines are a non-parametric method which have been defined as: "a piecewise third-order polynomial function that passes through a set of m (or degrees of freedom) control points; it can have a very simple form locally, yet be globally flexible and smooth" (taken from de Onis et al. [99] , page xvi). An advantage of cubic splines over parametric methods such as fractional polynomials for fitting growth curves is that they typically better accommodate periods of rapid change, such as during the pubescent growth spurt [98].

Assumptions when using the BCCG distribution to model the relationship between a measure and age include that the observations are independent [95,96]. I was aware that in this thesis, data may be clustered at the level of the individual, with eight studies having more than one wave of data collection. However it is common practice to use repeat measures in the production of cross-sectional normative data, albeit with consideration of whether repeat measures may have the effect of artificially improving results from tests of model fit [99]. One of the sensitivity analyses that I undertook (see section 2.5.4) was to restrict the data to the first observation per individual.

2.5.2 The GAMLSS library

The GAMLSS library is a flexible framework for regression analysis which allows the response variable to be modelled using a range of distributions. The parameters of each distribution can in turn be modelled using a range of parametric and non-parametric approaches [96]. I carried out sex-stratified analyses using the Box-Cox Cole and Green distribution with cubic splines to describe the relationships between each of the distribution parameters for grip strength and age, as summarised in Table 2.d. The set of cubic splines for each of the three parameters had a number of degrees of freedom; I describe the means by which these were determined in the following section. The GAMLSS uses the terminology mu, sigma and nu for the median, spread and skew parameters. However for consistency I continue to refer to these as M, S and L, respectively.

Table 2.d Parameters in Box-Cox Cole and Green distribution for grip strength

Parameter	**Model**
M (median)	cs(x = age, df = d_M)
S (spread)	cs(x = age, df = d_S)
L (skew)	cs(x = age, df = d_L)

cs: cubic splines. df: degrees of freedom (for further details see section 2.5.2.1, below).

2.5.2.1 Identification of optimum degrees of freedom for each model parameter

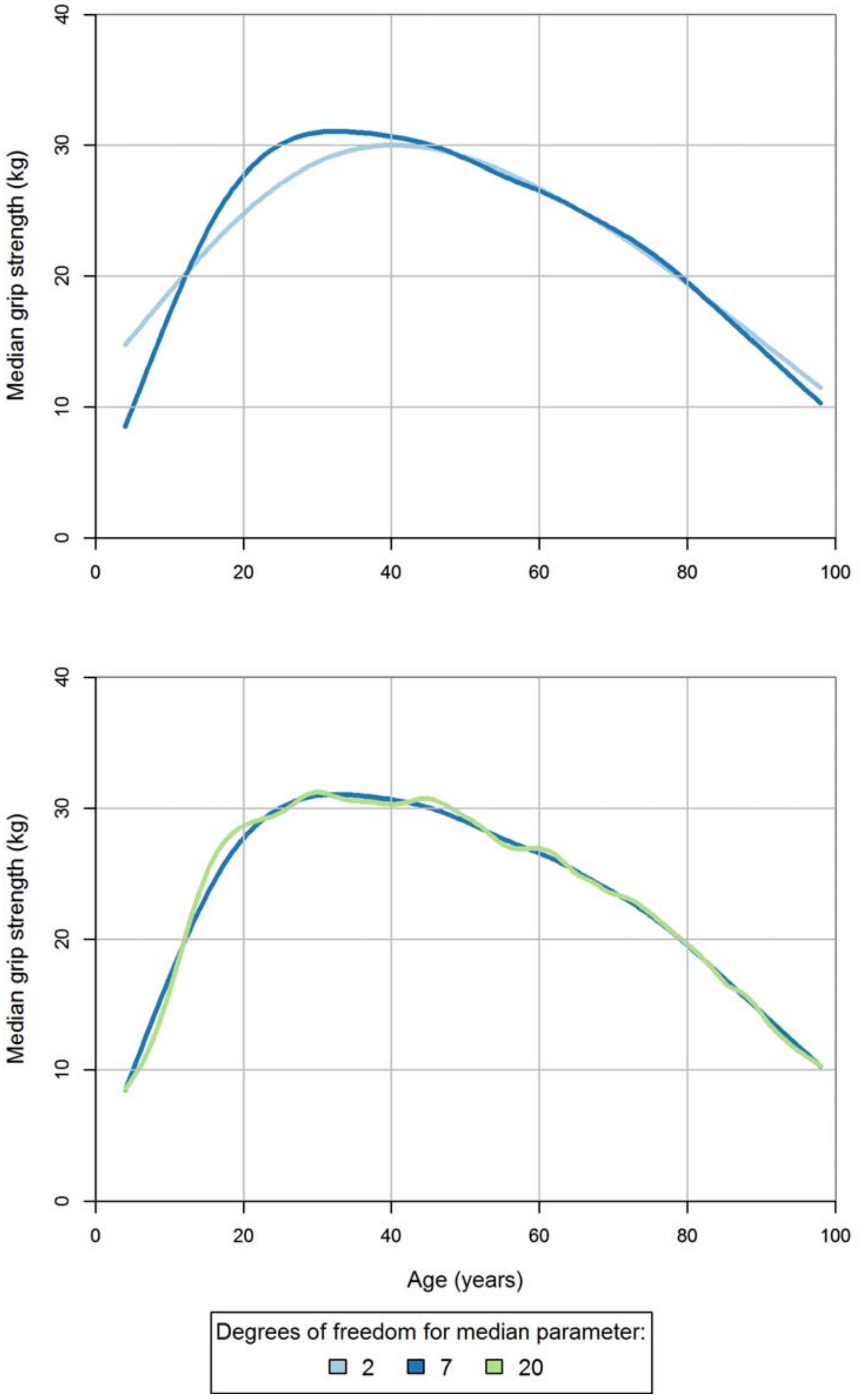
The selection of a number of degrees of freedom for each model parameter is a balance between producing a curve that over-simplifies the relationship, and one that becomes overly "data-driven" as the number of degrees of freedom increases as shown in Figure 2.c on page 29. For this reason, an upper limit of seven degrees of freedom would be typical [52] and I used this as the limit in my analyses. I considered that the curve with 20 degrees of freedom shown in Figure 2.c also modelled essentially the same relationship as the curve with seven degrees of freedom, and hence any increase beyond the latter value was not justified.

I used the GAMLSS command find.hyper to automate the selection of the number of degrees of freedom for each model parameter, beginning with the median curve and followed by the spread and then finally skew curves. This command uses an iterative process to find the model which best fits the data whilst favouring simpler curves over more complex ones. To do this, the command attempts to minimise a value known as the generalised Akaike information criterion. This combines a measure of how far the observed values deviate from the fitted model with a user-defined penalty for each degree of freedom. I found that the standard penalty of two was too small to exert an influence towards simpler curves, since the deviance values when handling the entire dataset were in the order of 200,000. I therefore experimented with different values for the penalty and settled on using a value of 30. I found this value avoided the curves for the spread and skew parameters from appearing overly “data-driven”, whilst still allowing the curve for the median parameter to take the maximum permissible number of degrees of freedom, seven.

2.5.2.2 Assessment of model fit using Z-scores

In order to assess if the centile curves that I produced using GAMLSS were a good fit for the grip strength data from which they were derived, I produced Z-scores for each observation using Equation 2.b on page 26. I then examined the distribution of these Z-scores. I expected that if the centile curves fitted the data well, then the Z-scores would be normally distributed with a mean of zero and a standard deviation of one. I also examined the Z-scores from each study in the same way, to check that the grip strength observations from any individual study were not poorly modelled by the centile curves.

Figure 2.c Median cubic splines with varying degrees of freedom



The two graphs compare a curve for median female grip strength with seven degrees of freedom to a curve with two (upper graph) and a curve with 20 (lower graph) degrees of freedom. The simpler curve is considered to poorly represent the growth period, whereas the more complex one adds unnecessary extra detail.

2.5.3 Estimates of prevalence of low grip strength

In addition to the centile curves produced using the BCCG distribution, I explored the mean and standard deviation of grip strength across the life course in order to determine the gender-specific prevalence of weak grip strength in mid and late adult life. The approach I used was analogous to the use of T-scores for bone density measurements in the diagnosis of osteoporosis. In that setting, a person's bone density measurement is expressed as a multiple of the number of standard deviations (SDs) below the young adult mean value for their gender; values 2.5 or more SDs below the mean are consistent with the diagnosis [47]. I therefore produced gender-specific values for the mean and SD of grip using the normal distribution, in place of the BCCG distribution, in GAMLSS as shown in Table 2.e. I then identified the age at which the peak mean value occurred: using the peak value and its associated SD, I was able to calculate cut-off values 2.5 SDs below the peak mean, as used in osteoporosis, and also 2 SDs below the peak mean, as used in previous research on grip strength [100].

Table 2.e Parameters in normal distribution for grip strength

Parameter	**Model**
Mean	cs(x = age, df = 7)
Standard deviation	cs(x = age, df = 7)

cs: cubic splines. df: degrees of freedom.

I then estimated how the prevalence of grip strength equal to or below these cut-offs changed with age. To do this I used the L, M and S values from the main BCCG models in a modified version of Equation 2.b (see page 26) to do this, as shown in Equation 2.c, below.

Equation 2.c Calculation of prevalence of low grip strength

$$\text{Prevalence (\%)} = \text{pnorm}\left(\frac{\left[{}^{\text{c}}/_{\text{M(t)}}\right]^{\text{L(t)}} - 1}{\text{S(t)L(t)}}\right) \times 100$$

pnorm: the cumulative normal distribution function, based on a mean of 0 and SD of 1.
c: cut-off value for grip strength (kg) of interest. L(t) etc.: L, M and S values from the BCCG model at age t years for which prevalence is required.

2.5.4 Sensitivity analyses

I carried out a series of sensitivity analyses by producing further sets of centile curves, as described below. In all additional models, I used the same number of degrees of freedom for each model parameter as I did when I produced the main results. This was to prevent differences in the centiles being the result of differences in the model specification. I was not aware of any previous techniques for comparing differences between set of centiles, so I elected to do this by pre-specifying an upper limit for what I considered to be acceptably similar findings across the 10th, median and 90th centiles. To account for the variation in the magnitude of grip strength values with age, I elected to do this on a percentage basis, setting the upper limit for a difference to be 10 percent either side of the centile values from my main results.

Firstly, I looked for evidence of kurtosis (peakedness) in the grip strength values by using the Box-Cox power exponential distribution [101]. This distribution includes a fourth parameter (in addition to L, M and S) for kurtosis. I established the optimum number of degrees of freedom for this in the same way as for the other parameters (see section 2.5.2.1 on page 27).

Secondly, I restricted the data to the first observation for each individual. I did this to see if the repeat measurements included in some studies showed evidence of biasing the results. This could occur due to loss-to-follow up bias, with those completing repeat measurements presumably being stronger on average than those who did not.

Thirdly, I produced dynamometer-specific sets of centiles. To do this, I created indicator variables for each dynamometer (except Jamar, which formed the baseline group). I then included terms related to these variables in the models for the three distribution parameters. I allowed the median, spread and skew curves to be shifted upwards or downwards by an amount for each dynamometer (intercept terms). I also allowed the median curve to be scaled by a factor for each dynamometer (slope terms), as shown in Table 2.f.

Table 2.f Models for grip strength including dynamometer terms

Parameter	**Model**
M (median)	$(\alpha_1.d_1 + \alpha_2.d_2 ..) + cs(x = age, df = 7).(\beta_1.d_1 + \beta_2.d_2 ..)$
S (spread)	$(\alpha_1.d_1 + \alpha_2.d_2 ..) + cs(x = age, df = 7)$
L (skew)	$(\alpha_1.d_1 + \alpha_2.d_2 ..) + cs(x = age, df = 1)$

cs: cubic splines. df: degrees of freedom. d_1 etc.: indicator variables for each dynamometer type (with Jamar being baseline group). α_1 etc.: intercept terms for each dynamometer type. β_1 etc.: slope terms (only included for the median parameter).

As an extension of this third sensitivity analysis, I attempted to produce estimates (with 95% confidence intervals) for the effect of dynamometer type on grip strength, whilst controlling for the effect of other study factors. I did this using multiple linear regression of the grip strength Z-scores (as described in section 2.5.2.2 on page 28), with explanatory terms for the different types of dynamometer and for the 12 different studies. I found that the dynamometer terms dropped out of the models due to collinearity with the study terms.

The fourth sensitivity analysis I carried out looked at the impact of the position of grip strength measurement: standing or sitting, with the latter divided into those who were sitting as per protocol and those who chose to sit or were unable to stand. I created indicator variables for standing and choosing to sit (with sitting as per protocol forming the baseline group). I included these in the models for the three parameters in the same way as for dynamometer type. Again I attempted to produce estimates using multiple linear regression but found that the position terms were collinear with the study terms.

In the fifth sensitivity analysis, I examined whether truncating all participants’ ages to integer values (as is the case by default for the UKHLS, ADNFS and ELSA studies) affected the centile values obtained.

Finally I checked if any one study was unduly influencing the results obtained by creating centile curves based on data which excluded each study in turn.

3. Normative data from 12 British studies: results

In this chapter, I describe the data used for the main analyses and show the results from the main set of centile curves, including estimates of the prevalence of weak grip strength. I finish by showing the results from the sensitivity analyses, including the impact of aspects of measurement protocol and the influence of individual studies.

3.1 Descriptive statistics

In total, 60,803 measurements of grip strength (from 49,964 individual participants) were available for the analyses. As shown in Table 3.a, these measurements represented a high proportion, 94.8% overall, of the potential measurements from all those seen in each wave of each study. There did not appear to be a substantially lower proportion of those with a valid grip measurement in studies which focused on older people, such as N85. In terms of the number of trials completed, the majority of measurements (60,013 or 98.7%) were based on the full set of trials as required in each study’s protocol.

Table 3.a Valid measurements of grip strength from each wave of each study

Study	Age range (y)	N seen[*]	N with valid grip measure (%)	
SWS	4 – 5	1,035	968	(93.5)
	6 – 7	522	462	(88.5)
ALSPAC	10 – 14	7,159	6,701	(93.6)
ADNFS	16 – 74	3,024	2,602	(86.0)
UKHLS	16 – 102	15,591	14,678	(94.1)
SWSp	18 – 58	1,520	1,265	(83.2)
SWSm	21 – 40	1,634	1,563	(95.7)
T-07	35 – 37	923	880	(95.3)
	52 – 62	991	913	(92.1)
	74 – 78	654	587	(89.8)
ELSA	52 – 89	7,666	7,477[†]	(97.5)
	50 – 89	8,210	7,965[‡]	(97.0)
NSHD	53	2,984	2,847[§]	(95.4)
	60 – 64	2,229	2,069	(92.8)
HCS	59 – 73	2,997	2,987	(99.7)
	65 – 75	642	639	(99.5)
HAS	63 – 73	717	717	(100)
	72 – 83	294	292	(99.3)
LBC1936	68 – 70	1,091	1,086	(99.5)
	72 – 73	866	865	(99.9)
LBC1921	78 – 80	550	544	(98.9)
	82 – 84	321	321	(100)
	86 – 87	237	204	(86.1)
N85	84 – 86	849	819	(96.5)
	85 – 88	632	603	(95.4)
	87 – 89	486	453	(93.2)
	89 – 91	344	296	(86.0)
Overall		**64,168**	**60,803**	**(94.8)**

[*] The number here refers to the number of participants seen at the stage of the study where grip strength would normally be measured (e.g. at a clinic visit). I typically took these values from study documentation, or otherwise from the study data file.

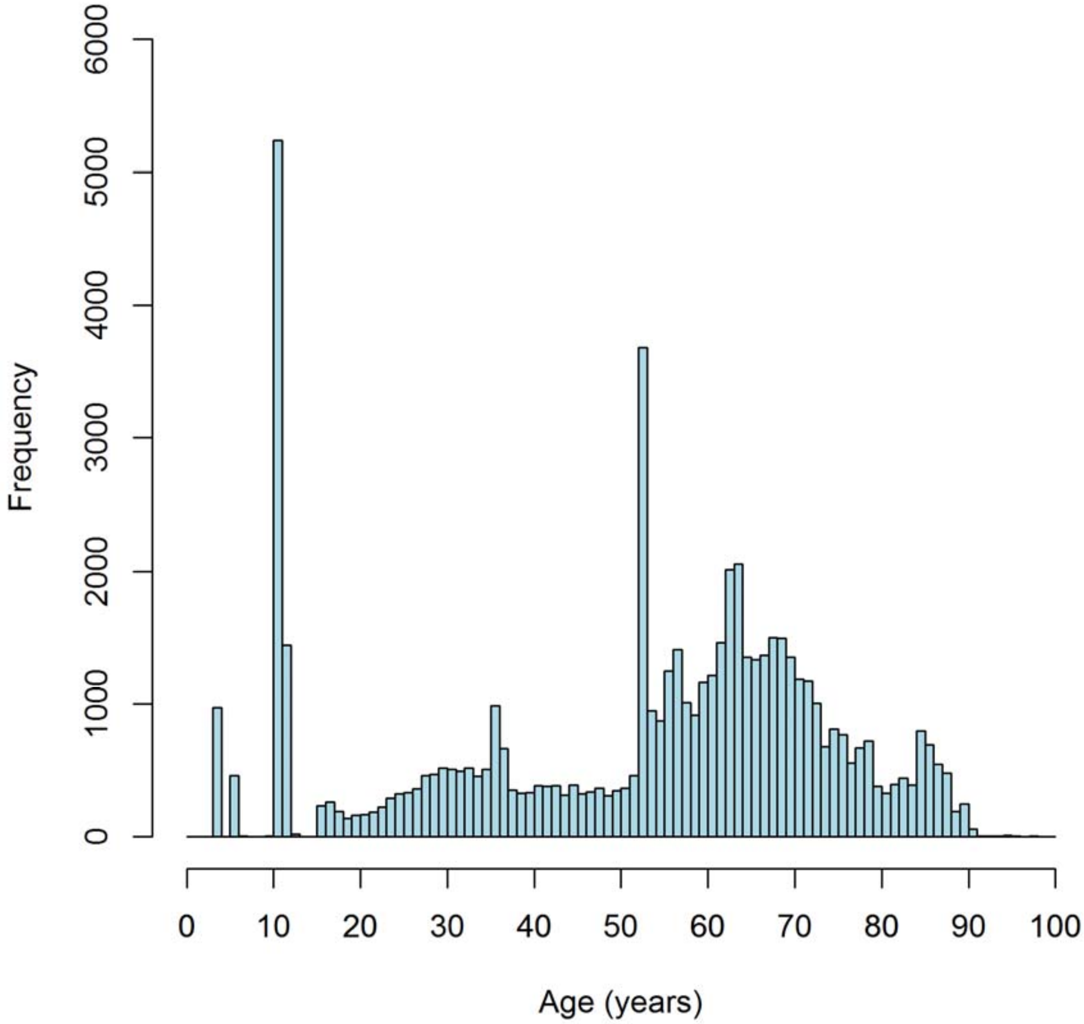
[†] In the first wave of ELSA to include grip strength, 75 of the 80 participants aged 90+ completed a measurement but were not included as their exact age was not available.

[‡] Similarly in the second wave of ELSA to include grip strength, 87 of the 91 participants aged 90+ had a valid grip strength measurement but were not included.

[§] In this wave of NSHD, there were 2,850 individuals with measurements but three were excluded as they were females with grip strength > 60kg (considered to be an error).

Eight of the twelve studies had measured grip strength in mid-late adult life, as reflected by the age distribution of the observations: median 58 years (IQR 36 – 69 years). There was still reasonable coverage of the life course except for some small gaps in childhood and adolescence, as shown by the histogram Figure 3.a, below.

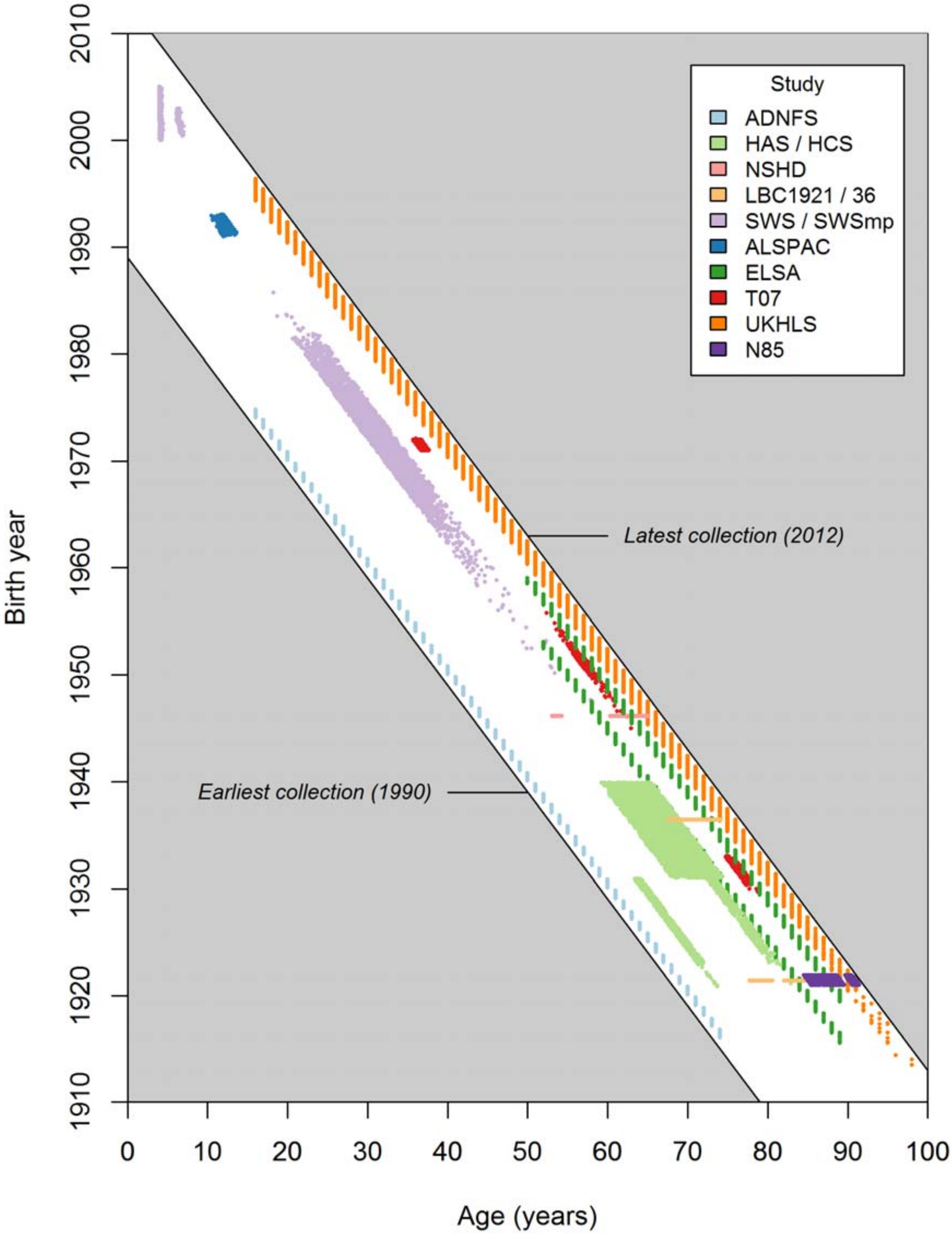
Figure 3.a Frequency of grip strength measurements by age



Small gaps in the coverage of the life course exist around the two waves of SWS (4-5 and 6-7 years), ALSPAC (10-14 years) and ADNFS/UKHLS (both age 16 onwards).

The data collection for the included studies took place in a recent timeframe between 1990 and 2012. As such, age and birth year were strongly linked with younger individuals having been born more recently as shown in Figure 3.b.

Figure 3.b Ages and birth years for each grip strength measurement, by study

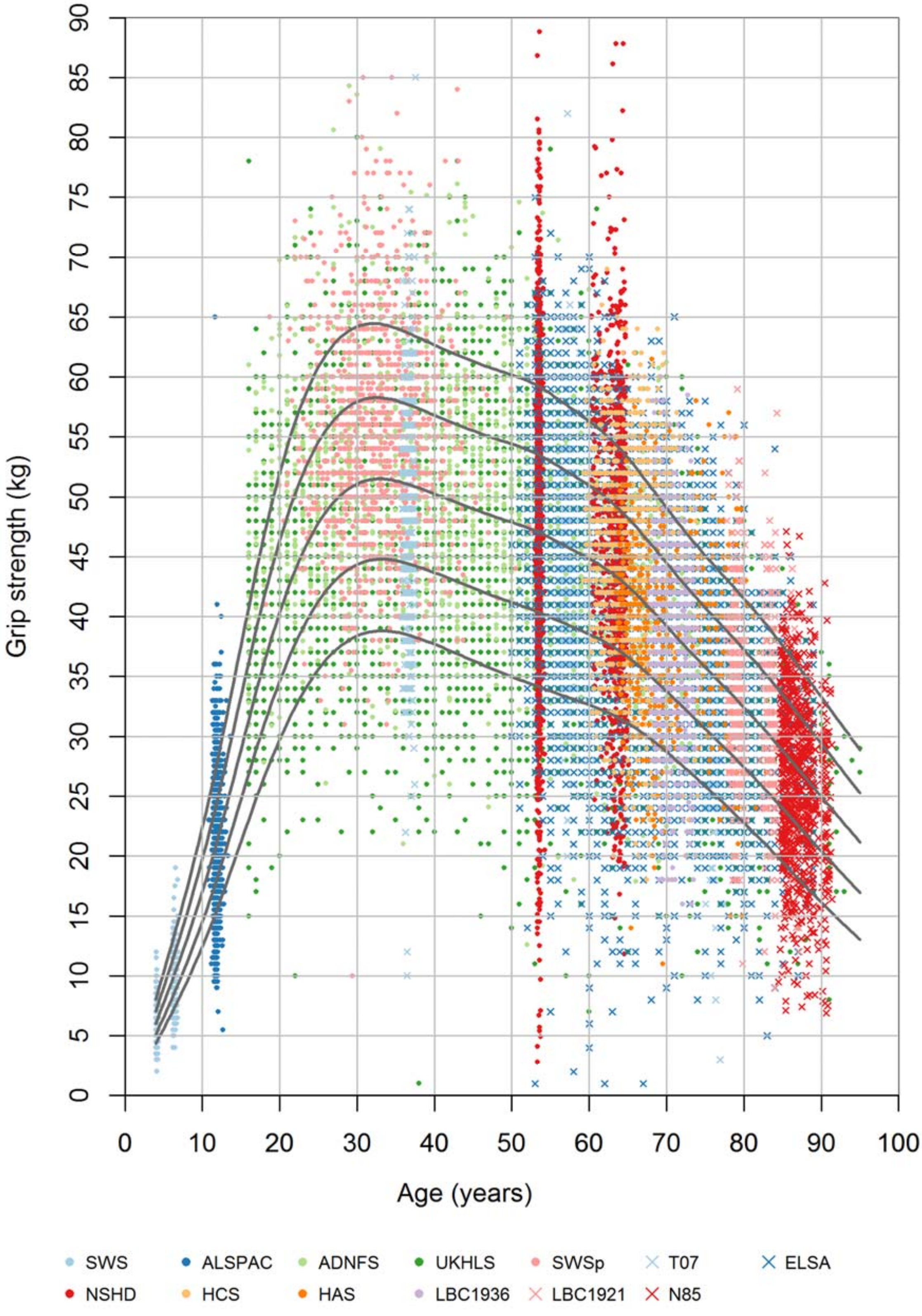


The data collection for the included studies occurred between 1990 and 2012; as such for any given age there is a limited range of birth years, as shown. For studies where the data was obtained from the Economic and Social Data Service (ADNFS, ELSA and UKHLS), there was no information provided on month of birth hence all ages are integer values.

3.2 Centile curves for grip strength

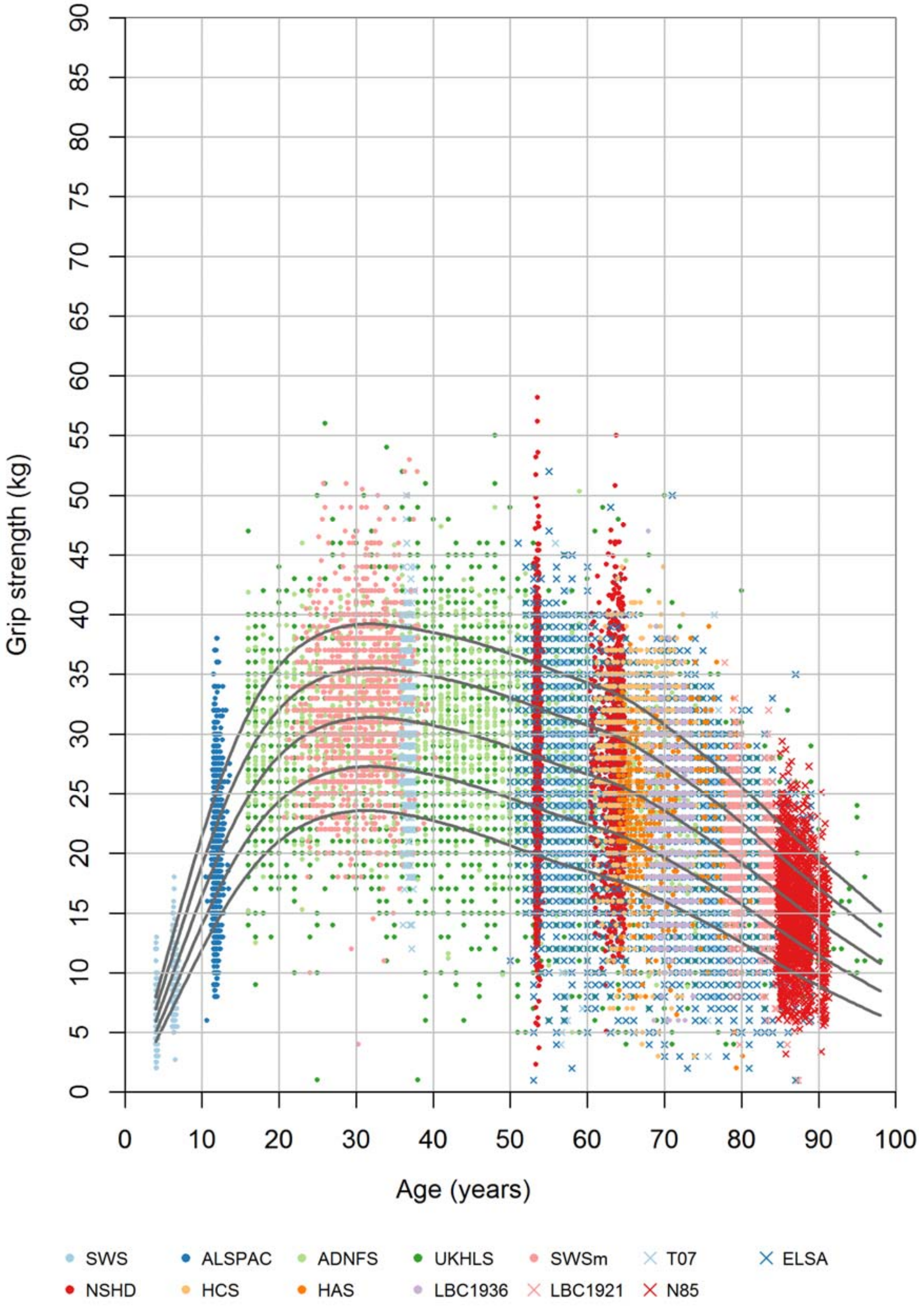
The centile curves for males and females based on the Box-Cox Cole and Green (BCCG) distribution are shown in Figure 3.c and Figure 3.d, overleaf, with the corresponding normative values shown in Table 3.b on page 40. They suggested three overall periods: an increase to peak in early adult life, broad maintenance through to midlife and decline from midlife onwards. Males reached a peak median grip of 51kg (rounded to the nearest whole kg) between ages 29 and 39, compared to the peak female median grip of 31kg between ages 26 and 42.

Figure 3.c Cross-cohort centile curves for male grip strength



Centiles shown 10th, 25th, 50th, 75th and 90th. Studies ordered by age at first grip measurement; for abbreviations see Table 2.a on page 19.

Figure 3.d Cross-cohort centile curves for female grip strength



Centiles shown 10th, 25th, 50th, 75th and 90th. Studies ordered by age at first grip measurement; for abbreviations see Table 2.a on page 19.

Table 3.b Normative values for grip strength

		Grip strength normative values at age shown (kg)						
Age (years)	**Observations**[*]	**Centiles**					**Mean (SD)**	
		10th	**25th**	**50th**	**75th**	**90th**		
Males								
5	730	6	7	8	9	10	7.8	(1.9)
10	3222	12	15	17	20	22	17.2	(3.7)
15	288	21	25	29	33	38	29.1	(6.5)
20	354	30	35	40	46	52	40.5	(9.4)
25	574	36	41	48	55	61	48.0	(10.3)
30	984	38	44	51	58	64	51.3	(10.0)
35	1380	39	45	51	58	64	51.5	(9.7)
40	880	38	44	50	57	63	50.2	(9.6)
45	798	36	42	49	56	61	48.8	(9.7)
50	820	35	41	48	54	60	47.6	(10.1)
55	3743	34	40	47	53	59	46.2	(9.9)
60	2683	33	39	45	51	56	44.6	(9.3)
65	3947	31	37	43	48	53	42.3	(8.7)
70	3286	29	34	39	44	49	39.1	(7.8)
75	1883	26	31	35	41	45	35.6	(7.4)
80	1115	23	27	32	37	42	32.2	(7.4)
85	1134	19	24	29	33	38	28.5	(7.2)
90	431	16	20	25	29	33	24.7	(6.9)
95+	5[†]							
(Total)	(28,257)							
Females								
5	700	6	7	8	9	10	7.8	(2.2)
10	3339	12	14	16	19	21	16.6	(3.6)
15	345	17	20	24	27	30	23.8	(5.0)
20	463	21	24	28	32	36	28.4	(5.8)
25	870	23	26	30	35	38	30.6	(6.0)
30	1423	24	27	31	35	39	31.4	(6.0)
35	1785	23	27	31	35	39	31.3	(6.0)
40	968	23	27	31	35	39	30.7	(6.3)
45	952	22	26	30	34	38	29.9	(6.1)
50	1019	21	25	29	33	37	28.7	(6.4)
55	4250	19	23	28	32	35	27.5	(6.5)
60	2943	18	22	27	31	34	26.5	(6.2)
65	4171	17	21	25	29	33	25.3	(6.0)
70	3473	16	20	24	27	31	23.5	(5.7)
75	2135	14	18	21	25	28	21.4	(5.4)
80	1361	13	16	19	23	26	19.1	(5.1)
85	1632	11	14	17	20	23	16.6	(4.7)
90	702	9	11	14	17	20	14.2	(4.3)
95+	15[†]							
(Total)	(32,546)							

The centiles and mean (SD) values were derived for the exact ages shown.

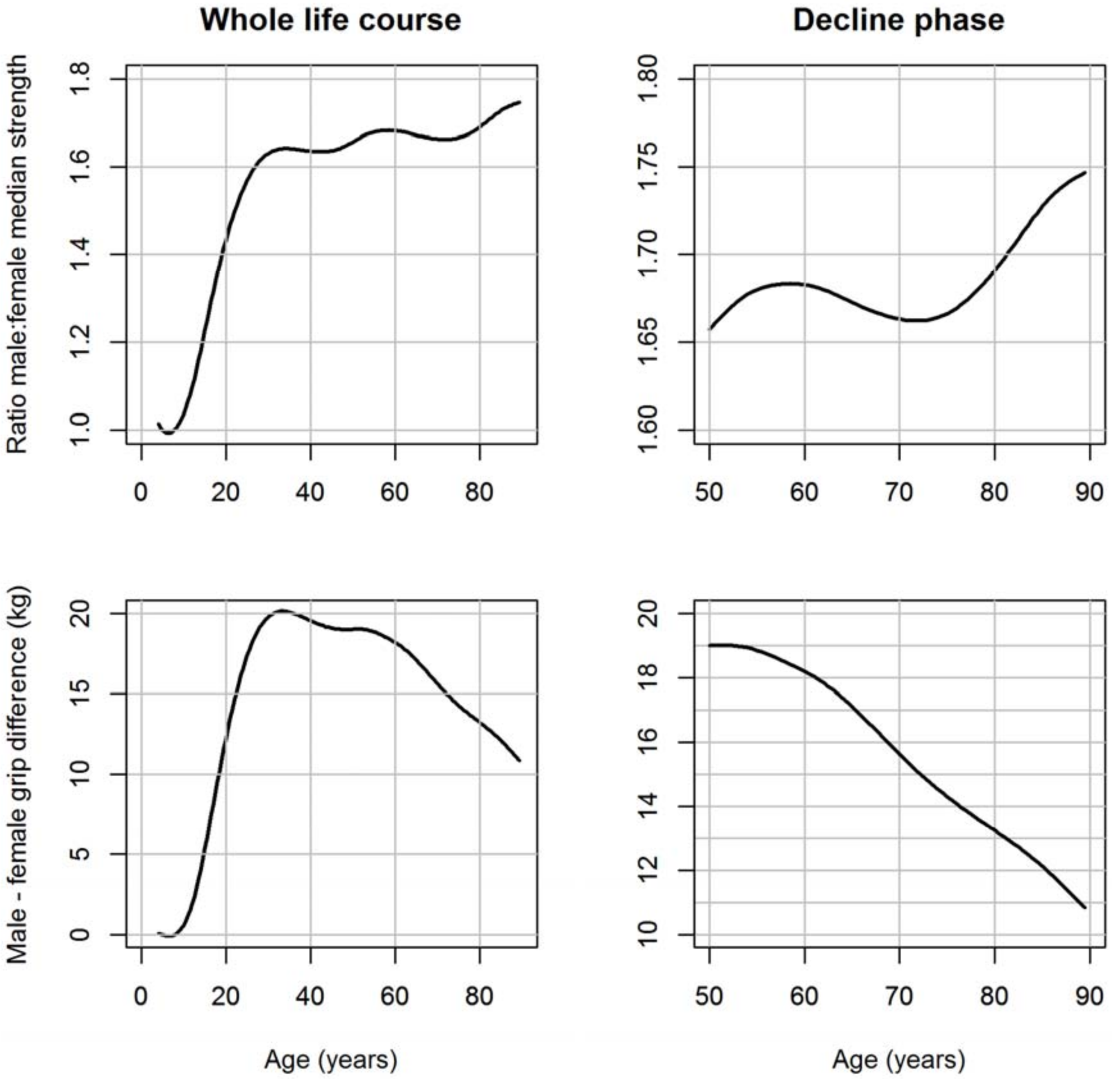
[*] Number of grip strength observations refers to the number of individuals at age shown ± 2.5 years (to give an indication of the sample size at different ages).

[†] Limited data were available in the 95+ years category so centile values are not shown.

3.2.1 Gender differences in median grip strength

Males were stronger on average than females from adolescence onwards; by age 25, males' median strength was 1.6 times that of females and this ratio increased slightly to 1.7 and remained relatively constant during the decline phase as shown in Figure 3.e. The gender difference in median strength is also shown; males' median strength was 20kg higher than females' at age 30. This difference between the genders' median values reduced as they both became proportionately weaker with increasing age.

Figure 3.e Gender differences in median grip

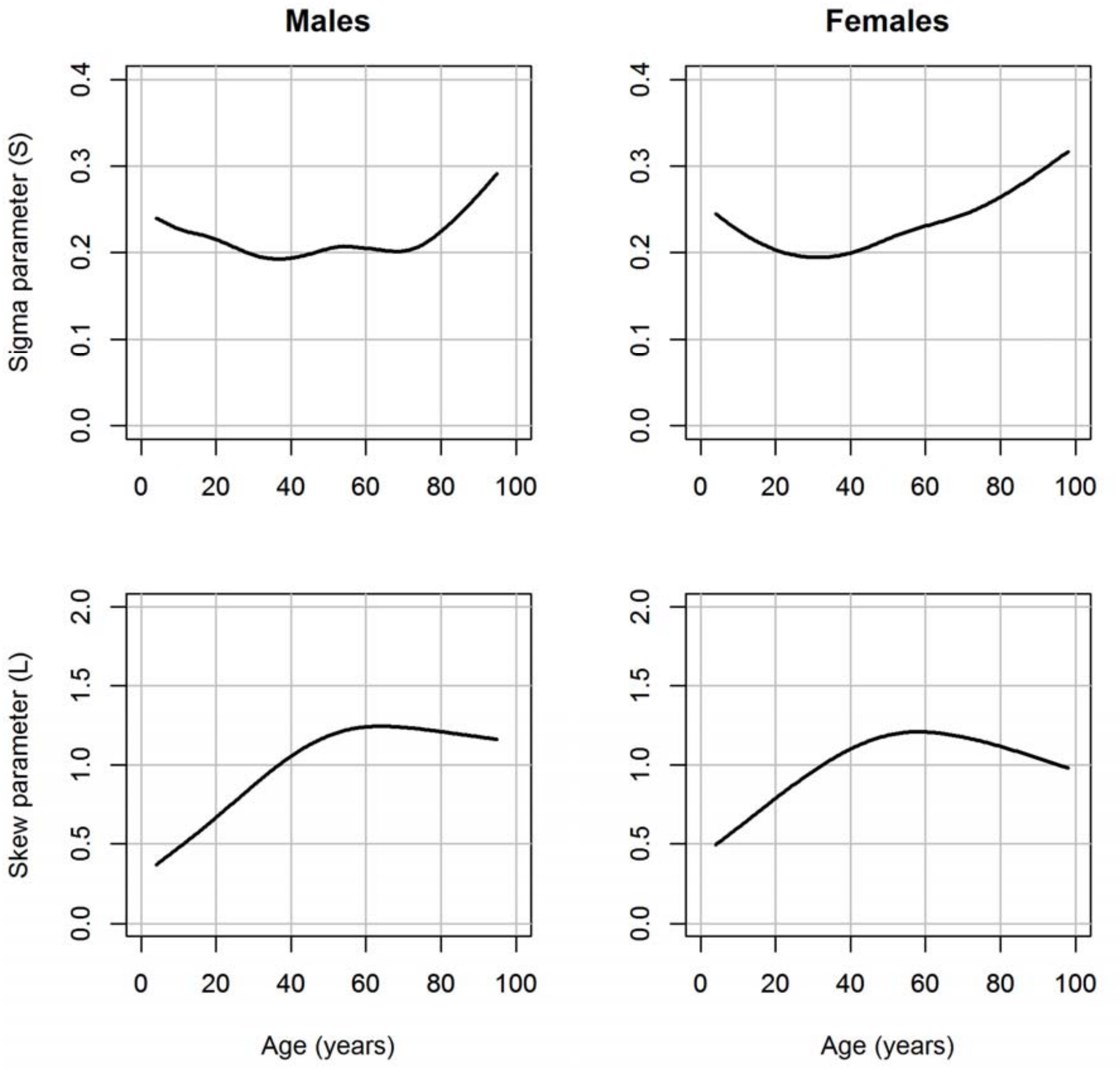


The two charts on the left side show the ratio and difference between male and female median grip strength across the life course. The two on the right focus on the decline phase (age 50 onwards).

3.2.2 Findings for the other model parameters

The relationships between age and the spread of grip strength values relative to the median (S, the sigma parameter from the BCCG model, an approximation to the coefficient of variation), and between age and skew parameter (L) are shown in Figure 3.f, below.

Figure 3.f Sigma and skew parameters in relation to age



The sigma parameter increased slightly in later life, from 0.20 in the fourth decade in men and women, rising to 0.25 and 0.29 in the ninth decade in men and women, respectively. This change translates to a minor increase in the spread of the centile values produced; for example, the 10th and 90th centile values in the ninth decade are each approximately 2kg further away from the median than they would be if the sigma parameter had remained at 0.20.

I found no evidence of skew in the grip strength data. The values for the skew parameter (L) across the life course had median (IQR) 1.2 (0.8, 1.2) in males and 1.1 (0.9, 1.2) in females, consistent with no marked skew. As shown in Figure 3.f, above, the skew parameter took a value of approximately 0.5 during childhood, suggesting a skew towards higher values of grip strength. However the effect of this skew on the centile values observed was minimal, as shown from the centile values for the relevant ages in Table 3.b on page 40.

3.2.3 Z-scores for grip strength observations

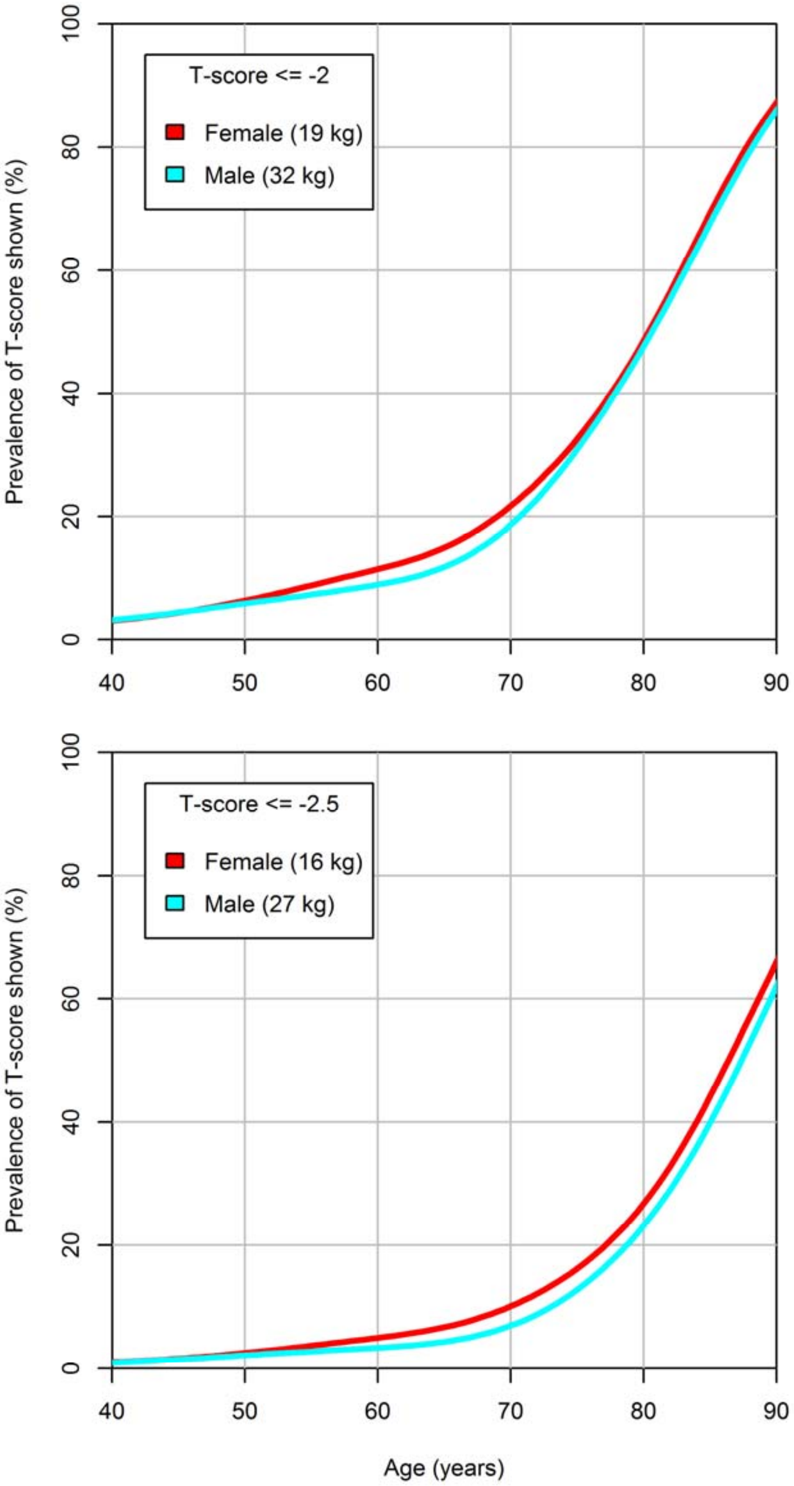
I used the centile curves to produce Z-scores for each of the grip strength observations. As I expected, these Z-scores were normally distributed with a mean of 0.0 and standard deviation of 1.0 in both males and females. I also examined the Z-scores by study and found that they largely followed a similar distribution, with Z-score means of ± 0.3 and standard deviations between 0.9 and 1.1. There were two exceptions. Firstly, participants in SWSp (the partners of SWS mothers) were stronger than the average from my centiles with a mean Z-score of 0.4 (0.9). Secondly, participants in NSHD had similar average grip strength to my centiles but a slightly broader spread of values with a mean Z-score of 0.1 (1.3). The histograms and results for the Z-scores overall and by study are shown in Appendix 1 starting on page 117.

3.3 Estimates of prevalence of low grip strength

The values for the mean and standard deviation of grip strength are shown in Table 3.b. There was little difference between the mean and median values for grip strength at any given age, in keeping with the finding of no evidence of skew in the BCCG model.

The estimated prevalences of weak grip strength in mid and late adult life, defined by gender-specific T-scores of less than or equal to -2 and -2.5, are shown in Figure 3.g. These were derived relative to the peak mean (SD) for grip strength of 51.7 (9.8) kg in males and 31.5 (6.0) kg in females, both occurring at age 32. Females and males had similar prevalence of weak grip strength during the decline phase. The prevalence of weak grip increased rapidly in late adult life; using a T-score of -2.5, my results suggested that by age 80, around a quarter of participants had weak grip strength (23% of males and 27% of females).

Figure 3.g Prevalence of weak grip strength using T-scores of ≤ -2 and -2.5



This figure shows the age range associated with decline (40 onwards). The values shown in brackets are the gender-specific cut-off values calculated by subtracting the relevant number of standard deviations (2 or 2.5) from the young adult peak mean.

3.4 Sensitivity analyses

In summary, I found that the centile curves were robust across the six types of sensitivity analysis that I carried out. The results of each analysis are described below and the charts comparing the 10th, median and 90th centiles from the sensitivity analyses to the main findings are shown in Figures on pages 48 - 51 and in Appendices 2 and 3.

The inclusion of a parameter (tau) for kurtosis using the Box-Cox power exponential distribution [101] in place of the BCCG distribution revealed slight evidence of leptokurtosis (peakedness) in the data, with values for tau below 2 (the value in the case of a normal distribution). The median (IQR) for the tau parameter across all ages in males was 1.64 (1.61, 1.70) and in females 1.66 (1.61, 1.71). However this made no difference to the centile values produced as shown in Figure 3.h.

Restriction of the dataset to the first observation for each individual led to acceptably similar centiles except in the tenth decade of life, where the values approached 10% higher than the main findings (see Figure 3.i). The available data are somewhat sparse at these ages, being drawn from observations made in UKHLS (n=58) and the fourth wave of N85 (n=270). Restriction to the first observation led to the N85 data being excluded; the remaining UKHLS values are on average higher than those from N85 and this appears to account for the difference in the centiles shown.

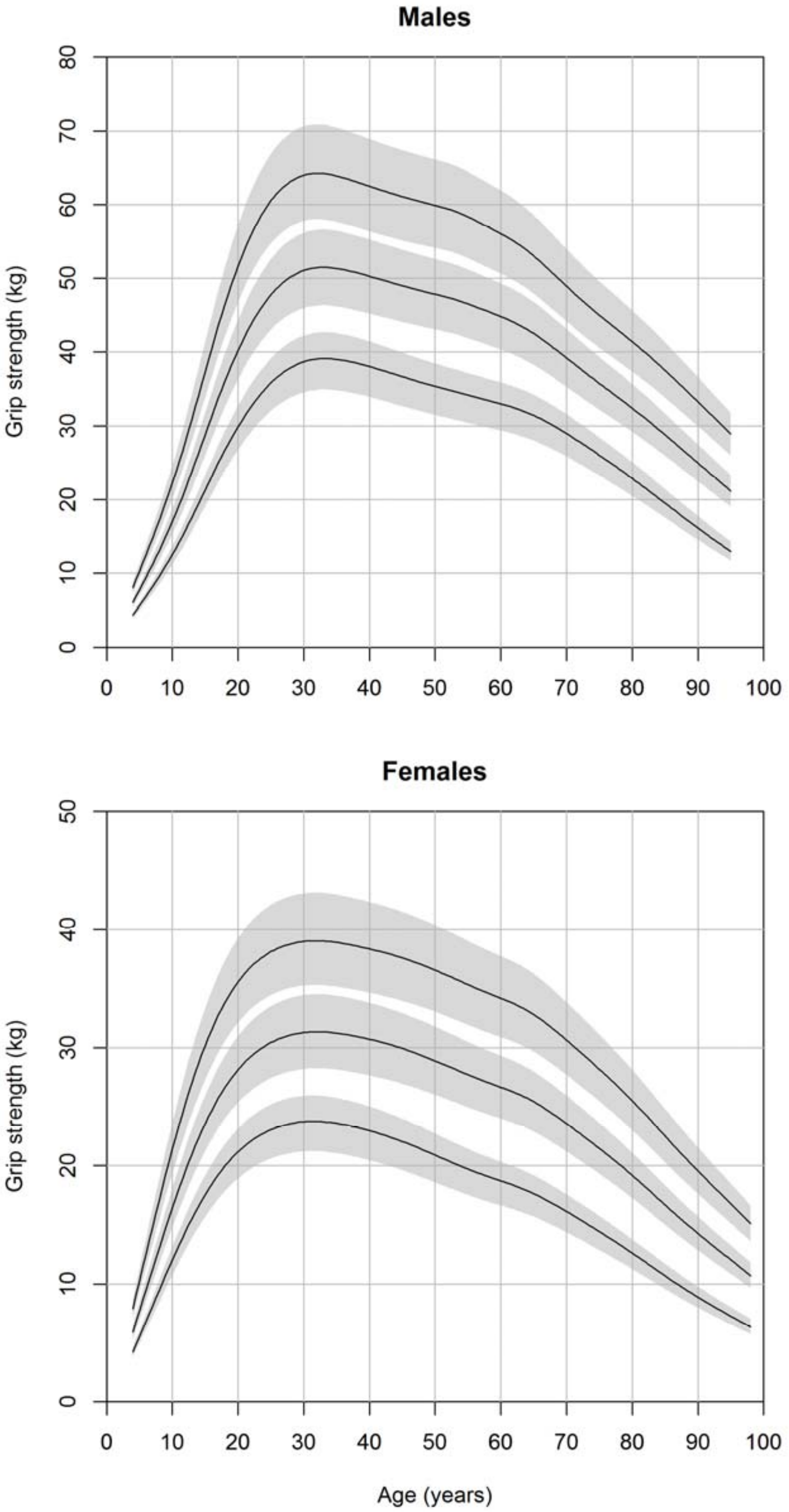
Overall the dynamometer-specific centiles were similar to the main results as shown in Figure 3.j. However the 90th centile values for the Nottingham dynamometer in early adult life in males were elevated greater than 10% above the main centiles. As no other study used the Nottingham dynamometer in this age range, it is unclear if these differences are due to the dynamometer or to other study factors. There was some evidence that selection bias may have occurred with the ADNFS males in the 16-20 age group, towards taller (and hence stronger) individuals. Whereas males in ADNFS in the 20-40 age group tended to be shorter than those from other studies (typically by around 2cm), those in the 16-20 age group were around the same height as those seen in the data collection for UKHLS which took place around 20 years later.

The centiles stratified by position showed similar findings to the main results for participants who were seated (as per protocol) or standing (see Figure 3.k). Perhaps unsurprisingly, those who chose to sit or were unable to stand tended to be weaker and this difference became more pronounced with age until the ninth decade when their 10th centile values approached 10 per cent lower than the combined results.

The truncation of all participants' ages to integer values had the effect of slightly increasing the centile values for grip strength during childhood, as shown in Figure 3.l. This is perhaps not surprising since the non-integer portion of an age in childhood (for example 0.5 years in the case of a child aged 4 years and 6 months) is a relatively larger proportion of their age than in adulthood; removing this therefore makes it appear that they have attained a given strength at a younger age. This finding led me to consider whether the truncated ages in ADNFS, UKHLS and ELSA might have led to higher grip strength centile values, particularly the data from ADNFS and UKHLS and the associated centile values during adolescence. In retrospect, it might have been better to assume that the non-integer portion of the participants' ages in these studies was 0.5 (e.g. six months) on average as opposed to zero. I therefore carried out a further sensitivity analysis (see Appendix 3) using this assumption. I did not observe a difference in the centiles when I did so.

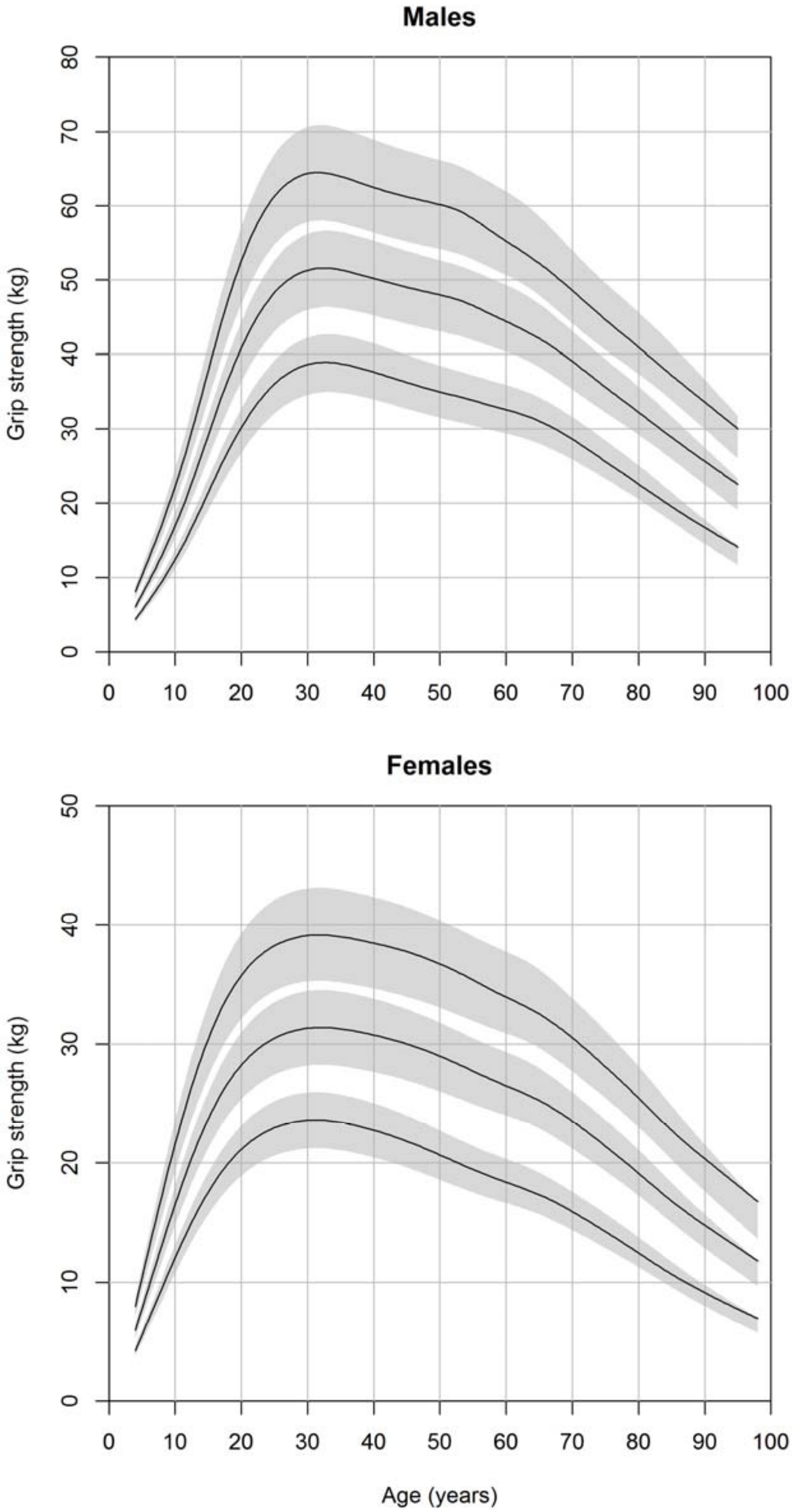
Finally, the centiles produced from analyses excluding each study in turn (see Appendix 2) were acceptably similar except for two instances. The exclusion of N85 data led to centiles which were greater than 10% higher than the main findings in the tenth decade of life. The exclusion of ALSPAC data also led to centiles in males which were more than 10% greater than the main findings during adolescence. Both instances appear to be explained by the sparse or absent data in the relevant age ranges when those particular studies were excluded.

Figure 3.h Centiles comparison: model including kurtosis



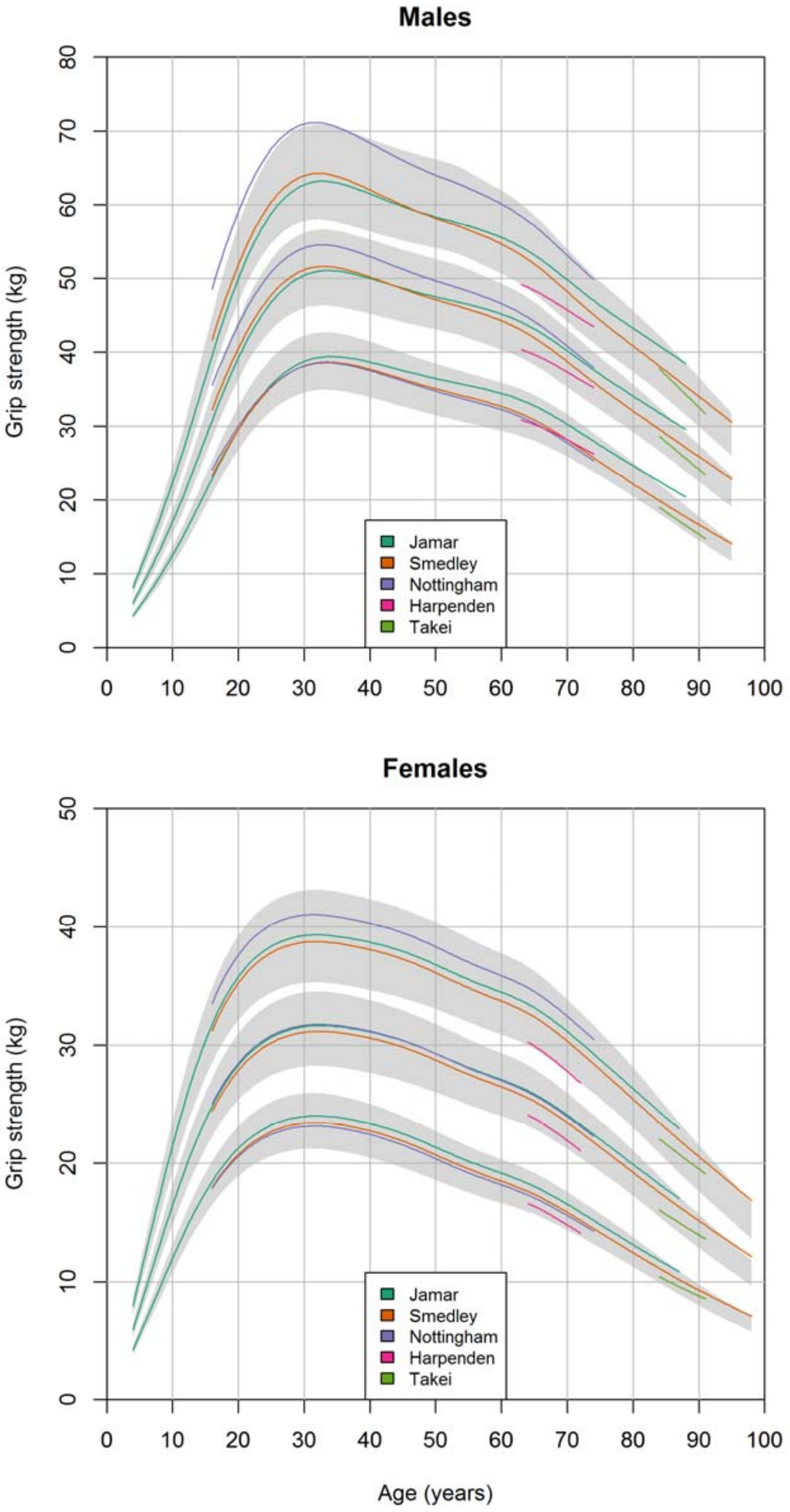
The lines represent the 10th, median and 90th centiles from the sensitivity analysis which included a parameter for kurtosis. The grey areas show the range produced if the values from the 10th, median and 90th centiles in the main results are increased or decreased by 10 per cent.

Figure 3.i Centiles comparison: restriction to first observation for each individual



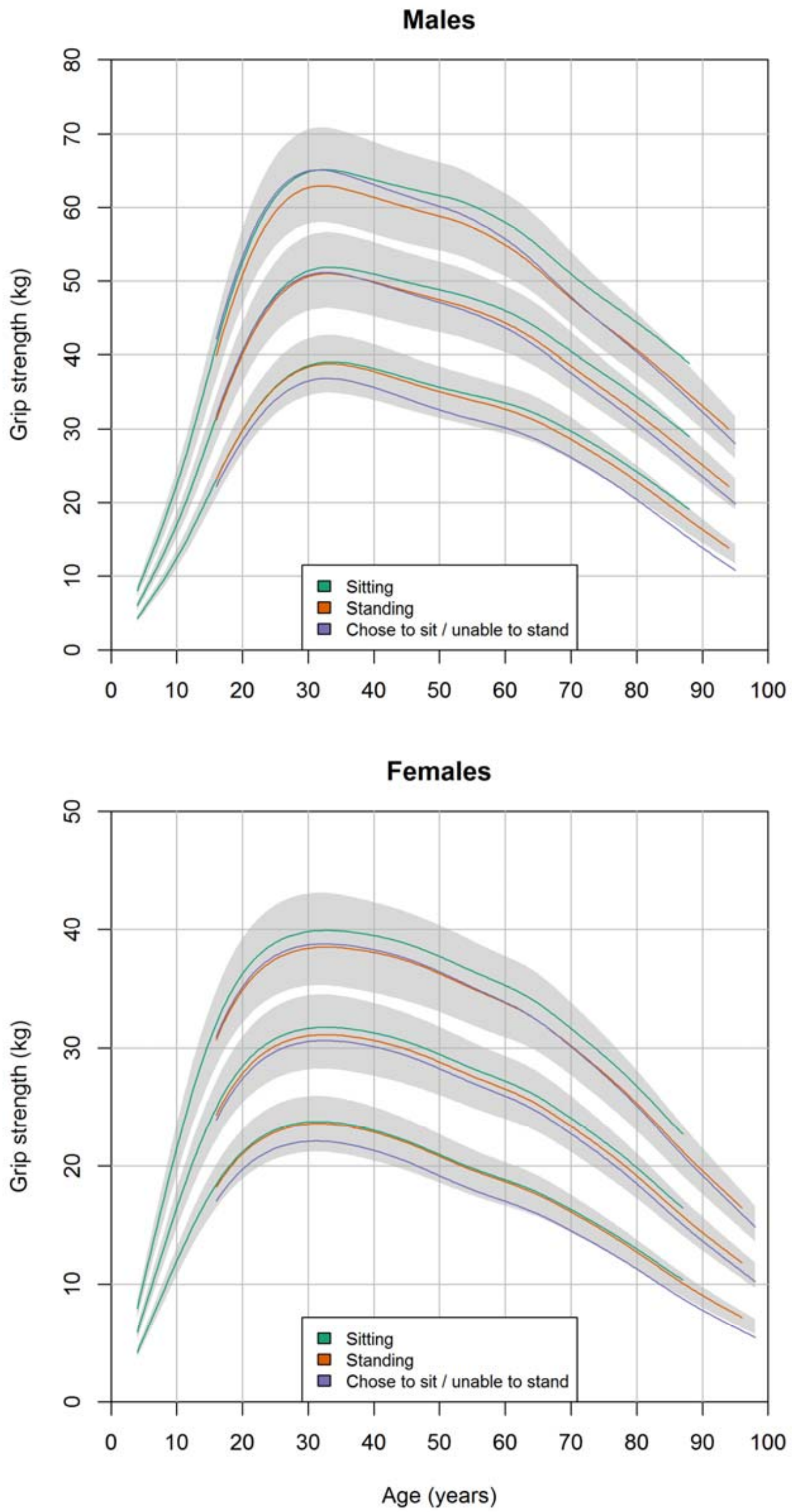
The lines represent the 10th, median and 90th centiles from the sensitivity analysis where the dataset was restricted to the first observation for each individual. The grey areas show the range produced if the values from the 10th, median and 90th centiles in the main results are increased or decreased by 10 per cent.

Figure 3.j Centiles comparison: stratification by dynamometer type



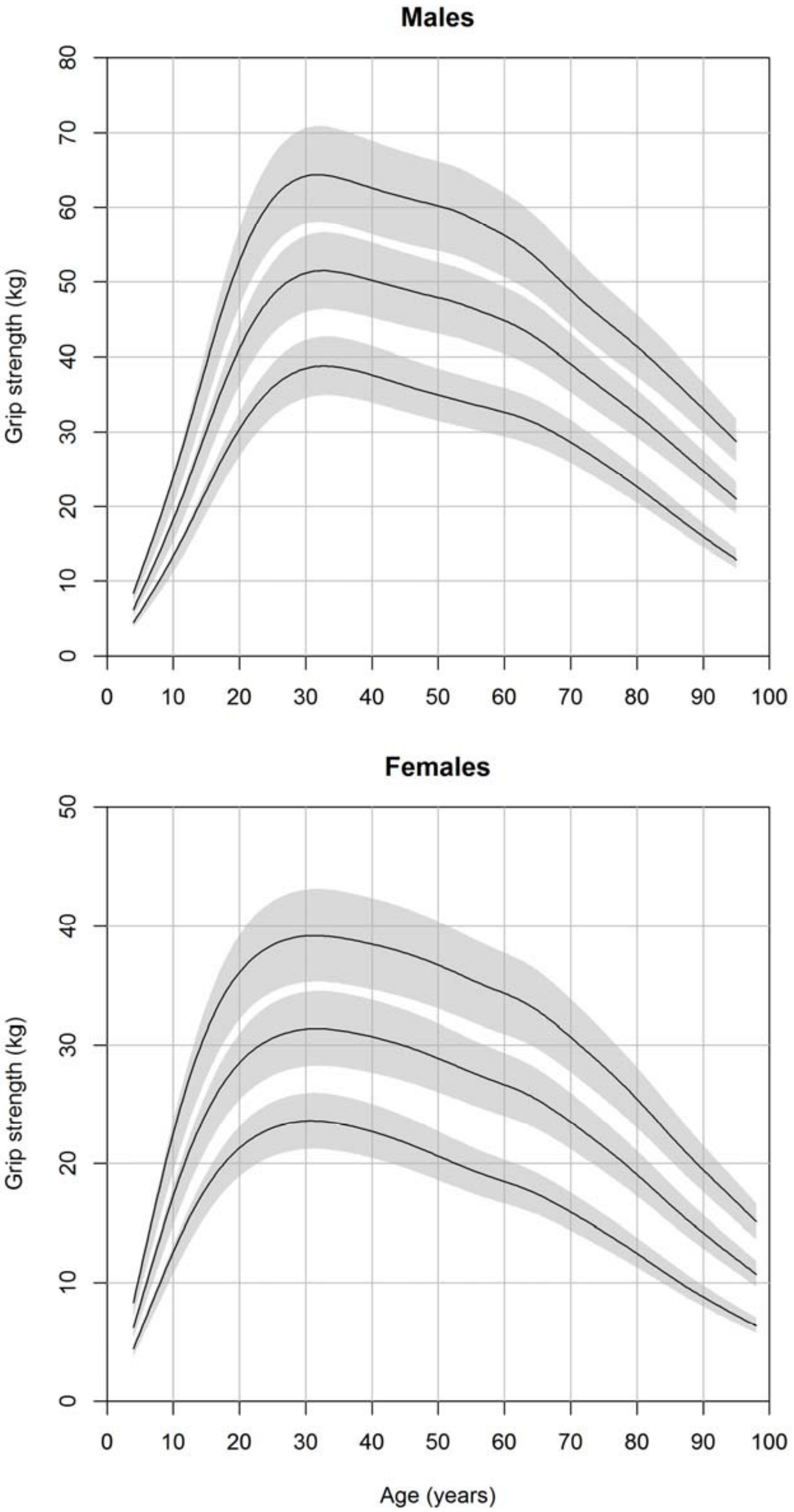
The lines represent the 10th, median and 90th centiles from the sensitivity analysis where the centile curves were stratified by dynamometer type. The grey areas show the range produced if the values from the 10th, median and 90th centiles in the main results are increased or decreased by 10 per cent.

Figure 3.k Centiles comparison: stratification by position of measurement



The lines represent the 10th, median and 90th centiles from the sensitivity analysis where the centile curves were stratified by the position of measurement. The grey areas show the range produced if the values from the 10th, median and 90th centiles in the main results are increased or decreased by 10 per cent.

Figure 3.l Truncation of all participants' ages to integer values



The lines represent the 10th, median and 90th centiles when all ages were truncated to integers. The grey areas show the range produced if the values from the 10th, median and 90th centiles in the main results are increased or decreased by 10 per cent.

4. Normative data from systematic literature review: methods

4.1 Objectives of this project

The objectives for this project:

- To compare the normative values produced from British studies to those in the literature, including investigation of differences in grip strength by world region
    - A secondary objective is to investigate the differences in published grip strength by aspects of measurement protocol and reporting.

In the following chapter, I describe how I searched for relevant papers, how I extracted data from them and I how stored and analysed those data.

4.2 Literature search and inclusion criteria

I developed the terms shown in Table 4.a, below, to carry out a systematic literature search of the databases MEDLINE (including in-process citations) and EMBASE. The search query returned articles which had at least one of the terms relating to grip strength and at least one of the terms relating to normative data. I also added steps to the search to remove articles which were duplicates from the two databases, those concerning animals only, non-English articles and those published before 1980. I ran the search on 11th August 2014 using the Ovid search system. I used Microsoft Excel to store the 806 abstracts returned by the search and to record my assessment of each of them.

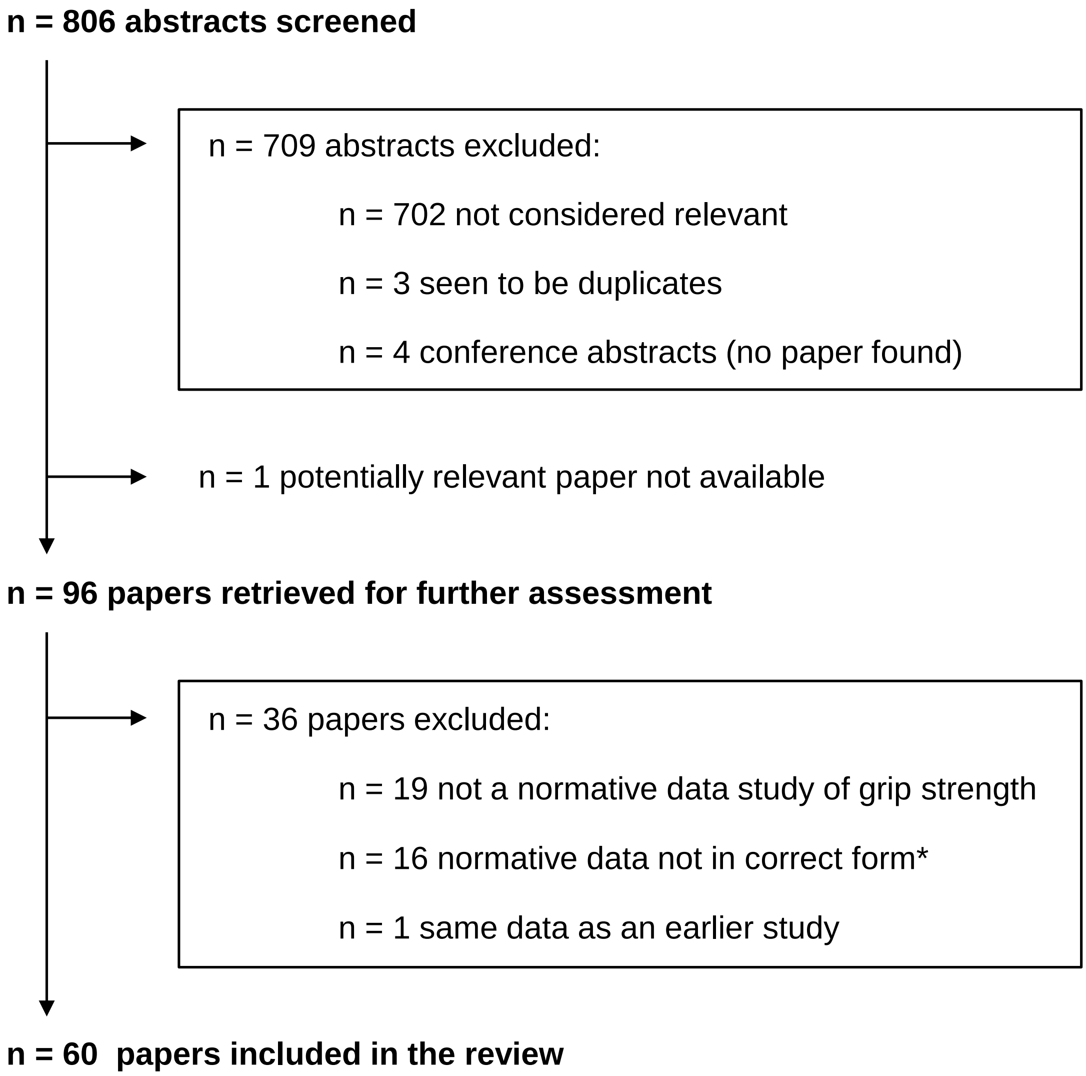
Table 4.a Search query used to identify articles

Step	Search string	Abstracts returned
1	(Hand Strength/ or Muscle Strength Dynamometer/ or "grip strength".ti,ab or "hand strength".ti,ab or "handgrip strength".ti,ab or "grip dynamometer".ti,ab)	26480
2	Reference Values/ or "reference values".ti,ab. or "normative".ti,ab. or (association* adj2 age).ab. or (relationship adj2 age).ab. or "age related".ti. or "age-related".ti. or "normal values".ti,ab	334730
3	1 and 2	1167
4	remove duplicates from 3 (with preference towards MEDLINE)	860
5	(4 and humans/) or (4 not (humans/ or animals/))	840
6	limit 5 to english language	811
7	limit 6 to yr="1980 -Current"	806

Search run on 11th August 2014 using databases MEDLINE (including in-process citations) and EMBASE.

A flow diagram summarising my assessment of the 806 abstracts is shown in Figure 4.a, below. I did not attempt to include information from conference abstracts in my review, although where a conference abstract appeared relevant I did check if a paper on the same work had been published subsequently. In all four cases, I was unable to find a related paper.

Figure 4.a Flow chart showing included papers



***** Reasons for normative data not being in the correct form included not presenting data in the form of a table, not stratifying normative values by gender, including a mean but no measure of spread such as standard deviation, and having an age range wider than 15 years.

I identified 97 papers where the abstract suggested that the paper might contain normative data for grip strength. I was able to obtain 96 of these for further assessment, with one paper [102] remaining unavailable despite an inter-library loans request.

There were two criteria for inclusion in the review. Firstly, papers needed to have reported normative data for grip strength from a sample of the general population.

Secondly, they must have reported normative values for grip strength stratified by age and by gender, where the sample contained both males and females.

Following these criteria, I excluded 36 of the 96 papers that I assessed. These exclusions fell into two main groups as described in the two paragraphs below.

Firstly, I excluded nineteen papers as they were not a study of normative data for grip strength of the general population. For example, I excluded papers where the data presented concerned specific patient or occupational groups, for example children with cystic fibrosis or papers contrasting grip strength between employees with manual and non-manual occupations. I also excluded papers that had assessed grip strength using the Martin vigorimeter, since this pneumatic device measures grip pressure, not grip force. Finally in this group, I excluded review articles on the measurement and interpretation of grip strength, although I did check their reference lists. I did not identify any further relevant papers for the review by doing this.

Secondly, I excluded 16 papers as they had not presented normative data for grip strength in the correct form. I excluded papers which had used a means other than tables stratified by age and gender to present their data, such as graphs or equations. I also required papers to include both a measure of average grip, such as mean or median and a measure of spread of grip strength values, such as standard deviation or interquartile range, for each item of normative data. I also excluded one paper where the age groups provided were too broad (in excess of 15 years).

I also excluded one paper as it contained the same data as an earlier study. This left 60 papers which I proceeded to extract the normative data from as described in the next section.

4.3 Data extraction

From each paper I extracted details at the study level, such as the sample and measurement protocol used, as well as the details of each item of normative data, such as the age range and the mean value for grip strength. I created a database in Microsoft

Access to facilitate data-entry and also to allow the overall details of each paper to be linked to the normative data items contained within it.

4.3.1 Study level details

I extracted information about the sample, protocol and statistical methods described in each paper as shown in Table 4.b on page 60. In terms of the sample used, I recorded the country and at what level the sample was drawn from such as national or regional. To facilitate later analyses, I used the International Organization for Standardisation (ISO) 3166 alpha-3 codes [103] to record the country setting such as "GBR" for the United Kingdom. This approach to coding also allowed me to plot a map showing the countries in which the samples were based, using the library rworldmap [104] for the statistical program, R [97].

I assessed whether the sample was drawn by approaching individuals using a sampling frame, such as a national registry or telephone directory, or whether the sample was a convenience one such as by recruiting participants at a shopping centre or by displaying posters. I recorded the total sample size contributing to the normative data in each paper. I did this for two reasons: firstly, to allow me to calculate the number of observations lost due to the need to exclude open-ended age ranges (described further in section 4.3.2, below), and secondly so that I could calculate an average number of observations in each age group where sample sizes for each individual age group were not provided in a paper.

In terms of the protocol used, I recorded the dynamometer make and model. If not already stated in the paper, I attempted to determine which type of device the dynamometer was: hydraulic, pneumatic or electronic. I also extracted information on the position of measurement, hands tested and number of trials, as shown in Table 4.b. Where possible, I extracted information on grip strength based on the maximum value from several trials of both hands, as recommended in published guidance [89]. Where values were stratified by the hand of measurement, I extracted data for the right or dominant hand, as available.

I classified the statistical methods used to produce the normative values into simple descriptive statistics, a parametric method such as linear regression or a non-parametric method such as restricted cubic splines. I also noted if each paper stratified grip strength by different height groups.

Table 4.b Study level details extracted

Variable	**Comments**
Paper details	
First author	(with additional information, e.g. abbreviated journal title, if more than one relevant paper by same author in the same year)
Year of publication	
Study sample	
Country	
Sample level	Options: national, regional (county or equivalent), local (single city), facility (e.g. a single university or hospital)
Sample type	Options: sampling frame*, convenience, not specified
Sample description	Brief description: e.g. "participants of a university-run well-being programme"
Total sample size (males)	Number of participants contributing to normative data for grip strength
Total sample size (females)	
Year of data collection (earliest)	Value zero if not specified
Year of data collection (latest)	
Study protocol	
Dynamometer make (and model)	Model if specified, e.g. Takei 5001 Grip A
Dynamometer type	Options: hydraulic, pneumatic, electronic
Measurement position	Seated or standing
Arm support	Supported or unsupported
Total repetitions	Across both hands if both tested
Hand(s) tested	Both, left, right, dominant or non-dominant
Hand(s) data extracted for	Both, left, right, dominant or non-dominant
Summary measure	Maximum or mean
Units of measurement	Options: newtons, and kg and pounds force.
Other protocol details	Free text for other details regarding protocol
Statistical methods	
Stratified by height	For studies that stratify results by height, number of height groups included
Analysis approach	Options: Descriptive statistics, linear regression, cubic splines, not specified

* This refers to any study where the sample was obtained by approaching individuals using a sampling frame – whether a national registry or telephone directory, etc.

4.3.2 Details for each item of normative data

For each item of normative data, I extracted details of the gender and age stratum which it related to, along with the mean and standard deviation as shown in Table 4.c, below. Three papers had further stratified normative data by height categories, either into two groups (above and below median height) [52], or into seven [105] or eight [106] categories. For the paper using two groups, I extracted the normative data for both groups, and for the other two papers, I extracted data for the group containing the median height for my British normative data sample at the same age.

I excluded normative data items where the age range given was open-ended, for example “75+ years”. I extracted data in the same format as used in the paper: for example, using a separate field to record the upper and lower 95% confidence intervals for a mean when these were provided but a standard deviation was not. In a similar way, I did not manually convert units to kg force, but rather entered the data as shown in the paper and noted as part of the study level details which units had been used.

Table 4.c Variables extracted concerning each normative data item

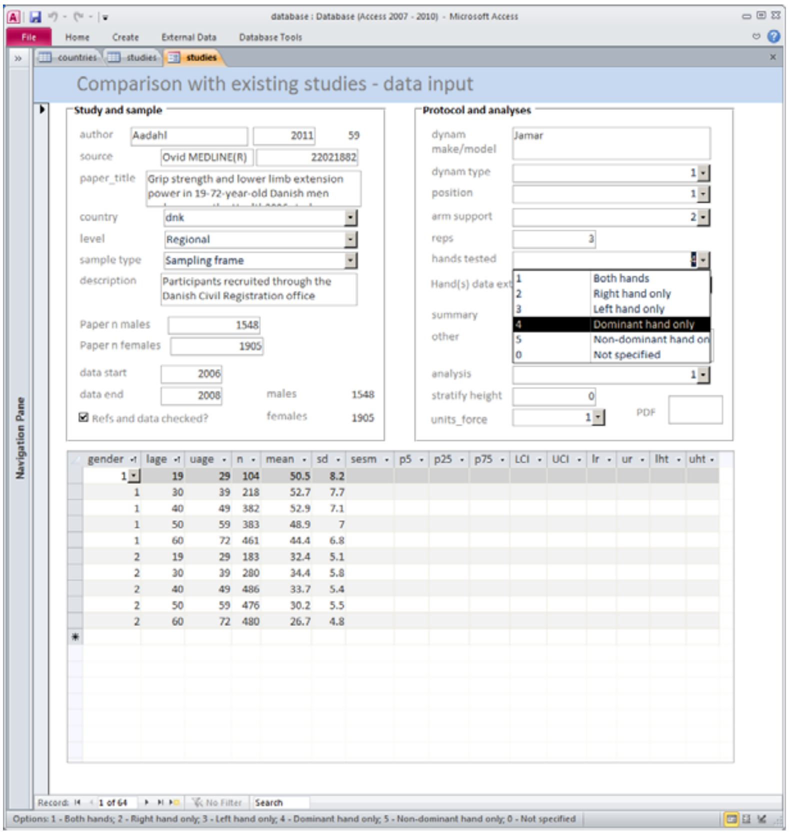
Variable	Comments
Specific sample	
Gender	Male or female
Lower age limit (years)	
Upper age limit (years)	
Sample size	Zero if not-specified
Grip strength values	
Grip strength mean	
Grip strength SD (or standard error of sample mean, or IQR, or 5th centile, or reference range[*] or 95% CI for mean)	Where SD not given in the paper but one of the values in brackets given, equations[†] used to calculate SD
Height values (if relevant)	
Height lower limit (cm)	If multiple height groups extracted, initial plan will be to extract middle group.
Height upper limit (cm)	

[*] Referring to the mean value ± two standard deviations.
[†] For equations used, see section 4.4 Data management on page 62.

4.3.3 Data entry

I designed a relational database using Microsoft Access to store the information I extracted from each paper in a standardised way ready for data management and analysis tasks. A screenshot of the main data-entry form is shown in Figure 4.b. Where possible, I designed the form so that details could be selected from drop-down lists such as for the hands tested in a given study. The main relationship in the database was that each study (the top half of the screenshot) could give rise to multiple normative data items (the bottom half of the screenshot).

Figure 4.b Screenshot of data-entry form in Microsoft Access



Comparison with existing studies - data input

Study and sample

author: Aadahl 2011 59
source: Ovid MEDLINE(R) 22021882
paper_title: Grip strength and lower limb extension power in 19-72-year-old Danish men
country: dnk
level: Regional
sample type: Sampling frame
description: Participants recruited through the Danish Civil Registration office
Paper n males: 1548
Paper n females: 1905
data start: 2006
data end: 2008
males: 1548
females: 1905
☑ Refs and data checked?

Protocol and analyses

dynam make/model: Jamar
dynam type: 1
position: 1
arm support: 2
reps: 3
hands tested: 4
Hand(s) data ext
summary
other
analysis: 1
stratify height: 0
units_force: 1
PDF

1	Both hands
2	Right hand only
3	Left hand only
4	Dominant hand only
5	Non-dominant hand on
0	Not specified

gender	lage	uage	n	mean	sd	sesm	p5	p25	p75	LCI	UCI	lr	ur	lht	uht
1	19	29	104	50.5	8.2										
1	30	39	218	52.7	7.7										
1	40	49	382	52.9	7.1										
1	50	59	383	48.9	7										
1	60	72	461	44.4	6.8										
2	19	29	183	32.4	5.1										
2	30	39	280	34.4	5.8										
2	40	49	486	33.7	5.4										
2	50	59	476	30.2	5.5										
2	60	72	480	26.7	4.8										

Options: 1 - Both hands; 2 - Right hand only; 3 - Left hand only; 4 - Dominant hand only; 5 - Non-dominant hand only; 0 - Not specified

4.4 Data management

I created a query in Access which converted the data to long format, where every item of normative data had its own row complete with all the details for the study it was taken from. I then imported the query results into Stata version 12.0 [94] to carry out data management tasks as described below.

As described in the previous section, several studies had not reported the mean, standard deviation and number of observations for their normative data, but rather had provided other descriptive statistics from which they could be calculated. I show the formulae I used to carry out the necessary conversions in Table 4.d.

Table 4.d Formulae used to produce descriptive statistics from alternatives provided

Descriptive statistic not provided	Alternative provided in paper	Formula used for conversion
Mean, $\bar{x}$	Reference range (lower and upper), $R_L = \bar{x} - 2s$ and $R_U = \bar{x} + 2s$	$\bar{x} = \frac{R_L + R_U}{2}$
	Median[*], P_{50}	$\bar{x} = P_{50}$
Standard deviation, s	Lower 95 % CI for mean CI_L and n	$s = \frac{(\bar{x} - CI_L) * \sqrt{n}}{1.96}$
	Standard error of the sample mean se and n	$s = se * \sqrt{n}$
	Interquartile range[*] P_{25} and P_{75} (based on the N(0,1) distribution, P_{25} and P_{75} are 0.674 SDs either side of the mean, so the difference between them represents 1.348 SDs).	$s = \frac{P_{75} - P_{25}}{1.348}$
	Fifth centile P_5 (as above, P_5 is 1.645 SDs below the mean)	$s = \frac{(\bar{x} - P_5)}{1.645}$
Sample size, n	Standard error of the sample mean se and s	$n = round\left[\left(\frac{s}{se}\right)^2\right]$

[*] From my earlier work on normative data, I considered it reasonable to assume that grip strength was normally distributed and indeed on inspection of the data I extracted from studies reporting a median and interquartile range for grip strength, there was very little evidence of skew.

Where papers did not present a sample size for individual groups, or a standard error and standard deviation from which to calculate one from, I calculated an approximate sample size based on the assumption that the overall sample size for each given gender was evenly distributed across the age groups presented:

$$n_{approx} = \frac{N}{g}$$

Overall sample size for given gender N and number of groups g.

One paper [106] had stratified normative data for each gender into six different age groups, and then further stratified each age group into eight height groups. The paper only provided the overall sample size for each gender. It was therefore necessary to assume that the sample for each gender was evenly distributed across the six age groups. Furthermore, I then assumed that the sample within each gender and age stratum was evenly distributed across the eight height groups. As described in section 4.3.2, above, I extracted the normative data for height group containing the median height for my British sample at the same age.

I converted values to kg force when they were provided in the units of pounds force or Newtons. The conversion factors I used to do this are shown in Table 4.e, below. Finally I halved values from studies that reported summed values from both hands.

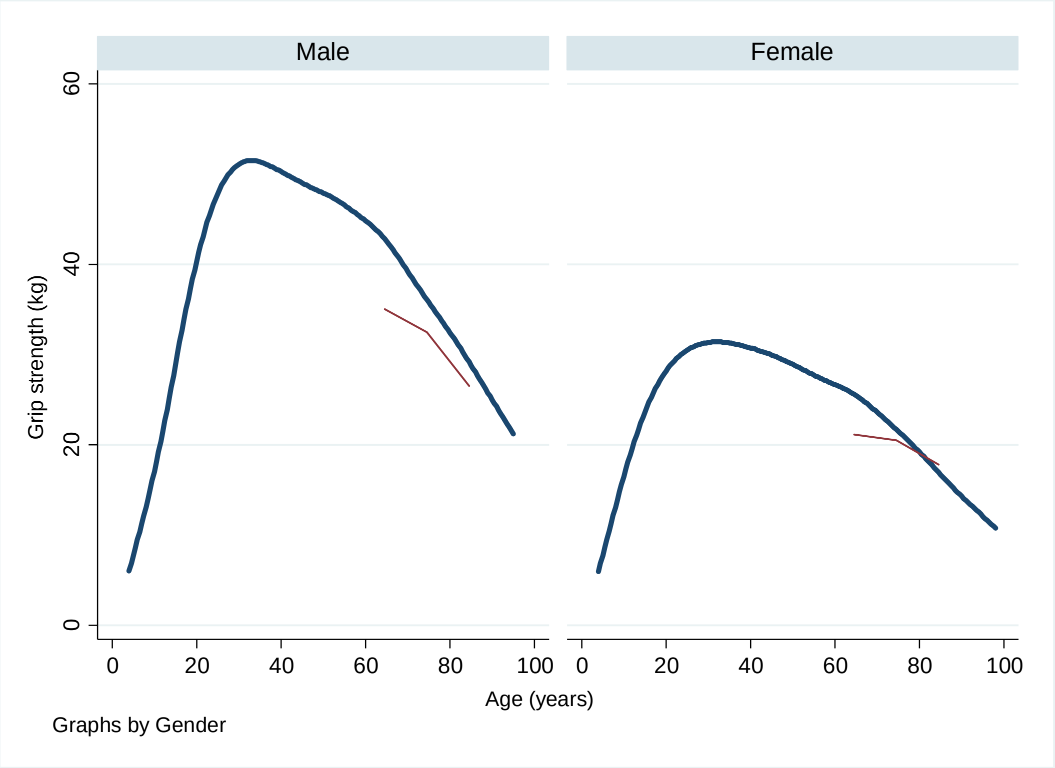
Table 4.e Factors used to convert extracted values to kilograms force

Unit	**Conversion factor***
Pounds force	0.453594
Newtons	0.101972

I multiplied values by the relevant factor to obtain the equivalent in kilograms force.
*I used publically available conversion factors [107].

Prior to analysis I checked the data I had entered by producing graphs showing the results from each study. These took the form of line plots where the mid-point of each age range was shown against the mean grip strength for that age range. I included the mean values from my British normative data on the graph as a reference. An example is shown in Figure 4.c. If the plot suggested an inconsistent pattern of results relative to my normative data, I re-checked that I had entered the data from the paper correctly.

Figure 4.c Sample plot used to check data entry



This example shows the data from the paper by Wang et al. [108]. The norms they reported across three age groups are shown as the red line with my norms from British studies shown in blue for comparison.

4.5 Statistical analyses

I classified countries into geographical regions using the groupings provided by the United Nations Statistics Division [109]. These groupings include whether a region is classed overall as developed or developing. I also used the economic groupings from the World Bank [110] to classify each country as either low/middle or high income. The two approaches gave broadly similar groupings, with most countries in developing regions having low/middle income. There were exceptions, such as Saudi Arabia: a high-income country in the Asia (except Japan) region, which is classed as developing.

I initially produced summary tables and charts to describe the characteristics of the included studies and to show the broad pattern of normative data when grouped by factors such as UN region.

In my strategy for subsequent analyses I aimed to meet the following two objectives:

i. To consider the precision of individual items of normative data. I was aware that several studies had small sample sizes within individual age groups, so it was important to take the precision of different studies' estimates into account when pooling or comparing results.
ii. To take account of the effect of age when exploring the role of explanatory factors. Studies had considered different stages of the life course, such as childhood and old age, and also used different age ranges at each stage, for example by classifying into five or 10 year age bands. When looking at the overall effect of a study level factor like geographical region, I wanted to be able to convert the results from each study into a form that took account of these age differences.

In terms of the first objective, I calculated the standard error, se of each sample mean in my dataset using the standard deviation for the sample, s and the number of observations in the sample, n as shown below.

Equation 4.a Calculation of standard error of the sample mean

$$se = \frac{s}{\sqrt{n}}$$

4.5.1 Calculation of z-scores

To address the second analysis objective, I used my own normative data from 12 British studies to convert each particular result from included papers into a Z-score. In summary, this involved calculating the mean and standard deviation from my normative data over the same age range as that used for each given result. I then used the calculated mean and standard deviation to express each paper's results as Z-scores. I describe the steps I used to do this using an example, below.

To illustrate the process, I show the steps involved in the calculation of a z-score for one of the items of normative data in Denmark reported by Aadahl et al. [111]. For the age range 30-39 years in men, they report a mean of 52.7kg and a standard deviation of 7.7kg based on 218 observations.

Whereas their mean and standard deviation refer to a range of ages, my normative values from British studies are taken from cubic spline functions and hence refer to exact ages. To produce an equivalent mean and standard deviation for the same age range as the Aadahl et al. sample, I therefore pooled my mean and standard deviation values across the age range 30 to 40 years, using the techniques described below. The reason for using the higher upper limit (40 as opposed to 39 years) is that a participant in the Aadahl et al. sample could conceivably have been aged over 39 years and 6 months, and hence have been closer to age 40 than age 39.

To pool the means from my data, I took the mean of the 21 mean values in men across the age range 30 to 40 years, in steps of 0.5 years. This resulted in a pooled mean, $\bar{x}_p$ of 51.2kg, slightly lower than that reported by Aadahl et al. (52.7kg). It is important to point out that throughout this pooling approach, I made an assumption that the observations in the Aadahl sample were evenly distributed across the age range.

To pool the relevant standard deviations from my data, I calculated a value known as the total mean square, as used in an analysis of variance, and then took the square root of this value [112]. The formulae for doing this are shown in Equation 4.b, below, and the application of the formulae to the age range of 30-40 years in men is shown in Table 4.f on page 69.

The process for pooling standard deviations required an assumption about the number of observations contributing to each standard deviation value that I was pooling. Since my standard deviation values were drawn from cubic spline functions of age, they did not have a number of observations associated with them directly. I experimented with different values for the assumed sample size when calculating pooled standard deviations. I found that values of 50 and above produced similar results, and so used 50 as my assumed sample size. I also considered this to be a reasonable approach as there were very few examples in my dataset of British normative data of years of age which did not have at least 100 observations, or 50 per half year.

Equation 4.b Formulae to calculate pooled standard deviation

The following are based on the guide “Composite standard deviations” by David A. Burton [112].

$$ess = \sum_{i=1}^{k} {s_i}^2 * (n - 1)$$

ess, the overall error sum of squares calculated by summing the error sum of squares based on the standard deviation, s, of k groups (in this example, 21) each containing n observations (assumed to be 50, see text above).

$$gss = \sum_{i=1}^{k} \left(\bar{x}_i - \bar{x}_p \right)^2 * n$$

$$\bar{x}_p = \frac{1}{k} * \sum_{i=1}^{k} \bar{x}_i$$

gss, the overall group sum of squares calculated by summing the group sum of squares based on each group’s mean, $\bar{x}_i$ and the overall pooled mean, $\bar{x}_p$.

$$s_p = \sqrt{\frac{ess + gss}{N - 1}}$$

s_p, the pooled standard deviation calculated using ess, gss and N the sum of the observations across the k groups (in this example there are 21 groups assumed to have 50 observations each, so N is 1,050).

Applying the formulae in Equation 4.b to the age range 30-40 years in men produced a pooled standard deviation of 9.7kg. I show how the formulae produced this value in Table 4.f, below.

Table 4.f Example calculation of a pooled standard deviation

Age (y)	Mean grip, $\bar{x}$ (kg)	SD grip, s (kg)	$s^2 * (n-1)$	$(\bar{x} - \bar{x}_p)^2 * n$
30.0	51.29	10.04	4938.97	0.39
30.5	51.42	10.00	4899.15	2.42
31.0	51.52	9.96	4859.69	5.17
31.5	51.60	9.92	4821.01	7.78
32.0	51.64	9.88	4783.53	9.69
32.5	51.66	9.84	4747.61	10.61
33.0	51.66	9.81	4713.42	10.47
33.5	51.64	9.77	4681.10	9.36
34.0	51.59	9.74	4650.83	7.52
34.5	51.53	9.71	4622.74	5.30
35.0	51.45	9.69	4596.97	3.07
35.5	51.36	9.66	4573.67	1.24
36.0	51.26	9.64	4553.13	0.16
36.5	51.15	9.62	4535.57	0.15
37.0	51.03	9.61	4520.94	1.48
37.5	50.91	9.59	4509.19	4.35
38.0	50.78	9.58	4500.19	8.96
38.5	50.65	9.58	4493.81	15.43
39.0	50.51	9.57	4490.03	23.89
39.5	50.37	9.57	4488.84	34.41
40.0	50.23	9.57	4490.32	47.02
Calculated values (for formulae see Equation 4.b, above)				
	$\bar{x}_p = 51.20$		$ess = 97470.70$	$gss = 208.87$
Pooled standard deviation, $s_p = \sqrt{\frac{ess+gss}{N-1}} = \sqrt{\frac{97470.70 + 208.87}{1050 - 1}} = 9.7$kg				

The table shows the mean and standard deviation values for men from my British normative data for the ages shown.
N, total sample size, assumed to be 1,050 (50 observations per group across 21 groups).

I then used the pooled mean, $\bar{x}_p$ and pooled standard deviation, s_p to calculate how many standard deviations above my pooled mean the value from the Aadahl et al. example was, i.e. the mean on the Z-score scale. In this case, the Aadahl et al. mean value was 0.15 standard deviations above my equivalent mean:

$$Z = \frac{52.7 - 51.2}{9.7} = \frac{1.5}{9.7} = 0.15$$

In order to include normative data items in metaregression analyses, it was also necessary to calculate their standard errors of the sample means on the Z-score scale. Continuing with the Aadahl et al. example, I converted the standard deviation of 7.7kg on to the Z-score scale. Since my equivalent pooled standard deviation is 9.7kg, this means the Aadahl et al. standard deviation on the Z-score scale is 7.7kg divided by 9.7kg, equal to 0.79. I could then calculate the standard error of the sample mean on Z-score scale, using Equation 4.a on page 66:

$$se = \frac{s}{\sqrt{n}} = \frac{0.79}{\sqrt{218}} = 0.054$$

There were examples of studies which had modelled the mean and standard deviation of grip strength as a function of age using approaches such as cubic splines. These studies typically reported normative values for exact ages and where this was the case, I did not need to pool the means and standard deviations for my normative data but rather use the values corresponding to the same ages.

In conclusion, calculating Z-scores using my British normative data as a reference allowed me to address the second aim of my analytical strategy: to make values from different stages of the life course comparable and also to take into account the varying age ranges used by the included studies. I could then use these Z-score values to explore the role of explanatory factors in metaregression, as described in the following section.

4.5.2 Metaregression

In order to investigate the association between factors such as world region and the Z-scores of the normative data items from the included papers, I carried out random-effects meta-regression using the *metareg* command in Stata version 12.0 [94]. This allowed me to investigate to what extent a range of covariates accounted for the variance between the normative data items, and also to produce pooled estimates of Z-scores for different groups [113].

In each model, I generated indicator variables to denote each category, such as for normative data items from European settings in the analysis of mean Z-score by region. I then carried out metaregression using the mean Z-scores of the normative data items (and their associated standard errors) as the outcome and the indicator variables as the predictors. I used the postestimation command *predict* to calculate the pooled mean Z-score value and 95% confidence interval for each category. I also reported the proportion of variance between the normative data items which was explained by the covariates in each model. This value is reported in the output of *metareg* as the adjusted R^2 statistic.

I chose several factors to investigate prior to carrying out the analyses. For the primary objective (see page 55) of this project, I explored the mean Z-scores by world region, classified as described at the start of this statistical analysis section on page 65. As per the secondary objective, I also investigated mean Z-scores by dynamometer type, by whether measurement was carried out in the seated or standing positions, and by the hand to which the extracted normative data related: right/dominant, non-dominant or both. I also looked at whether grip strength differed between papers that reported the maximum or mean value as their summary measure.

As described in the results chapter on page 78, initial charts suggested that the normative data items from countries in developed regions might have higher Z-scores in early adulthood compared to other ages. I therefore carried out additional sensitivity analyses to estimate the mean Z-scores at different stages of the life course. I carried out these analyses separately for countries from developing and developed regions.

Finally I used a cut-off value of ± 0.4 SDs as the threshold for a meaningful difference between a pooled Z-score and my British norms. This is consistent with the ± 10% difference in mean values in kg that I previously used in sensitivity analyses (see section 2.5.4 on page 31). This is because I previously found the coefficient of variation for grip strength, or the standard deviation divided by the mean, to be approximately 0.25. It therefore follows that 10% either side of a mean value for grip strength in kg is equivalent to approximately 0.1 divided by 0.25 = 0.4 SDs on the Z-score scale.

5. Normative data from systematic literature review: results

In this chapter, I describe the characteristics of the papers included in the review and the overall patterns of normative data that I extracted, before reporting the findings from the metaregression analyses that I carried out.

A full list of the included papers and their details is provided in Appendix 4, starting on page 133. Where I cite an included paper in this chapter, I also state the first author's name along with the year if needed to identify the paper. This is to aid the reader if they wish to locate the cited paper in the table in Appendix 4, which is sorted by first author.

5.1 Description of included papers

My systematic literature search resulted in 60 papers for inclusion in the review as shown in the last chapter (see Figure 4.a on page 57). In this section I summarise the characteristics of these included papers, shown for developing and developed countries separately as well as for both combined.

Three of these papers each contained two sets of normative data: Kaur et al. [114] reported data from both urban and rural settings, Massy-Westropp et al. (2004) [57] used two different dynamometers in the same population, and Rodrigues-Barbosa et al. [115] reported data from two countries. I treated these three papers as if they were each two separate publications and hence the total number of papers described in this section is 63.

5.1.1 Characteristics of samples used

The country setting of the included papers is shown in Table 5.a and Figure 5.a, below. Approximately two thirds (n=44) of the papers contained normative data from developed countries. The two regions with the most papers were Europe (29 papers) and Asia excluding Japan (12 papers).

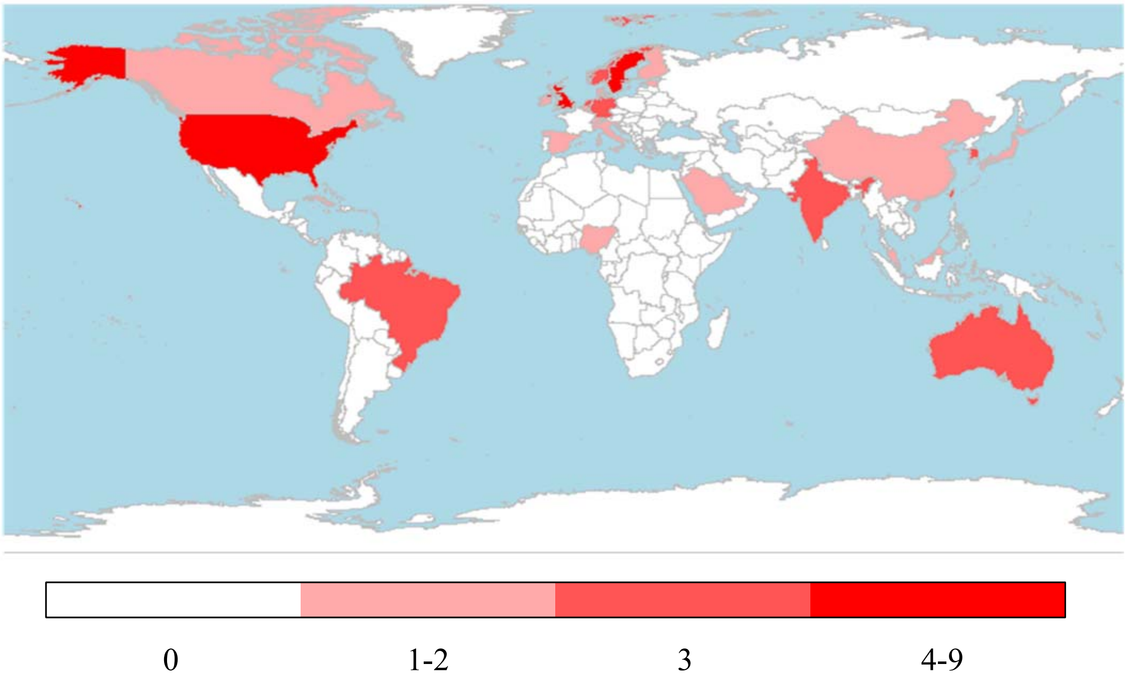
Table 5.a Country setting of included papers, by UN region

Developed status	Region	Country	n
Developing (n=19)	Africa (n=2)	Nigeria	2
	Americas excluding N America (n=5)	Barbados*	1
		Brazil	3
		Cuba	1
	Asia excluding Japan (n=12)	China	1
		India	3
		Korea, Republic of*	3
		Malaysia	1
		Saudi Arabia*	1
		Taiwan, Province of China	3
Developed (n=44)	Australia and New Zealand (n=3)	Australia	3
	Europe (n=29)	Belgium	1
		Denmark	2
		Estonia	1
		Finland	1
		Germany	3
		Ireland	2
		Italy	1
		Netherlands	3
		Norway	3
		Slovenia	1
		Spain	1
		Sweden	4
		Switzerland	1
		United Kingdom	5
	Japan (n=2)	Japan	2
	Northern America (n=10)	Canada	1
		United States	9

* Three countries in developing regions have high-income economies as per the World Bank classification. For more information, see section 4.5 on page 65.

The number of papers for each of the 28 included countries varied, with the majority of countries (n=17) having one or two papers, eight countries having three papers and three countries having more than this: Sweden (4 papers), the United Kingdom (5 papers) and the United States (9 papers).

Figure 5.a Map showing countries of included papers



Colour-coding indicates the number of papers from each country.
Note the rworldmap software highlights Alaska as part of the United States, although all nine studies were from the mainland United States.

The characteristics of the included papers are shown in Table 5.b on page 76. The majority of the papers had been published in the last decade and had produced normative data from convenience samples drawn from a local area or single facility. Around two thirds of the papers (n=45) contained normative data on adult life, with the majority of these including data on individuals aged both below and above 50. Only four papers reported normative data that covered childhood, adolescence and adult ages, such as that by Balogun et al. [91] which had an age range of 7 – 69 years. The overall median sample size per paper was 473 individuals (IQR 199, 1119), with sample size tending to be larger in papers relating to developed (median 514 individuals) as opposed to developing countries (median 336 individuals).

Table 5.b Sample and analysis characteristics of included papers, by region

Characteristic		Developed status n (%)[*]					
		Developing N=19		Developed N=44		Both N=63	
Economy	Low/middle income	14	(74)	0	(100)	14	(22)
	High income	5	(26)	44	0	49	(78)
Year of publication	1985 - 1994	2	(11)	6	(14)	8	(13)
	1995 – 2004	2	(11)	15	(34)	17	(27)
	2005 – 2014	15	(79)	23	(52)	38	(60)
Sample level	National	1	(5)	6	(14)	7	(11)
	Regional	3	(16)	10	(23)	13	(21)
	Local / facility / NS	15	(79)	28	(64)	43	(68)
Sample type	Sampling frame	3	(16)	14	(32)	17	(27)
	Convenience / NS	16	(84)	30	(68)	46	(73)
Gender	Males and females	13	(68)	41	(93)	54	(86)
	Males only	4	(21)	2	(5)	6	(10)
	Females only	2	(11)	1	(2)	3	(5)
Sample size[†]	Median (IQR)	336	(120, 840)	514	(270, 1479)	473	(199, 1119)
Stage of life course	Child / adol. ≤ 18 y	3	(16)	11	(25)	14	(22)
	Adults all < 50 y	2[‡]	(11)	2	(5)	4	(6)
	Adults all ≥ 50 y	4	(21)	9	(20)	13	(21)
	Adults, both ages	8	(42)	20[§]	(45)	28	(44)
	All stages above	2	(11)	2	(5)	4	(6)

NS, not specified.

[*] Unless otherwise specified. Please note all percentages are rounded to the nearest whole percentage point, and hence the total for each group may not equal 100.

[†] This refers to the sample size for the age ranges extracted from each paper. This value is smaller than the sample size provided in papers which had included open-ended age ranges such as 75+ years (see section 4.3.2 on page 61).

[‡] The paper by Chatterjee et al. [116] had an age range of 10-49 years and for the purpose of this table I classed this as a young adult paper.

[§] The paper by Backman et al. [117] had an age range of 17-70 years and I classed this as adults, both ages.

5.1.2 Protocol for grip measurement and reporting of normative data

Several characteristics of the protocols used for grip strength measurement and the reporting of normative data items are shown in Table 5.c, below. The majority of papers did state the device used, with the Jamar hydraulic dynamometer being the most common and used in approximately half of the included papers. Other manufacturers of hydraulic dynamometers included Takei as used in six papers, and Baseline and

Smedley, both in three papers. Finally nine papers reported using a variety of electronic dynamometers.

The majority of papers had measured grip in the seated position, with the remainder having measured grip standing or not describing the position used. Some papers did include further information such as elbow positioning and support, although I did not attempt to extract these details as they were not described in the majority.

I had looked to extract normative data for participants' maximum grip strength taken from multiple trials of both hands, as described in section 4.3.1 on page 59. In fact the majority of papers reported grip strength stratified by hand, as either right and left, or dominant and non-dominant, and so for such papers I extracted data from the right / dominant hand as available. Most papers had used either two or three trials per hand.

In terms of reporting of grip strength, half of papers reported the maximum value from multiple trials, with the remainder reporting the mean or not stating the descriptive statistic they used. Only three of the 63 papers had stratified grip strength by height: Frederiksen et al. [105], Kenny et al. [52] and Spruit et al. [106]. The majority of papers had used descriptive statistics to generate the normative data items, with four papers using a modelling technique such as cubic splines.

Table 5.c Protocol and reporting characteristics of included papers, by region

		Developed status n (%)[*]					
		Developing N=19		Developed N=44		Both N=63	
Characteristic							
Dynamometer	Jamar hydraulic	8	(42)	23	(52)	31	(49)
	Other - hydraulic	6	(32)	12	(27)	18	(29)
	Electronic	3	(16)	6	(14)	9	(14)
	NS	2	(11)	3	(7)	5	(8)
Position	Seated	11	(58)	32	(73)	43	(68)
	Standing	5	(26)	7	(16)	12	(19)
	NS	3	(16)	5	(11)	8	(13)
Hand(s) described in extracted data	Right / dominant	17	(89)	32	(72)	49	(78)
	Non-dominant	0	(0)	4	(9)	4	(6)
	Both	2	(11)	8	(18)	10	(16)
Summary of trials	Maximum	12	(63)	22	(50)	34	(54)
	Mean	5	(26)	13	(30)	18	(29)
	NS	2	(11)	9	(20)	11	(17)
Analysis	Descriptive / NS[†]	19	(100)	40	(91)	59	(94)
	Model fitted to data	0	(0)	4	(9)	4	(6)

NS, not specified.

[*] Unless otherwise specified. Please note all percentages are rounded to the nearest whole percentage point, and hence the total for each group may not equal 100.

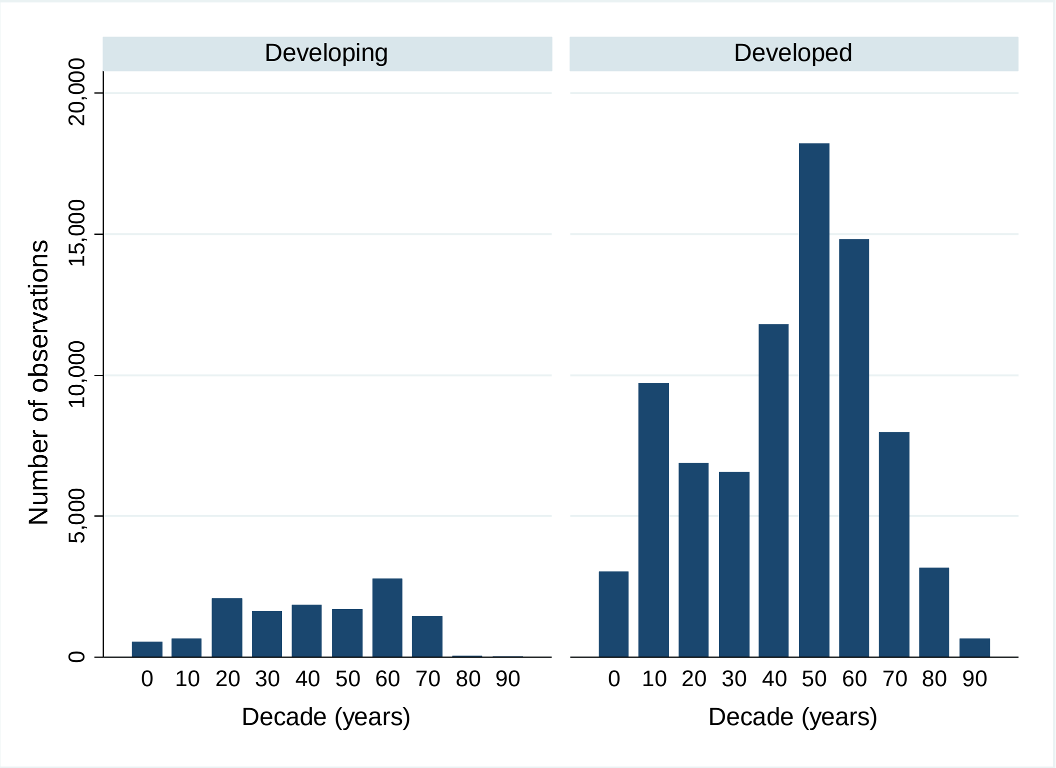
[†] I assumed that descriptive statistics had been used when the paper did not specify otherwise.

5.2 Description of extracted normative data

In total, I extracted 730 normative data items relating to approximately 95,625 grip strength observations. The value was approximate as in the paper by Spruit et al. [106] it was necessary to make the assumption that the overall sample sizes for men and women they provided were equally distributed across the eight height groups into which they had stratified their normative data. Twenty-nine of the 63 papers had also included open-ended age ranges; on average this meant discarding 18% of their samples since I did not include open-ended age ranges in my analyses.

There was reasonable coverage of the life course in both developed and developing regions, although the majority of observations (82,856 or 87%) came from developed regions as shown in Figure 5.b, below. Of the observations from developed regions, the majority were from the European region (68,686 or 83%).

Figure 5.b Number of observations by age and developed status

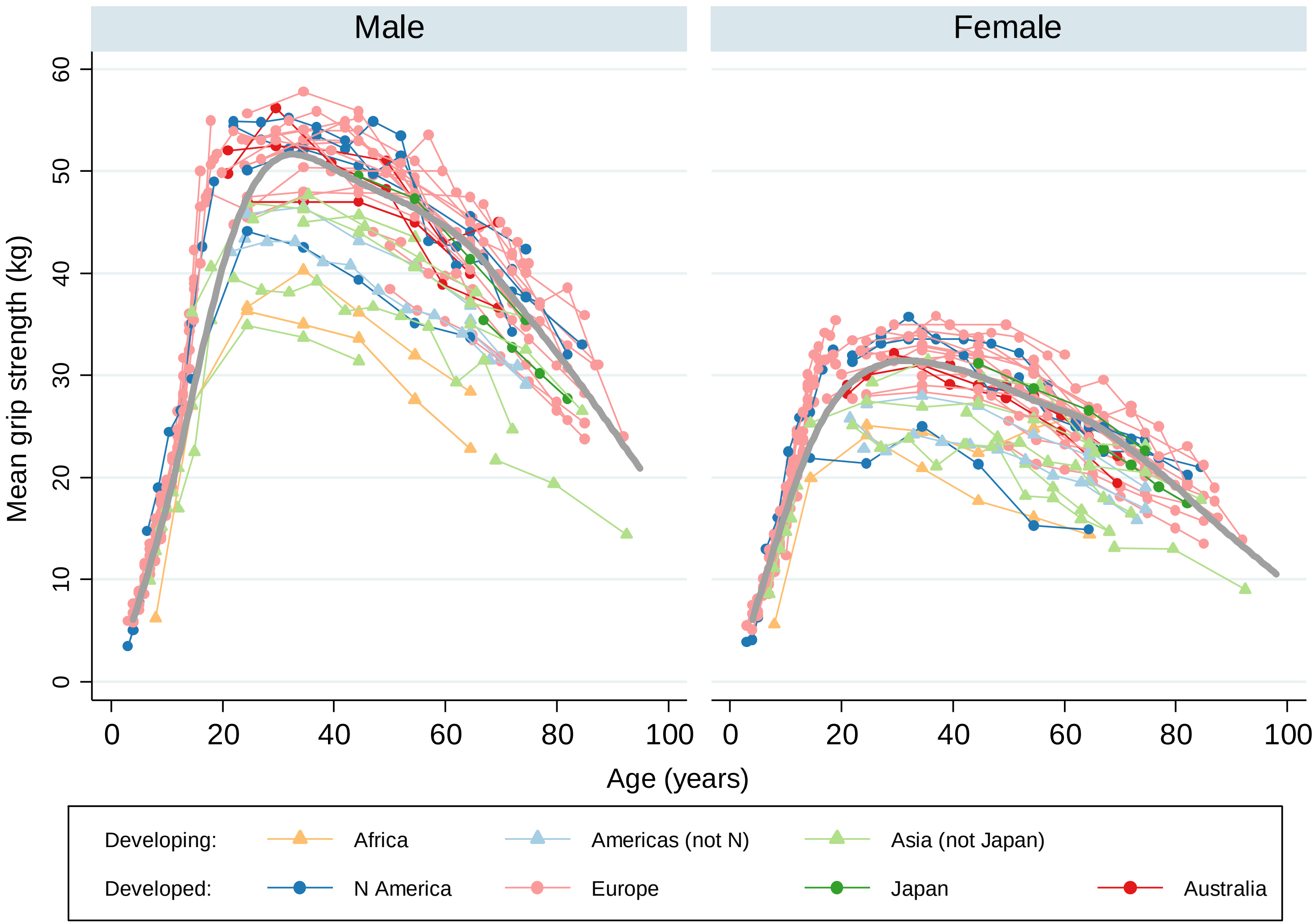


I plotted the normative data items from the included papers, grouped by UN region as shown in Figure 5.c, below. I included my curve of mean grip strength from 12 British studies for comparison. The broad pattern of mean grip strength across the life course from the included papers appeared similar to my findings from 12 British studies. In both males and females there was an increase to peak in early adult life, broad maintenance through to midlife and decline from midlife onwards.

There was also a clear separation between papers based in developed regions, which were typically located around or slightly above the mean curve from the 12 British studies, and papers from developing regions, which were typically beneath the mean curve.

Figure 5.c Grip strength mean values from included papers, by region

Each point represents the mean value of grip strength for each item of normative data, plotted against the mid-point of the age range it relates to. Values from the same paper are connected. Data from developing and developed regions are shown with triangles and circles, respectively. For comparison, the grey line shows the mean values from my normative data for 12 British studies.



I considered that the appearance of the plots in Figure 5.c, specifically the similar broad pattern of normative data items to my British studies across the life course, supported the use of Z-scores to convert the normative data items into a form suitable for metaregression analyses as previously described in section 4.5.1 on page 66. These analyses included the estimation of a single pooled Z-score for each UN region at all ages, and again Figure 5.c suggested that such an approach was justified given the reasonably consistent separation of UN regions across the life course.

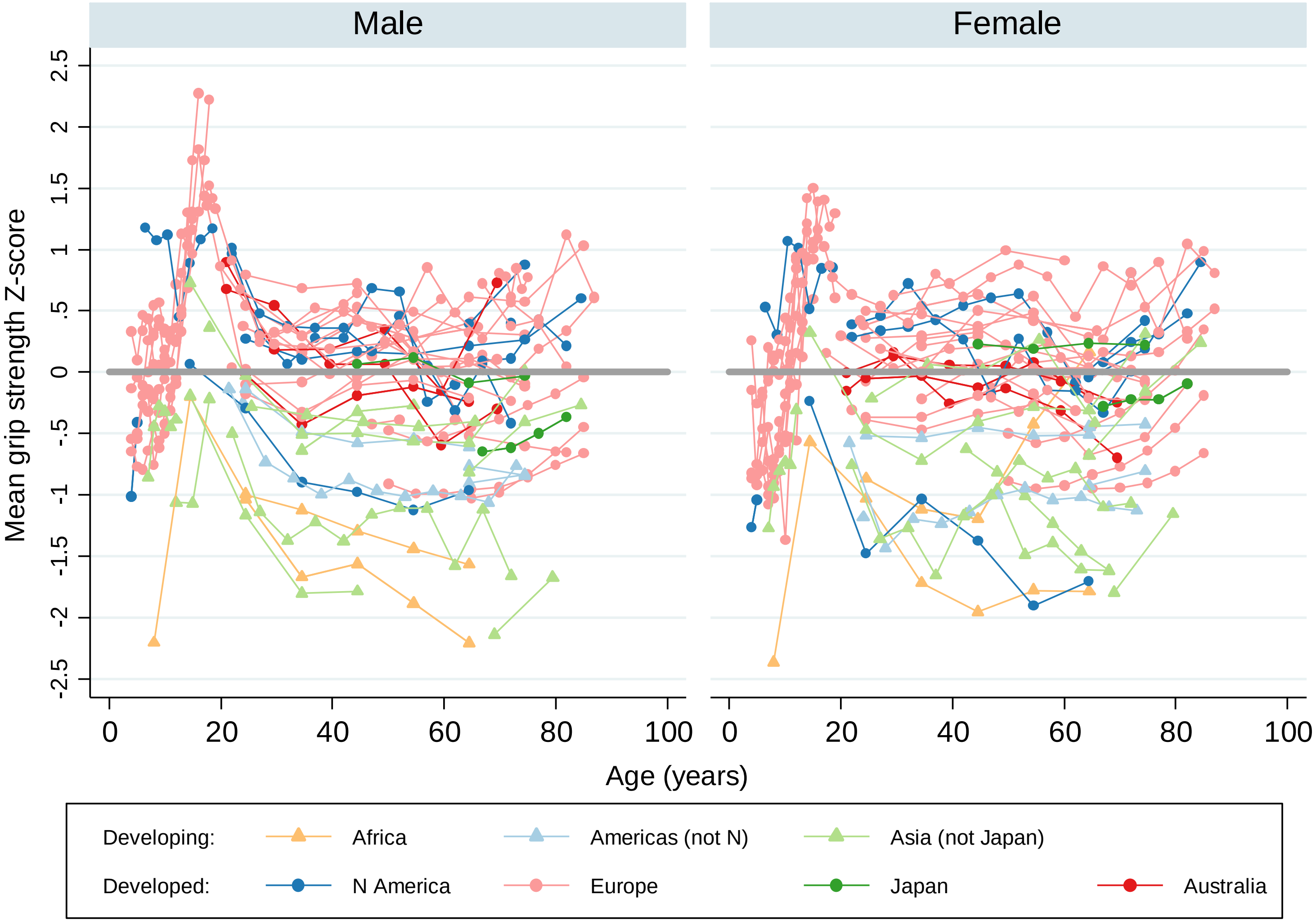
Ten items of normative data from five papers [105,118–121] had an age range outside my British norms (ages 4 to 90 years). They were therefore excluded when I converted the normative data items into Z-scores, leaving 720 items of normative data for subsequent analysis.

Figure 5.d, below, shows these items in the same way as previously used in Figure 5.c, except using the Z-scores of the normative data items. As such the mean values from my British studies are shown as a line with a value of zero throughout.

The use of the Z-score scale highlighted a small group of papers at young ages based in the European region with high mean grip strength values. Specifically, the papers by Hager Ross [49], Lang [121] and Rauch [122] contained results in males between ages 15 and 20 that were over 1.5 SDs above the corresponding mean values from my British studies. I consider these differences further in section 5.3.3, Grip strength by stage of the life course.

Figure 5.d Grip strength Z-scores from included papers, by region

Each point represents the Z-score for the mean value of grip strength provided in the paper, plotted against the mid-point of the age range it relates to. Values from the same paper are connected. Data from developing and developed regions are shown with triangles and circles, respectively. For comparison, the grey line shows the mean values from my normative data for 12 British studies (for which by definition, Z = 0).



5.3 Findings from metaregression analyses

5.3.1 Grip strength by world region

The pooled grip strength Z-scores by world region are shown in Table 5.d, below. The pooled Z-score from the 19 countries in developing regions was substantially below my British normative values at -0.86 (95% CI: -0.95, -0.77). This compared to that from developed regions which was only slightly above my British values at 0.12 (95% CI: 0.07, 0.17).

Table 5.d Pooled Z-scores by different country classifications

Classification	N [*]	Pooled Z-score	(95% CI)	Adjusted R^2 [†]
None	63	-0.09	(-0.15, -0.04)	-
UN region status				34.1%
Developing	19	-0.86	(-0.95, -0.77)	
Developed	44	0.12	(0.07, 0.17)	
Economic status				32.4%
LMIC	14	-0.97	(-1.08, -0.86)	
HIC	49	0.08	(0.03, 0.13)	
UN world region (with references shown)				36.3%
Africa [91,123]	2	-1.34	(-1.57, -1.11)	
Americas excluding N America [115,124–126]	5	-0.80	(-0.97, -0.63)	
Asia excluding Japan [108,114,116,120,127–133]	12	-0.76	(-0.88, -0.64)	
Australia and New Zealand [57,134]	3	-0.01	(-0.20, 0.18)	
Europe (See below[‡])	29	0.13	(0.07, 0.19)	
Japan [135,136]	2	-0.13	(-0.41, 0.15)	
Northern America [48,118,137–144]	10	0.16	(0.04, 0.28)	

Results shown are from separate metaregression models of all 720 normative data items, with model term(s) those for each classification shown.

[*] N, number of papers contributing to each subgroup.

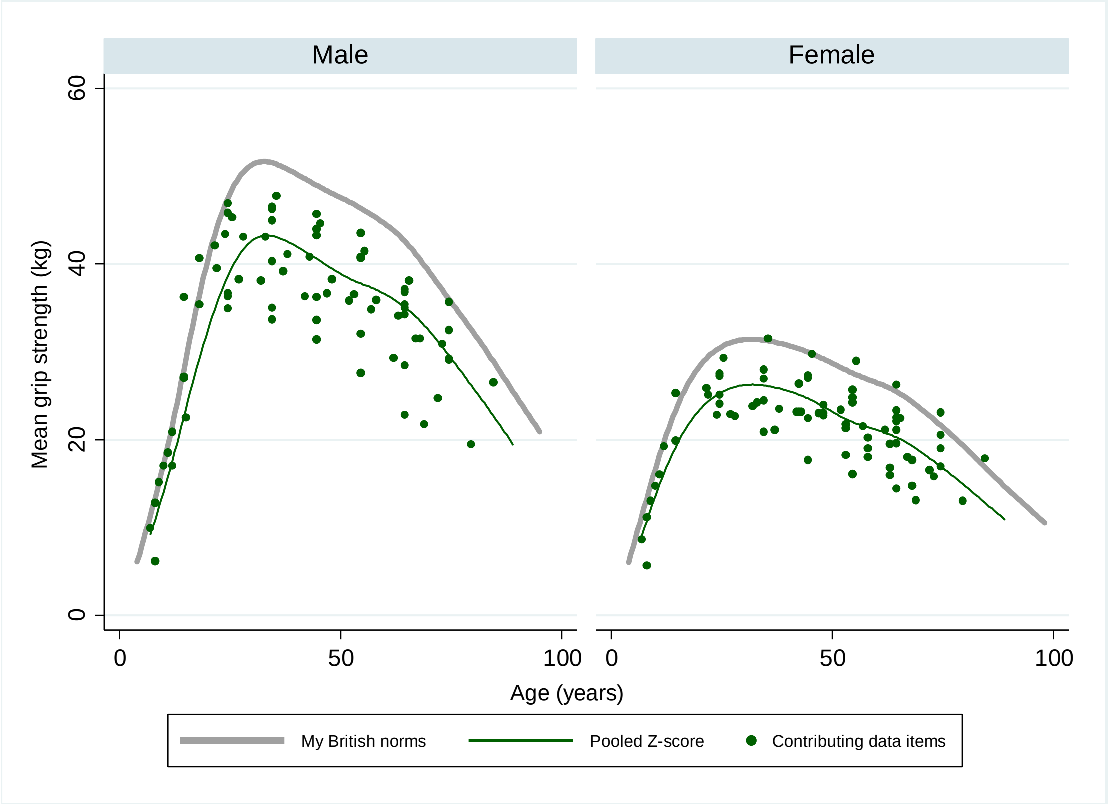
[†] The adjusted R^2 is the proportion of variance between each item of normative data explained by each of classifications.

[‡] References for Europe as follows: [49,50,52,56,63,85,105,106,111,117,119,121,122,145–160]

Figure 5.e and Figure 5.f, below, show the pooled Z-scores from developing and developed regions, converted back to the kg scale, alongside the contributing normative data items. They suggested that either side of the pooled value, there was substantial variation in the normative data items for each type of region. I also pooled normative data items by their countries’ economic status and by specific world regions. Both of these further classifications gave similar results as using whether a region was

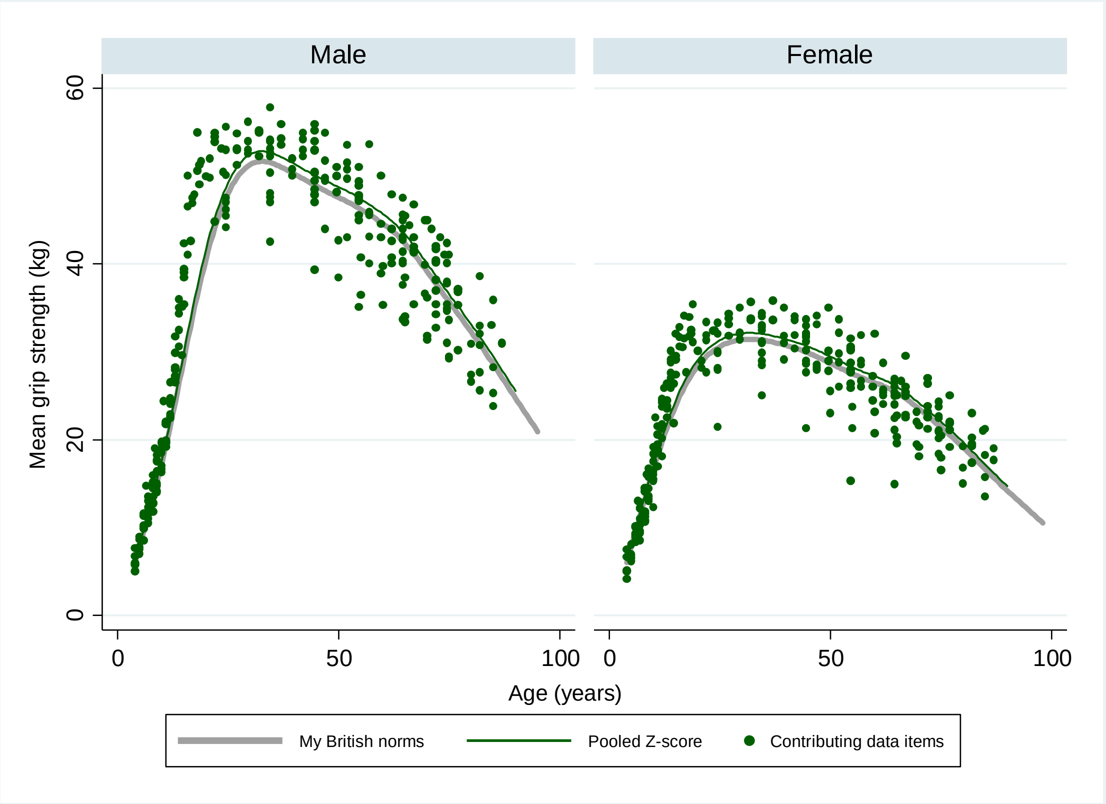
developed or developing, including explaining a similar proportion of the variance between normative data items (the adjusted R^2 statistic) as shown in Table 5.d.

Figure 5.e Pooled Z-score in developing regions



This chart shows the pooled Z-score of -0.86 for developing regions, plotted as grip strength in kg alongside the mean curve from my British normative data. The 157 normative data items contributing to the pooled Z-score are also shown.

Figure 5.f Pooled Z-score in developed regions



This chart shows the pooled Z-score of +0.12 for developed regions, plotted as grip strength in kg alongside the mean curve from my British normative data. The 563 normative data items contributing to the pooled Z-score are also shown.

The above figures suggested that there clearly was variance between items of normative data in developing and developed regions. I chose to explore this variation further by focussing on the European region, for two reasons: firstly this region had the largest number of included papers, and secondly because I wished to test if the pooled Z-score from British papers was different to my British normative data.

The pooled Z-scores for each European country are shown in Table 5.e, below, and also in map form in Figure 5.g on page 89. The majority were within ± 0.4 SDs of my normative data from 12 British studies, including the pooled value from the five papers based in the United Kingdom. One of these papers, by Nevill et al. [85], contained the data from one of the 12 British studies. The exclusion of this paper made no difference to the pooled Z-score value: 0.06 (95% CI: -0.10, 0.22).

Three countries fell outside the limits of ± 0.4 SDs, either below in the case of Ireland (pooled Z-score of -0.62), or above in the case of Germany (pooled Z-score of 0.53) and Switzerland (pooled Z-score of 0.60). These results were based on a small number of papers in each country. There were two papers based in Ireland: Corish et al. [148] and Kenny et al. [52], the latter being a large representative sample at national level.

Two of the three papers based in Germany, Lang et al. [121] and Rauch et al. [122] were samples based in childhood and adolescence. As already described in section 5.2 on page 78, the Z-scores of the normative data items from these studies were substantially above my British norms. I calculated the pooled Z-score for the remaining paper based in Germany, a convenience sample of adults by Gunther et al. [119] and found it to be 0.30 (95% CI: 0.18, 0.42). This suggested that the effect of the other two papers in early life was to inflate the pooled result for Germany overall.

Finally there was one paper based in Switzerland, by Werle et al. [158]. They had used a convenience sample from a range of locations including local shopping centres.

Table 5.e Pooled Z-scores for papers based in Europe

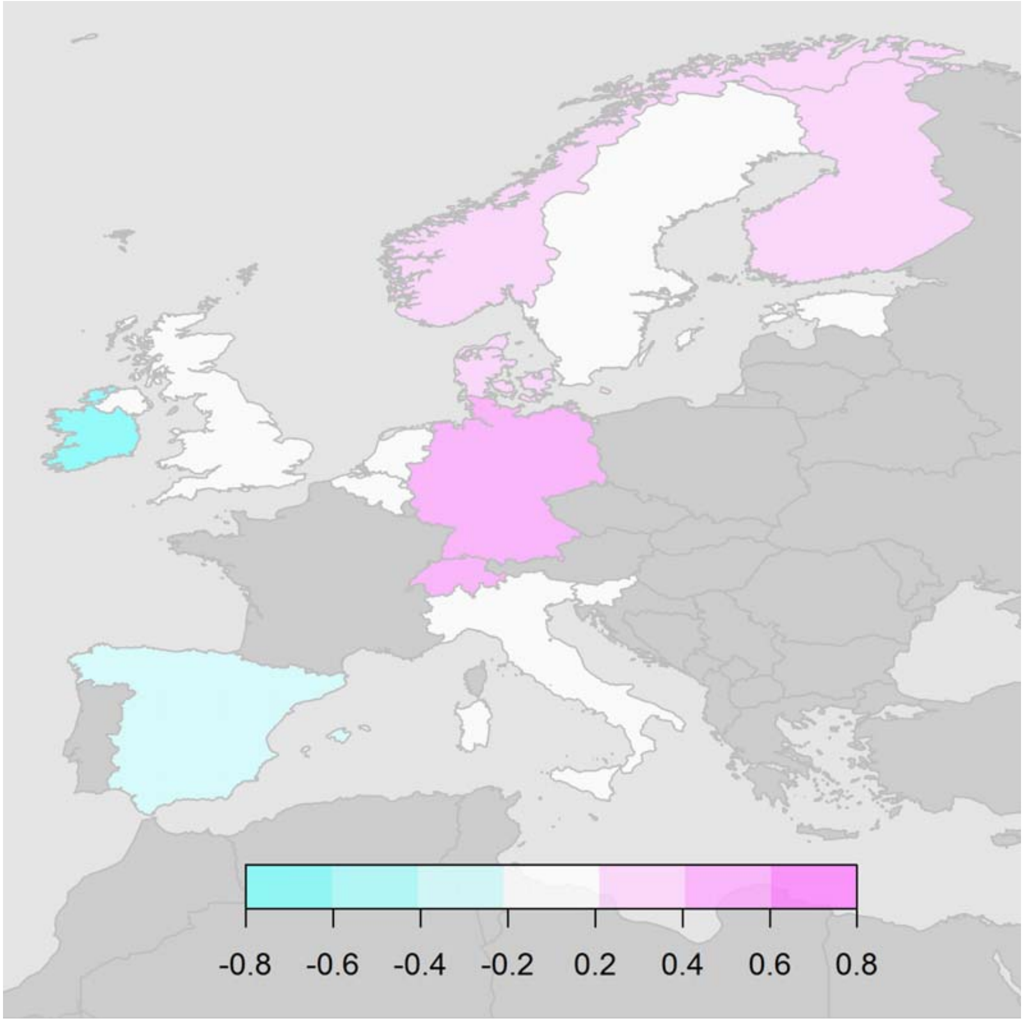
Classification		N *	Pooled Z-score	(95% CI)	Adjusted R^2 †
None		29	0.13	(0.07, 0.19)	-
Country	**Reference(s)**				33.8%
Ireland	[52,148]	2	-0.62	(-0.77, -0.47)	
Spain	[56]	1	-0.21	(-0.50, 0.08)	
Estonia	[146]	1	-0.19	(-0.50, 0.12)	
Italy	[149]	1	-0.13	(-0.80, 0.54)	
Netherlands	[63,150,151]	3	-0.06	(-0.20, 0.08)	
Belgium	[145]	1	0.06	(-0.16, 0.28)	
United Kingdom	[50,85,106,159,160]	5	0.09	(-0.04, 0.22)	
Slovenia	[155]	1	0.14	(-0.22, 0.50)	
Sweden	[49,117,156,157]	4	0.19	(0.05, 0.33)	
Denmark	[105,111]	2	0.24	(0.06, 0.42)	
Norway	[152–154]	3	0.33	(0.17, 0.49)	
Finland	[147]	1	0.36	(-0.14, 0.86)	
Germany	[119,121,122]	3	0.53	(0.40, 0.66)	
Switzerland	[158]	1	0.60	(0.41, 0.79)	

Results shown are from metaregression models using the 419 normative data items from the European region. The pooled Z-scores for normative data items from each European country are shown, ordered from lowest to highest.

* N, number of papers in each subgroup.

† The adjusted R^2 is the proportion of variance between each item of normative data explained by the use of countries as predictor variables.

Figure 5.g Pooled Z-scores for each European country



The map shows the pooled Z-score for each European country for which papers were included, with shading indicating the value. Countries without included papers are shown in dark grey.

5.3.2 Grip strength by protocol and reporting of normative data

Overall I saw no major differences between normative data items which had been collected with different dynamometer types or in the seated or standing positions, as shown in Table 5.f, below. Similarly I saw little difference by the hand for which normative data were described and the summary measure of separate trials. A small number of papers had not included the relevant information on protocol and reporting in their methods; the five papers which had not reported the dynamometer type used did have a pooled Z-score below my British norms at -0.53 (95% CI: -0.75, -0.31).

Table 5.f Pooled Z-scores by protocol and reporting factors

Classification	N [*]	Mean Z-score	(95% CI)	Adjusted R^2 [†]
None	63	-0.09	(-0.15, -0.04)	-
Dynamometer				7.9%
Jamar hydraulic	31	0.08	(0.01, 0.15)	
Other - hydraulic	18	-0.28	(-0.38, -0.18)	
Electronic	9	-0.21	(-0.34, -0.08)	
NS	5	-0.53	(-0.75, -0.31)	
Position				7.6%
Seated	43	0.03	(-0.03, 0.09)	
Standing	12	-0.35	(-0.46, -0.24)	
NS	8	-0.45	(-0.62, -0.28)	
Hand(s) described in extracted data				5.1%
Right / dominant	49	-0.11	(-0.17, -0.05)	
Non-dominant	4	0.35	(0.19, 0.51)	
Both	10	-0.28	(-0.39, -0.17)	
Summary of trials				0.6%
Maximum	34	-0.13	(-0.20, -0.06)	
Mean	18	-0.09	(-0.20, 0.02)	
NS	11	0.01	(-0.11, 0.13)	

Results shown are from separate metaregression models of all 720 normative data items, with model term(s) those for each classification shown.
NS, not specified.
[*] N, number of papers in each subgroup.
[†] The adjusted R^2 is the proportion of variance between each item of normative data explained by the use of protocol and reporting factors as predictor variables.

5.3.3 Grip strength by stage of the life course

I previously identified normative data items in early life with a Z-score substantially above my British norms, as described in section 5.2 on page 78. I therefore undertook sensitivity analyses to examine the pooled Z-scores for each stage of the life course. I separated the life course into the following stages: under 15 years, 15 to 25 years (where the Z-scores were higher), 25 to 45 years (the approximate age range of peak grip strength) and greater than 45 years. The results are shown in Table 5.g and Table 5.h, below.

In countries in developing regions, there was some evidence that normative data items in the two age groups below age 25 were closer to my British norms than those above age 25. For example, the pooled Z-score between ages 15 and 24 was -0.59 (95% CI: -0.85, -0.33) compared to -0.98 (95% CI: -1.15, -0.81) between ages 25 and 44.

Table 5.g Pooled Z-scores in different age groups in developing regions

Classification	N [*]	Mean Z-score	(95% CI)	Adjusted R^2 [†]
None	19	-0.86	(-0.95, -0.77)	-
Age group				4.2%
< 15 y	5	-0.66	(-0.90, -0.42)	
≥ 15 y and < 25 y	10	-0.59	(-0.85, -0.33)	
≥ 25 y and < 45 y	11	-0.98	(-1.15, -0.81)	
≥ 45 y	14	-0.91	(-1.03, -0.79)	

Results shown are from metaregression models using the 157 normative data items from developing countries. The pooled Z-scores for normative data items from each age group are shown.

[*] N, number of papers in each subgroup. Note each paper could contribute to more than one age group and hence the total N across the four subgroups is greater than 19.

[†] The adjusted R^2 is the proportion of variance between each item of normative data explained by the use of age groups as predictor variables.

In countries in developed regions, the pooled Z-scores across the different age groups were similar to my British norms except between ages 15 and 24. Here the pooled Z-score was considerably above my British norms, at 0.71 (95% CI: 0.58, 0.84).

Table 5.h Pooled Z-scores in different age groups in developed regions

Classification	N [*]	Mean Z-score	(95% CI)	Adjusted R^2 [†]
None	44	0.12	(0.07, 0.17)	-
Age group				14.3%
< 15 y	12	0.02	(-0.07, 0.11)	
≥ 15 y and < 25 y	23	0.71	(0.58, 0.84)	
≥ 25 y and < 45 y	21	0.17	(0.06, 0.28)	
≥ 45 y	31	0.00	(-0.07, 0.07)	

Results shown are from metaregression models using the 563 normative data items from developed countries. The pooled Z-scores for normative data items from each age group are shown.

[*] N, number of papers in each subgroup. Note each paper could contribute to more than one age group and hence the total N across the four subgroups is greater than 44.

[†] The adjusted R^2 is the proportion of variance between each item of normative data explained by the use of age groups as predictor variables.

6. Discussion: findings, strengths and limitations

6.1 Main findings

I begin this discussion chapter by summarising the main findings from my thesis.

6.1.1 Normative data from 12 British studies

I combined data from 12 general population studies conducted in Great Britain to produce normative data for grip strength across the life course. This has shown that grip strength increases to a peak in early adult life, and is then followed by a period of broad maintenance prior to decline with increasing age.

This thesis also shows that the strength of males and females is similar until adolescence, after which males' strength increases to a higher peak median of 51kg between ages 29 and 39, compared to the peak female median grip of 31kg between ages 26 and 42. The prevalence of weak grip strength, defined as strength at least 2.5 SDs below the gender-specific peak mean, increased sharply with age, reaching 23% in males and 27% in females by age 80.

Sensitivity analyses demonstrated that the normative data produced by this thesis are robust to a range of dynamometer types and also to measurement in the seated or standing positions.

These normative data for grip strength will facilitate the study of influences on grip strength across the life course and inform the development of future interventions. They will help with the clinical interpretation of grip strength measurements, such as by helping to establish thresholds of low muscle strength for the identification of sarcopenia in clinical practice. I expand on these areas in the next chapter.

6.1.2 Normative data from systematic literature review

I carried out a systematic literature review of published normative data for grip strength returning 60 papers, three of which had included two sets of normative data. The majority were based in countries in developed regions according to the UN classification. The extracted normative data followed the same pattern across the life course as my findings from 12 British studies. There was evidence of clear separation between papers based in developing and developed regions, with pooled Z-scores of -0.86 (95% CI: -0.95, -0.77) from the former and 0.12 (95% CI: 0.07, 0.17) from the latter.

I found that published normative data using different types of dynamometer, as well as in the seated and standing positions had acceptably similar pooled Z-score values. This was also the case when I grouped papers by reporting of the hand(s) measured and the summary used for multiple trials.

As consensus definitions for sarcopenia are developed, the question of whether a single set of normative data for grip strength can be applied across a range of different countries is an important one. The additional analyses I undertook of results from Europe suggest that in many cases this may be possible, although they also highlight how future work in this area would benefit from the use of samples at a national level to produce norms for each country.

6.2 Interpretation of findings

I now consider the findings from my thesis in more detail. Where possible, I draw together findings from both the 12 British studies and the systematic literature review.

6.2.1 The pattern of grip strength across the life course

The pattern of grip strength shown by my normative data from 12 British studies is similar to the trajectory for a range of physiological measures described as part of the life course framework, with growth to peak and subsequent decline [161]. I also saw this pattern across a range of different countries in the results from my systematic literature review. This pattern was also shown by Bruce [162] who plotted four sources of normative data for grip strength spanning between 1842 and 1990. He shows them on a relative scale, with the data from each plotted as a percentage of the peak value from that time period. This approach highlights that in the more recent cohorts, the onset of age-related decline appears to have occurred later than it does in the historical cohorts.

I saw some evidence that the mean curve for grip strength that I modelled may have underestimated the rate of growth in adolescence and early adulthood. Specifically I noted this with regard to the ADNFS study when carrying out dynamometer-specific analyses (section 3.4 on page 46) and also from the graph of normative data items' Z-scores (Figure 5.d on page 82). This was not seen for all studies included in my British norms nor for all papers in my systematic literature search, however. Another explanation is therefore that biases in recruitment may have led to selection of taller and stronger individuals in the relevant samples. It is recognised that the young adult age group may be difficult to recruit to cohort studies, particularly in men [163].

I described a period of broad maintenance following growth to peak and preceding age-related decline. It could be argued that the pattern is more simply growth reaching an instantaneous peak before decline. I considered that the fourth decade in men and women, when mean grip strength remained unchanged to the nearest whole kg, did represent a period of broad maintenance. Nahhas et al. [164] examined trajectories of grip strength and chose to model these using a plateau phase where grip was constrained to remain constant. They estimated the plateau to begin in the fourth decade and extend to age 56 in men and age 50 in women.

6.2.2 Gender differences in grip strength

My results from 12 British studies (Figure 3.e, see page 41) showed that males were stronger on average than females from adolescence onwards. At age 50, males' grip strength was approximately 1.7 times that of females and that this ratio remained the same with increasing age. Cooper et al. [69] previously carried out a meta-analysis of gender differences in grip strength using five of the studies included in this work (NSHD, ELSA, HCS, HAS and LBC1921), covering mean ages 53 to 79 years. They reported the gender difference within each study after adjustment for age, height and weight. The adjustments likely explain why my findings for the unadjusted difference in median grip strength across these ages were similar in pattern but larger in magnitude. For example, they reported that men were on average 10kg stronger than women in LBC1921 (mean age 79) after adjustments; in comparison, I found a difference in median grip strength between men and women at age 80 of 13kg.

6.2.3 Comparison of my normative data to other published British norms

My systematic literature review provided an opportunity to compare the mean from my normative data from 12 British studies to other published values. My literature search returned five such papers and their pooled Z-score suggested they were consistent with my findings for mean grip strength, as shown in Table 5.e on page 88.

The five papers covered all stages of the life course. Cohen et al. [159] reported findings from the East of England Healthy Hearts study in childhood and adolescence. Nevill et al. [85] used the ADNFS to look at ages from adolescence to old age. Spruit et al. [106] reported findings from UK Biobank, between ages 45 and 64. Finally Pearl et al. [160] and Skelton et al. [50] used convenience samples across adult ages and in old age, respectively.

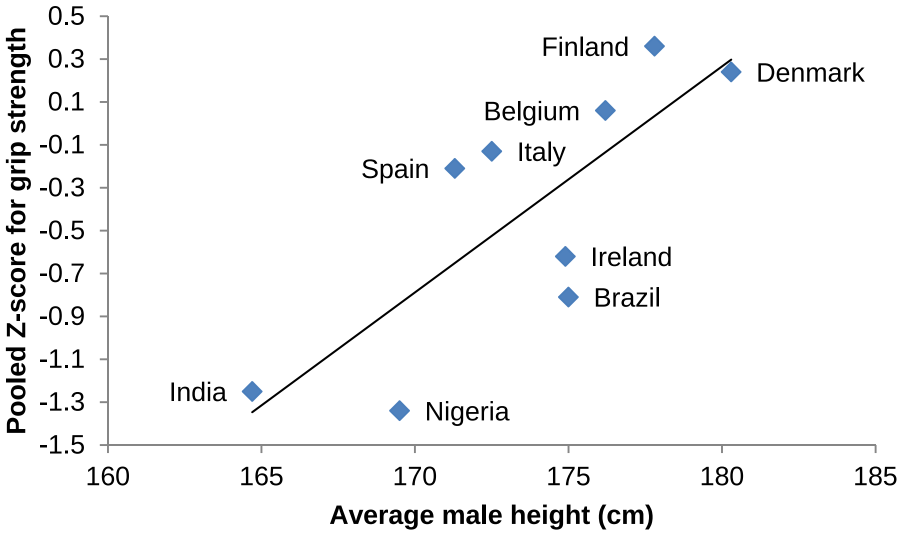
When I researched studies for my British norms, I found the ADNFS and accessed data from it using the Economic and Social Data Service. I was not aware of the grip strength data in UK Biobank and the paper by Spruit et al. [106] was not published until after I had produced my centile curves. I was also not aware of the East of England Healthy Hearts Study. However the pooled Z-score result for British papers in my review suggests that if I had been able to include these additional resources, my centile values would be unchanged.

6.2.4 Differences in grip strength by country

I saw clear separation between published normative data from developed and developing regions. Published data from developed regions were broadly similar to my British norms, whereas those from developing regions were 0.86 SDs lower on average. To illustrate this, the pooled Z-score I found for developing regions is equivalent to mean grip strength at age 30 of 43 kg in men, as opposed to 51 kg as seen in my 12 British studies. I saw less marked differences when I investigated the variation of pooled Z-scores for countries within the European region.

There are likely to be multiple factors which are patterned differently between countries and that may partly account for the variation observed in mean grip strength values. An obvious example is height which is positively associated with grip [165]. I therefore explored if there was evidence of an ecological association between average height and pooled Z-scores at the country level. I used adult heights for men born in 1950-55 for six countries from the European Community Household project [166], a more recent Nigerian cohort [167] and an existing compilation of average heights for Brazil and India [168]. As shown in Figure 6.a, below, there appeared to be a correlation between height and grip strength.

Figure 6.a Pooled Z-scores for selected countries in relation to average height



For source of average male height values, see preceding text. Pooled Z-scores for grip strength from my systematic literature review.

It is likely that grip strength and height both reflect a variety of exposures affecting growth such as nutrition, genetic and epigenetic factors. Grip strength may additionally be influenced by factors affecting body composition, and differences in the patterning of these factors may therefore also account for the differences seen between countries.

An alternative explanation for the country differences is that they relate to sample factors. This is of particular relevance for countries where I only had a small number of papers available. In this situation a recruitment bias in one paper towards healthier individuals could then lead to a higher pooled Z-score for a given country. The secular increase in height, and hence likely in grip strength, is also known to be considerable in some countries. If included papers tended to sample in the same period from one country at younger ages and another country at older ages, this could have led to an apparent difference between the pooled Z-scores of the two countries which in fact reflects the difference in the age groups used.

6.2.5 Differences in grip strength by protocol and reporting factors

From the sensitivity analyses in my British normative data, I conclude that the different dynamometers used, namely the Jamar, Smedley, Nottingham electronic, Takei, and Harpenden dynamometers, produce acceptably similar normative data, albeit within the limits at which measurements were observed using each device (the latter two devices being used only in older cohorts and in relatively small numbers of people). I also recognise that in these data, it is not possible to unpick the effect of dynamometer from other study effects since the two are collinear. My systematic literature review also did not find evidence of differences between Jamar, other hydraulic and electronic dynamometers. I am not aware of any other studies which have compared the normative data obtained from general population samples using different dynamometer types.

Two of the studies reviewed in the introduction looking at the effect of dynamometer type on the measurement value recorded (section 1.4.1, page 10) made comparisons that were relevant to the types of dynamometer used in my project on British normative data. Amaral et al. [53] compared measurements from the Jamar hydraulic and Takei digital dynamometers among 18 volunteers (eight male and 10 female) at mean age 20 years. They reported statistically significant differences between the mean values observed with the two dynamometers, with the Jamar dynamometer producing values which were on average 17% stronger. Guerra et al. [54] compared measurements from the Jamar hydraulic and Smedley dynamometers among 55 volunteers (42 women and 13 men) aged approximately 80 years. They found that the Jamar values were on average 3.3kg higher than those from the Smedley in women (mean 12.2kg) and 2.6kg higher in men (mean 22.2kg). Overall, it appears that further studies with a greater number of participants and across a wider age range would be needed to establish if measures taken from the same individual with different dynamometers are comparable or not.

In terms of the position of measurement, my results from both projects show that normative data from studies using the seated and standing positions are comparable. In my British normative data project, I saw that older individuals who chose not to stand or were unable to do so tended to have weaker grip, as would be expected. As described in the introduction, three small studies of repeat measurements investigating the role of measurement position have also not found evidence of a difference between the seated and standing positions [66–68].

Finally from my systematic review I did not see evidence of difference in grip strength by the hand used for measurement, or by whether the mean or maximum was used to summarise repeat trials.

Overall my thesis has not found evidence of differences in grip strength due to measurement protocol and reporting. Nevertheless this does not detract from the importance of recent calls for standardisation of the measurement of grip strength in future data collections [89,169].

6.3 Strengths and limitations

6.3.1 Normative data from 12 British studies

The project on normative data from 12 British studies had some limitations. First, my data contained a limited range of birth years (at most 32 years) for any given ten year age group (see Figure 3.b, page 36). As such I cannot be certain that the relationships shown with age do not partly represent cohort effects as demonstrated in a study where grip strength had been measured in successive birth cohorts [164]. However, the aim of this project was to produce normative data for current use and as such, the recent period of data collection (with its associated wide range of birth years) seems appropriate.

Second, I emphasise that the normative data for grip are cross-sectional and are likely to underestimate individual decline in grip strength; the centiles should therefore not be used for monitoring individual trajectories of grip strength [105,170,171].

Third, this project did not consider the potential impact of other recognised determinants of grip strength, such as height, on the centile values presented. This could be an area for future research, although it would be important to first consider the clinical relevance of further stratification of grip strength, as discussed further in section 7.2.2 on page 107.

Finally I cannot exclude the possibility that selection and loss-to-follow up biases may have influenced my centile values; however I have included a wide range of population based studies from different geographical regions of Great Britain and the centile curves were robust to the exclusion of any individual study.

This project also had many strengths. First, I included data from many large general population studies in Great Britain resulting in centiles which, for the first time, cover all stages of the life course. Second, I used a modelling approach (GAMLSS) which allowed grip strength to vary as a smooth function of age and to incorporate any non-normality in grip (skewness or kurtosis).

Third, I conducted extensive sensitivity analyses and demonstrated that the centile curves for grip strength are robust to the dynamometer used for measurement and differences in the position (seated or standing). Finally, I was able to implement my centiles as a reference standard against which to compare values from the published literature.

6.3.2 Normative data from systematic literature review

The systematic literature review project had some limitations. First in terms of the literature search, it is possible that there are other examples of normative data for grip strength not published in medical journals, such as in government reports. There are also likely to be numerous cohort studies which have measured grip strength but not published normative data. However both sources could potentially be time-consuming to access in a systematic manner.

Second, many of the included papers were based on small convenience samples of the local area or one facility. This may have led to pooled estimates for some countries which were not representative of the population as a whole, although I did use a statistical technique, random effects metaregression, which anticipated variance between estimates and weighted them according to their standard errors. In future studies of different countries, it could be helpful to identify large studies of the general population which have measured grip strength and attempt to access the relevant data, as I did when producing my British normative data.

Third, I have not been able to explore to what extent differences in height account for the differences in grip strength between regions, as suggested by the ecological plot in section 6.2.4 on page 97. This is because the included papers typically did not include information on height, especially in a gender- and age-stratified form which would have allowed me to include height as an explanatory variable in my analyses.

This project also had many strengths. I undertook a comprehensive literature search which yielded papers on grip strength from all world regions. There was considerable variation in how papers reported their normative data, such as the age ranges, descriptive statistics and units used. To address this, I adopted a thorough approach to data management and analysis which allowed me to convert the normative data items into a comparable form.

I used my British norms as a reference, generating Z-scores which allowed me to then pool over 700 items of normative data using metaregression analyses. As far as I am aware, such an approach has not been used before and this allowed me to investigate differences in grip strength between countries. In a similar way as in my project on British centiles, I found the differences between normative data items related to measurement protocol to be acceptably small.

7. Discussion: relevance and future work

In this chapter, I firstly consider the relevance of this work to our understanding of the life course epidemiology of grip strength, including how this work may help to develop future interventions across the life course. I then move on to its relevance to the clinical care of older people. I finish by discussing future work in these areas.

7.1 Relevance to the life course epidemiology of grip strength

The pattern of grip strength across the life course identified in this thesis is similar to that proposed in the life course epidemiology framework for a range of physiological measures. This is important since it supports the idea that an individual's grip strength increases to a peak in early adult life, prior to entering a period of decline with age. The aetiology of weak grip strength in older adults, a key component of sarcopenia and frailty, may therefore be viewed in terms of factors influencing growth to peak and the timing and rate of decline.

7.1.1 Associations during growth to peak grip strength

A range of factors have been associated with grip strength during the periods of growth towards, and then broad maintenance of, peak strength. Grip strength is recognised to have a heritable component [172] and genes related to the myostatin pathway have been linked to knee strength in young men [173]. Growth during foetal life may also represent a critical period for subsequent grip strength, as first suggested by the finding of a positive association between birth weight abstracted from historical records and grip strength at mean age 68 years [41]. A systematic review and meta-analysis of this and 12 other studies has shown a mean increase in grip strength of 0.86 kg per additional kilogram of birth weight, including adjustment for height which typically attenuates but does not fully explain the relationship [1]. One explanation is that intrauterine development, assessed using birth weight as a proxy, has lasting effects on both muscle quantity and quality.

Discussion: relevance and future work

Height and grip strength are correlated, as seen in studies which stratified normative data for grip strength into age and height groups: as one would expect, taller individuals are stronger on average [52,105,106]. My pooled Z-scores for grip strength suggested a similar ecological association at the country level. It is likely on entering adulthood, an individual's height and grip strength share past exposures to a degree such as nutrition.

I used the data from Understanding Society to explore to what extent an individual's grip strength can be predicted by their height. Specifically, I examined the proportion of variance in grip strength at the time of peak in the fourth decade that is explained by a linear term for height. I saw positive associations although the proportions of variance explained were low: for example, in women a 1cm increase in height was associated with a 0.2kg increase in grip strength and the proportion of variance explained was 6%.

I considered that this high residual variance in grip strength was consistent with other differences between height and grip strength. Firstly, in comparison with grip strength, peak height is reached at a younger age and the age-related decline in height is slower: again, using cross-sectional values from Understanding Society, peak height has been reached by age 20 (as opposed to during the fourth decade for grip). The age-related decline by age 80 is then only 4% below the peak (as opposed to 38% for grip). Secondly, the associations between height and all-cause mortality are less marked than those for grip strength [174].

I therefore conclude that although there is likely to be some overlap in the determinants of adult grip strength and height, these are not the same. I go on to consider whether it is necessary to produce height-stratified cut-points for grip strength as part of the clinical relevance section 7.2.2 on page 107.

Finally, there is relatively little known about the role of physical activity and diet in relation to the growth to peak grip strength. Cross-sectional relationships show that children who are more physically active tend to have stronger grip [45,175]. I am not aware of studies that have related diet to peak grip strength, although there is evidence that longer duration of breastfeeding is associated with increased lower body explosive strength in adolescence, as assessed by standing long jump tests [176].

7.1.2 Associations during the decline in grip strength

Genetic and early life factors have also been examined in relation to grip strength during the decline phase. The HALCyon collaboration did not find an association between polymorphisms of the GH/IGF axis and grip strength [177]. Several studies have found an association between birth weight and grip strength during the decline phase, as described above [1]. Finally longer duration of breastfeeding has been linked to higher grip strength in men at mean age 66 in the Hertfordshire Cohort Study [178].

Diet and grip strength at mean age 66 have also been investigated cross-sectionally in the Hertfordshire Cohort Study. Consumption of fatty fish was found to predict higher grip strength in men and women, as was following an overall prudent diet pattern, characterised by high consumption of fruit, vegetables and whole-grain cereals as well as fatty fish [179].

The findings so far in this section typically describe an exposure at a single time point in relation to grip strength at a single time point; of course in the case of cross-sectional studies, both assessments have been made at the same time point. There are also studies which have used repeat measures of an exposure, repeat measures of grip strength or both to investigate the aetiology of grip strength. For example, in the MRC National Survey of Health and Development, a cumulative benefit of increased leisure time physical activity across ages 36, 43, 53 and 60-64 has been found for grip strength at age 60-64 years [3]. Similarly, participation in sport was associated with a more rapid increase in grip strength in early adult life in women in the Fels Longitudinal Study [164]. Finally data from the Swedish Adoption/Twin Study of Aging have been used to investigate factors associated with decline in grip strength from age 50 onwards: a range of associations were found such as a more rapid decline in grip strength among women who had previously smoked [180].

7.1.3 The development of future interventions

The life course approach to grip strength described above also has implications for future interventions to prevent sarcopenia and frailty. Observational evidence regarding the factors which promote a higher peak, and attenuate the decline of, grip strength has the potential to guide intervention strategies. Importantly these interventions can be targeted at all stages of the life course. There is recognition that a minor modification of risk trajectory as early as at the mother and infant stage has the potential to exert marked effects in later life [181]. Such an intervention for future bone health is currently being assessed: the Maternal Vitamin D Osteoporosis Study, a trial of vitamin D supplementation in pregnancy in relation to the bone mineral content of the infant [182].

The normative data in this thesis have the potential to contribute to interventions across the life course. In older age, this could be in the form of inclusion criteria in studies examining the treatment of sarcopenia and frailty [183]. Across the life course, it could assist in the identification of individuals with grip strength below the level expected for their age. This would effectively constitute screening and so associated questions would follow, such as the ability of grip strength to correctly identify those at risk and the availability of an intervention. I return to consider the identification of those at risk in the section on future work (7.3) on page 108.

7.2 Relevance to clinical practice

7.2.1 Cut-points for grip strength

The life course trajectory identified for grip strength in this study is similar to the well-established life course trajectory of bone mineral density (BMD) [47]. This supports the use of peak values from early adult life to define cut-offs for weak grip at subsequent ages using T-scores. I have used this approach to estimate the prevalence of weak grip in the British population based on T-scores of both -2 and -2.5. A T-score of less than or equal to -2 has previously been used by Lauretani et al. [100] for grip strength, although the prevalence figures for weak strength that they report using this value, especially those for men, are considerably higher than those in this thesis. This difference may have arisen as in their sample, they include 25 men at ages 20-29 with mean (SD) grip 61.1 (10.5) kg. The cut-off for weak grip in men is not stated in their paper but I presume it is then 40 kg (61.1 less 2 x 10.5) – substantially higher than this thesis' value

(32kg). By fitting centile curves that span all stages of the life course, I hope that I have established more informative peak values on which to base T-scores.

I still found a high prevalence of weak grip strength based on a T-score of -2 or below (equivalent to 19kg in females and 32kg in males, or weaker) with almost half of participants at or below this level at age 80. It may therefore be that a T-score of -2.5 or below (equivalent to 16kg in females and 27kg in males, or weaker) produces a more discriminatory cut-off for weak grip – with 23% of males and 27% of females at or below this level at age 80.

It is important that any cut-off values are shown to relate to relevant outcomes. I am aware of three studies that have looked at optimal cut-offs for detecting mobility disability in a cross-sectional fashion. Lauretani et al. [100] examined the optimum grip strength values for detecting slow measured gait speed and self-reported difficulty in walking 1 km; they found that grip strength of 30kg in males and 19kg in females provided the optimum balance between sensitivity and specificity. Alley et al. [184] proposed cut-offs for intermediate and marked levels of grip strength weakness in relation to risk of impaired gait speed; they found values of 33 and 26kg, respectively, for men and 21 and 16kg, respectively, for women. Sallinen et al. [185] looked at self-reported difficulties with mobility and found similar overall cut-offs: 37kg in males and 21kg in females.

Clearly there is a need to examine similar relationships in a longitudinal fashion if individual values of grip strength are to be used as a marker of those at risk of adverse outcomes.

7.2.2 Stratification of grip strength by height

I did not stratify my normative data from 12 British studies by height and neither did all but three of the papers in my systematic literature review. As described in section 7.1.1 on page 103, grip strength and height are positively correlated and hence the question arises: should we assess grip in light of an individual’s height, as well as their age and gender?

The measurement of height requires additional time which may not always be feasible in clinical settings, as well as the need to estimate standing height in those unable to stand. Another challenge is the interpretation of height at young and older ages, when an individual's height may partly reflect their stage of growth towards their young adult height and the degree of any subsequent decline from this, respectively.

It is also necessary to consider whether height in combination with grip strength provides additional information about an individual's current health and risk of subsequent ill health. In analyses undertaken as part of the Foundation for the National Institutes of Health Sarcopenia Project, Alley et al. found that cut-points based on grip strength in combination with BMI were more sensitive than grip strength alone for detecting mobility impairment in a cross-sectional fashion. However they considered the benefit was not sufficient to justify the use of a more complex measure in a clinical setting [184].

7.3 Future work

I now discuss possibilities for future work arising from this thesis. I divide these in the same way as the previous two sections: firstly by considering future projects on the life course epidemiology of grip strength and then those related to clinical practice.

7.3.1 The life course epidemiology of grip strength

The normative data presented in this thesis for Great Britain can be used as a reference standard against which an individual grip measurement at a given gender and age can be compared. This can be done both in terms of a Z-score, capturing the difference between the measured value and that expected at the same age and gender, and as a T-score, capturing the difference between a measured value and the peak mean value for the relevant gender.

Such external comparisons are commonly made in epidemiological studies, for example using the Child Growth Foundation standards for weight and height [186]. They assist authors in showing how their sample compares to a national average and also by allowing grip strength readings at a range of ages and in both genders to be combined for analyses. A future project could therefore be to produce a function in statistical software that produces Z- and T-scores for grip strength readings automatically.

The pooling of grip strength data in my systematic literature review has allowed me to investigate differences between countries. In the case of many of the countries, the data were drawn from convenience samples over a small geographical area. As such, it would not seem appropriate to attempt to produce country-specific reference standards from these results. As previously described, an area of future work could involve the production of reference data for other countries using large general population samples. An example of a potential source of grip strength measurements would be the SHARE study which has collected data in ten European countries [187].

The majority of both the 12 studies used to produce my British normative data and the papers included in my systematic literature review had only measured grip strength on a single occasion. This parallels studies which have investigated the determinants of weak grip strength and its outcomes, which are again typically based on a single measurement of grip strength.

There is growing interest in using repeat measures of grip strength in order to improve our understanding of aetiological factors, including at which stage of the life course they exert their main effect. It is possible that an individual’s grip strength trajectory could provide more a useful prediction of their subsequent health than a single measure. This is supported by the finding that rate of decline in grip strength is associated with mortality [16,17].

A substantial area of future work is therefore to examine the trajectory of grip strength across the life course, with the aim of producing British normative data as I did in a cross-sectional manner in this thesis. There are several challenges that would need to be overcome in doing this. Firstly, studies with repeat measures across different stages of the life course would need to be identified. Additional measurement waves for studies such as ELSA which have become available since I accessed the data would be helpful in this regard. A second issue would be to develop the analytical approach to modelling the trajectory and describing its findings. The FALCon project has already carried out work in this area on trajectories of systolic blood pressure [70,188]. The longitudinal analysis of grip strength, including the role of exposures such as physical activity, has the potential to contribute valuable information on guidance for a healthy lifestyle at all ages [189].

7.3.2 Clinical practice

This thesis demonstrates that the measurement of grip strength has been undertaken on a large scale in epidemiological studies, suggesting that it is acceptable for research participants and data collection teams. I am aware of fewer examples of grip strength data collected in clinical settings, particularly among in-patients [29,30,120,190]. The clinical setting presents additional challenges such as training and the safe storage of equipment. A future area of research would therefore be to explore the translation of grip strength measurement into clinical practice. The normative data in this thesis could form part of the work, in assisting healthcare professionals with the interpretation of measurements.

I have proposed cut-points for weak grip strength that could be used as a quick way of assessing measurements in the clinical setting. As previously described in section 7.2.1 on page 106, it is important that any cut-points chosen relate to relevant outcomes. Existing research in this regard has been conducted in a cross-sectional manner and whilst this helps to inform cut-points, it does not address the clinically relevant question: what can an older person’s grip strength tell us about their future health?

In future work, cohort studies with information on relevant outcomes could be used to explore the predictive power of grip strength. An example is the Hertfordshire Cohort Study, where participants had grip strength measured as part of the baseline clinic. Linked records then provide subsequent follow-up for hospital admission and death over at least five years [191].

Using studies such as the Hertfordshire Cohort Study, it would be possible to carry out analyses such as the area under the receiver operating curve (ROC). This would assess the probability that a measurement of grip strength correctly predicts whether an individual goes on to experience the outcome of interest. In the future it might be possible to develop a web-based tool for the assessment of grip strength in the clinical setting, similar to the WHO fracture risk assessment tool (FRAX).

8. Conclusions

In conclusion, I have used existing data from a range of studies conducted in Great Britain to produce centile curves for grip strength which cover the entire life course. I was able to describe the increase in grip strength to peak in early adult life, a period of broad maintenance and then decline.

I found that published international normative data show a similar pattern of results, but with clear differences in the magnitude of grip strength between countries in developing and developed regions.

I used data from 12 British studies and 60 published papers. In keeping with clinical practice, both had used a variety of different measurement protocols; sensitivity analyses suggested that the results were robust to these differences.

The findings in this thesis have the potential to inform the clinical assessment of grip strength which is recognised as an important part of the identification of people with sarcopenia and frailty.

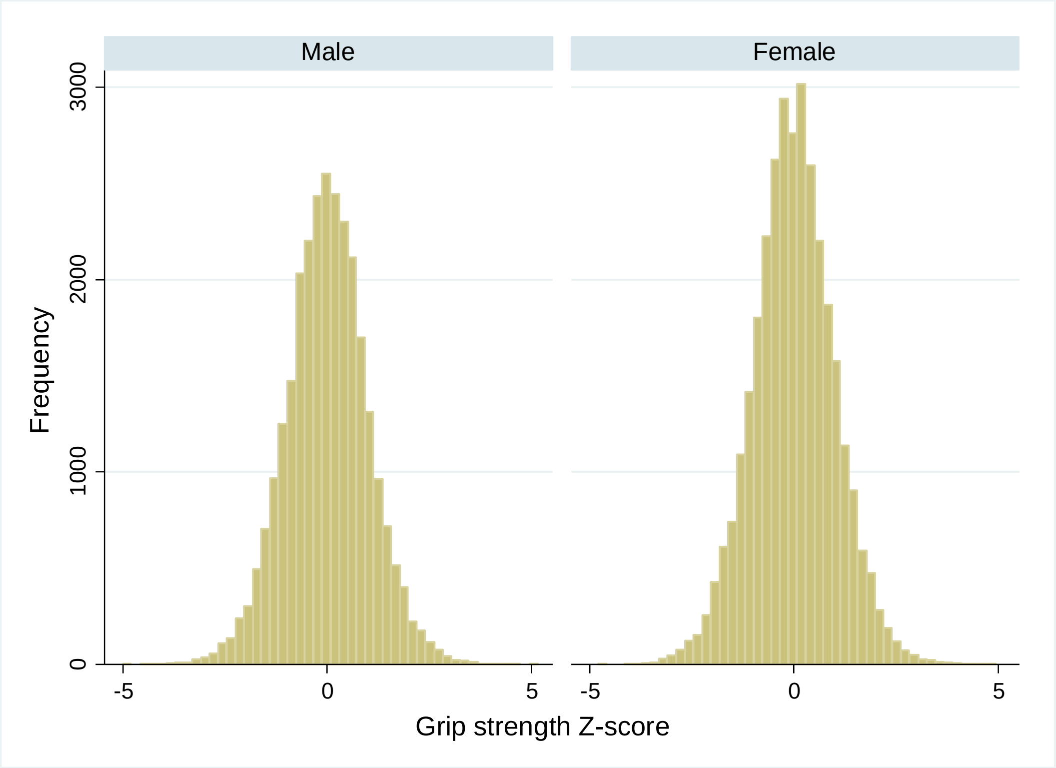
Appendices

Appendix 1 is overleaf.

Appendix 1. Z-scores for British grip strength observations

Here I show further results from the Z-scores of the grip strength observations, as previously described in section 3.2.3 on page 43. Please note that for consistency, I drew the x-axis on all charts between -5 and 5. I therefore excluded the small number of observations (n=9) which fell outside this range.

The Z-scores for all males and all females were both normally distributed with mean 0.0 and standard deviation 1.0, as shown in the below histograms and table:



Gender	**N**	**Z-score mean**	**Z-score SD**
Male	28,257	0.0	1.0
Female	32,546	0.0	1.0
Total	**60,803**	**0.0**	**1.0**

The Z-scores by study are shown in the table on the next page. The results for males and females are combined, except in the case of the SWS mothers and partners. The histograms for each study follow the table, shown separately for males and females.

Appendix 1

Study	**N**	**Z-score mean**	**Z-score SD**
SWS	1,430	-0.0	1.1
ALSPAC	6,701	-0.0	1.0
USoc	14,678	-0.1	1.0
ADNFS	2,602	0.2	1.0
SWSm	1,563	0.2	1.0
SWSp	1,265	0.4	0.9
T07	2,380	-0.2	1.0
NSHD	4,916	0.1	1.3
ELSA	15,442	-0.0	1.0
HCS	3,626	0.3	0.9
HAS	1,009	-0.1	1.0
LBC1936	1,951	-0.2	0.9
LBC1921	1,069	0.2	1.0
N85	2,171	-0.1	1.0
Total	**60803**	**0.0**	**1.0**

For study abbreviations see Table 2.a on page 19.

The below histograms and tables show the individual results for each study, with results for males and females shown separately.

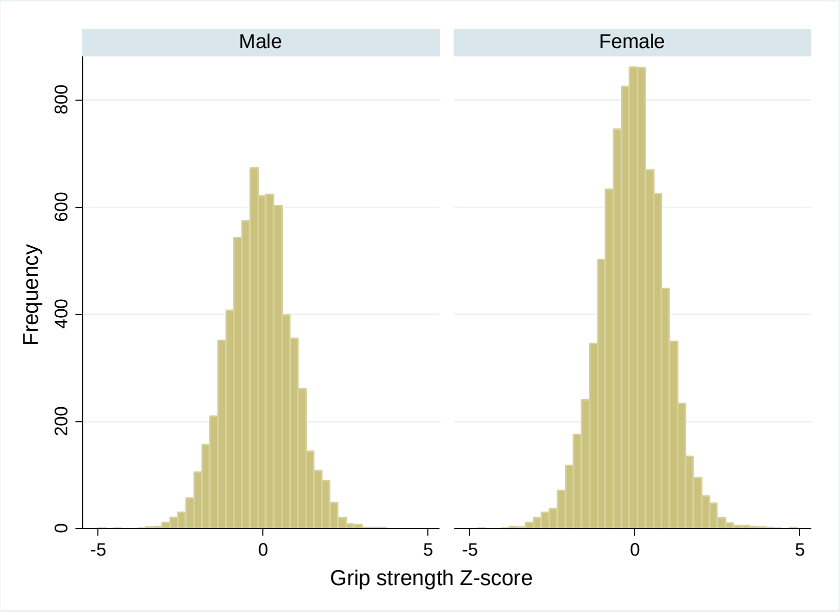
SWS

	N	**Z-score mean**	**Z-score SD**
Male	730	0.0	1.1
Female	700	-0.1	1.1
Total	1430	-0.0	1.1

ALSPAC

	N	Z-score mean	Z-score SD
Male	3290	-0.1	0.9
Female	3411	0.0	1.0
Total	6701	-0.0	1.0

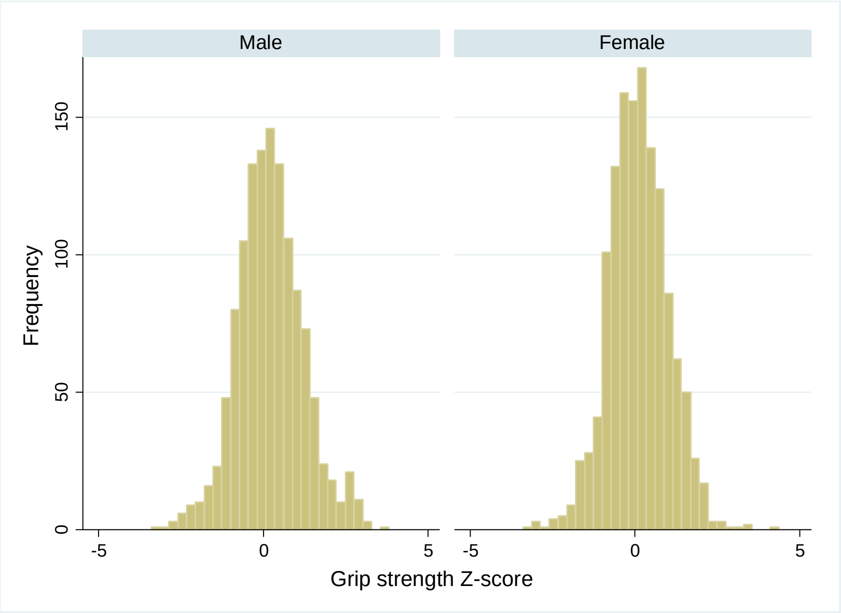
USoc



	N	Z-score mean	Z-score SD
Male	6461	-0.1	1.0
Female	8217	-0.1	1.0
Total	14678	-0.1	1.0

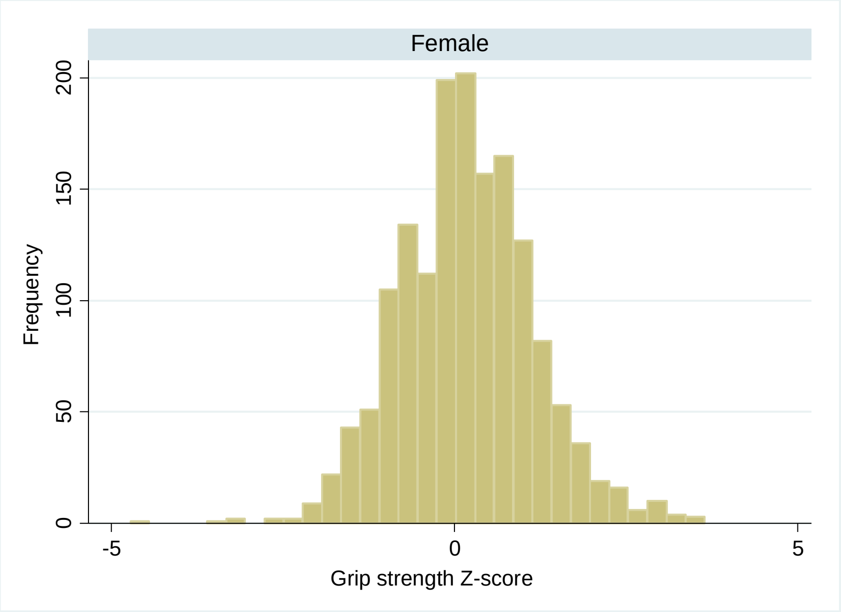
Appendix 1

ADNFS



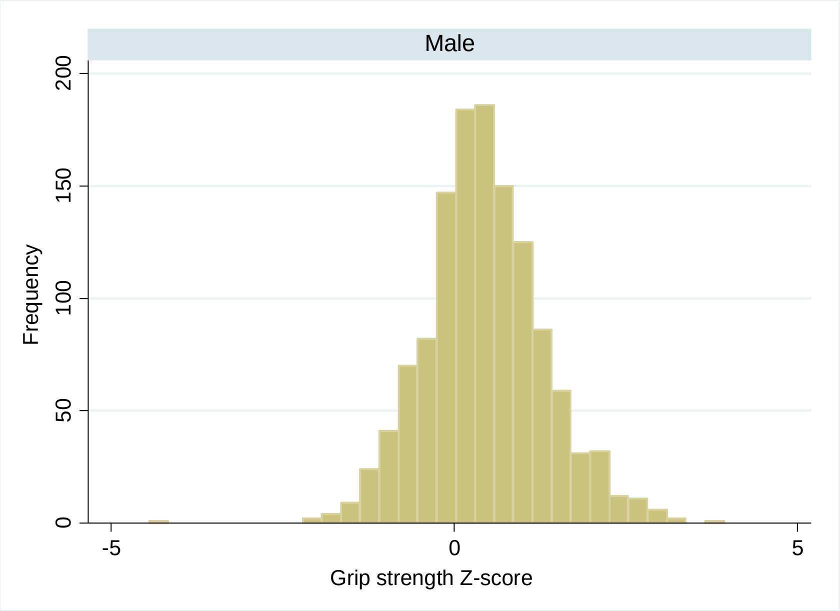
	N	Z-score mean	Z-score SD
Male	1254	0.2	1.0
Female	1348	0.1	0.9
Total	2602	0.2	1.0

SWSm



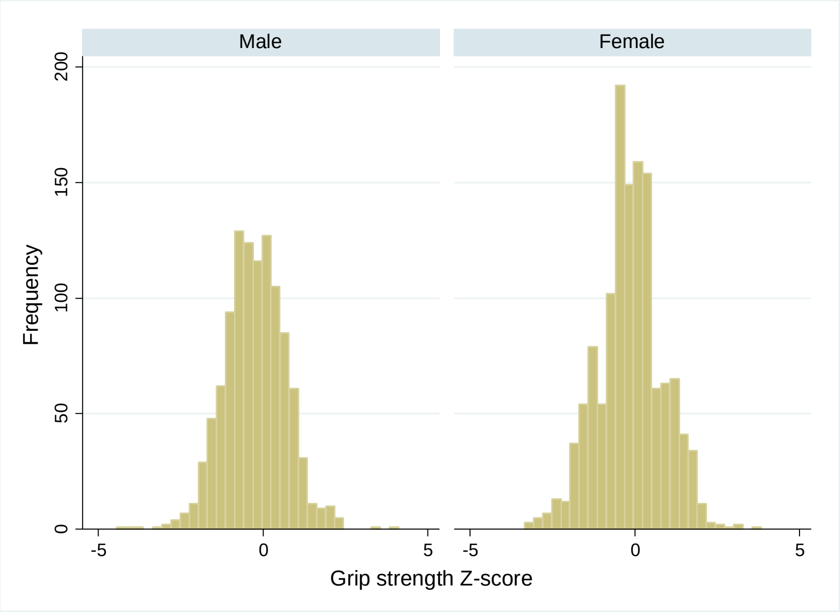
	N	Z-score mean	Z-score SD
Female	1563	0.2	1.0
Total	1563	0.2	1.0

SWSp



	N	Z-score mean	Z-score SD
Male	1265	0.4	0.9
Total	1265	0.4	0.9

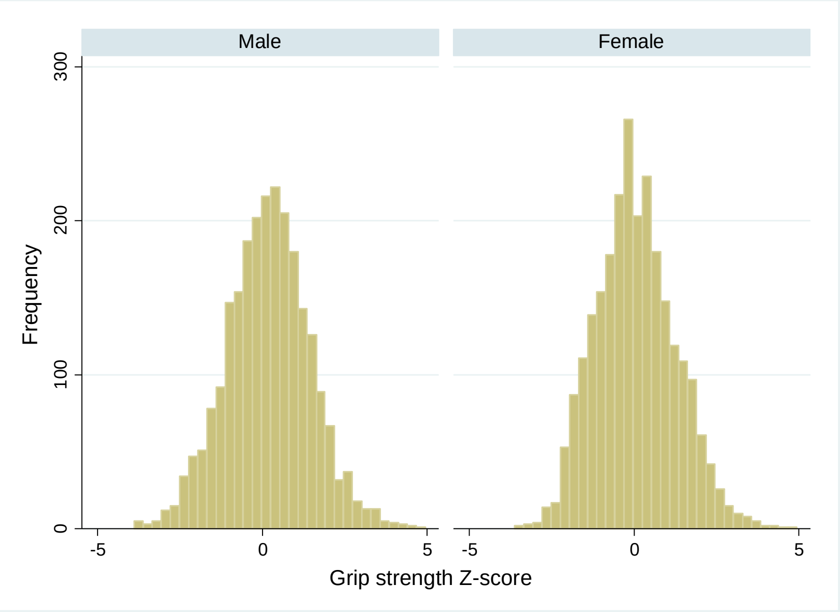
T07



	N	Z-score mean	Z-score SD
Male	1076	-0.2	0.9
Female	1304	-0.1	1.0
Total	2380	-0.2	1.0

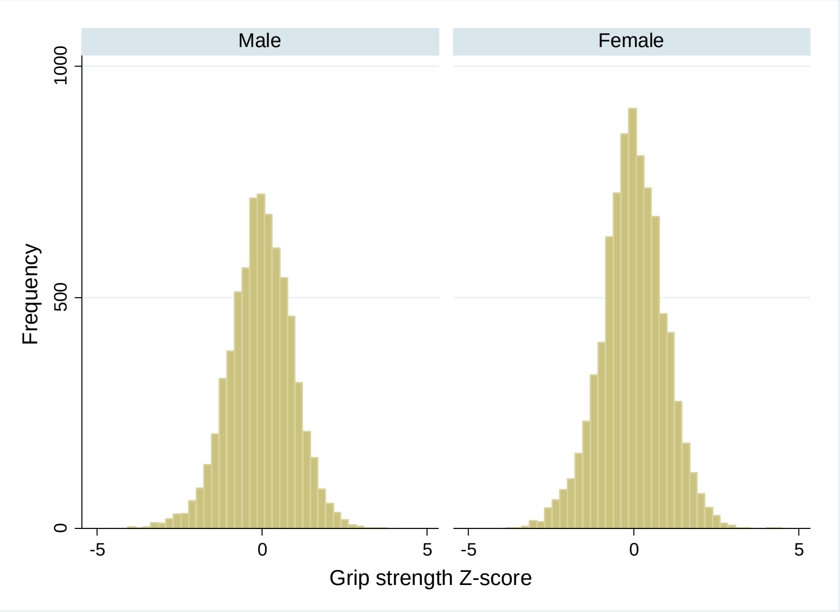
Appendix 1

NSHD



	N	Z-score mean	Z-score SD
Male	2411	0.2	1.3
Female	2505	0.1	1.2
Total	4916	0.1	1.3

ELSA



	N	Z-score mean	Z-score SD
Male	7004	-0.0	1.0
Female	8438	-0.0	1.0
Total	15442	-0.0	1.0

HCS

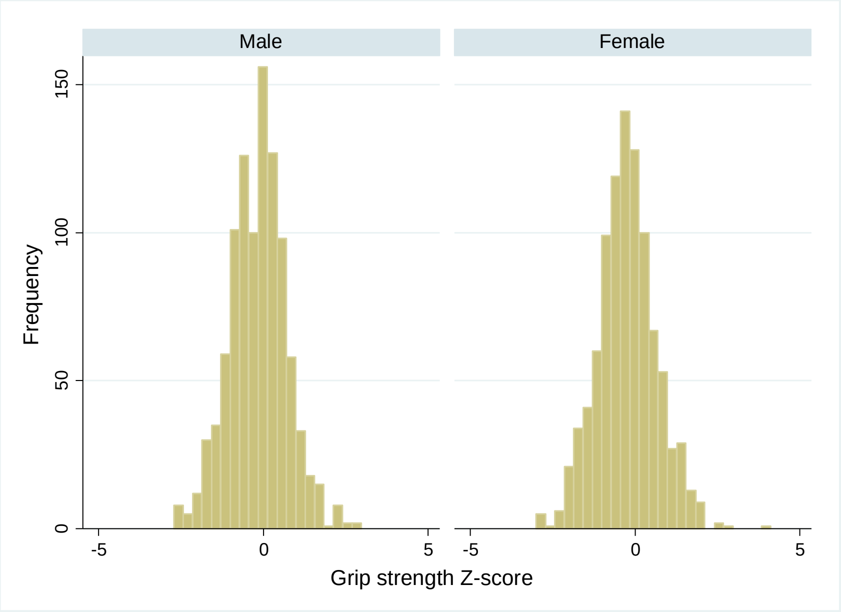
	N	Z-score mean	Z-score SD
Male	1893	0.3	0.9
Female	1733	0.3	1.0
Total	3626	0.3	0.9

HAS

	N	Z-score mean	Z-score SD
Male	583	-0.0	1.0
Female	426	-0.1	1.0
Total	1009	-0.1	1.0

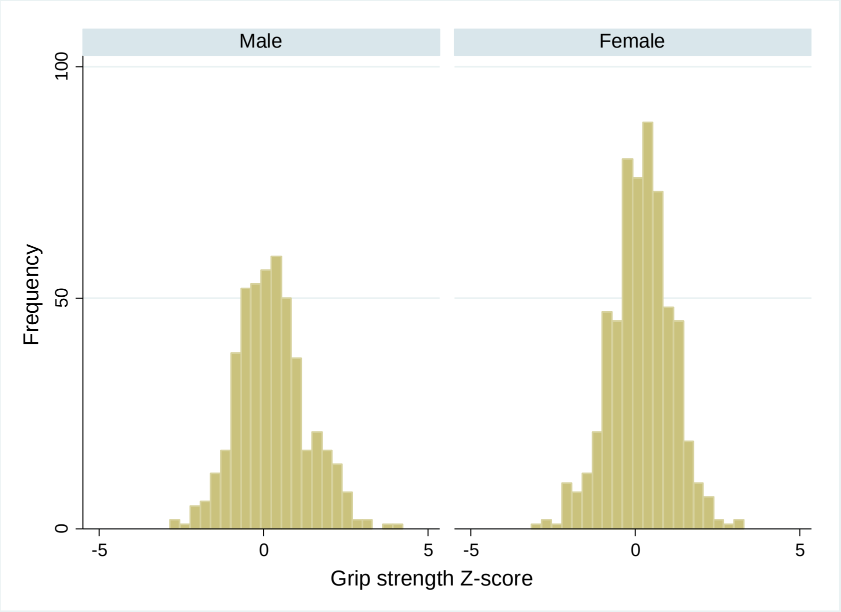
Appendix 1

LBC1936



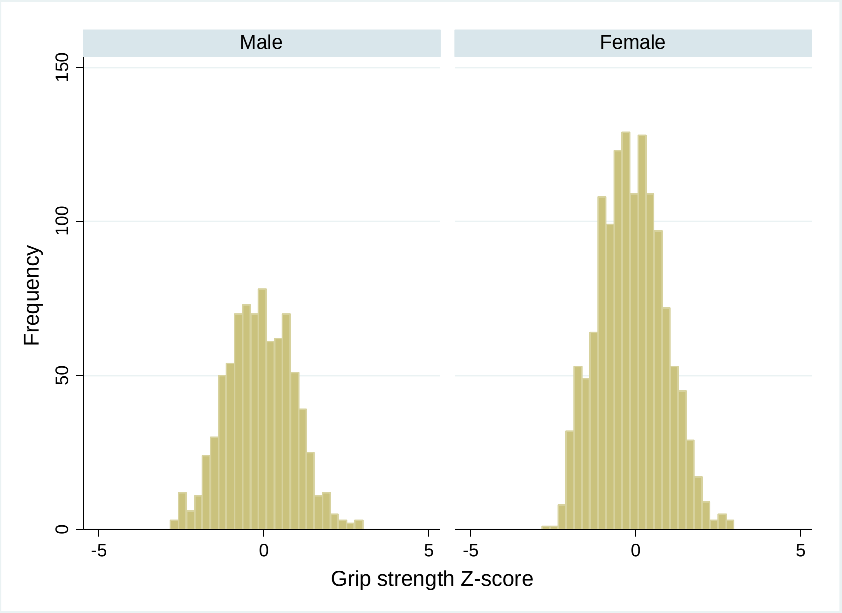
	N	Z-score mean	Z-score SD
Male	994	-0.2	0.9
Female	957	-0.2	0.9
Total	1951	-0.2	0.9

LBC1921



	N	Z-score mean	Z-score SD
Male	471	0.3	1.1
Female	598	0.2	0.9
Total	1069	0.2	1.0

N85



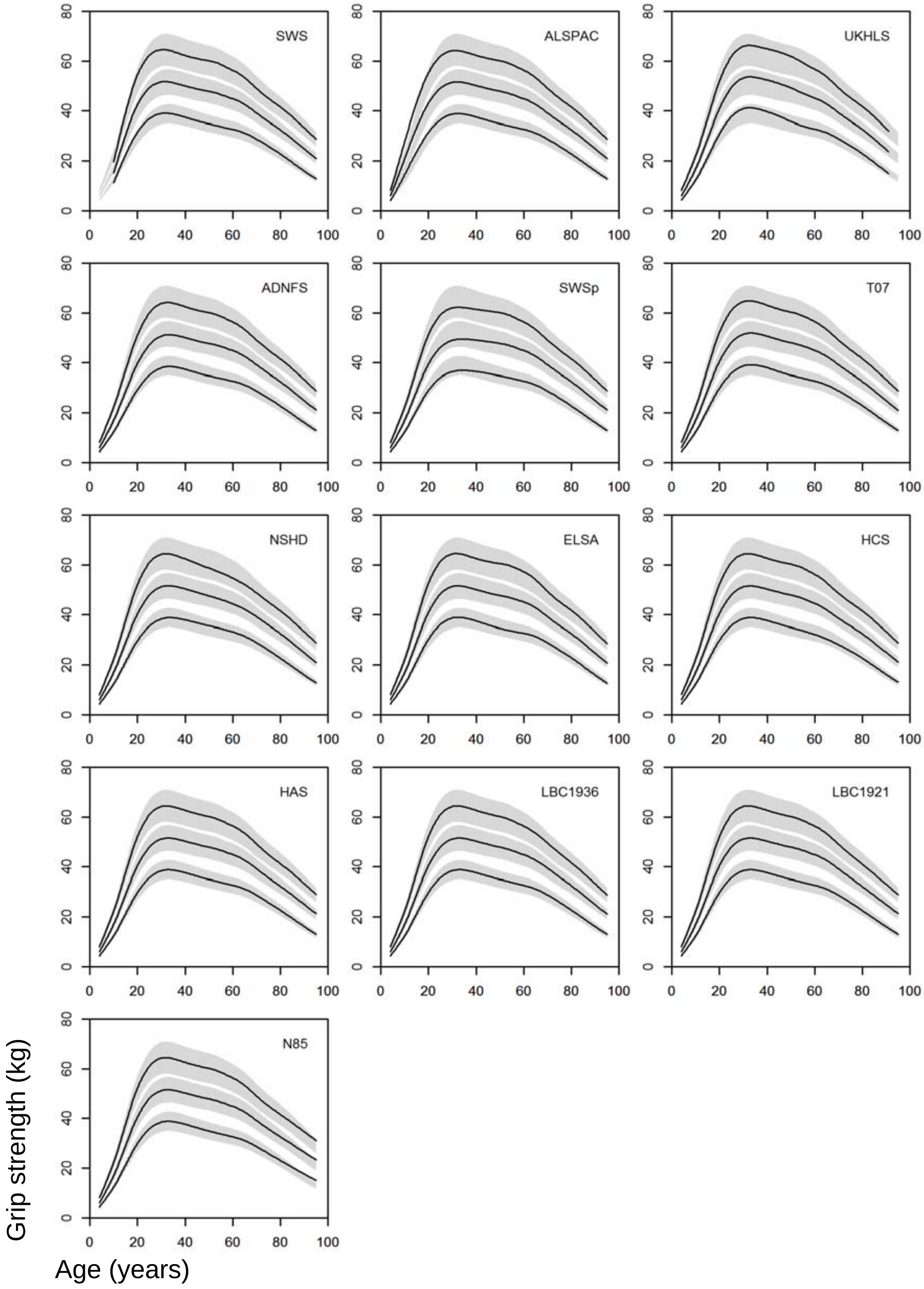
	N	**Z-score mean**	**Z-score SD**
Male	825	-0.1	1.0
Female	1346	-0.1	1.0
Total	2171	-0.1	1.0

Appendix 2. Results of sensitivity analyses excluding each study in turn

These are shown on the following two pages.

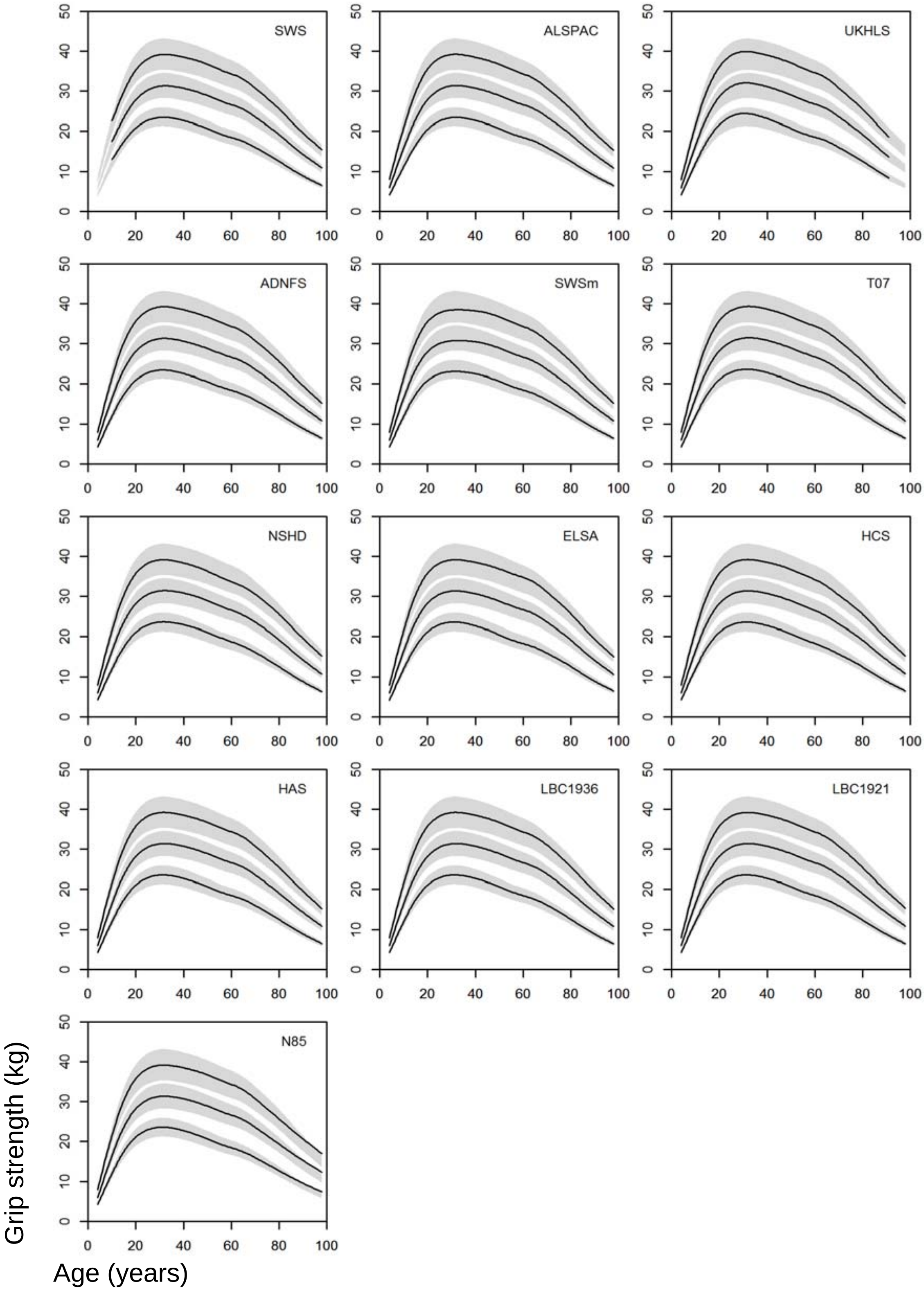
Appendix 2

Males



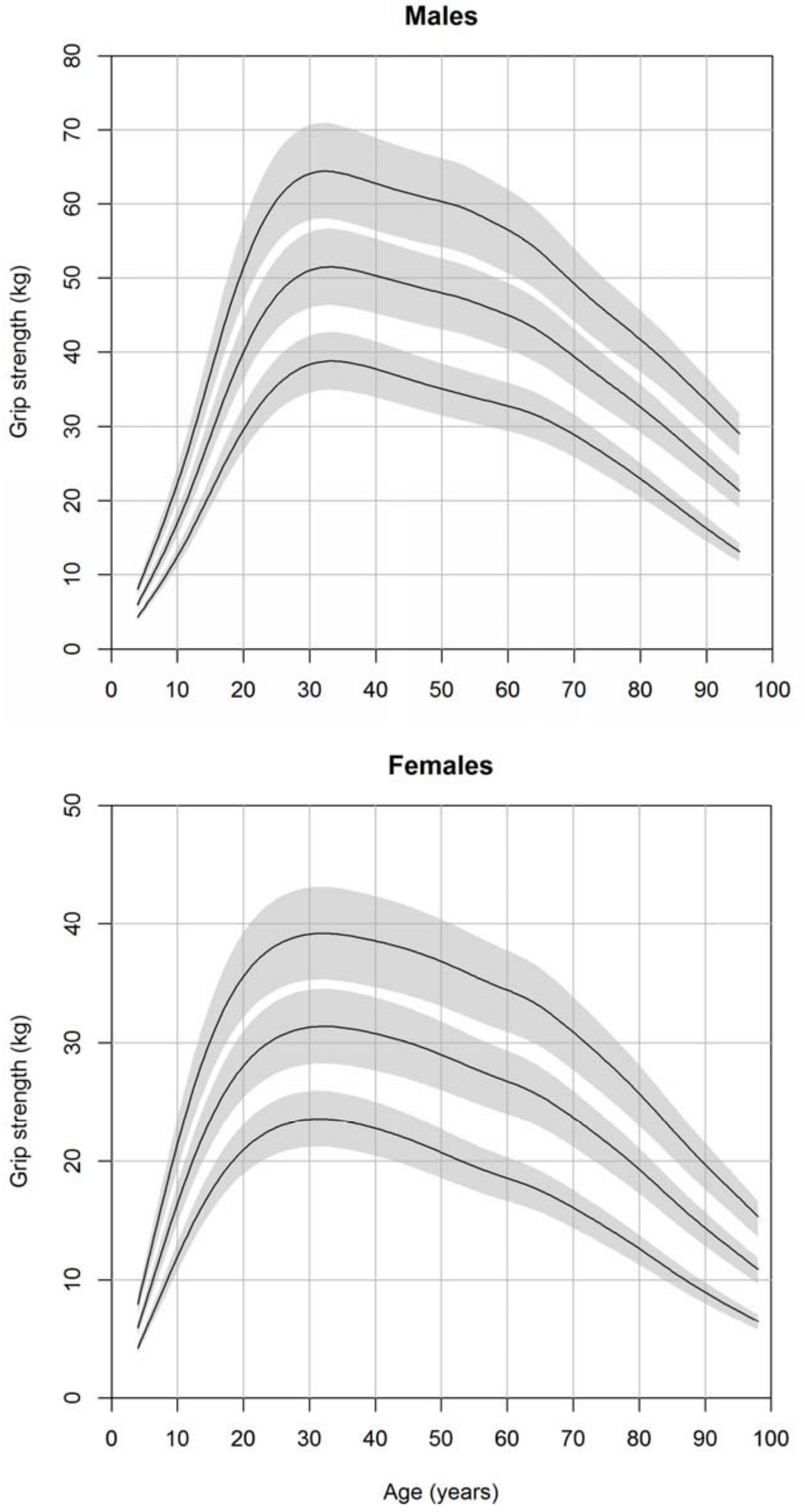
The lines represent the 10th, median and 90th centiles when the study shown is excluded. The grey areas show the range produced if the values from the 10th, median and 90th centiles in the main results are increased or decreased by 10 per cent.

Females



The lines represent the 10th, median and 90th centiles when the study shown is excluded. The grey areas show the range produced if the values from the 10th, median and 90th centiles in the main results are increased or decreased by 10 per cent.

Appendix 3. Result of further sensitivity analysis on age



The lines represent the 10th, median and 90th centiles from the sensitivity analysis where six months were added to the age of participants from ADNFS, UKHLS and ELSA. The grey areas show the range produced if the values from the 10th, median and 90th centiles in the main results are increased or decreased by 10 per cent.

Appendix 4. Details of extracted studies

Studies ordered by first author and then by year. C, convenience sample. NS, not specified. Sf, sampling frame used.
[*] The age range shown is that for the normative data items that I extracted from each paper. I excluded open-ended age ranges, such as 70+ years.
[†] N, the number of individuals with grip strength measurements in the age range specified. These are notably lower than the figures in the published papers by Frederiksen et al. and Spruit et al., since in these two studies I chose to extract details for a single height group only.
[‡] In the paper by Frederiksen et al., sample sizes for individual normative data items were not provided. Rather the sample size shown is approximated based on the standard deviation and standard error of the sample mean, which were provided for each item.

Author, year Ref	**Type**	**Country**	**Level**	**Sample description**	**Dynamometer**	**Age range (y)[*]**	**N[†]**
Aadahl, 2011 [111]	Sf	Denmark	Regional	Participants recruited through the Danish Civil Registration office across in 11 municipalities in the western area of the Capital Region of Denmark.	Jamar	19 - 72	3453
Adedoyin, 2009 [123]	C	Nigeria	Facility	Participants recruited by advertisement and invitations from Obafemi Awolowo University, Ile-Ife.	Takei TKK 84466	20 - 69	745
Ahn, 2013 [128]	C	Korea, Republic of	Facility	Recruited from healthy participants visiting the Occupational and Environmental Health Center over a 2 month period.	Camry Electronic	30 - 59	120
Almuzaini, 2007 [131]	C	Saudi Arabia	Local	Drawn from three local schools.	NS	11 - 19	44
Backman, 1995 [117]	Sf	Sweden	NS	Two sources mentioned in paper; appears approached all healthy adults in a small area of Linköping.	Rank Stanley Cox strain gauge	17 - 70	128

Appendix 4

Author, year **Ref**	**Type**	**Country**	**Level**	**Sample description**	**Dynamometer**	**Age range (y)**[*]	**N**[†]
Balogun, 1991 [91]	C	Nigeria	Local	Participants were recruited from community residential quarters, shopping centers, churches, and schools.	Harpenden	7 - 69	840
Bear-Lehman, 2002 [118]	C	United States	Local	From 4 preschools in New York City.	Jamar	3 - 5	81
Brennan, 2004 [138]	C	United States	Local	Noninstitutionalised women who participated in health screenings at one of five community senior centers in the state of Connecticut.	Jamar	60 - 89	104
Budziareck, 2008 [124]	C	Brazil	Local	Three locations: a hospital, centre for older people and a local city square.	Jamar	18 - 30	100
Chatterjee, 1991 [116]	NS	India	NS	Normal healthy male subjects.	Simple handgrip dynamometer -INCO made in India	10 - 49	81
Chuang, 1997 [132]	C	Taiwan, Province of China	Facility	From one junior college; participants paid NT$ 50 (approx 2 US $) for every hour attending session.	Takei TKK Muscular Power Measuring Device with digital dynamometer	16 - 20	120
Cohen, 2010 [159]	Sf	United Kingdom	Regional	23 state primary and secondary schools in East of England Healthy Hearts study.	Takei T.K.K.5001 Grip A	10 - 15	6683
Corish, 2003 [148]	C	Ireland	Local	Recruited from interest groups for the active retired.	Takei	65 - 85	874

Appendix 4

Author, year Ref	**Type**	**Country**	**Level**	**Sample description**	**Dynamometer**	**Age range (y)**[*]	**N**[†]
De Smet, 2001 [145]	NS	Belgium	NS	No sample details provided.	Jamar	5 - 15	419
Desrosiers, 1995 [137]	Sf	Canada	Local	Random sampling (with replacement) from the electoral list	Jamar	60 - 79	240
Frederiksen, 2006 [105]	Sf	Denmark	National	Participants of three nationwide population-based surveys.	Smedley	45 - 94	2926[‡]
Gunther, 2008 [119]	C	Germany	Regional	Volunteers randomly chosen from different locations including hospitals, public recreations areas and homes for the elderly.	Baseline digital hydraulic dynamometer	20 - 95	769
Hager-Ross, 2002 [49]	C	Sweden	Local	From 20 randomly chosen day care centres and schools in the municipality of Umea.	Grippit	4 - 16	530
Hanten, 1999 [139]	C	United States	NS	NS.	Jamar	20 - 64	1182
Harkonen, 1993 [147]	NS	Finland	NS	Volunteers working in the food and medicine industries.	Jamar	30 - 49	115
Holm, 2008 [152]	C	Norway	Local	Schools in the Oslo area up to 4-5km from hospital where study based.	Jamar	7 - 29	376
Horowitz, 1997 [140]	C	United States	Local	Two Suffolk County, Long Island senior citizen community organisations.	Jamar	70 - 74	47
Jansen, 2008 [141]	C	United States	Local	Recruited from local health fairs, a geriatric primary-care clinic and senior-citizen community events.	Jamar	65 - 84	196

Appendix 4

Author, year Ref	**Type**	**Country**	**Level**	**Sample description**	**Dynamometer**	**Age range (y)**[*]	**N**[†]
Kallman, 1990 [142]	Sf	United States	Regional	Baltimore Longitudinal Study of Ageing	Smedley	20 - 89	842
Kaur (rural), 2009 [114]	NS	India	Regional	Samples of rural Jat (the most prominent caste) females from Haryana, North India.	NS	40 - 70	300
Kaur (urban), 2009 [114]	NS	India	Regional	Samples of urban Jat(the most prominent caste) females from Haryana, North India.	NS	40 - 70	300
Keevil, 2013 [120]	C	Malaysia	Facility	Patients admitted to Geriatrics Ward of University Malaya Medical Centre, Kuala Lumpur	Jamar	64 - 100	80
Kenny, 2013 [52]	Sf	Ireland	National	Nationally representative sample of adults.	Baseline	50 - 85	5819
Lang, 2013 [121]	NS	Germany	Facility	All participants from Tuebingen Waldorf School	Jamar	3 - 19	869
Luna-Heredia, 2005 [56]	C	Spain	Local	Workers of the Móstoles Hospital, Madrid, relatives of patients visiting the hospital and elderly subjects from senior residences in two cities near Madrid.	Baseline and Grip-D (two devices used, considered exchangeable)	30 - 84	473
Massy-Westropp (Grippit), 2004 [57]	C	Australia	Local	From several sources including a large teaching hospital, a high pedestrian-traffic area of a Medical Centre and community centres.	Grippit	18 - 74	362

Appendix 4

Author, year Ref	**Type**	**Country**	**Level**	**Sample description**	**Dynamometer**	**Age range (y)***	**N†**
Massy-Westropp (Jamar), 2004 [57]	C	Australia	Local	From several sources including a large teaching hospital, a high pedestrian-traffic area of a Medical Centre and community centres.	Jamar	18 - 74	359
Massy-Westropp, 2011 [134]	Sf	Australia	Regional	Data obtained from the North West Adelaide Health Study - random sampling using telephone directory. NB Sample size not divided into males and females, so total divided by two and split equally across age groups.	Jamar	20 - 69	2629
Mathiowetz, 1985 [143]	C	United States	Regional	Recruited from shopping centers, fairs, senior citizen centers, a rehabiliation center (staff) and a university.	Jamar	20 - 74	577
Mathiowetz, 1986 [48]	C	United States	Regional	Participants from schools in the seven-county Milwaukee area.	Jamar	6 - 19	471
Molenaar, 2010 [63]	C	Netherlands	Facility	Children from a local primary school.	Lode	4 - 12	225
Montalcini, 2013 [149]	C	Italy	Facility	Healthy university students.	Hersteller	19 - 25	335
Nevill, 2000 [85]	Sf	United Kingdom	National	Random sample of English population with subsample having physical appraisal.	Nottingham electronic	16 - 74	2632

Appendix 4

Author, year **Ref**	**Type**	**Country**	**Level**	**Sample description**	**Dynamometer**	**Age range (y)***	**N†**
Nilsen, 2012 [153]	C	Norway	Local	Several settings including shopping malls, workplaces and community centres for the elderly in the region of Oslo.	Grippit	20 - 79	498
Pearl, 1993 [160]	C	United Kingdom	Facility	Subject attending BUPA Health Screening Centre, London. Of those over 50, only those who exercised regularly completed grip strength assessment.	NS	20 - 69	16980
Peolsson, 2001 [156]	Sf	Sweden	Facility	Age stratified sample of hospital staff.	Jamar	25 - 65	101
Peters, 2011 [150]	C	Netherlands	Local	University, hospital and secondary school personnel, homes for the elderly and sports clubs.	Jamar	20 - 79	614
Ploegmakers, 2013 [151]	C	Netherlands	Regional	Schools approached in the four northern provinces of The Netherlands.	Jamar	4 - 14	2241
Puh, 2010 [155]	C	Slovenia	NS	Recruited at locations including shopping centres, fairs and nursing homes.	Baseline	20 - 79	199
Rauch, 2002 [122]	NS	Germany	Regional	Participants in the Dortmund Nutritional and Anthropometric Longitudinally Designed study.	Jamar	7 - 18	305
Ribom, 2011 [157]	Sf	Sweden	Regional	MrOS (osteoporotic fractures in men) Sweden cohort in Uppsala.	Jamar	70 - 75	548

Appendix 4

Author, year Ref	**Type**	**Country**	**Level**	**Sample description**	**Dynamometer**	**Age range (y)***	**N†**
Rodrigues-Barbosa (Barbados), 2011 [115]	Sf	Barbados	Local	Data taken from SABE (Survey on Health, Aging and Well Being in Latin America and the Caribbean), specifically Bridgetown.	Takei TK 1201	60 - 79	1119
Rodrigues-Barbosa (Cuba), 2011 [115]	Sf	Cuba	Local	Data taken from SABE (Survey on Health, Aging and Well Being in Latin America and the Caribbean), specifically Havana.	Takei TK 1201	60 - 79	1425
Schlussel, 2008 [125]	Sf	Brazil	Local	Three stage sampling procedure in the city of Niterói.	Jamar	20 - 69	2802
Seino, 2014 [135]	Sf	Japan	National	Six cohort studies participating in TMIG-LISA (Tokyo Metropolitan Institute of Gerontology-Longitudinal Interdisciplinary Study on Aging).	Smedley-like	65 - 84	4443
Sella, 2001 [144]	C	United States	Facility	Retrospective analysis of data collected from an occupational physician's patients (none had upper limb pathology).	Jamar	10 - 69	860
Semproli, 2007 [146]	C	Estonia	Local	Several schools in Tartu.	Takei TKK 5001	6 - 10	461
Shim, 2013 [129]	C	Korea, Republic of	Facility	Patients visiting a hospital for normal health screening visits.	Jamar	10 - 79	336

Appendix 4

Author, year Ref	Type	Country	Level	Sample description	Dynamometer	Age range (y)*	N†
Skelton, 1994 [50]	C	United Kingdom	Local	Volunteers recruited through local and national newspapers to attend Human Performance Laboratory in Hampstead, London.	Takei Kiki Kogyo Handgrip mechanical dynamometer	65 - 89	100
Spruit, 2013 [106]	C	United Kingdom	National	Recruitment via centrally coordinated identification and invitation from population-based registers (such as those held by the NHS) of potentially eligible people living within a reasonable travelling distance of an assessment centre.	Jamar	45 - 64	18735
Tsang, 2005 [127]	C	China	Regional	From 22 hospitals and clinics of the Hospital Authority in Hong Kong.	Jamar	21 - 70	544
Tveter, 2014 [154]	C	Norway	Local	Volunteers recruited from a range of work sites, schools, community centres for older adults.	Baseline	18 - 90	370
Vianna, 2007 [126]	C	Brazil	Facility	Those attending a private exercise medicine clinic.	Takei Digital Grip Dynamometer	18 - 75	2477
Wang, 2010 [108]	NS	Taiwan, Province of China	NS	Volunteers but source(s) NS.	Jamar	60 - 89	176
Werle, 2009 [158]	C	Switzerland	Local	Shopping centres and malls, secondary schools, senior sports groups and senior residences.	Jamar	18 - 84	922

Appendix 4

Author, year Ref	**Type**	**Country**	**Level**	**Sample description**	**Dynamometer**	**Age range (y)[*]**	**N[†]**
Wu, 2009 [133]	C	Taiwan, Province of China	National	The research team visited universities, mountain villages, public parks, markets, community halls, churches and temples. Access to volunteers was gained through community gatekeepers, district nurses, priests, and local community leaders.	Jamar	20 - 74	435
Yim, 2003 [130]	C	Korea, Republic of	Facility	Students in an elementary school in Suwon city, Korea	Jamar	7 - 12	712
Yoshimura, 2011 [136]	Sf	Japan	National	Second wave of a large-scale population cohort study: the ROAD study (research on osteoarthritis / osteopororis against disability)	Toei Light handgrip dynamometer	40 - 79	1776

Studies ordered by first author and then by year. C, convenience sample. NS, not specified. Sf, sampling frame used.

[*] The age range shown is that for the normative data items that I extracted from each paper. I excluded open-ended age ranges, such as 70+ years.

[†] N, the number of individuals with grip strength measurements in the age range specified. These are notably lower than the figures in the published papers by Frederiksen et al. and Spruit et al., since in these two studies I chose to extract details for a single height group only.

[‡] In the paper by Frederiksen et al., sample sizes for individual normative data items were not provided. Rather the sample size shown is approximated based on the standard deviation and standard error of the sample mean, which were provided for each item.

Appendix 5. Copy of PLoS ONE paper

This paper [5] is included overleaf.

Appendix 5

PLOS | ONE

RESEARCH ARTICLE

Grip Strength across the Life Course: Normative Data from Twelve British Studies

Richard M. Dodds[1]*, Holly E. Syddall[1], Rachel Cooper[2], Michaela Benzeval[3], Ian J. Deary[4], Elaine M. Dennison[1], Geoff Der[5], Catharine R. Gale[1,4], Hazel M. Inskip[1], Carol Jagger[6], Thomas B. Kirkwood[6], Debbie A. Lawlor[7], Sian M. Robinson[1], John M. Starr[4], Andrew Steptoe[8], Kate Tilling[7], Diana Kuh[2], Cyrus Cooper[1], Avan Aihie Sayer[1]

1. MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, United Kingdom, **2.** MRC Unit for Lifelong Health and Ageing at UCL, London, United Kingdom, **3.** Institute for Social and Economic Research, University of Essex, Colchester, United Kingdom, **4.** Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh, Edinburgh, United Kingdom, **5.** Social & Public Health Sciences Unit, Medical Research Council, Glasgow, United Kingdom, **6.** Institute for Ageing and Health, Newcastle University, Campus for Ageing and Vitality, Newcastle upon Tyne NE4 5PL, United Kingdom, **7.** MRC Integrative Epidemiology Unit, University of Bristol, Bristol, United Kingdom, **8.** Department of Epidemiology and Public Health, University College London, London, United Kingdom

*rd@mrc.soton.ac.uk

Citation: Dodds RM, Syddall HE, Cooper R, Benzeval M, Deary IJ, et al. (2014) Grip Strength across the Life Course: Normative Data from Twelve British Studies. PLoS ONE 9(12): e113637. doi:10.1371/journal.pone.0113637

Editor: Jose Vina, University of Valencia, Spain

Received: September 3, 2014

Accepted: October 27, 2014

Published: December 4, 2014

Data Availability: The authors confirm that, for approved reasons, some access restrictions apply to the data underlying the findings. All data used for this study are owned by third parties. Data access arrangements for the various datasets are described in the Supporting Information files.

Funding: RD is supported by a Wellcome Trust Fellowship (Grant number WT099055AIA). RC and DK are supported by the UK Medical Research Council (programme code MC_UU_12019/4). CJ is supported by the AXA Research Fund. MB is funded by the University of Essex and ESRC. DAL and KT work in a unit that receives support from the UK Medical Research Council (MC_UU_12013/5 and MC_UU_12013/9, respectively). Core support for the ALSPAC study is provided by the UK Medical Research Council and Wellcome Trust (092731). Acknowledgements: We are extremely grateful to all of the families who took part in this study, the midwives for recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses. The English Longitudinal Study of Ageing was developed by a team of researchers based at University College London, the Institute for Fiscal Studies and the National Centre for Social Research. The funding is provided by the National Institute on Aging (grants 2RO1AG7644-01A1 and 2RO1AG017644) and a consortium of UK government departments coordinated by the Office for National Statistics. The Hertfordshire Ageing Study and the Hertfordshire Cohort Study were funded by the UK Medical Research Council, the Wellcome Trust, Arthritis Research United Kingdom and the University of Southampton. The Lothian Birth Cohort 1921 was funded by the Biotechnology and Biological

Abstract

Introduction: Epidemiological studies have shown that weaker grip strength in later life is associated with disability, morbidity, and mortality. Grip strength is a key component of the sarcopenia and frailty phenotypes and yet it is unclear how individual measurements should be interpreted. Our objective was to produce cross-sectional centile values for grip strength across the life course. A secondary objective was to examine the impact of different aspects of measurement protocol.

Methods: We combined 60,803 observations from 49,964 participants (26,687 female) of 12 general population studies in Great Britain. We produced centile curves for ages 4 to 90 and investigated the prevalence of weak grip, defined as strength at least 2.5 SDs below the gender-specific peak mean. We carried out a series of sensitivity analyses to assess the impact of dynamometer type and measurement position (seated or standing).

Results: Our results suggested three overall periods: an increase to peak in early adult life, maintenance through to midlife, and decline from midlife onwards. Males were on average stronger than females from adolescence onwards: males' peak median grip was 51 kg between ages 29 and 39, compared to 31 kg in females between ages 26 and 42. Weak grip strength, defined as strength at least 2.5 SDs below the gender-specific peak mean, increased sharply with age, reaching a prevalence of 23% in males and 27% in females by age 80. Sensitivity analyses

Sciences Research Council, by a Royal Society-Wolfson Research Merit Award, and by the Scottish Government's Chief Scientist Office. The Lothian Birth Cohort 1936 was funded by Age UK (Disconnected Mind project). The work was done within the Centre for Cognitive Ageing and Cognitive Epidemiology (Mr/K026992/1); funding from the Medical Research Council and the Biotechnology and Biological Sciences Research Council is appreciated. For collating and collecting data, we thank the LBC1921 and LBC1936 research teams and the research nurses and staff at the Wellcome Trust Clinical Research Facility at the Western General Hospital, Edinburgh. The MRC National Survey of Health and Development is funded by the UK Medical Research Council. The Newcastle 85+ Study was funded by grants from the UK Medical Research Council (G0500997), the Dunhill Medical Trust (R124/0509), and the Newcastle Healthcare Charity. The research was also supported by the National Institute for Health Research Newcastle Biomedical Research Centre, based at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University. The waves of the Southampton Women's Survey included in this analysis were funded by the Medical Research Council, the University of Southampton, Dunhill Medical Trust, Arthritis Research UK and the UK Food Standards Agency. UKHLS is funded by the Economic and Social Research Council (ESRC). The study is carried out by the Institute for Social and Economic Research and data are made available through the UK Data Service. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

suggested our findings were robust to differences in dynamometer type and measurement position.

Conclusion: This is the first study to provide normative data for grip strength across the life course. These centile values have the potential to inform the clinical assessment of grip strength which is recognised as an important part of the identification of people with sarcopenia and frailty.

Introduction

Grip strength is associated with a variety of ageing outcomes [1–3] and forms a key component of sarcopenia [4] and frailty [5, 6] phenotypes. There is considerable interest in its role as a marker of healthy ageing, as an outcome in intervention studies, and as a potential tool for clinical assessment [7–9]. The life course epidemiology framework recognises that factors which promote healthy ageing may operate both by increasing the peak grip strength obtained in early adult life as well as by attenuating decline thereafter [10]. There is therefore a requirement for normative data for grip strength which cover all stages of the life course.

Existing normative data have focussed mainly on older ages [11] with relatively few studies examining childhood, adolescence, and early adult life. Since no studies have measured grip strength at all stages of the life course, it is necessary to combine data from studies at different ages. Bohannon et al [12] have previously combined data from 12 studies in adulthood; however, these studies were predominantly modestly-sized samples drawn from the USA. Cohort and cross-sectional studies of the general population conducted in Great Britain (GB) contain a wealth of grip strength data, which in keeping with clinical practice, have been collected using a variety of measurement protocols.

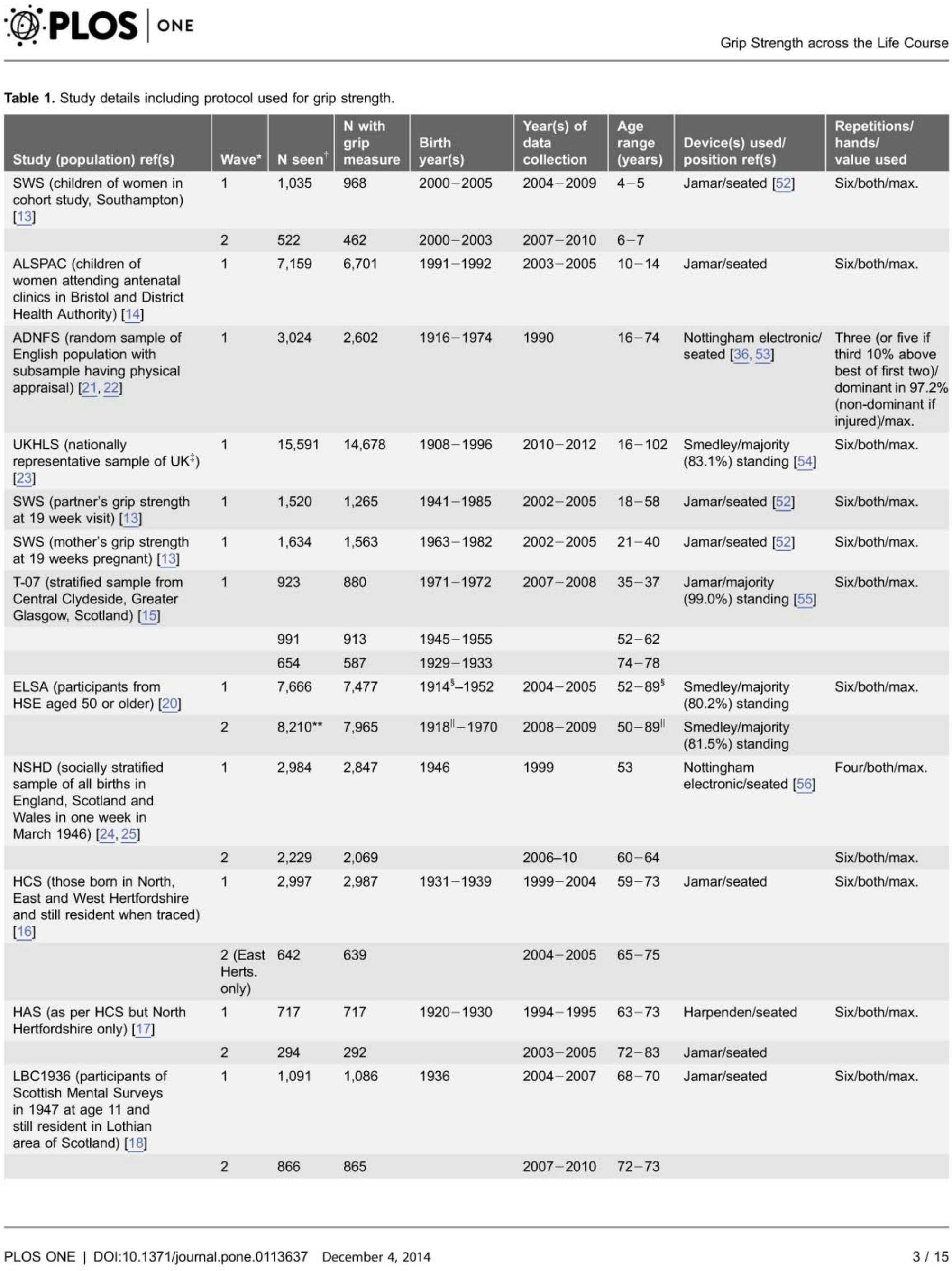
The objective of this paper was to produce cross-sectional centile values for grip strength across the life course by pooling data from a range of general population studies conducted in GB. A secondary objective was to examine the impact of different aspects of measurement protocol on the centile values obtained.

Methods

Data sources

We combined data from 12 studies conducted in GB as shown in Table 1. These were all samples of the general population, with eight studies including individuals from specific regions (SWS [13], ALSPAC [14], T-07 [15], HCS [16], HAS [17], LBC1936 [18], LBC1921 [18] and N85 [19]) and four drawing from one (ELSA [20] and ADNFS [21, 22]) or all three countries of GB (UKHLS [23] and NSHD [24, 25]). All included males and females. When combined, studies'

Appendix 5



PLOS | ONE

Grip Strength across the Life Course

Table 1. Study details including protocol used for grip strength.

Study (population) ref(s)	Wave*	N seen†	N with grip measure	Birth year(s)	Year(s) of data collection	Age range (years)	Device(s) used/ position ref(s)	Repetitions/ hands/ value used
SWS (children of women in cohort study, Southampton) [13]	1	1,035	968	2000–2005	2004–2009	4–5	Jamar/seated [52]	Six/both/max.
	2	522	462	2000–2003	2007–2010	6–7		
ALSPAC (children of women attending antenatal clinics in Bristol and District Health Authority) [14]	1	7,159	6,701	1991–1992	2003–2005	10–14	Jamar/seated	Six/both/max.
ADNFS (random sample of English population with subsample having physical appraisal) [21, 22]	1	3,024	2,602	1916–1974	1990	16–74	Nottingham electronic/ seated [36, 53]	Three (or five if third 10% above best of first two)/ dominant in 97.2% (non-dominant if injured)/max.
UKHLS (nationally representative sample of UK‡) [23]	1	15,591	14,678	1908–1996	2010–2012	16–102	Smedley/majority (83.1%) standing [54]	Six/both/max.
SWS (partner's grip strength at 19 week visit) [13]	1	1,520	1,265	1941–1985	2002–2005	18–58	Jamar/seated [52]	Six/both/max.
SWS (mother's grip strength at 19 weeks pregnant) [13]	1	1,634	1,563	1963–1982	2002–2005	21–40	Jamar/seated [52]	Six/both/max.
T-07 (stratified sample from Central Clydeside, Greater Glasgow, Scotland) [15]	1	923	880	1971–1972	2007–2008	35–37	Jamar/majority (99.0%) standing [55]	Six/both/max.
		991	913	1945–1955		52–62		
		654	587	1929–1933		74–78		
ELSA (participants from HSE aged 50 or older) [20]	1	7,666	7,477	1914§–1952	2004–2005	52–89§	Smedley/majority (80.2%) standing	Six/both/max.
	2	8,210**	7,965	1918‖–1970	2008–2009	50–89‖	Smedley/majority (81.5%) standing	
NSHD (socially stratified sample of all births in England, Scotland and Wales in one week in March 1946) [24, 25]	1	2,984	2,847	1946	1999	53	Nottingham electronic/seated [56]	Four/both/max.
	2	2,229	2,069		2006–10	60–64		Six/both/max.
HCS (those born in North, East and West Hertfordshire and still resident when traced) [16]	1	2,997	2,987	1931–1939	1999–2004	59–73	Jamar/seated	Six/both/max.
	2 (East Herts. only)	642	639		2004–2005	65–75		
HAS (as per HCS but North Hertfordshire only) [17]	1	717	717	1920–1930	1994–1995	63–73	Harpenden/seated	Six/both/max.
	2	294	292		2003–2005	72–83	Jamar/seated	
LBC1936 (participants of Scottish Mental Surveys in 1947 at age 11 and still resident in Lothian area of Scotland) [18]	1	1,091	1,086	1936	2004–2007	68–70	Jamar/seated	Six/both/max.
	2	866	865		2007–2010	72–73		

PLOS ONE | DOI:10.1371/journal.pone.0113637 December 4, 2014 3 / 15

Table 1. Cont.

Study (population) ref(s)	Wave*	N seen†	N with grip measure	Birth year(s)	Year(s) of data collection	Age range (years)	Device(s) used/ position ref(s)	Repetitions/ hands/ value used
LBC1921 (as per LBC1936 but participants in 1932 at age 11) [18]	1	550	544	1921	1999–2001	78–80	Jamar/seated [57]	Six/both (values from dominant hand used in analyses)/max.
	2	321	321		2003–2005	82–84		
	3	237	204		2007–2008	86–87		
N85 (those registered with a Newcastle/North Tyneside general practice) [19]	1	849	819	1921	2006–2007	84–86	Takei digital/standing	Four/both/max.
	2	632	603		2007–2009	85–88		
	3	486	453		2009–2010	87–89		
	4	344	296		2011–2012	89–91		

Studies ordered by age at first wave of data collection, youngest first.

*With measurement of grip strength.

†The number here typically refers to the number of participants seen at the stage of the study where grip strength would normally be measured (e.g. at a clinic visit).

‡The wave 2 nurse health assessment in which grip strength was measured was only carried out in England, Scotland and Wales.

⁎In the first wave of ELSA to measure grip (wave 2), only core study members (n=8,780) were eligible to take part in the nurse visit and this was completed in the number shown.

§80 individuals were aged 90 or older and their exact age is not available.

**In the second wave of ELSA to measure grip strength (wave 4) only core study members (n=9,886) core members were eligible to take part in the nurse visit and this was completed in the number shown.

||91 individuals were aged 90 or older and their exact age is not available.

ADNFS Allied Dunbar National Fitness Survey, ALSPAC Avon Longitudinal Study of Parents and Children, ELSA English Longitudinal Study of Ageing, HAS Hertfordshire Ageing Study, HCS Hertfordshire Cohort Study, HSE Health Survey for England, LBC1921 and LBC1936 Lothian Birth Cohorts of 1921 and 1936, N85 Newcastle 85+ Study, NSHD Medical Research Council National Survey of Health and Development, SWS Southampton Women's Survey, T-07 West of Scotland Twenty-07 Study, UKHLS Understanding Society: the UK Household Panel Study.

doi:10.1371/journal.pone.0113637.t001

grip measurements covered ages 4 to 90+ years with measurements occurring between 1990 and 2012. Three studies had prospectively recruited participants at or shortly after birth (SWS, ALSPAC and NSHD) and in SWS, grip strength measurements were also available from the mother during her pregnancy and from her partner. The majority (n=10) of studies had measured grip strength at one or two waves, with LBC1921 and N85 having data from three and four waves, respectively. All studies had received relevant ethical approval and all participants gave informed consent.

Grip strength measurement

Information on the grip strength measurement protocols is shown in Table 1. Seven studies used the Jamar dynamometer (including the second wave of HAS, which used the Harpenden dynamometer at the first wave), two studies (ELSA and UKHLS) used the Smedley dynamometer, two studies used the Nottingham electronic dynamometer (ADNFS and NSHD), and N85 used the Takei dynamometer. The majority (n=8) of studies measured grip in the seated position for all participants.

All studies took measurements from both hands except ADNFS which used the dominant hand only (except in case of injury), and LBC1921 which measured both hands but provided values from only the dominant hand for analyses. The majority of studies used three trials from each hand, except for N85 and the first wave of NSHD, which used two trials. Taken together, this meant that the total number of grip strength values we could use in analyses varied: either three (ADNFS and LBC1921), four (N85 and the first wave of NSHD) or six (the remainder). We therefore always used the maximum of these values for our analyses, since the maximum is less likely to be affected by the number of trials than the mean [26].

Statistical analyses

Our main analyses used all available data, including values for individuals who had had grip strength measured at more than one age. We produced gender-specific cross-sectional centiles for grip strength using the Box-Cox Cole and Green (BCCG) distribution (also known as the LMS method [27]) implemented in the Generalised Additive Models for Location, Scale and Shape (GAMLSS) library [28] for the statistical program, R [29]. We used restricted cubic splines to model the relationship between age and each of the three model parameters: the median, variation and skewness. We identified the optimum number of degrees of freedom for each parameter using the GAMLSS command find.hyper. We anticipated a smooth relationship with age and therefore used a maximum number of degrees of freedom of seven and increased the standard penalty. We looked for evidence of kurtosis in the grip strength values by using the Box-Cox power exponential distribution. We modelled the mean and SD of grip at each age using the normal distribution in GAMLSS.

We defined a T-score for grip strength as an individual's value expressed as a multiple of the number of standard deviations below the peak mean value encountered in young adult life. This is the same as the approach applied to measurements of bone density in the diagnosis of osteoporosis [30], except we used gender-specific peak mean values for grip strength. We explored the gender-specific prevalence of weak grip strength in mid and late adult life in two ways. Firstly, using a T-score for grip strength of equal to or less than −2 as used previously [31], and secondly using a T-score of equal to or less than −2.5, as widely used in the diagnosis of osteoporosis.

We carried out sensitivity analyses by producing further sets of centile curves and comparing these to our main findings. We restricted the data to the first observation for each individual. We produced dynamometer-specific sets of centile curves by allowing the median, variation and skewness curves to vary by dynamometer type. Similarly we considered the impact of the position of grip strength measurement: standing or sitting, with the latter divided into those who were sitting as per protocol and those who chose to sit or were unable to stand.

Finally we checked if any one study was unduly influencing the results obtained by excluding each study in turn. To compare each additional model to the main findings, we examined absolute differences for the 10th, median and 90th centiles; we considered that a 10 percent difference or less in the centile values at any given age provided evidence of acceptably similar findings. We carried out data management using Stata version 12.0 [32].

Results

We used a total of 60,803 observations of grip strength from 49,964 participants to produce the centile values for grip strength as shown in Table 2 and Figure 1. Eight of the twelve studies had measured grip strength in mid-late adult life, as reflected by the median age of the observations: 58 years (IQR 36–69 years).

The centile curves (Figure 1) suggested three overall periods: an increase to peak in early adult life, broad maintenance through to midlife and decline from midlife onwards. Males were stronger on average than females from adolescence onwards; by age 25, males' median strength was 1.6 times that of females and this ratio increased slightly to 1.7 from age 50 onwards. Males reached a peak median grip of 51 kg (to the nearest whole kg) between ages 29 and 39, compared to the peak female median grip of 31 kg between ages 26 and 42.

The spread of grip strength values relative to the median (the sigma parameter from the BCCG model, an approximation to the coefficient of variation) increased slightly in later life, from 0.20 in the fourth decade in men and women, rising to 0.25 and 0.29 in the ninth decade in men and women, respectively. We found no evidence of skewness or kurtosis in grip strength at any age.

Estimated prevalence of weak grip strength in mid and late adult life, defined by gender-specific T-scores of less than or equal to −2 and −2.5, are shown in Figure 2. These were derived relative to the peak mean (SD) for grip strength of 51.9 (9.9) kg in males and 31.4 (6.1) kg in females, both occurring at age 32. Females and males had similar prevalence of weak grip strength during the decline phase. The prevalence of weak grip increased rapidly in late adult life; using a T-score of −2.5, our results suggested that by age 80, around a quarter had weak grip strength (23.0% of males and 26.6% of females).

Sensitivity analyses (see Figures S1, S2, and S3 in File S1) suggested that the centile curves were robust to the inclusion of repeat measurements of grip strength and protocol differences between studies. In comparison to our main results, we generally saw centile differences of less than 10 per cent when restricting the data to the first observation for each individual, and when producing centile curves stratified by dynamometer type. This was also the case for centiles stratified by whether participants were seated (as per protocol) or standing. Those who chose to sit or were unable to stand tended to be weaker and this difference became more pronounced with age until the ninth decade when their 10th centile values approached 10 per cent lower than the combined results. Finally, the centiles produced from analyses excluding each study in turn (not

Appendix 5

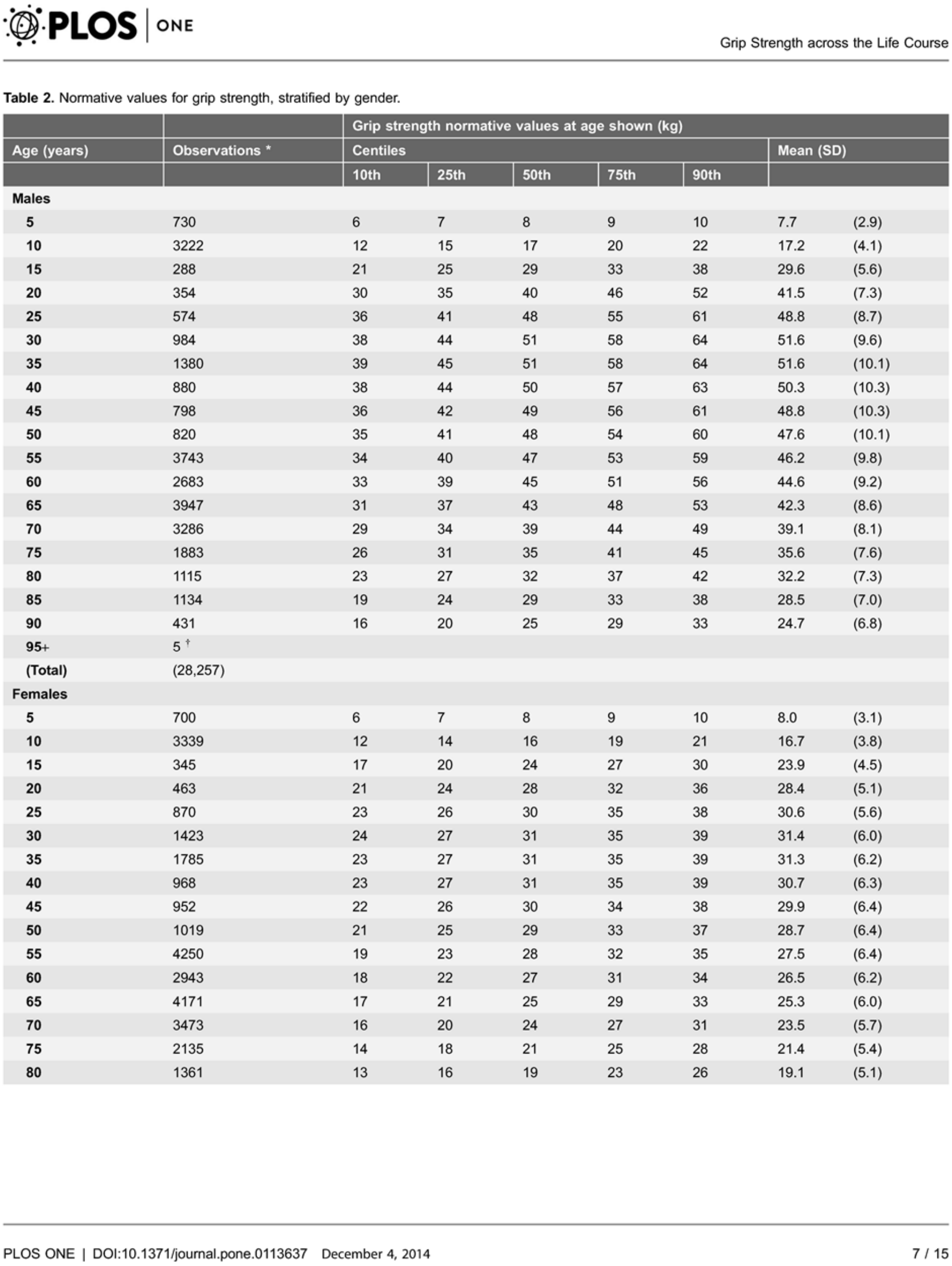


Table 2. Normative values for grip strength, stratified by gender.

		Grip strength normative values at age shown (kg)						
Age (years)	**Observations ***	**Centiles**					**Mean (SD)**	
		10th	**25th**	**50th**	**75th**	**90th**		
Males								
5	730	6	7	8	9	10	7.7	(2.9)
10	3222	12	15	17	20	22	17.2	(4.1)
15	288	21	25	29	33	38	29.6	(5.6)
20	354	30	35	40	46	52	41.5	(7.3)
25	574	36	41	48	55	61	48.8	(8.7)
30	984	38	44	51	58	64	51.6	(9.6)
35	1380	39	45	51	58	64	51.6	(10.1)
40	880	38	44	50	57	63	50.3	(10.3)
45	798	36	42	49	56	61	48.8	(10.3)
50	820	35	41	48	54	60	47.6	(10.1)
55	3743	34	40	47	53	59	46.2	(9.8)
60	2683	33	39	45	51	56	44.6	(9.2)
65	3947	31	37	43	48	53	42.3	(8.6)
70	3286	29	34	39	44	49	39.1	(8.1)
75	1883	26	31	35	41	45	35.6	(7.6)
80	1115	23	27	32	37	42	32.2	(7.3)
85	1134	19	24	29	33	38	28.5	(7.0)
90	431	16	20	25	29	33	24.7	(6.8)
95+	5 †							
(Total)	(28,257)							
Females								
5	700	6	7	8	9	10	8.0	(3.1)
10	3339	12	14	16	19	21	16.7	(3.8)
15	345	17	20	24	27	30	23.9	(4.5)
20	463	21	24	28	32	36	28.4	(5.1)
25	870	23	26	30	35	38	30.6	(5.6)
30	1423	24	27	31	35	39	31.4	(6.0)
35	1785	23	27	31	35	39	31.3	(6.2)
40	968	23	27	31	35	39	30.7	(6.3)
45	952	22	26	30	34	38	29.9	(6.4)
50	1019	21	25	29	33	37	28.7	(6.4)
55	4250	19	23	28	32	35	27.5	(6.4)
60	2943	18	22	27	31	34	26.5	(6.2)
65	4171	17	21	25	29	33	25.3	(6.0)
70	3473	16	20	24	27	31	23.5	(5.7)
75	2135	14	18	21	25	28	21.4	(5.4)
80	1361	13	16	19	23	26	19.1	(5.1)

Table 2. Cont.

		Grip strength normative values at age shown (kg)						
Age (years)	**Observations ***	**Centiles**					**Mean (SD)**	
		10th	**25th**	**50th**	**75th**	**90th**		
85	1632	11	14	17	20	23	16.6	(4.7)
90	702	9	11	14	17	20	14.2	(4.4)
95+	15 †							
(Total)	(32,546)							

The centiles and mean (SD) values were derived from the GAMLSS models for the exact ages shown.
*Number of grip strength observations refers to the number of individuals at age shown ±2.5 years (to give an indication of the sample size at different ages).
†Limited data were available in the 95+ years category so centile values are not shown.

doi:10.1371/journal.pone.0113637.t002

shown) were acceptably similar, except for ALSPAC (males only) and N85 (both males and females); this was perhaps not surprising as the exclusion of each of these studies led to sparse or absent data in the relevant age ranges.

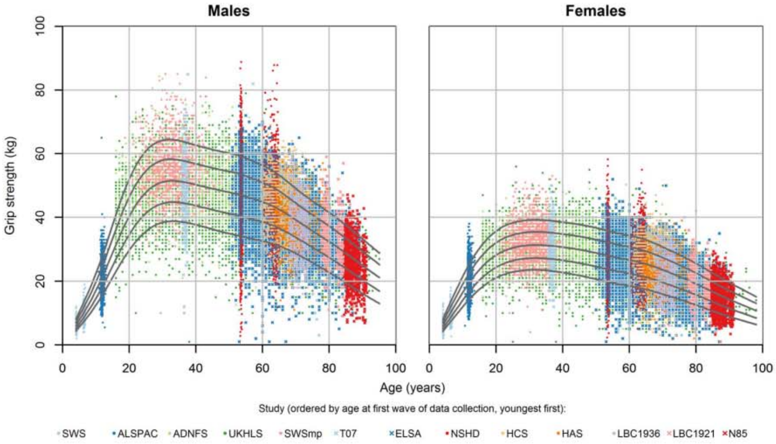


Figure 1. Cross-cohort centile curves for grip strength. Centiles shown 10, 25th, 50th, 75th and 90th. ADNFS Allied Dunbar National Fitness Survey, ALSPAC Avon Longitudinal Study of Parents and Children, ELSA English Longitudinal Study of Ageing, HAS Hertfordshire Ageing Study, HCS Hertfordshire Cohort Study, LBC1921 and LBC1936 Lothian Birth Cohorts of 1921 and 1936, N85 Newcastle 85+ Study, NSHD Medical Research Council National Survey of Health and Development, SWS Southampton Women's Survey, SWSmp mothers and their partners from the SWS, T-07 West of Scotland Twenty-07 Study, UKHLS Understanding Society: the UK Household Panel Study.

doi:10.1371/journal.pone.0113637.g001

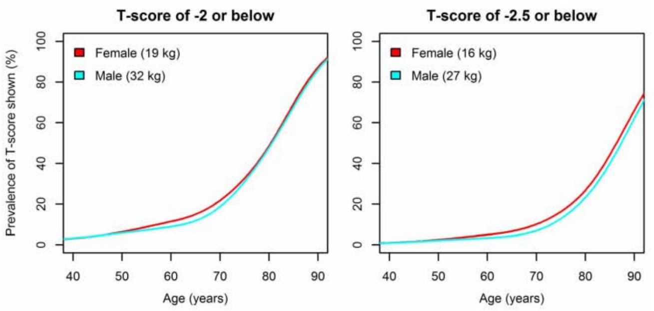


Figure 2. Gender-specific prevalence of weak grip strength based on T-scores of −2 and −2.5. Values shown in brackets are the gender-specific cut-off values calculated by subtracting the relevant number of standard deviations (2 or 2.5) from the young adult peak mean.

doi:10.1371/journal.pone.0113637.g002

Discussion

Main findings

We have combined data from 12 general population studies conducted in GB to produce normative data for grip strength across the life course. We have shown that grip strength increases to a peak in early adult life, and is then followed by a period of broad maintenance prior to decline with increasing age. Our study shows that the strength of males and females is similar until adolescence, after which males began to gain strength more rapidly to a higher peak median of 51 kg between ages 29 and 39, compared to the peak female median grip of 31 kg between ages 26 and 42. Sensitivity analyses demonstrated that the normative data produced by this study are robust to a range of dynamometer types and also to measurement in the seated or standing positions. Our normative data for grip strength across the life course will inform the clinical interpretation of grip strength measurements and will help to establish thresholds for identification of low muscle strength for use in clinical practice and the operationalization of consensus definitions of sarcopenia and frailty.

Comparison with other studies

Our study is the first to produce normative data for grip strength across the whole life course in GB (or in any other setting, as far as we are aware) so we elected to compare our results with previously published studies of grip strength in international as well as British settings, grouped by the stage(s) of the life course they addressed. We considered differences between previously published mean values and our median values for grip strength at a selection of ages, expressed as a percentage of our value. Normative data from studies identified in childhood and adolescence varied in their relationship to our findings: either broadly similar

[33], consistently higher [34] (on average 27%), or similar at young ages and higher at older ages [35] (on average 9% higher overall). However the three previously published studies may not provide reliable estimates of the general population since they contained small numbers of individuals at each given age and gender: at most 43 (mean 22) in each of the ages compared.

We also compared our values to those from four studies addressing adult ages either side of the peak (ages 20–80). Three of these [12, 36, 37] showed agreement with our results, with average differences of around 6%. In one case [36] this is not surprising, since the article reported results from the ADNFS, a study included in our analysis. The second study was the meta-analysis by Bohannon et al [12] which combined data from a range of studies in developed country settings. The third study [37] reported normative data for male participants in the Baltimore Longitudinal Study of Ageing. The normative values from the fourth study [38], based in Switzerland, were on average 11% higher than ours.

Finally, we compared our values to those from three studies which considered age-related differences in grip strength during the decline phase. Normative values from UK Biobank were stratified into eight height groups [39]; in comparison to the average of the middle two groups, our values were on average 7% higher. The TILDA study in Ireland [11] stratified values into two height groups; our values were around 15% higher the average of the groups. Finally a study from Denmark [40] stratified values into five height groups, the middle of which were similar to our own values.

Our results expand on the range of ages as well as the contributing sample sizes of existing studies presenting normative data for grip strength. They also broadly agree with previously published results for adults from developed country settings. Fewer normative data for grip strength in children and adolescents were available for comparison.

We are not aware of any other studies which have compared the centile values obtained from general population samples using different dynamometer types. Several small studies (with 104 or fewer participants) have used comparisons of repeat measurements with two or more dynamometers to investigate whether similar readings are produced. Their findings have varied, with some reporting that readings from different dynamometers are comparable [41–44], or can be converted using an equation [45], and others concluding that the limits of agreement are too broad and the devices are not interchangeable in either way [41, 46]. From our results, we conclude that the different dynamometers used produce acceptably similar normative data, albeit within the ages at which measurements were observed.

Similarly, studies investigating the role of measurement position are inconsistent, with one finding no difference [47] and another suggesting that standing produces higher values [48]. Our results show that normative data from studies using the seated and standing positions are comparable, although unsurprisingly individuals who chose not to stand or were unable to do so had weaker grip. Although our centiles appeared to be robust to differences in measurement protocol, this does not detract from the importance of recent calls for standardisation in future data collections [26, 49].

Clinical relevance of findings

Our findings have confirmed that grip strength increases to a peak in early adult life and is then followed by a period of maintenance prior to decline with increasing age and that this age related decline in grip strength starts as early as the fifth decade of life in both men and women. The life course trajectory identified for grip strength in our study is similar to the well-established life course trajectory of bone mineral density (BMD) [30]. This supports the use of peak values from early adult life to define cut-offs for weak grip at subsequent ages using T-scores. We have used this approach to estimate the prevalence of weak grip based on T-scores of both −2 and −2.5. A T-score of less than or equal to −2 has previously been used by Lauretani et al [31] for grip strength, although the prevalence figures for weak strength that they report using this value, especially those for men, are considerably higher than our own. This difference may have arisen as in their sample, they include 25 men at ages 20–29 with mean (SD) grip 61.1 (10.5) kg. The cut-off for weak grip in men is not stated in their paper but we presume it is then 40 kg (61.1 less 2 × 10.5) – substantially higher than our own (32kg). By fitting centile curves that span all stages of the life course, we have established more informative peak values on which to base T-scores.

In our data, we still found a high prevalence of weak grip strength based on a T-score of −2 or below (equivalent to 19 kg in females and 32 kg in males, or weaker) with almost half of participants at or below this level at age 80. It may therefore be that a T-score of −2.5 (equivalent to 16 kg in females and 27 kg in males) produces a more discriminatory cut-off for weak grip – with 23.0% of males and 26.6% of females at or below this level at age 80.

It is important that any cut-off values relate to relevant outcomes. Two studies have done this in a cross-sectional fashion. Lauretani et al [31] examined the optimum grip strength values for detecting slow measured walking speed and self-reported difficulty in walking 1 km; they found that grip strength of 30 kg in males and 19 kg in females provided the optimum balance between sensitivity and specificity. Sallinen et al [9] looked at self-reported difficulties with mobility and found similar overall cut-off s: 37 kg in males and 21 kg in females. Clearly there is a need to examine similar relationships in a longitudinal fashion if individual values of grip strength are to be used as a marker of those at risk of adverse outcomes.

Strengths and limitations

This study had some limitations. First, our data contained a limited range of birth years (at most 32 years) for any given ten year age group. As such the relationships shown with age may partly represent cohort effects [45]. However as the aim of this paper was to produce normative data for current use, the recent period of data collection seems appropriate. Second, our normative data for grip are cross-sectional and are likely to underestimate individual decline; our centiles should therefore not be used for monitoring individual trajectories in grip strength [40, 50, 51]. Third, we have not considered the potential impact of recognised determinants of grip strength, such as height, on the centile values presented. This is an area for future research. Finally selection and loss-to-follow up biases may have influenced our centile values; however we included a wide range of population based studies from different geographical regions of GB and the centile curves were robust to the exclusion of any individual study.

Our study also had many strengths. First, we included data from many large general population studies in GB covering all stages of the life course. Second, we used a modelling approach which allowed grip strength to vary as a smooth function of age and to incorporate any non-normality in grip (skewness or kurtosis). Finally, extensive sensitivity analyses demonstrated that our centile curves for grip strength are robust to differences in the position (seated or standing) and the dynamometer used for measurement.

Conclusions

In conclusion, we have used existing data from a range of studies conducted in GB to produce centile curves for grip strength across the life course. These centile values have the potential to inform the clinical assessment of grip strength which is recognised as an important part of the identification of people with sarcopenia and frailty.

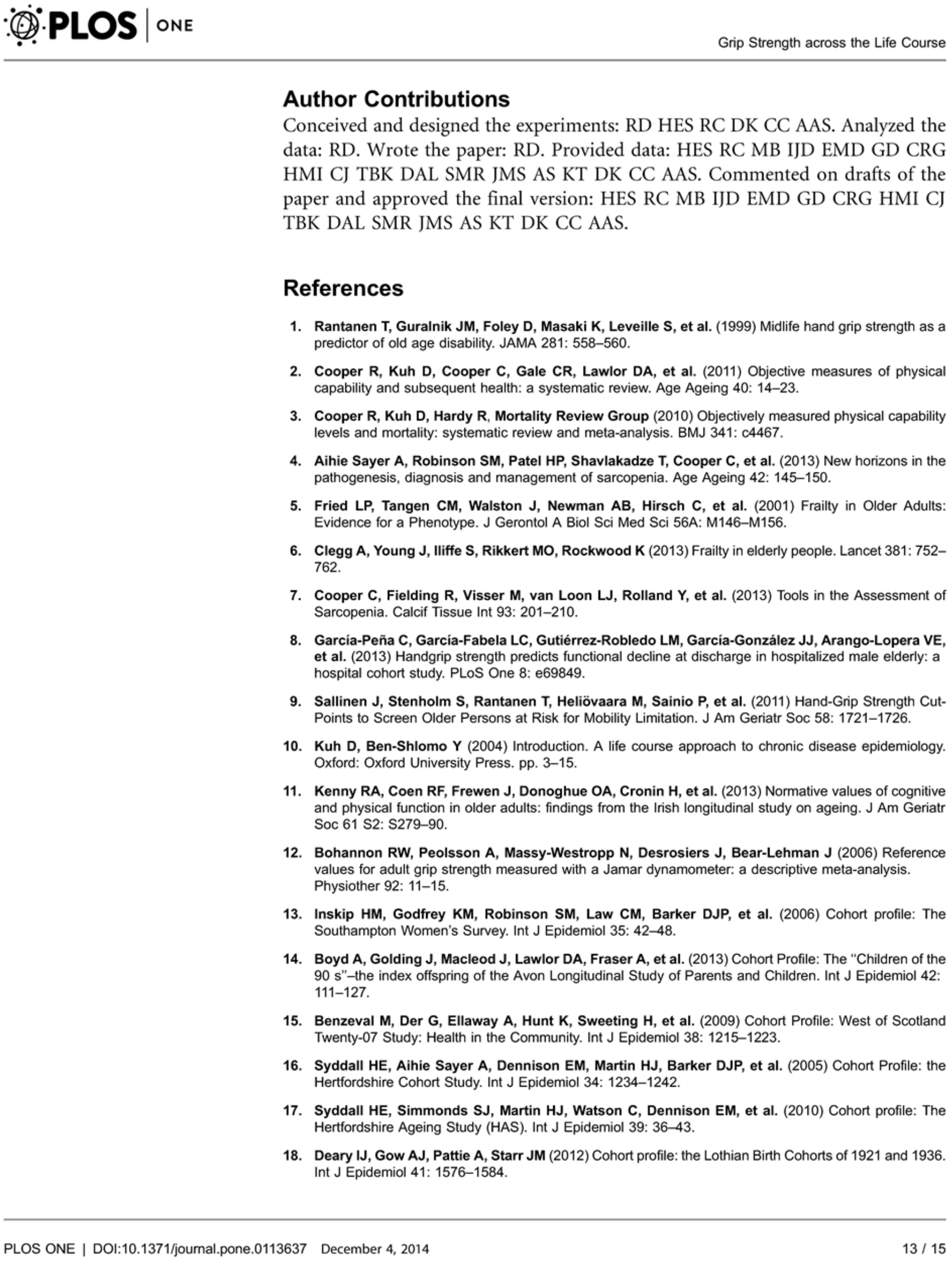
Supporting Information

File S1. Figure S1, Centiles from first observation per individual only. Figure S2, Centiles stratified by dynamometer type. Figure S3, Centiles stratified by position of measurement.
doi:10.1371/journal.pone.0113637.s001 (DOCX)

File S2. Data access details for 12 included studies.
doi:10.1371/journal.pone.0113637.s002 (DOCX)

Acknowledgments

We are grateful to the participants and data collection teams of all the included studies.
We would like to thank Prof. Clive Osmond, PhD (MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK) for his help with the approach of using centile curves to describe the grip strength data.



Author Contributions

Conceived and designed the experiments: RD HES RC DK CC AAS. Analyzed the data: RD. Wrote the paper: RD. Provided data: HES RC MB IJD EMD GD CRG HMI CJ TBK DAL SMR JMS AS KT DK CC AAS. Commented on drafts of the paper and approved the final version: HES RC MB IJD EMD GD CRG HMI CJ TBK DAL SMR JMS AS KT DK CC AAS.

References

1. **Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, et al.** (1999) Midlife hand grip strength as a predictor of old age disability. JAMA 281: 558–560.
2. **Cooper R, Kuh D, Cooper C, Gale CR, Lawlor DA, et al.** (2011) Objective measures of physical capability and subsequent health: a systematic review. Age Ageing 40: 14–23.
3. **Cooper R, Kuh D, Hardy R, Mortality Review Group** (2010) Objectively measured physical capability levels and mortality: systematic review and meta-analysis. BMJ 341: c4467.
4. **Aihie Sayer A, Robinson SM, Patel HP, Shavlakadze T, Cooper C, et al.** (2013) New horizons in the pathogenesis, diagnosis and management of sarcopenia. Age Ageing 42: 145–150.
5. **Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, et al.** (2001) Frailty in Older Adults: Evidence for a Phenotype. J Gerontol A Biol Sci Med Sci 56A: M146–M156.
6. **Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K** (2013) Frailty in elderly people. Lancet 381: 752–762.
7. **Cooper C, Fielding R, Visser M, van Loon LJ, Rolland Y, et al.** (2013) Tools in the Assessment of Sarcopenia. Calcif Tissue Int 93: 201–210.
8. **García-Peña C, García-Fabela LC, Gutiérrez-Robledo LM, García-González JJ, Arango-Lopera VE, et al.** (2013) Handgrip strength predicts functional decline at discharge in hospitalized male elderly: a hospital cohort study. PLoS One 8: e69849.
9. **Sallinen J, Stenholm S, Rantanen T, Heliövaara M, Sainio P, et al.** (2011) Hand-Grip Strength Cut-Points to Screen Older Persons at Risk for Mobility Limitation. J Am Geriatr Soc 58: 1721–1726.
10. **Kuh D, Ben-Shlomo Y** (2004) Introduction. A life course approach to chronic disease epidemiology. Oxford: Oxford University Press. pp. 3–15.
11. **Kenny RA, Coen RF, Frewen J, Donoghue OA, Cronin H, et al.** (2013) Normative values of cognitive and physical function in older adults: findings from the Irish longitudinal study on ageing. J Am Geriatr Soc 61 S2: S279–90.
12. **Bohannon RW, Peolsson A, Massy-Westropp N, Desrosiers J, Bear-Lehman J** (2006) Reference values for adult grip strength measured with a Jamar dynamometer: a descriptive meta-analysis. Physiother 92: 11–15.
13. **Inskip HM, Godfrey KM, Robinson SM, Law CM, Barker DJP, et al.** (2006) Cohort profile: The Southampton Women's Survey. Int J Epidemiol 35: 42–48.
14. **Boyd A, Golding J, Macleod J, Lawlor DA, Fraser A, et al.** (2013) Cohort Profile: The "Children of the 90 s"–the index offspring of the Avon Longitudinal Study of Parents and Children. Int J Epidemiol 42: 111–127.
15. **Benzeval M, Der G, Ellaway A, Hunt K, Sweeting H, et al.** (2009) Cohort Profile: West of Scotland Twenty-07 Study: Health in the Community. Int J Epidemiol 38: 1215–1223.
16. **Syddall HE, Aihie Sayer A, Dennison EM, Martin HJ, Barker DJP, et al.** (2005) Cohort Profile: the Hertfordshire Cohort Study. Int J Epidemiol 34: 1234–1242.
17. **Syddall HE, Simmonds SJ, Martin HJ, Watson C, Dennison EM, et al.** (2010) Cohort profile: The Hertfordshire Ageing Study (HAS). Int J Epidemiol 39: 36–43.
18. **Deary IJ, Gow AJ, Pattie A, Starr JM** (2012) Cohort profile: the Lothian Birth Cohorts of 1921 and 1936. Int J Epidemiol 41: 1576–1584.

19. **Collerton J, Davies K, Jagger C, Kingston A, Bond J, et al.** (2009) Health and disease in 85 year olds: baseline findings from the Newcastle 85+ cohort study. BMJ 399: b4904.

20. **Marmot M et al. n.d.)** English Longitudinal Study of Ageing: Wave 0 (1998, 1999 and 2001) and Waves 1–5 (2002–2011) [computer file]. 18th Edition. Colchester, Essex: UK Data Archive [distributor], February 2013. SN: 5050, http://dx.doi.org/10.5255/UKDA-SN-5050-4.

21. **Activity and Health Research. Allied Dunbar National Fitness Survey** (1992) A report on Activity Patterns and Fitness levels: Main Findings. London: Sports Council and Health Education Authority.

22. **Activity and Health Research Limited (n.d.)** Allied Dunbar National Fitness Survey, 1990 [computer file]. Colchester, Essex: UK Data Archive [distributor], May 1995. SN: 3303, http://dx.doi.org/10.5255/UKDA-SN-3303-1.

23. **University of Essex (n.d.)** Institute for Social and Economic Research and National Centre for Social Research, Understanding Society: Waves 1–2, 2009–2011 [computer file]. 4th Edition. Colchester, Essex: UK Data Archive [distributor], December 2012. SN: 6614.

24. **Wadsworth M, Kuh D, Richards M, Hardy R** (2006) Cohort Profile: The 1946 National Birth Cohort (MRC National Survey of Health and Development). Int J Epidemiol 35: 49–54.

25. **Kuh D, Pierce M, Adams J, Deanfield J, Ekelund U, et al.** (2011) Cohort profile: updating the cohort profile for the MRC National Survey of Health and Development: a new clinic-based data collection for ageing research. Int J Epidemiol 40: e1–9.

26. **Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, et al.** (2011) A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing 40: 423–429.

27. **Cole TJ, Green PJ** (1992) Smoothing reference centile curves: the LMS method and penalized likelihood. Stat Med 11: 1305–1319.

28. **Stasinopoulos DM, Rigby RA** (2007) Generalized Additive Models for Location Scale and Shape (GAMLSS) in R. J Stat Soft 23.

29. **R Core Team** (2013) R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. Available: http://www.R-project.org/.

30. **Kanis J** (2002) Diagnosis of osteoporosis and assessment of fracture risk. Lancet 359: 1929–1936.

31. **Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, et al.** (2003) Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol 95: 1851–1860.

32. **StataCorp** (2011) Stata Statistical Software: Release 12.

33. **Molenaar HMT, Selles RW, Zuidam JM, Willemsen SP, Stam HJ, et al.** (2010) Growth diagrams for grip strength in children. Clin Orthop Relat Res 468: 217–223.

34. **Mathiowetz V, Wiemer DM, Federman SM** (1985) Grip and Pinch Strength: Norms for 6- to 19-Year-Olds. Am J Occ Ther 40: 705–711.

35. **De Smet L, Vercammen A** (2001) Grip strength in children. J Pedr Ortho B 10: 352–354.

36. **Nevill AM, Holder RL** (2000) Modelling handgrip strength in the presence of confounding variables: results from the Allied Dunbar National Fitness Survey. Ergonomics 43: 1547–1558.

37. **Kallman D, Plato C, Tobin J** (1990) The role of muscle loss in the age-related decline of grip strength: cross-sectional and longitudinal perspectives. J Gerontol 45: M82–8.

38. **Werle S, Goldhahn J, Drerup S, Simmen BR, Sprott H, et al.** (2009) Age- and gender-specific normative data of grip and pinch strength in a healthy adult Swiss population. J Hand Surg [Eur]. 34: 76–84.

39. **Spruit MA, Sillen MJH, Groenen MTJ, Wouters EFM, Franssen FME** (2013) New normative values for handgrip strength: results from the UK Biobank. JAMDA 14: 775.e5–11.

40. **Frederiksen H, Hjelmborg J, Mortensen J, McGue M, Vaupel JW, et al.** (2006) Age trajectories of grip strength: cross-sectional and longitudinal data among 8,342 Danes aged 46 to 102. Ann Epidemiol 16: 554–562.

41. **Amaral JF, Mancini M, Novo Júnior JM** (2012) Comparison of three hand dynamometers in relation to the accuracy and precision of the measurements. Rev Bras Fisioter 16: 216–224.

42. **Beaton DE, Driscoll SWO, Richards RR** (1995) Grip Strength Testing Using the BTE Work Simulator and the Jamar Dynamometer: A Comparative Study. J Hand Surg 20A: 293–298.

43. **Mathiowetz V** (2002) Comparison of Rolyan and Jamar dynamometers for measuring grip strength. Occup Ther Int 9: 201–209.

44. **Shechtman O, Gestewitz L, Kimble C** (2005) Reliability and validity of the DynEx dynamometer. J Hand Ther 18: 339–347.

45. **Nahhas RW, Choh AC, Lee M, Chumlea WMC, Duren DL, et al.** (2010) Bayesian longitudinal plateau model of adult grip strength. Am J Hum Biol 22: 648–656.

46. **Guerra RS, Amaral TF** (2009) Comparison of hand dynamometers in elderly people. J Nutr Heal Ageing 13: 907–912.

47. **Shechtman O, Mackinnon L, Locklear C** (2001) Using the BTE Primus to measure grip and wrist flexion strength in physically active wheelchair users: an exploratory study. Am J Occup Ther 55: 393–400.

48. **Balogun J, Akomolafe C, Amusa L** (1991) Grip strength: effects of testing posture and elbow position. Arch Phys Med Rehabil 72: 280–283.

49. **Reuben DB, Magasi S, McCreath HE, Bohannon RW, Wang Y-C, et al.** (2013) Motor assessment using the NIH Toolbox. Neurology 80: S65–75.

50. **Desrosiers J, Hébert R, Bravo G, Rochette A** (1998) Comparison of cross-sectional and longitudinal designs in the study of aging of upper extremity performance. J Gerontol A Biol Sci Med Sci 53A: B362–8.

51. **Kirkwood TBL** (1998) Alex Comfort and the measure of ageing. Exp Gerontol 33: 135–140.

52. **Dodds R, Macdonald-Wallis C, Kapasi T, Aihie Sayer A, Robinson S, et al.** (2012) Grip strength at. 4 years in relation to birth weight. J Devel Orig Heal Dis 3: 111–115.

53. **Fentem PH, Collins MF, Tuxworth W, Walker A, Hoinville E, et al.** (1994) Allied Dunbar National Fitness Survey. Technical Report. London: Sports Council.

54. **McFall S, Petersen J, Kaminska O, Lynn P** (2013) Understanding Society - The UK Household Longitudinal Study: Wave 2 Nurse Health Assessment, 2010–2012, Guide to Nurse Health Assessment (2013). Colchester: University of Essex.

55. **Der G, Batty GD, Benzeval M, Deary IJ, Green MJ, et al.** (2012) Is telomere length a biomarker for aging: cross-sectional evidence from the west of Scotland? PLoS One 7: e45166.

56. **Kuh D, Bassey J, Hardy R, Aihie Sayer A, Wadsworth M, et al.** (2002) Birth Weight, Childhood Size, and Muscle Strength in Adult Life: Evidence from a Birth Cohort Study. Am J Epidemiol 156: 627–633.

57. **Deary I, Johnson W** (2011) Losing one's grip: a bivariate growth curve model of grip strength and nonverbal reasoning from age 79 to 87 years in the Lothian Birth Cohort 1921. J Gerontol B Psych Sci 66: 699–707.

List of References

1. Dodds R, Denison HJ, Ntani G, *et al.* Birth weight and muscle strength: a systematic review and meta-analysis. J Nutr Heal. Ageing. 2012;16(7):609–15.

2. Dodds R, Macdonald-Wallis C, Kapasi T, *et al.* Grip strength at 4 years in relation to birth weight. J Devel Orig Heal. Dis. 2012;3(02):111–115.

3. Dodds R, Kuh D, Aihie Sayer A, Cooper R. Physical activity levels across adult life and grip strength in early old age : updating findings from a British birth cohort. Age Ageing. 2013;42(6):794–798.

4. Denison HJ, Syddall HE, Dodds R, *et al.* Effects of aerobic exercise on muscle strength and physical performance in community-dwelling older people from the Hertfordshire Cohort Study: a randomized controlled trial. J Am Geriatr Soc. 2013;61(6):1034–1036.

5. Dodds RM, Syddall HE, Cooper R, *et al.* Grip Strength across the Life Course: Normative Data from Twelve British Studies. PLoS One. 2014;9(12):e113637.

6. Waldo B. Grip strength testing. Strength Condit J. 1996;18(5):32–5.

7. Kent M. The Oxford Dictionary of Sports Science & Medicine. 3rd ed.; 2006.

8. Lanska D. William Hammond, the Dynamometer, the Dynamograph. Arch Neurol. 2014;57(11):1649–1653.

9. Francis Galton as Anthropologist. Available at: http://galton.org/anthropologist.htm. Accessed June 4, 2014.

10. Life of Francis Galton by Karl Pearson Vol 2 : image 0438. Available at: http://galton.org/cgi-bin/searchImages/galton/search/pearson/vol2/pages/vol2_0438.htm. Accessed June 4, 2014.

11. Cooper R, Kuh D, Hardy R, Mortality Review Group. Objectively measured physical capability levels and mortality: systematic review and meta-analysis. BMJ. 2010;341:c4467.

12. De Buyser SL, Petrovic M, Taes YE, Toye KRC, Kaufman J-M, Goemaere S. Physical function measurements predict mortality in ambulatory older men. Eur J Clin Invest. 2013;43(4):379–86.

13. Hamer M, Bates CJ, Mishra GD. Depression, Physical Function, and Risk of Mortality: National Diet and Nutrition Survey in Adults Older Than 65 Years. Am J Geriatr Psych. 2011;19(1):72–8.

14. McDermott MM, Liu K, Tian L, *et al.* Calf muscle characteristics, strength measures, and mortality in peripheral arterial disease: a longitudinal study. J Am Coll Cardiol. 2012;59(13):1159–67.

15. Cooper R, Strand B, Hardy R, Patel K, Kuh D. Physical capability in mid-life and survival over 13 years of follow-up: British birth cohort study. BMJ. 2014;348:g2219.

16. Hirsch CH, Buzková P, Robbins JA, Patel K V, Newman AB. Predicting late-life disability and death by the rate of decline in physical performance measures. Age Ageing. 2012;41(2):155–61.

17. Xue Q-L, Beamer BA, Chaves PHM, Guralnik JM, Fried LP. Heterogeneity in rate of decline in grip, hip, and knee strength and the risk of all-cause mortality: the Women's Health and Aging Study II. J Am Geriatr Soc. 2010;58(11):2076–84.

18. Den Ouden MEM, Schuurmans MJ, Arts IEMA, van der Schouw YT. Physical performance characteristics related to disability in older persons: a systematic review. Maturitas. 2011;69(3):208–19.

19. Vermeulen J, Neyens JCL, van Rossum E, Spreeuwenberg MD, de Witte LP. Predicting ADL disability in community-dwelling elderly people using physical frailty indicators: a systematic review. BMC Geriatr. 2011;11(1):33.

20. Onder G, Penninx BWJH, Ferrucci L, Fried LP, Guralnik JM, Pahor M. Measures of Physical Performance and Risk for Progressive and Catastrophic Disability: Results From the Women's Health and Aging Study. J Gerontol A Biol Sci Med Sci. 2005;60(1):74–79.

21. Rothman MD, Leo-Summers L, Gill TM. Prognostic significance of potential frailty criteria. J. Am. Geriatr. Soc. 2008;56(12):2211–116.

22. Den Ouden MEM, Schuurmans MJ, Brand JS, Arts IEMA, Mueller-Schotte S, van der Schouw YT. Physical functioning is related to both an impaired physical ability and ADL disability: a ten year follow-up study in middle-aged and older persons. Maturitas. 2013;74(1):89–94.

23. Hicks GE, Shardell M, Alley DE, *et al.* Absolute strength and loss of strength as predictors of mobility decline in older adults: the InCHIANTI study. J. Gerontol. A. Biol. Sci. Med. Sci. 2012;67(1):66–73.

24. Cooper R, Kuh D, Cooper C, *et al.* Objective measures of physical capability and subsequent health: a systematic review. Age Ageing. 2011;40(1):14–23.

25. Sayer AA, Syddall HE, Dennison EM, *et al.* Grip strength and the metabolic syndrome: findings from the Hertfordshire Cohort Study. QJM. 2007;100(11):707–13.

26. Yang EJ, Lim S, Lim J-Y, Kim KW, Jang HC, Paik N-J. Association between muscle strength and metabolic syndrome in older Korean men and women: the Korean Longitudinal Study on Health and Aging. Metabolism. 2012;61(3):317–24.

27. Aihie Sayer A, Dennison EM, Syddall HE, Gilbody HJ, Phillips DIW, Cooper C. Type 2 diabetes, muscle strength, and impaired physical function: the tip of the iceberg? Diab Care. 2005;28(10):2541–2.

28. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. J. Geriatr. Phys. Ther. 2008;31(1):3–10.

29. García-Peña C, García-Fabela LC, Gutiérrez-Robledo LM, García-González JJ, Arango-Lopera VE, Pérez-Zepeda MU. Handgrip strength predicts functional decline at discharge in hospitalized male elderly: a hospital cohort study. PLoS One. 2013;8(7):e69849.

30. Roberts HC, Syddall HE, Cooper C, Aihie Sayer A. Is grip strength associated with length of stay in hospitalised older patients admitted for rehabilitation? Findings from the Southampton grip strength study. Age Ageing. 2012;41(5):641–6.

31. Rosenberg I. Summary comments. Am J Clin Nutr. 1989;(50):1231–1233.

32. Janssen I, Shepard DS, Katzmarzyk PT, Roubenoff R. The healthcare costs of sarcopenia in the United States. J. Am. Geriatr. Soc. 2004;52(1):80–5.

33. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, *et al.* Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010;39(4):412–23.

34. Manini TM, Clark BC. Dynapenia and aging: an update. J. Gerontol. A. Biol. Sci. Med. Sci. 2012;67(1):28–40.

35. Newman AB, Kupelian V, Visser M, *et al.* Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. J. Gerontol. A. Biol. Sci. Med. Sci. 2006;61(1):72–7.

36. Goodpaster BH, Park SW, Harris TB, *et al.* The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. J Gerontol A Biol Sci Med Sci. 2006;61A(10):1059–64.

37. Drey M. Sarcopenia - pathophysiology and clinical relevance. Wien. Med. Wochenschr. 2011;161(17-18):402–8.

38. Wolfe RR. The underappreciated role of muscle in health and disease. Am J Clin Nutr. 2006;84(3):475–82.

39. Syddall H, Cooper C, Martin F, Briggs R, Aihie Sayer A. Is grip strength a useful single marker of frailty ? Age Ageing. 2003;32:650–656.

40. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752–62.

41. Aihie Sayer A, Cooper C, Evans JR, *et al.* Are rates of ageing determined in utero? Age Ageing. 1998;27(5):579–83.

42. Sayer AA, Syddall HE, Gilbody HJ, Dennison EM, Cooper C. Does sarcopenia originate in early life? Findings from the Hertfordshire Cohort Study. J Gerontol A Biol Sci Med Sci. 2004;59(9):M930–4.

43. Kuh D, Ben-Shlomo Y. Introduction. In: A life course approach to chronic disease epidemiology. 2nd ed. Oxford: Oxford University Press; 2004:3–15.

44. Aihie Sayer A, Syddall H, Martin H, Patel H, Baylis D, Cooper C. The developmental origins of sarcopenia. J Nutr Heal. Ageing. 2008;12(7):427–432.

45. Inskip H, Macdonald-Wallis C, Kapasi T, *et al.* Associations between grip strength of parents and their 4-year-old children: findings from the Southampton Women's Survey. Paediatr. Perinat. Epidemiol. 2012;26(1):27–33.

46. Stenholm S, Tiainen K, Rantanen T, *et al.* Long-term determinants of muscle strength decline: prospective evidence from the 22-year mini-Finland follow-up survey. J Am Geriatr Soc. 2012;60(1):77–85.

47. Kanis J. Diagnosis of osteoporosis and assessment of fracture risk. Lancet. 2002;359:1929–36.

48. Mathiowetz V, Wiemer DM, Federman SM. Grip and Pinch Strength: Norms for 6- to 19-Year-Olds. Am J Occ Ther. 1986;40(10):705–11.

49. Häger-Ross C, Rösblad B. Norms for grip strength in children aged 4-16 years. Acta Paediatr. 2002;91(6):617–25.

50. Skelton DA, Greig CA, Davies JM, Young A. Strength, Power and Related Functional Ability of Healthy People Aged 65–89 Years. Age Ageing. 1994;23(5):371–377.

51. Bohannon RW, Peolsson A, Massy-Westropp N, Desrosiers J, Bear-Lehman J. Reference values for adult grip strength measured with a Jamar dynamometer: a descriptive meta-analysis. Physiother. 2006;92(1):11–15.

52. Kenny RA, Coen RF, Frewen J, Donoghue OA, Cronin H, Savva GM. Normative values of cognitive and physical function in older adults: findings from the Irish Longitudinal Study on Ageing. J Am Geriatr Soc. 2013;61 S2:S279–90.

53. Amaral JF, Mancini M, Novo Júnior JM. Comparison of three hand dynamometers in relation to the accuracy and precision of the measurements. Rev. Bras. Fisioter. 2012;16(3):216–24.

54. Guerra RS, Amaral TF. Comparison of hand dynamometers in elderly people. J Nutr Heal. Ageing. 2009;13(10):907–12.

55. King TI. Interinstrument Reliability of the Jamar Electronic Dynamometer and Pinch Gauge Compared With the Jamar Hydraulic Dynamometer and B & L Engineering Mechanical Pinch Gauge. Am J Occ Ther. 2013;67(4):480–3.

56. Luna-Heredia E, Martín-Peña G, Ruiz-Galiana J. Handgrip dynamometry in healthy adults. Clin Nutr. 2005;24(2):250–8.

57. Massy-Westropp N, Rankin W, Ahern M, Krishan J, Hearn TC. Measuring grip strength in normal adults: reference ranges and a comparison of electronic and hydraulic instruments. J Hand Surg Am. 2004;29(3):514–9.

58. Mathiowetz V, Vizenor L, Melander D. Comparison of Baseline instruments to the Jamar dynamometer and the B and L Engineering pinch gauge. Occ Ther J Res. 2000;20(3):147–62.

59. Mathiowetz V. Comparison of Rolyan and Jamar dynamometers for measuring grip strength. Occup. Ther. Int. 2002;9(3):201–9.

60. Bohannon RW. Parallel comparison of grip strength measures obtained with a MicroFET 4 and a Jamar dynamometer. Percept Mot. Ski. 2005;100:795–8.

61. Shechtman O, Gestewitz L, Kimble C. Reliability and validity of the DynEx dynamometer. J Hand Ther. 2005;18(3):339–47.

62. Svantesson U, Nordé M, Svensson S, Brodin E. A comparative study of the Jamar® and the Grippit® for measuring handgrip strength in clinical practice. Isokinet. Exerc Sci. 2009;17:85–91.

63. Molenaar HMT, Selles RW, Zuidam JM, Willemsen SP, Stam HJ, Hovius SER. Growth diagrams for grip strength in children. Clin. Orthop. Relat. Res. 2010;468(1):217–23.

64. Gerodimos V. Reliability of handgrip strength test in basketball players. J Hum Kinet. 2012;31:25–36.

65. Bohannon RW, Schaubert KL. Test-retest reliability of grip-strength measures obtained over a 12-week interval from community-dwelling elders. J. Hand Ther. 2005;18(4):426–7.

66. Shechtman O, Mackinnon L, Locklear C. Using the BTE Primus to measure grip and wrist flexion strength in physically active wheelchair users: an exploratory study. Am J Occup Ther. 2001;55(4):393–400.

67. Balogun J, Akomolafe C, Amusa L. Grip strength: effects of testing posture and elbow position. Arch Phys Med Rehabil. 1991;72(5):280–3.

68. Liao W-C, Wang C-H, Yu S-Y, Chen L-Y, Wang C-Y. Grip strength measurement in older adults: A comparison of three testing positions. Austr J Ageing. 2014;33(4):278–82.

69. Cooper R, Hardy R, Aihie Sayer A, *et al.* Age and Gender Differences in Physical Capability Levels from Mid-Life Onwards: The Harmonisation and Meta-Analysis of Data from Eight UK Cohort Studies. PLoS One. 2011;6(11):e27899.

70. Wills AK, Lawlor DA, Matthews FE, *et al.* Life Course Trajectories of Systolic Blood Pressure Using Longitudinal Data from Eight UK Cohorts. PLoS Med. 2011;8(6):e1000440.

71. Marmot M et al. English Longitudinal Study of Ageing: Wave 0 (1998, 1999 and 2001) and Waves 1-5 (2002-2011) [computer file]. 18th Edition. Colchester, Essex: UK Data Archive [distributor], February 2013. SN: 5050, http://dx.doi.org/10.5255/UKDA-SN-5050-4.

72. Syddall HE, Aihie Sayer A, Dennison EM, Martin HJ, Barker DJP, Cooper C. Cohort Profile: The Hertfordshire Cohort Study. Int. J. Epidemiol. 2005;34(6):1234–42.

73. Syddall HE, Simmonds SJ, Martin HJ, *et al.* Cohort Profile: The Hertfordshire Ageing Study (HAS). Int. J. Epidemiol. 2010;39(1):36–43.

74. Deary IJ, Gow AJ, Pattie A, Starr JM. Cohort profile: the Lothian Birth Cohorts of 1921 and 1936. Int J Epidemiol. 2012;41(6):1576–84.

75. Wadsworth M, Kuh D, Richards M, Hardy R. Cohort Profile: The 1946 National Birth Cohort (MRC National Survey of Health and Development). Int. J. Epidemiol. 2006;35(1):49–54.

76. Kuh D, Pierce M, Adams J, *et al.* Cohort profile: updating the cohort profile for the MRC National Survey of Health and Development: a new clinic-based data collection for ageing research. Int J Epidemiol. 2011;40(1):e1–9.

77. Boyd A, Golding J, Macleod J, *et al.* Cohort Profile: The “Children of the 90s”--the index offspring of the Avon Longitudinal Study of Parents and Children. Int J Epidemiol. 2013;42(1):111–27.

78. Benzeval M, Der G, Ellaway A, *et al.* Cohort Profile: West of Scotland Twenty-07 Study: Health in the Community. Int J Epidemiol. 2009;38(5):1215–23.

79. Activity and Health Research. Allied Dunbar National Fitness Survey. A report on Activity Patterns and Fitness levels: Main Findings. London: Sports Council and Health Education Authority.; 1992.

80. Collerton J, Davies K, Jagger C, *et al.* Health and disease in 85 year olds: baseline findings from the Newcastle 85+ cohort study. BMJ. 2009;399:b4904.

81. Inskip HM, Godfrey KM, Robinson SM, Law CM, Barker DJP, Cooper C. Cohort profile: The Southampton Women's Survey. Int J Epidemiol. 2006;35(1):42–8.

82. University of Essex. Institute for Social and Economic Research and National Centre for Social Research, Understanding Society: Waves 1-2, 2009-2011 [computer file]. 4th Edition. Colchester, Essex: UK Data Archive [distributor], December 2012. SN: 6614.

83. McFall S, Petersen J, Kaminska O, Lynn P. Understanding Society - The UK Household Longitudinal Study: Wave 2 Nurse Health Assessment, 2010 - 2012, Guide to Nurse Health Assessment. (2013). Colchester: University of Essex. 2013.

84. Fentem PH, Collins MF, Tuxworth W, *et al.* Allied Dunbar National Fitness Survey. Technical Report. London: Sports Council.; 1994.

85. Nevill AM, Holder RL. Modelling handgrip strength in the presence of confounding variables: results from the Allied Dunbar National Fitness Survey. Ergonomics. 2000;43(10):1547–58.

86. Der G, Batty GD, Benzeval M, *et al.* Is telomere length a biomarker for aging: cross-sectional evidence from the west of Scotland? PLoS One. 2012;7(9):e45166.

87. Kuh D, Bassey J, Hardy R, Aihie Sayer A, Wadsworth M, Cooper C. Birth Weight, Childhood Size, and Muscle Strength in Adult Life: Evidence from a Birth Cohort Study. Am J Epidemiol. 2002;156(7):627–633.

88. Deary I, Johnson W. Losing one's grip: a bivariate growth curve model of grip strength and nonverbal reasoning from age 79 to 87 years in the Lothian Birth Cohort 1921. J Gerontol B Psych Sci. 2011;66:699–707.

89. Roberts HC, Denison HJ, Martin HJ, *et al.* A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing. 2011;40(4):423–9.

90. National Centre for Social Research. Nurse Protocols for Measurements and samples used by the National Centre for Social Research.; 2010:33–5.

91. Balogun JA, Adenlola SA, Akinloye AA. Grip strength normative data for the Harpenden dynamometer. J Orthop Sport. Phys Ther. 1991;14(4):155–60.

92. Physical Company. Takei A5401 Digital Hand Grip Dynamometer - Fitness Assessment. 2014. Available at: http://www.physicalcompany.co.uk/takei-a5401-digital-hand-grip-dynamometer-pid2801.html. Accessed April 3, 2014.

93. Takei Scientific Instruments Co Ltd. Takei Scientific Instruments Co.,Ltd. | Health Promotion | Physical Fitness Measurement Instruments. 2014. Available at: http://www.takei-si.co.jp/en/productinfo/detail/49.html. Accessed April 3, 2014.

94. StataCorp. Stata Statistical Software: Release 12. 2011.

95. Cole TJ, Green PJ. Smoothing reference centile curves: the LMS method and penalized likelihood. Stat Med. 1992;11(10):1305–19.

96. Stasinopoulos DM, Rigby RA. Generalized Additive Models for Location Scale and Shape (GAMLSS) in R. J Stat Soft. 2007;23(7).

97. R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/. 2013.

98. Cole TJ. Growth references and the LMS method. In: Human growth from conception to maturity. 1st ed. London, UK; 2002:69–77.

99. De Onis M, Onyango A, Borghi E, Siyam A, Pinol A. WHO child growth standards : length/height-for-age, weight-for-age, weight-for-length, weight-for- height and body mass index-for-age : methods and development. Geneva; 2006.

100. Lauretani F, Russo CR, Bandinelli S, *et al.* Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol. 2003;95(5):1851–60.

101. Rigby RA, Stasinopoulos DM. Smooth centile curves for skew and kurtotic data modelled using the Box—Cox power exponential distribution. Stat Med. 2004;23:3053–76.

102. Ho RW, Chang SY, Wang CW, Hwang MH. Grip and key pinch strength: norms for 15- to 22-year-old Chinese students. Chin. Med. J. (Engl). 2000;63(1):21–7.

103. International Organization for Standardization. ISO 3166 - Country codes. Available at: http://www.iso.org/iso/home/standards/country_codes.htm. Accessed December 9, 2014.

104. South A. rworldmap: A New R package for Mapping Global Data. R J. 2011;3(1):35–43.

105. Frederiksen H, Hjelmborg J, Mortensen J, McGue M, Vaupel JW, Christensen K. Age trajectories of grip strength: cross-sectional and longitudinal data among 8,342 Danes aged 46 to 102. Ann Epidemiol. 2006;16(7):554–62.

106. Spruit MA, Sillen MJH, Groenen MTJ, Wouters EFM, Franssen FME. New normative values for handgrip strength: results from the UK Biobank. JAMDA. 2013;14:775.e5–11.

107. Engineering Department University of Cambridge. Unit Conversion Tables. Available at:

http://www3.eng.cam.ac.uk/DesignOffice/cad/proewild3/usascii/proe/promec/getstart/units/reference/units_conv.htm. Accessed February 26, 2015.

108. Wang C-Y. Hand dominance and grip strength of older Asian adults. Percept Mot. Ski. 2010;110:897–900.

109. United Nations Statistics Division. Composition of macro geographical (continental) regions, geographical sub-regions, and selected economic and other groupings. 2013. Available at: http://unstats.un.org/unsd/methods/m49/m49regin.htm. Accessed December 9, 2014.

110. World Bank Group. Country and Lending Groups. 2015. Available at: http://data.worldbank.org/about/country-and-lending-groups. Accessed January 12, 2015.

111. Aadahl M, Beyer N, Linneberg A, Thuesen BH, Jørgensen T. Grip strength and lower limb extension power in 19-72-year-old Danish men and women: the Health2006 study. BMJ Open. 2011;1(2):e000192.

112. Burton DA. Composite standard deviations. Available at: http://www.burtonsys.com/climate/composite_standard_deviations.html. Accessed December 11, 2014.

113. Harbord RM, Higgins JPT. Meta-regression in Stata. Stata J. 2008;8(4):493–519.

114. Kaur M. Age-related changes in hand grip strength among rural and urban Haryanvi Jat females. Homo. 2009;60(5):441–50.

115. Rodrigues-Barbosa A, Miranda LM De, Vieira-Guimaraes A, Xavier-Corseuil H, Weber-Corseuil M. Age and gender differences regarding physical performance in the elderly from Barbados and Cuba. Rev salud pública. 2011;13(1):54–66.

116. Chatterjee S, Chowdhuri BJ. Comparison of grip strength and isometric endurance between the right and left hands of men and their relationship with age and other physical parameters. J Hum. Ergol. 1991;20:41–50.

117. Backman E, Johansson V, Hager B, Sjoblom P, Henriksson KG. Isometric muscle strength and muscular endurance in normal persons aged between 17 and 70 years. Scand J Rehab Med. 1995;27:109–117.

118. Bear-Lehman J, Kafko M, Mah L, Mosquera L, Reilly B. An exploratory look at hand strength and hand size among preschoolers. J. Hand Ther. 15(4):340–6.

119. Gunther CM, Burger A, Rickert M, Crispin A, Schulz C. Grip strength in healthy caucasian adults: reference values. J Hand Surg Am. 2008;33(4):558–65.

120. Keevil VL, Mazzuin Razali R, Chin AV, Jameson K, Aihie Sayer A, Roberts H. Grip strength in a cohort of older medical inpatients in Malaysia: A pilot study to

describe the range, determinants and association with length of hospital stay. Arch Gerontol Ger. 2013;56:155–159.

121. Lang I, Busche P, Rakhimi N, Rawer R, Martin DD. Mechanography in childhood: References for grip force, multiple one-leg hopping force and whole body stiffness. J Musculoskelet Neuronal Interact. 2013;13(2):227–35.

122. Rauch F, Neu CM, Wassmer G, *et al.* Muscle analysis by measurement of maximal isometric grip force: new reference data and clinical applications in pediatrics. Pediatr. Res. 2002;51(4):505–10.

123. Adedoyin RA, Ogundapo FA, Mbada CE, *et al.* Reference Values for Handgrip Strength Among Healthy Adults in Nigeria. Hong Kong Physiother. J. 2009;27(1):21–29.

124. Budziareck MB, Pureza Duarte RR, Barbosa-Silva MCG. Reference values and determinants for handgrip strength in healthy subjects. Clin Nutr. 2008;27(3):357–62.

125. Schlüssel MM, dos Anjos LA, de Vasconcellos MTL, Kac G. Reference values of handgrip dynamometry of healthy adults: a population-based study. Clin Nutr. 2008;27(4):601–7.

126. Vianna LC, Oliveira R, Araujo CGS. Age-related decline in handgrip strength differs according to gender. J Strength Cond Res. 2007;21(4):1310–14.

127. Tsang RCC. Reference Values for 6-Minute Walk Test and Hand-Grip Strength in Healthy Hong Kong Chinese Adults. Hong Kong Physiother. J. 2005;23(1):6–12.

128. Ahn R, Yoo C-I, Lee H, *et al.* Normative data for neuromuscular assessment of the hand-arm vibration syndrome and its retrospective applications in Korean male workers. Int. Arch. Occup. Environ. Health. 2013;86(7):837–44.

129. Shim JH, Roh SY, Kim JS, *et al.* Normative measurements of grip and pinch strengths of 21st century Korean population. Arch. Plast. Surg. 2013;40(1):52–6.

130. Yim SY, Cho JR, Lee IY. Normative data and developmental characteristics of hand function for elementary school children in Suwon area of Korea: grip, pinch and dexterity study. J Korean Med Sci. 2003;18(4):552–8.

131. Almuzaini KS. Muscle function in Saudi children and adolescents: relationship to anthropometric characteristics during growth. Pediatr. Exerc. Sci. 2007;19(3):319–33.

132. Chuang MC, You M, Cai D, Chen CC. Isometric muscle strength of Chinese young males in Taiwan. Ergonomics. 1997;40(5):576–90.

133. Wu S-W, Wu S-F, Liang H-W, Wu Z-T, Huang S. Measuring factors affecting grip strength in a Taiwan Chinese population and a comparison with consolidated norms. Appl. Ergon. 2009;40(4):811–5.

134. Massy-Westropp NM, Gill TK, Taylor AW, Bohannon RW, Hill CL. Hand Grip Strength: age and gender stratified normative data in a population-based study. BMC Res Notes. 2011;4(1):127.

135. Seino S, Shinkai S, Fujiwara Y, *et al.* Reference values and age and sex differences in physical performance measures for community-dwelling older Japanese: a pooled analysis of six cohort studies. PLoS One. 2014;9(6):e99487.

136. Yoshimura N, Oka H, Muraki S, *et al.* Reference values for hand grip strength, muscle mass, walking time, and one-leg standing time as indices for locomotive syndrome and associated disability: the second survey of the ROAD study. J Orthopaed Sci. 2011;16(6):768–77.

137. Desrosiers J, Bravo G, Hébert R, Dutil É. Normative data for grip strength of elderly men and women. Am J Occ Ther. 1995;49(7):637–44.

138. Brennan P, Bohannon R, Pescatello L, Marschke L, Hanson S, Murphy M. Grip strength norms for elderly women. Percept Mot. Ski. 2004;99:899–902.

139. Hanten WP, Chen W-Y, Austin AA, *et al.* Maximum grip strength in normal subjects from 20 to 64 years of age. J. Hand Ther. 1999;12(3):193–200.

140. Horowitz BP, Tollin R, Cassidy G. Grip Strength : Collection of Normative Data with Community Dwelling Elders. Phys Occ Ther Ger. 1997;15(1):53–64.

141. Jansen CWS, Niebuhr BR, Coussirat DJ, Hawthorne D, Moreno L, Phillip M. Hand force of men and women over 65 years of age as measured by maximum pinch and grip force. J. Aging Phys. Act. 2008;16(1):24–41.

142. Kallman D, Plato C, Tobin J. The role of muscle loss in the age-related decline of grip strength: cross-sectional and longitudinal perspectives. J Gerontol. 1990;45(3):M82–8.

143. Mathiowetz V, Kashman N, Volland G, Weber K, Dowe M, Rogers S. Grip and pinch strength: normative data for adults. Arch Phys Med Rehabil. 1985;66:69–74.

144. Sella GE. The hand grip : gender , dominance and age considerations. Eur Med Phys. 2001;37(3):161–170.

145. De Smet L, Vercammen A. Grip strength in children. J Pedr Ortho B. 2001;10:352–4.

146. Semproli S, Brasili P, Toselli S, Ventrella A, Jurimae J, Jurimae T. The influence of anthropometric characteristics to the handgrip and pinch strength in 6-10-year old children. Anthr. Anz. 2007;65(3):293–302.

147. Harkonen R, Piirtomaa M, Alaranta H. Grip strength and hand position of the dynamometer in 204 Finnish adults. J Hand Surg [Eur]. 1993;18B:129–32.

148. Corish CA, Kennedy NP. Anthropometric measurements from a cross-sectional survey of Irish free-living elderly subjects with smoothed centile curves. Br. J. Nutr. 2003;89(1):137–45.

149. Montalcini T, Migliaccio V, Yvelise F, *et al.* Reference values for handgrip strength in young people of both sexes. Endocrine. 2013;43:342–45.

150. Peters MJH, van Nes SI, Vanhoutte EK, *et al.* Revised normative values for grip strength with the Jamar dynamometer. J. Peripher. Nerv. Syst. 2011;16(1):47–50.

151. Ploegmakers JJW, Hepping AM, Geertzen JHB, Bulstra SK, Stevens M. Grip strength is strongly associated with height, weight and gender in childhood: a cross sectional study of 2241 children and adolescents providing reference values. J. Physiother. 2013;59(4):255–61.

152. Holm I, Fredriksen P, Fosdahl M, Vøllestad N. A normative sample of isotonic and isokinetic muscle strength measurements in children 7 to 12 years of age. Acta Paediatr. 2008;97(5):602–7.

153. Nilsen T, Hermann M, Eriksen CS, Dagfinrud H, Mowinckel P, Kjeken I. Grip force and pinch grip in an adult population: reference values and factors associated with grip force. Scand J Occ Ther. 2012;19(3):288–96.

154. Tveter AT, Dagfinrud H, Moseng T, Holm I. Health-related physical fitness measures: reference values and reference equations for use in clinical practice. Arch. Phys. Med. Rehabil. 2014;95(7):1366–73.

155. Puh U. Age-related and sex-related differences in hand and pinch grip strength in adults. Int J Rehab Res. 2010;33:4–11.

156. Peolsson A, Hedlund R, Oberg B. Intra- and inter-tester reliability and reference values for hand strength. J Rehab Med. 2001;33:36–41.

157. Ribom EL, Mellström D, Ljunggren Ö, Karlsson MK. Population-based reference values of handgrip strength and functional tests of muscle strength and balance in men aged 70-80 years. Arch Gerontol Ger. 2011;53(2):e114–7.

158. Werle S, Goldhahn J, Drerup S, Simmen BR, Sprott H, Herren DB. Age- and gender-specific normative data of grip and pinch strength in a healthy adult Swiss population. J Hand Surg [Eur]. 2009;34(1):76–84.

159. Cohen DD, Voss C, Taylor MJD, Stasinopoulos DM, Delextrat A, Sandercock GRH. Handgrip strength in English schoolchildren. Acta Paediatr. 2010;99(7):1065–72.

160. Pearl A, Robinson D, Hale A. Fitness in a U.K. screening sample - a comparison with the Canadian Population. Meth Inf. Med. 1993;32:203–5.

161. Ben-shlomo Y, Kuh D. A life course approach to chronic disease epidemiology : conceptual models , empirical challenges and interdisciplinary perspectives. Int J Epidemiol. 2002;31:285–293.

162. Bruce S. Muscle Strength. In: Tallis R, Fillit H, Brocklehurst JC, eds. Geriatric Medicine and Gerontology. 5th ed. Edinburgh: Churchill Livingstone; 1998:1107–1114.

163. Medical Research Council. Maximising the value of UK population cohorts. London; 2014.

164. Nahhas RW, Choh AC, Lee M, *et al.* Bayesian longitudinal plateau model of adult grip strength. Am J Hum Biol. 2010;22(5):648–56.

165. Bassey EJ. The effects of aging on exercise capacity. In: Whipp BJ, Sargeant AJ, eds. Physiological determinants of exercise tolerance in humans. 1st ed. London: Portland Press; 1999:153–67.

166. Garcia J, Quintana-Domeque C. The evolution of adult height in Europe: A brief note. Econ. Hum Biol. 2007;5:340–349.

167. Ayoola O, Ebersole K, Omotade OO, *et al.* Relative Height and Weight among Children and Adolescents of Rural Southwestern Nigeria. Ann Hum Biol. 2009;36(4):388–399.

168. Template:Average height around the world. Available at: http://en.wikipedia.org/wiki/Template:Average_height_around_the_world#cite_note-16. Accessed April 10, 2015.

169. Reuben DB, Magasi S, McCreath HE, *et al.* Motor assessment using the NIH Toolbox. Neurology. 2013;80:S65–75.

170. Desrosiers J, Hébert R, Bravo G, Rochette A. Comparison of cross-sectional and longitudinal designs in the study of aging of upper extremity performance. J Gerontol A Biol Sci Med Sci. 1998;53A(5):B362–8.

171. Kirkwood TBL. Alex Comfort and the measure of ageing. Exp Gerontol. 1998;33(1-2):135–40.

172. Arden NK, Spector TD. Genetic influences on muscle strength, lean body mass, and bone mineral density: a twin study. J Bone Min. Res. 1997;12(12):2076–2081.

173. Huygens W, Thomis M a I, Peeters MW, Aerssens J, Vlietinck R, Beunen GP. Quantitative trait loci for human muscle strength: linkage analysis of myostatin pathway genes. Physiol. Genomics. 2005;22(3):390–7.

174. Davey Smith G, Hart C, Upton M, *et al.* Height and risk of death among men and women: aetiological implications of associations with cardiorespiratory disease and cancer mortality. J. Epidemiol. Community Health. 2000;54:97–103.

175. Ruiz JR, Rizzo NS, Hurtig-Wennlöf A, Ortega FB, Wärnberg J, Sjöström M. Relations of total physical activity and intensity to fitness and fatness in children: the European Youth Heart Study. Am. J. Clin. Nutr. 2006;84(2):299–303.

176. Artero EG, Ortega FB, Espan V, *et al.* Longer Breastfeeding Is Associated with Increased Lower Body Explosive Strength. J Nutr. 2010;140:1989–95.

177. Alfred T, Ben-shlomo Y, Cooper R, *et al.* A Multi-Cohort Study of Polymorphisms in the GH / IGF Axis and Physical Capability : The HALCyon Programme. PLoS One. 2012;7(1):e29883.

178. Robinson SM, Simmonds SJ, Jameson KA, *et al.* Muscle strength in older community-dwelling men is related to type of milk feeding in infancy. J. Gerontol. A. Biol. Sci. Med. Sci. 2012;67(9):990–6.

179. Robinson SM, Jameson KA, Batelaan SF, *et al.* Diet and its relationship with grip strength in community-dwelling older men and women: the Hertfordshire cohort study. J. Am. Geriatr. Soc. 2008;56(1):84–90.

180. Sternang O, Reynolds CA, Finkel D, Ernsth-Bravell M, Pedersen NL, Dahl Aslan AK. Factors associated with grip strength decline in older adults. Age Ageing. 2014;0:1–6.

181. Hanson M, Godfrey KM, Lillycrop KA, Burdge GC, Gluckman PD. Developmental plasticity and developmental origins of non-communicable disease: theoretical considerations and epigentic mechanisms. Prog Biophys Mol Biol. 2011;106(1):272–80.

182. Harvey NC, Javaid K, Bishop N, *et al.* MAVIDOS Maternal Vitamin D Osteoporosis Study: study protocol for a randomized controlled trial. The MAVIDOS Study Group. Trials. 2012;13:13.

183. Cooper C, Fielding R, Visser M, *et al.* Tools in the Assessment of Sarcopenia. Calcif Tissue Int. 2013;93:201–210.

184. Alley DE, Shardell MD, Peters KW, *et al.* Grip strength cutpoints for the identification of clinically relevant weakness. J Gerontol A Biol Sci Med Sci. 2014;69(5):559–66.

185. Sallinen J, Stenholm S, Rantanen T, Heliövaara M, Sainio P, Koskinen S. Hand-Grip Strength Cut-Points to Screen Older Persons at Risk for Mobility Limitation. J Am Geriatr Soc. 2011;58(9):1721–1726.

186. Cole TJ, Freeman J V, Preece MA. British 1990 growth reference centiles for weight, height, body mass index and head circumference fitted by maximum penalized likelihood. Stat Med. 1998;17:407–29.

187. Santos-Eggimann B, Cuénoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. J. Gerontol. A. Biol. Sci. Med. Sci. 2009;64(6):675–81.

188. Muniz-Terrera G, Bakra E, Hardy R, Matthews FE, Lunn D. Modelling life course blood pressure trajectories using Bayesian adaptive splines. Stat. Methods Med. Res. 2014;(epub).

189. Department of Health. Start Active, Stay Active: A report on physical activity from the four home countries' Chief Medical Officers.; 2011.

190. Kerr A, Syddall HE, Cooper C, Turner GF, Briggs RS, Aihie Sayer A. Does admission grip strength predict length of stay in hospitalised older patients? Age Ageing. 2006;35(1):82–4.

191. Simmonds SJ, Syddall HE, Walsh B, *et al.* Understanding NHS hospital admissions in England: linkage of Hospital Episode Statistics to the Hertfordshire Cohort Study. Age Ageing. 2014;43(5):653–60.