The influence of an intense training program on hypermobility and correlation between hypermobility and incidence of injury

By

Henri-Charl Terblanche

Submitted in fulfilment of the requirements for the degree:

Magister Scientiae in Human Physiology

In the

Department of Physiology

Faculty of Health Sciences

University of Pretoria

Supervisor: Prof. P J du TOIT

2015
ACKNOWLEDGEMENTS

“If all things are equal and only knowledge remains
If context is lost
There’ll be no wisdom to gain”

HC Terblanche, 2015

With thanks and dedication:

To all institutions and their staff who contributed to the completion of this study: University of Pretoria’s Department of Physiology, South African National Defence Force & National Research Fund.

To my academic mentor and supervisor Prof. Peet du Toit, for guidance, commitment, opportunities and an “everything is possible” attitude.

To my colleagues Jason, Vangi and Michael for all their support. Together we endured hours of testing and data capturing...most importantly, we endured.

To all my family and my close friends who are family, for unwavering support and encouragement, and for sustaining me with laughter and life through times of perseverance.

To my parents, who were steadfast in faith and all manner of support, who fervently prayed towards the realisation that this could be done, who also instilled in me the faith and ambition to accept and relish new challenges.

To my wife, who endlessly supports and acknowledges my efforts, whose unquenchable desire to know and understand inspires me, whose joy is infectious and whose love sustains me.

To my Lord and Saviour Jesus Christ, Your grace and favour and all-encompassing Love, that I might know Life in abundance.
RESEARCH OUTPUTS

Publications in peer-reviewed or refereed journals:


**Participation in conferences and seminars:**

**2013: Neuroscience day (UP – May 2013)**


**2012: International Conference on Sport and Exercise Science, Paris, France, 2012**

2012: Suid Afrikaanse Akademie vir Wetenskap en Kuns (North-West University – October 2012)


20. *Various Posters*


22. *The effect of Sports Vision Exercises on the visual skills of university students.* J Armstrong; AF Mahomed; E Henning; M Kleynhans; **HC Terblanche**; N Coetzee; P Wood; C Grant; P du Toit (Poster).


2011: Conference hosted by the University of the Western Cape (August 2011)


2011: Faculty of Health Sciences Day


2011: Neuroscience day (UP – May 2011)


2010: Neuroscience day (UP – May 2010)


2010: Faculty Day (University of Pretoria – Faculty Health Sciences)


2010: Suid Afrikaans Akademie vir Wetenskap en Kuns (Pretoria – October 2010)


# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acknowledgements</td>
<td>I</td>
</tr>
<tr>
<td>Research Output</td>
<td>II</td>
</tr>
<tr>
<td>Table of Content</td>
<td>VIII</td>
</tr>
<tr>
<td>Abbreviation Index</td>
<td>XIV</td>
</tr>
<tr>
<td>List of Figures</td>
<td>XV</td>
</tr>
<tr>
<td>List of Tables</td>
<td>XVI</td>
</tr>
<tr>
<td>Abstract</td>
<td>XVII</td>
</tr>
<tr>
<td>Abstrak</td>
<td>XX</td>
</tr>
</tbody>
</table>

## CHAPTER 1 : INTRODUCTION

1.1 Background                                   | 1    |
1.2 Research rational                            | 6    |
  1.2.1 Aim                                       | 6    |
  1.2.2 Research approach                        | 7    |
  1.2.3 Research motivation                      | 7    |
  1.2.3.1 Sex differences in the Beighton nine-point hypermobility test | 7    |
  1.2.3.2 Comparison of the Beighton nine-point hypermobility scores between males and females with relation to altered muscular component | 8    |
  1.2.3.3 Correlation between joint hypermobility and incidence of musculoskeletal injury in an intense training population | 10   |
1.3 References                                   | 13   |
## CHAPTER 2: LITERATURE REVIEW

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 A brief historical overview</td>
<td>17</td>
</tr>
<tr>
<td>2.2 Distinguishing hypermobility classifications</td>
<td>17</td>
</tr>
<tr>
<td>2.2.1 General Ligamentous Laxity</td>
<td>18</td>
</tr>
<tr>
<td>2.2.2 Hypermobility, Joint hypermobility, General joint hypermobility</td>
<td>18</td>
</tr>
<tr>
<td>2.2.3 Joint hypermobility syndrome, Benign joint hypermobility syndrome</td>
<td>19</td>
</tr>
<tr>
<td>2.2.4 All joint laxity does not equate to a joint hypermobility syndrome</td>
<td>22</td>
</tr>
<tr>
<td>2.2.5 Classifications of Benign joint hypermobility syndrome</td>
<td>25</td>
</tr>
<tr>
<td>2.3 The physiology of hypermobility</td>
<td>27</td>
</tr>
<tr>
<td>2.3.1 Musculoskeletal and connective tissue</td>
<td>27</td>
</tr>
<tr>
<td>2.3.2 Neurologic, proprioceptive and algesic features of hypermobility</td>
<td>31</td>
</tr>
<tr>
<td>2.3.3 Postural adaptations</td>
<td>35</td>
</tr>
<tr>
<td>2.3.4 Neuropathological features associated with hypermobility</td>
<td>36</td>
</tr>
<tr>
<td>2.3.4.1 Carpal tunnel syndrome</td>
<td>36</td>
</tr>
<tr>
<td>2.3.4.2 Chronic fatigue syndrome</td>
<td>37</td>
</tr>
<tr>
<td>2.3.4.3 Psychological and cephalalgia factors in hypermobility</td>
<td>38</td>
</tr>
<tr>
<td>2.3.5 Other extra-articular features associated with JHS</td>
<td>39</td>
</tr>
<tr>
<td>2.3.6 Endocrine factors in hypermobility</td>
<td>41</td>
</tr>
<tr>
<td>2.4 Hypermobility and Injury</td>
<td>44</td>
</tr>
<tr>
<td>2.4.1 GLL and injury in military subgroups</td>
<td>45</td>
</tr>
<tr>
<td>2.4.2 GLL and injury in sport</td>
<td>48</td>
</tr>
<tr>
<td>2.5 References</td>
<td>51</td>
</tr>
</tbody>
</table>

## CHAPTER 3: SEX DIFFERENCES IN THE BEIGHTON NINE-POINT TEST SCORES

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Key focus of the study</td>
<td>60</td>
</tr>
<tr>
<td>3.2 Background of the study</td>
<td>60</td>
</tr>
</tbody>
</table>

© University of Pretoria
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.3</td>
<td>Research objectives</td>
<td>60</td>
</tr>
<tr>
<td>3.4</td>
<td>Review of literature</td>
<td>61</td>
</tr>
<tr>
<td>3.5</td>
<td>Research design and methods</td>
<td>62</td>
</tr>
<tr>
<td>3.5.1</td>
<td>Research approach</td>
<td>62</td>
</tr>
<tr>
<td>3.5.2</td>
<td>Ethical considerations</td>
<td>62</td>
</tr>
<tr>
<td>3.5.3</td>
<td>Participants</td>
<td>62</td>
</tr>
<tr>
<td>3.5.3.1</td>
<td>Inclusion/Exclusion criteria</td>
<td>63</td>
</tr>
<tr>
<td>3.5.3.2</td>
<td>Participant screening and informed consent</td>
<td>63</td>
</tr>
<tr>
<td>3.5.3.3</td>
<td>Discontinuation criteria</td>
<td>63</td>
</tr>
<tr>
<td>3.6</td>
<td>General Procedures and Measurements</td>
<td>64</td>
</tr>
<tr>
<td>3.6.1</td>
<td>Biographical data and questionnaires</td>
<td>64</td>
</tr>
<tr>
<td>3.6.2</td>
<td>Beighton nine-point scale testing</td>
<td>66</td>
</tr>
<tr>
<td>3.6.3</td>
<td>Anthropometric testing</td>
<td>67</td>
</tr>
<tr>
<td>3.7</td>
<td>Data processing and statistical analysis</td>
<td>69</td>
</tr>
<tr>
<td>3.8</td>
<td>Results</td>
<td>70</td>
</tr>
<tr>
<td>3.9</td>
<td>Discussion</td>
<td>71</td>
</tr>
<tr>
<td>3.10</td>
<td>Conclusion</td>
<td>73</td>
</tr>
<tr>
<td>3.11</td>
<td>Suggestions for future research</td>
<td>74</td>
</tr>
<tr>
<td>3.12</td>
<td>References</td>
<td>75</td>
</tr>
</tbody>
</table>

**CHAPTER 4: COMPARISON OF THE BEIGHTON NINE-POINT HYPERMOBILITY SCORES BETWEEN MALES AND FEMALES WITH RELATION TO ALTERED MUSCULAR COMPONENT**

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>Key focus of the study</td>
<td>77</td>
</tr>
<tr>
<td>4.2</td>
<td>Background of the study</td>
<td>77</td>
</tr>
<tr>
<td>4.3</td>
<td>Research objectives</td>
<td>78</td>
</tr>
<tr>
<td>4.4</td>
<td>Review of literature</td>
<td>78</td>
</tr>
</tbody>
</table>
4.5 Research design and methods 81
4.5.1 Research approach 81
4.5.2 Ethical considerations 81
4.5.3 Participants 82
4.5.3.1 Inclusion/Exclusion criteria 82
4.5.3.2 Discontinuation criteria 82
4.5.4 Data collection timeframe 83

4.6 General Procedures and Measurements 83
4.6.1 Biographical data and questionnaires 83
4.6.2 Beighton nine-point scale testing 83
4.6.3 Anthropometric measures 85
4.6.4. Intervention Protocol 86

4.7 Data processing and statistical analysis 87

4.8 Results 88
4.9 Discussion 91
4.10 Conclusion 94
4.11 Suggestions for future research 95
4.12 References 97

CHAPTER 5 : CORRELATION BETWEEN HYPERMOBILITY AND INCIDENCE OF INJURY IN A TRAINING POPULATION
5.1 Key focus of the study 100
5.2 Background of the study 100
5.3 Research objectives 101
5.4 Review of literature 102
5.5 Research design and methods 104
Appendix A: 1 Military hospital research ethical consent ...........................................130
Appendix B: Informed consent ..................................................................................132
Appendix C: Data sheet ............................................................................................138
# ABBREVIATION INDEX

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACL</td>
<td>Anterior cruciate ligament</td>
</tr>
<tr>
<td>BJHS</td>
<td>Benign joint hypermobility syndrome</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>BW</td>
<td>Body weight</td>
</tr>
<tr>
<td>CFS</td>
<td>Chronic fatigue syndrome</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CTS</td>
<td>Carpal tunnel syndrome</td>
</tr>
<tr>
<td>EDS</td>
<td>Ehlers-Danlos syndrome</td>
</tr>
<tr>
<td>EMG</td>
<td>Electromyography</td>
</tr>
<tr>
<td>FGID</td>
<td>Functional gastro-intestinal disorder</td>
</tr>
<tr>
<td>GJH</td>
<td>General joint hypermobility</td>
</tr>
<tr>
<td>GLL</td>
<td>General ligamentous laxity</td>
</tr>
<tr>
<td>HDCT</td>
<td>Heritable disorder of connective tissue</td>
</tr>
<tr>
<td>HMS</td>
<td>Hypermobility syndrome</td>
</tr>
<tr>
<td>JH</td>
<td>Joint hypermobility</td>
</tr>
<tr>
<td>JHS</td>
<td>Joint hypermobility syndrome</td>
</tr>
<tr>
<td>JK</td>
<td>Joint kinaesthesia</td>
</tr>
<tr>
<td>JPS</td>
<td>Joint position sense</td>
</tr>
<tr>
<td>LBM</td>
<td>Lean body mass</td>
</tr>
<tr>
<td>MMP</td>
<td>Matrix metaloproteinases</td>
</tr>
<tr>
<td>MSI</td>
<td>Musculoskeletal injury</td>
</tr>
<tr>
<td>MVP</td>
<td>Mitral valve prolapse</td>
</tr>
<tr>
<td>PAR-Q</td>
<td>Physical activity readiness questionnaire</td>
</tr>
<tr>
<td>PT</td>
<td>Physical training</td>
</tr>
<tr>
<td>ROM</td>
<td>Range of motion</td>
</tr>
<tr>
<td>SANDF</td>
<td>South African national defence force</td>
</tr>
<tr>
<td>SAPD</td>
<td>South African police department</td>
</tr>
<tr>
<td>STR</td>
<td>Soft tissue rheumatism</td>
</tr>
<tr>
<td>USMA</td>
<td>United States military academy</td>
</tr>
</tbody>
</table>
LIST OF FIGURES

**Figure 1.1:** Structure of collagen with central glycine proteins  
2

**Figure 1.2:** Cycle of causative factors regarding diminished joint proprioception in hypermobile individuals  
4

**Figure 2.1:** Illustrated maneuvers of the Beighton nine-point hypermobility test  
19

**Figure 2.2:** Inter-relationship between the heritable connective tissue disorders  
20

**Figure 2.3:** Structure of collagen with central glycine proteins  
30

**Figure 2.4:** Cycle of causative factors regarding diminished joint proprioception in hypermobile individuals  
33

**Figure 2.5:** The Pathogenesis of chronic pain syndrome in JHS  
35

**Figure 2.6:** Injury rate in 1000 exposure hours by hypermobility status  
49

**Figure 3.1:** Maneuvers of the Beighton nine-point hypermobility test  
67

**Figure 3.2:** Box plot of sex specific results  
71

**Figure 4.1:** Maneuvers of the Beighton nine-point hypermobility test  
84

**Figure 4.2:** LBM adaptation between hypermobile and non-hypermobile participants  
91

**Figure 4.3:** Bar chart representing changes in hypermobility.  
92

**Figure 4.4:** Bar chart representing changes in LBM.  
93

**Figure 5.1:** Illustrated maneuvers of the Beighton nine-point hypermobility test  
107

**Figure 6.1:** Cycle of causative factors regarding diminished joint proprioception in hypermobile individuals.  
121
LIST OF TABLES

Table 1.1: Musculoskeletal and connective tissue predispositions of hypermobility 3

Table 2.1: Beighton nine-point hypermobility test 19
Table 2.2: Revised 1998 Brighton diagnostic criteria for joint hypermobility 21
Table 2.3: Objective measures of hypermobility 25
Table 2.4: Musculoskeletal and connective tissue predispositions of hypermobility 28

Table 3.1: Beighton nine-point hypermobility test 66
Table 3.2: Body fat recommendation Table for men 69
Table 3.3: Body fat recommendation Table for women 69
Table 3.4: Hypermobility incidence of sample populations. 70
Table 3.5: Sex specific incidence of hypermobility of sample populations. 70

Table 4.1: Beighton nine-point hypermobility test 84
Table 4.2: Outline of the military physical training intervention 87
Table 4.3: Paired T-test results for hypermobility correlation. 89
Table 4.4: Paired T-test results for lean body mass correlation. 90

Table 5.1: Beighton nine-point hypermobility test 107
Table 5.2: Outline of the military PT intervention. 108
Table 5.3: Contingency Table of MSI observation between hypermobile and non-hypermobile groups. 111
Table 5.4: Localization of MSI in the hypermobility group 112
Table 5.5: MSI localization of the non-hypermobility group 113
ABSTRACT

Title: The influence of an intense training program on hypermobility and correlation between hypermobility and incidence of injury

Candidate: Mr. HC Terblanche
Supervisor: Prof. PJ du Toit
Department: Physiology
Degree: MSc Human Physiology

Joint hypermobility (JH) in its various forms is in many ways misinterpreted and underdiagnosed. As a symptom of heritable disorders of connective tissue (HDCT), it is well known, whilst understanding around JH as a non-symptomatic occurrence in physically active populations is vague at best. With literature suggesting associations between JH and musculoskeletal injury (MSI), an inherent risk for populations undergoing intense physical training (PT) is implied. This dissertation set out to shed light on the incidence of hypermobility in a South African context, whilst seeking to clarify the implications of JH on intense PT and vice versa. The research was conducted by employing an in depth literature review on the broad spectrum of physiological factors linked to hypermobility, along with three comprehensive scientific studies which answered definitive questions relating to the paper’s main research objectives.

In investigating the causative factors of JH, literature indicated congenital amino-acid substitutions in collagen synthesis which compromises the molecular nano-mechanics of connective tissues, thus negating the structural integrity of collagen containing compounds such as tendons, ligaments, joint capsules, skin, demineralised bone and nerve receptors. This concept, along with current thinking which suggests that the shape of bones and low muscle tone may also contribute to hypermobility, clearly indicates compromised joint biomechanics in hypermobile individuals. A commonly linked neurologic factor of hypermobility i.e. diminished joint proprioceptive acuity, lead to our proposed concept of a closed cycle of “causative vs. symptomatic” factors, which perpetuates abnormal articular biomechanics.
The initial study which sought to investigate the incidence rates of hypermobility in the general South African population, employed a cross-sectional research approach with a sample population of 480 individuals from four wide-spread geographical areas. Individuals were tested for JH according to the Beighton nine-point hypermobility score with a diagnostic criteria of 4/9 or greater. Results indicated a 26.19% overall incidence of JH, with sex specific totals showing a 36.41% incidence for females compared to 13.96% for males. Thus concurring with contemporary studies indicating a significantly high prevalence of JH in the general population.

The second study which concerned the interactions between muscular component and hypermobility, correlated Beighton nine-point hypermobility scores and lean body mass (LBM) at three intervals during a 20 week intense training intervention period in a military sample. Linear regressions indicated a significant correlation between increased LBM and associated decreases in hypermobility, even though hypermobility peaked after 12 weeks of intense exercise. We proposed that the “hypermobility peak” leading up to week 12 can be clarified by initial training induced generalized flexibility, neural adaptation of exercise which increases ROM amongst other factors.

In aiming to clarify one of the most prevalent discussions in hypermobility research i.e. the association between JH and MSI, the final study compared MSI incidences between hypermobile and non-hypermobile individuals who endured 20 weeks of intense military basic training protocols. Odds ratios indicated that hypermobile individuals are 1.8 times more likely to sustain MSI when undergoing intense physical activity. Chi-square tests indicated a marginal, though significant association between JH and MSI. Ulterior results showed increased MSI prevalence amongst females as well as no significant difference in MSI location distribution amongst the hypermobile and control groups.

In considering all our findings we concluded that JH is an underdiagnosed common occurrence in the South African general population. The congenital influences on connective tissue development in hypermobile individuals sufficiently undermines musculoskeletal integrity to the extent where they are susceptible to increased risk of injury when participating in intense physical activity. These debilitating mechanisms can however be counteracted by the implementation of specific exercises promoting joint stabilization, proprioceptive acuity and increased muscular component.
Key terms: hypermobility, joint hypermobility, benign joint hypermobility syndrome, Beighton nine-point hypermobility score, military basic training, intense physical activity, lean body mass, musculoskeletal injury.
ABSTRAK

Titel: Die invloed van 'n intense oefen program op hipermobiliteit en korrelasie tussen hipermobiliteit en die voorkoms van beserings.

Kandidaat: Mr. HC Terblanche
Promotor: Prof. PJ du Toit
Departement: Fisiologie
Graad: MSc Menslike fisiologie

Gewrigshipermobiliteit (JH) in sy verskeie vorme word dikwels misinterpreteer en ongenoegsaam gediagnoseer. As 'n simptoom van oorerflke bindweefsel versteurings (HCDT) is dit welbekend, terwyl hipermobiliteit as 'n nie-simptomatiese gebeurtenis onder aktiewe populasies onvoldoende bestudeer is. Navorsing beweer dat daar 'n assosiasie tussen hipermobiliteit en muskuloskeletale beserings (MSI) bestaan, wat dus 'n inherente risiko vir aktiewe populasies inhou. Die verhandeling het onderneem om die insidensie van hipermobiliteit in 'n Suid Afrikaanse konteks te verduidelik, asook om die invloed van fisiese oefening op hipermobiliteit te verduidelik en vice versa. Ten einde die navorsingsdoelwitte te bereik is daar van 'n in diepe literatuur studie gebruik gemaak om die bredê spektrum van fisiologiese faktore wat met hipermobiliteit geassosieer is na te vors, asook is daar drie breedvoerige wetenskaplike studies onderneem om van die definitiewe vrae rakende hipermobiliteit te beantwoord.

Die literatuur dui aan dat JH veroorsaak word deur oorerflke faktore wat aminosuur substitusies veroorsaak tydens die vorming van kollageen, wat dan dienooreenkomstig die molekulêre nanomeganika van bindweefsel beïnvloed. Dus, word die structurele integriteit van samestellings soos tendons, ligamente, gewrigskapsules en senuwee reseptore wat almal kollageen bevat, pertinent in gedrang gebring. Die verduidelikking te same met onlangse navorsing wat voorstel dat been vorm en lae spiertonus ook bydrae tot hipermobiliteit, dui onomwonde aan dat die gewrigsbiomeganika van hipermobiele individue benadeel word. Die neurologiese verskynsel van verminderde gewrigspropriosepsie wat gereeld met hipermobiliteit geassosieer word, het ons geleid tot die veronderstelling van 'n geslote siklus waarin abnormale gewrigsbiomeganika as simptoom en oorsaak voortbestaan.

XX
Die aanvangklike studie het beoog om die insidensie van hipermobiliteit in 'n Suid-Afrikaanse konteks vas te stel. 'n Geografies wydverspreide groep van 480 individue is getoets volgens die Beighton nege-punt hipermobiliteitstelling met 'n afsnypunt van 4/9 of groter. Resultate het 'n 26.19% algehele insidensie aangedui, met n 36.41% vroue en 13.96% mans geslagsverspreiding van hipermobile individue. Die resultate strook met kontemporêre literatuur, wat 'n relatiewe hoë insidensie van hipermobiliteit in die populasie aandui.

Die tweede studie aangaande die wisselwerking tussen hipermobiliteit en spierkomponent het militêre soldate se Beighton nege-punt hipermobiliteitstellings en spiermassa (LBM) korrelear tydens drie tydsintervalle, gedurende 20 weke se deelname aan 'n intense oefeningsingryping. Lineêre regressies het aangedui dat verhoogde spiermassa beduidend assosieer met verlaagde hipermobiliteitstellings, ten spyte van 'n “hipermobiliteitspiek”, na 12 weke se ingryping. Ons het aangevoer dat die verhoogde hipermobiliteitstellings onder andere, aan oefeningsgeïnduseerde soepelheid en neurale aanpassing, asook verhoogde omvang van beweging te wyte kan wees.

Ten einde een van die mees prominente besprekings in hipermobiliteit te bestudeer d.w.s. die assosiasie tussen hipermobiliteit en MSI, het die finale studie die insidensie van MSI tussen hipermobiele en nie-hipermobiele toetsgroepie vergelyk tydens 20 weke se intense militêre basiese opleiding. Statistiese analyse van kans verhoudings het aangedui dat hipermobiele individue 1.8 keer meer waarskynlik is om MSI op te doen tydens intense fisiese oefening. Chi tot die tweede mag toetse, het 'n geringe, dog beduidende assosiasie tussen hipermobiliteit en MSI aangedui. Ander bevindinge het bewys dat vroue 'n verhoogde waarskynlikheid tot MSI het, asook dat daar geen verskil in lokale beseringsverspreiding tussen hipermobiliteitsgroepie aangedui is nie.

Met alle bevindinge in ag geneem het ons tot die slotsom gekom dat gewrigshipermobiliteit 'n algemene gebeurtenis is in die Suid-Afrikaanse populasie. Die oorferlike invloed op bindweefsel ontwikkeling in hipermobile individue ondermyn genoegsaam muskuloskeletale integriteit om die risiko vir beserings tydens intense fisiese aktiwiteit te verhoog. Nietemin, kan hierdie verswakkingsmeganismes
teengewerk word met die toepassing van spesifieke oefeninge wat poog daartoe om gewrigstabiliteit, spierkomponent en proprioepsie te verhoog.

**Sleutel terme:** hipermobiliteit, gewrigshipermobiliteit, Beighton nege-punt hipermobiliteitstelling, militêre basiese opleiding, intense fisiese oefening, spierkomponent, muskuloskeletale beserings.
Chapter 1: Introduction

1.1 Background

Joint hypermobility syndromes (JHS) are often misinterpreted and wrongfully diagnosed, seeing as the different types of this occurrence is so closely related. JH first appeared in rheumatology reports as an important entity in 1967 (1). Now, some 40 years on, it is better understood and more widely recognised. Although, through the years of studies and even as of late, there have been numerous changes in the identification and naming of JH diseases. Widely accepted nomenclature like HDCT has been shown to manifest features that closely overlap to rarer, better known disorders such as Marfan’s syndrome, EDS and Osteogenesis Imperfecta (2). Currently the widely accepted “all-inclusive” diagnosis for hypermobility disorders is known as Benign Joint Hypermobility Syndrome (BJHS). The occurrence of BJHS without chronic arthralgia should not be viewed as a disease, although acute bouts of joint pain may be experienced as well as localised symptoms like propensity to sprains and dislocations (3).

In literature, hypermobility has been shown to present with varied prevalence according to epidemiological and demographic factors such as age, sex and ethnicity. Thus far, predisposing factors that have been accepted by most include being female and of Asian or African ethnicity as opposed to European decent (4). Bridges and Larsson et al. reported prevalence in children and also the decrease of hypermobility with age (5). In 1983 Biro and colleagues estimated hypermobility to be 10% to 25% in children, with prevalence being more with girls (5, 6). Various epidemiological incidences have been reported through the years. Data from a West London rheumatology clinic was investigated by Hakim and Graham in 2003. They reported the JHS phenotype to be present in 58% of females and 29% of males in the sample (7). Adult incidences of hypermobility have been recorded to vary from 5% in the USA (8) and 43% in the Noruba tribe in Nigeria (9). Conclusive explanation of the higher female tendency have eluded researches, although reports that also link to the higher prevalence of female non-contact anterior cruciate ligament (ACL) injuries, suggest that cause might be found in female specific endocrine markers, or more specifically
influence of gonadotropic hormones relaxin and estradiol, as well as the influence of female specific joint angles (10,11).

For many years extensive research has been done on the physiological, pathological and genetic mechanisms that play a part in BJHS. Researchers currently understand that these are genetically-based conditions where, connective tissue proteins such as collagen are differently formed (12). Type 1 collagen is the most common collagen that tends to be affected and is contained in tendons, ligaments, joint capsules, skin, demineralised bone and nerve receptors (14).

The exact mechanism at work in BJHS is not established, although it can be linked to the same pathogenic process that causes hypermobility in patients suffering from osteogenesis imperfecta, where the deficiency arises from the substitution of the amino acid glycine (Figure 1.1) to bulkier amino acids in the triple helix structure of collagen. This exchange causes the larger amino acid side-chains to create steric hindrances that create a "bulge" in the collagen complex, which compromises both the molecular nano-mechanics as well as the interaction between the molecules (15). This results in the joints, muscles, tendons and ligaments being laxer and more fragile than is the case in the general population (16).

Considering the extensive network of collagen, not only regarding the musculoskeletal system, these changes invariably bring about multisystemic symptoms in hypermobile individuals. Table 1.1 summarizes several connective tissue related predispositions that all those with JHS, as commonly listed in literature.

![Figure 1.1: Structure of collagen with central glycine proteins (red)](13)
Table 1.1: Musculoskeletal and connective tissue predispositions of hypermobility.

<table>
<thead>
<tr>
<th>Listed predispositions of hypermobility in literature</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Susceptibility to soft-tissue injury</td>
<td>(17)</td>
</tr>
<tr>
<td>2. Impaired healing (collagen component of scar tissue)</td>
<td></td>
</tr>
<tr>
<td>3. Poor formation of superficial scarring (i.e. thin, shiny and often sunken below skin surface)</td>
<td></td>
</tr>
<tr>
<td>4. Tendency to sprains</td>
<td></td>
</tr>
<tr>
<td>5. Muscle tears</td>
<td></td>
</tr>
<tr>
<td>6. Tendon-bone attachment traction lesions</td>
<td></td>
</tr>
<tr>
<td>7. Meniscus tears</td>
<td></td>
</tr>
<tr>
<td>8. Stress fractures</td>
<td></td>
</tr>
<tr>
<td>9. Overuse lesions (work and performance related upper limb disorders)</td>
<td></td>
</tr>
<tr>
<td>10. Non-inflammatory spinal and joint pain</td>
<td></td>
</tr>
<tr>
<td>11. Varying degrees of degenerative joint disease</td>
<td></td>
</tr>
<tr>
<td>12. Tendency for joint “lock” at end range</td>
<td>(18)</td>
</tr>
<tr>
<td>13. Poor postural habits</td>
<td></td>
</tr>
<tr>
<td>14. Propensity to soft tissue rheumatism (STR) e.g. tendinitis, bursitis, fasciitis and fibromyalgia</td>
<td>(19)</td>
</tr>
<tr>
<td>15. Extensive skin laxity, striae and papyraceous scarring</td>
<td>(20)</td>
</tr>
<tr>
<td>16. Hallux Valgus (bunions) due to increased medial foot loading</td>
<td>(21)</td>
</tr>
<tr>
<td>17. Altered muscle activation pattern</td>
<td>(22)</td>
</tr>
<tr>
<td>Presentations in Adolescence</td>
<td></td>
</tr>
<tr>
<td>18. Motor delay</td>
<td>(17,23)</td>
</tr>
<tr>
<td>19. Ankle instability</td>
<td></td>
</tr>
<tr>
<td>20. Flat feet</td>
<td></td>
</tr>
<tr>
<td>21. Clumsiness</td>
<td></td>
</tr>
<tr>
<td>22. Fidgetiness</td>
<td></td>
</tr>
<tr>
<td>23. Development coordination disorder (dyspraxia)</td>
<td></td>
</tr>
</tbody>
</table>
Current thinking suggests that the shape of bones and low muscle tone may also contribute to hypermobility, especially in ball and socket joints that are shallow, which give rise to a greater range of motion (ROM) about the joint (24). Consequently, hypermobility influences some of the major contributors of movement that provides the functionality to perform physical activity.

According to the American College of Sports Medicine, physical fitness can be classified into seven fitness components, namely: cardio respiratory fitness and endurance, muscular strength, muscular endurance, flexibility, speed, power and agility (25). Due to the mechanical hindrance that hypermobility has on especially soft tissue and joints, it directly and indirectly affects most of these components. One of the most common neurologic features linked with hypermobility is diminished joint proprioceptive acuity (17). The strongest case for instigating factors of diminished proprioception in hypermobility, has been made against abated muscle spindle activation (26). In a closed cycle of “causative vs symptomatic” factors, as displayed in Figure 1.2, diminished proprioception plays its part by in turn influencing the initial causative factor i.e. abnormal articular biomechanics (18, 27).

![Figure 1.2: Cycle of causative factors regarding diminished joint proprioception in hypermobile individuals (3, 8, 18, 26, 27).](image)

* Constructed from various text as cited.
When considering the close association between hypermobility and physical activity, it comes as no surprise that two of the most prevalent populations reported on in hypermobility research are the military and sports subgroups. In a comprehensive meta-analysis done by Pacey and colleagues on generalized ligament laxity and the risk of lower-limb injury in sport, of the 4841 studies considered by Pacey et al., the 18 studies that met the inclusion criteria all used participant groups that were either specific to sports or the military (28). Due to the diverse nature of different sports and the many types of physical activity that can be engaged in, comparing research in this field in order to get conclusive evidence of how injuries and hypermobility relate can be quite challenging. In order to abridge this dilemma, some researchers have categorized sports as contact or collision sports, limited contact sports and noncontact sports (29).

Along with a high level of participation in sports that fall into all of the above mentioned categories, military servicemen also engage in other demanding and unique physical challenges. The most customary being PT which includes activities that require for example running and jumping under heavy load, muscular strength and endurance training with heavy objects of various shapes and sizes as well as calisthenics (30). All of these activities and sports with their specificity of impact load on joint angles, due to movement patterns that often requires cutting or jumping under heavy load or fatigue, invariably places an increased risk of musculoskeletal injuries on these populations (31).

Due to the comprehensive nature of collagen and connective tissue in the body, various systems are influenced when these components undergo structural adaptation. Thus, several factors apart from the musculoskeletal system have been shown to be affected by hypermobility and associated syndromes. In having a high collagenous attribution, skin abnormalities have been related to hypermobility. Some of these manifestations specifically associated with skin fragility, include ocular ptosis (drooping eyelids), varicose veins, excessive skin stretchiness and bruising (4). Another extra-articular associate of hypermobility is chronic fatigue syndrome (CFS). The main feature of CFS is debilitating fatigue present for a duration of no less than 6
months. This occurrence is often accompanied with other symptoms i.e. headaches, painful lymph nodes, myalgia and arthralgia, sleep disturbance and neurocognitive complaints. Impaired proprioception has again been marked as a primary cause in linking CFS and JHS (32). Some connotation with hypermobility and certain psychiatric states including phobic states and panic disorders have been reported, although more common psychological associations have been fatigue, depression and anxiety disorder (17, 33). Lesser known associations to hypermobility found in literature, include headaches, gastro-intestinal symptoms, fibromyalgia and mitral valve prolapse (MVP) to name a few (17). Several of these factors have however only been scarcely researched and lack sufficient substantiation.

It is evident that important correlations exist between the incidence of hypermobility and factors that influence physical activity such as musculoskeletal injuries and physiological adaptations to exercise. The greater percentile of research in this field has been devoted to analysing these correlations in very specific sample groups. This study will aim to investigate the correlation of hypermobility to physical activity factors in a sample that represents the general population of individuals in a South African context engaging in moderate to intense exercise with high frequency and duration.

1.2 Research Rationale

1.2.1 Aim

This study was aimed at investigating incidences of hypermobility in a South African context, and the influence of an intense training protocol on hypermobility. Differences in the occurrence of BJHS between males and females from a large sample group representative of a general population (aged 18-25) was studied, in order to establish representation of hypermobility between sexes. To research associations between hypermobility and intense exercise, LBM component was correlated with hypermobility in a military subgroup undergoing basic training. Whilst employing an applied research approach, this study aimed to provide answers on the incidences and typology of injuries amongst individuals with hypermobility, when subjected to a structured program of intense PT. As a collective objective this paper set out to shed light on the
commonly underdiagnosed and misinterpreted occurrence of JH in physically active populations.

1.2.2 Research approach

This investigation as a whole, into the influence of an intense training program on states of JH was approached from a multi-dimensional perspective and methodology. Three in-depth studies were conducted, to eventually combine as a detailed exposition on generalized joint hypermobility and interrelated physiological factors. Each of these studies followed varied designs specific to their outcomes. The first study followed a cross-sectional research approach in order to report on sex distributions and demographic prevalence. By employing a longitudinal repeated measures design, the second study investigated certain physiological training adaptations on states of hypermobility. Lastly, a prospective cohort study was conducted to comprehensively scrutinise and correlate factors relating JH and MSI.

1.2.3 Research motivation

1.2.3.1 Sex differences in the Beighton nine-point hypermobility test scores

Race and sex are factors that have well reported correlations with hypermobility. The evidence in these demographics are however conflicting. In a study which queried a military medical database in the United States of America, it was found that the prevalent race and sex associated with hypermobility was white females compared to black and “other” (34). These findings substantially contradict a study done in India, where a sample group of eight hundred and twenty nine Indian children between ages 3-19 were tested according to the Beighton nine-point protocol. They reported a 58.7% incidence of JH, and a near equal sex incidence (35). Thus it can be noted that there are still questions to be answered regarding sex, race and incidence of BJHS in general populations.

The aim of this study was to clarify the discrepancies in the comparison of males and females concerning the incidence of BJHS in a generalised population. It is generally
excepted that there is a predominance in females towards hypermobility, although many of these studies were not done in recent years, had seemingly small sample groups and were not particularly representative of the general population as the sample groups consisted of children, individuals diagnosed with hypermobility related syndromes and old-aged sufferers of rheumatism (36, 37).

Research Objectives

Objective 1:

Compare possible differences between male and female incidences of hypermobility in a sample group representative of the general population

Objective 2:

If significant difference was found, clarify the possible reasons for this occurrence.

Application and benefits of research outcomes

This particular study, also published as “Sex differences in the Beighton nine-point hypermobility test scores”, by Du Toit and colleagues are to the best of our knowledge, the only report on sex representation regarding hypermobility in the multicultural South African population. These results will significantly impact the approach of future research as well as sex based assumptions where hypermobility is implicated in physical activity prescription and injury precautions.

1.2.3.2 Comparison of the Beighton nine-point hypermobility scores between males and females with relation to altered muscular component

Musculoskeletal injuries have become seemingly synonymous with physical activity and intense exercise. However there is no denying the advances in performance brought about by PT in domains that require intense physical exertion i.e. professional sport, military, emergency services etc. Studies suggest that musculoskeletal injuries have a significant impact on military personnel readiness, whether at base or during deployment as well as costing military institutions millions of dollars (30). The prominence of MSI in sport is evident in the abundance of studies in literature relating specific sports and injuries. Coincidently the role that hypermobility might play in
musculoskeletal and joint injuries, have also been in the research spotlight over recent years. Various studies have reported contradictory results on the influence of hypermobility on musculoskeletal injuries, with most concluding that the impact is very much dependent on movement patterns, and joint angles specific to the physical activity.

Incidence of hypermobility has been reported to be as common as 36% in females and 14% in males (37). Due to the high numbers of personnel in military institutions participating in various types of physical activity on a frequent basis, hypermobility and musculoskeletal or joint injuries are bound to coincide. Military personnel do however formally engage in regular exercise and various resistance training programs which have been shown to increase proprioception and muscle torque as well as decrease muscle deconditioning in hypermobile individuals (27).

Considering this information and reviewed literature, it could be hypothesized that where physical activity/sports/exercise might lead to greater probability of MSI in hypermobile individuals, it could also concurrently lessen the degree of hypermobility in these individuals. To our knowledge, no studies have been done to investigate the interplay of physical activity and hypermobility in a military setting. This study attempted to quantify the interaction of a set military basic training exercise regime on the states of hypermobility, with relation to altered muscular component.

Research objectives

Objective 1:

Monitor and determine the changes in altered muscular component expressed as LBM, during 20 weeks of a military basic training program, and scrutinize the efficacy of the military basic training program to bring about changes in LBM

Objective 2:

Screen baseline and concurrent Beighton nine-point hypermobility scores of military recruits during an intervention period of 20 weeks basic training, and correlate results to changes in muscular component
Application and benefits of research outcomes

The outcome of this research would greatly advance understanding of the relationship between hypermobility and exercise. Resultant findings would verify the legitimacy of using the Beighton nine-point score to identify indicated JH in training populations. Advanced knowledge of the effects of an intense training regime on the state of hypermobility could give lead to altered criteria and training program design for hypermobile individuals participating in physical activity. Consequently, these findings might lead to refined approaches towards alleviating adverse hypermobility aspects, through physiological adaptations brought about by PT.

1.2.3.3. Correlation between JH and incidence of MSI in an intense training population

MSI, whether it be sprains, strains, soft tissue injuries or dislocations are practically synonymous with physically active populations. Military training populations in particular bear the brunt of lost man hours due to MSI. In their article entitled “The burden and management of sports-related musculoskeletal injuries and conditions within the US military”, Cameron and Owens states that musculoskeletal injuries significantly burdens military service personnel, as well as the military health system. It is deemed a leading cause of disability discharge (30). Sports and PT related injuries accounts for much lost duty time and also causes several non-battle related medical evacuations. They also found that these injuries were consistent with those commonly associated with athletic populations (30).

The majority of tissues in the musculoskeletal system (i.e. bone, tendons, ligaments, skin and cartilage) owe their physical integrity and extensive tensile strength to their considerable collagen component (17, 38). This marked reliance on the structural integrity of collagen for sound movement mechanics, inevitably challenges those with hypermobility severely. This is due to the fact that the foremost causative factor of hypermobility is genetically debilitated collagen formation (17, 18). Since the relationship between hypermobility and joint mechanics has been established, inevitably, questions regarding the association of generalized joint hypermobility and musculoskeletal injuries also arose. Therein lies the evident need for research to investigate JH as a possible risk factor of MSI in physically active populations. This
study aimed to shed light on the possible association between generalized joint hypermobility and MSI in a population burdened with the physiological stresses of an intense training program.

Research objectives

Objective 1:
Screen baseline and concurrent Beighton nine-point hypermobility scores of military recruits during a period of 20 weeks basic training and diagnose indicated JH according to a greater than four cut-off score.

Objective 2:
Analyse MSI occurrences as recorded by military medical personnel and compare injury observation ratios between participants with indicated JH (hypermobile group) and control counterparts (non-hypermobile group). Establish odds ratios between hypermobile and non-hypermobile for MSI and test hypothesis of independence between groups:

$H_0$: JH and MSI are independent.

$H_1$: JH and MSI are not independent.

Objective 3:
Utilize injury data to prospectively analyse the localized distribution of MSI as documented by the military medical staff, in order to draw comparisons between hypermobile and non-hypermobile groups.
Application and benefits of research outcomes

The resultant conclusions of this study is intended to be of use to military institutions and physical populations in determining the need for possible precautionary measures for participants with generalized joint hypermobility. Further understanding could also be supplemented into the treatment and rehabilitation of MSI for those with JH. In concurrence with the third objective of this study, a prospective benefit would be to identify whether a propensity to specific locational injury exists with hypermobile individuals, which would lead to the development of refined preventative protocols.
1.3 References


Chapter 2: Literature Review

2.1 A Brief Historical overview

Historically the occurrence of “double-jointedness” (as it is commonly referred to) was seen to be quite an oddity. Such was the fascination with the ability to contort bodily joints that it was enjoyed as entertainment at carnivals and festivals alike. To this day still, body contortionism has high entertainment value. It was only as time progressed and the field of medical research expanded that this rarity of hyperextending joints, was discovered to be more widespread than was initially expected. Soon, joint hyperextension was observed in various degrees and in some cases associated with musculoskeletal ailments, due to these occurrences intense investigation was warranted and the field of rheumatologic research attentively focused on incidences of hypermobility (1, 2).

Observations of excessive joint laxity have been recorded in history as early as the 4th century BC. It was in this era that Hippocrates hypothesized that the fall of the Scythians in India could have been attributed to the hyper laxity of their elbow and shoulder joints, which caused them to be meagre when drawing a bow or hurling spears (2, 3). In the late 15th to early 16th century the German artist Matthias Grunewald depicted “Saint Cyriaque” with hyper extended metacarpal phalangeal and interphalangeal joints in a painting on the Heller altarpiece in Frankfurt (3, 4). Even in music, mention was made of excessive joint laxity as the great musical mastery of Paganini in the 18th century was accredited to extreme mobility of the hands (3, 5). As the centuries progressed towards the end of the 19th century and towards the start of the 20th, the peculiarity around JH subsided and considerable clinical significance was recognized (3, 6).

2.2 Distinguishing hypermobility classifications

As research in this field increased over recent decades, excessive joint laxity was discovered to be associated with various ailments and disorders and presented itself in numerous ways. This great upsurge in research presented its own predicament in
terms of terminology and description. To properly comprehend all things pertaining to
the field of hypermobility, some clarification of the nomenclature is in order.

2.2.1 General Ligamentous Laxity (GLL)

In the majority of individuals that experience excessive joint laxity, this occurrence may
only be associated with crepitus and pain as musculoskeletal symptoms. In these
individuals, no genetic deviations are suspected to be the causative factors (7, 8). These
instances are commonly referred to as being cases of “generalized ligamentous
laxity” or “non-pathogenic hypermobility”. In these cases the ROM of various joints are
deemed to be significantly above the general population mean (7). Remvig et al. reported the occurrence of GLL amongst the general population to be between 5% and 15% (7, 9).

2.2.2 Hypermobility, Joint Hypermobility (JH), General Joint Hypermobility
(GJH)

The definition for JH describes a condition where several or most of an individual’s
synovial joints extend beyond normal limits. The normal limits for this description does
however take into consideration factors such as age, sex and ethnic background (3, 8). Several causative factors of JH have been implied through years of research. Child
et al. reported on hereditary influence, with Grahame making mention of an acquired
hypermobility due to years of stretching and training, as they found in their studies on
gymnasts and ballet dancers (3, 8, 10). In terms of the aforementioned demographic
factors, Grahame and Keer reported greater hypermobility scores in females, younger
individuals (children, adolescents, young adults) and people of African or Asian
ethnicity (11). Several scoring systems have been applied to clinically present JH. The
most widely used is certainly the Beighton nine-point scoring system as depicted in
Table 2.1 and Figure 2.1 below. In short, a Beighton score of greater than four is
indicative of prevalent JH (8, 12). The Beighton nine-point hypermobility scale will be
discussed in depth later on in the study, as we consider the methods and materials of
this paper.
### Table 2.1: Beighton nine-point hypermobility test (13).

<table>
<thead>
<tr>
<th>Joint</th>
<th>Set point limit criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>left little (fifth) finger</td>
<td>passive dorsiflexion beyond 90°</td>
<td>1</td>
</tr>
<tr>
<td>right little (fifth) finger</td>
<td>passive dorsiflexion beyond 90°</td>
<td>1</td>
</tr>
<tr>
<td>left thumb</td>
<td>passive dorsiflexion to the flexor aspect of the forearm</td>
<td>1</td>
</tr>
<tr>
<td>right thumb</td>
<td>passive dorsiflexion to the flexor aspect of the forearm</td>
<td>1</td>
</tr>
<tr>
<td>left elbow</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>right elbow</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>left knee</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>right knee</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>forward flexion of trunk with knees full extended</td>
<td>palms and hands can rest flat on the floor</td>
<td>1</td>
</tr>
</tbody>
</table>

#### Figure 2.1: Illustrated maneuvers of the Beighton nine-point hypermobility test (13).

### 2.2.3 Joint Hypermobility Syndrome (JHS), Benign Joint Hypermobility Syndrome (BJHS)

JHS distinguishes itself from JH as soon as mechanical joint indications appear. Thus, JH only becomes JHS as soon as symptoms attributable to JHS occur. Some symptoms that impact on the mechanical functionality of the joints include pain,
instability, dislocation and premature osteoarthritis (8). The severity and seriousness of JHS has long been overlooked and underdiagnosed. Only in recent years has JHS been classified as a multifaceted and multi-systemic HDCT (HDCT) (11). JHS is the most common HDCT, though it shares some features of other less common, yet more severe HDCT’s, such as Marfan’s syndrome, osteogenesis imperfect and EDS. The inter-relationship between these HDCT’s as illustrated by Grahame can be seen in the Figure 2.2 below (3, 8). So narrowly related are these conditions that leaders in the field consider Ehlers-Danlos hypermobility type (Ehlers-Danlos type III) to be indistinguishable from JHS (3, 8).

**Figure 2.2: Inter-relationship between the heritable connective tissue disorders (3, 11).**

Although the Beighton nine-point scale is an effective epidemiological device, it was deemed insufficient as a means of assertively diagnosing JHS (8). As such, the Brighton criteria was introduced for this purpose, by a special interest group on HDCT’s of the British Society for Rheumatology in 1998 (14). Similar to criteria for other HDCT’s, such as the Villefranche criteria for EDS (15) and the Ghent criteria for Marfan’s Syndrome (16), the Brighton criteria also discerns between major and minor classification criteria (8). The Brighton criteria does not solely rest on the presence of JH, but includes several aspects related to tissue laxity. These include excessive stretchiness of the skin, thin scarring, striae atropicae (growth spurt stretch marks) and also proof of weak visceral structure support such as abdominal wall hernia, genital prolapse and varicose veins (14). Interestingly two additional diagnostic pointers include the absence of the lingual frenulum as well as the ability to touch the tip of the
nose with one’s tongue, also known as Garlin’s sign (17). Table 2.2 below summarizes the Revised Brighton criteria of 1998 (8, 14).

Table 2.2: Revised 1998 Brighton diagnostic criteria for JHS* (8).

<table>
<thead>
<tr>
<th>Major criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A Beighton score of ≥ 4 of 9 points (either currently or historically)</td>
</tr>
<tr>
<td>2. Arthralgia for &gt; 3 months in four or more joints</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A Beighton score of 1, 2, or 3 of 9 points (0, 1, 2, or 3 points if ≥ 50 years old)</td>
</tr>
<tr>
<td>2. Arthralgia (≥ 3 months) in one to three joints or back pain (≥ 3 months), spondylosis, or spondylolysis/spondylolisthesis</td>
</tr>
<tr>
<td>3. Dislocation/subluxation in more than one joint, or in one joint on more than one occasion</td>
</tr>
<tr>
<td>4. STR: ≥ three lesions (e.g., epicondylitis, tenosynovitis, bursitis)</td>
</tr>
<tr>
<td>5. Marfanoid habitus (tall, slim, span/height ratio of &gt; 1.03; upper/lower segment ratio of &lt; 0.89; arachnodactyly [positive Steinberg/wrist signs])</td>
</tr>
<tr>
<td>6. Abnormal skin: striae, hyper extensibility, thin skin, papyraceous scarring</td>
</tr>
<tr>
<td>7. Eye signs: drooping eyelids, myopia, or antimongoloid slant</td>
</tr>
<tr>
<td>8. Varicose veins, hernia, or uterine/rectal prolapse</td>
</tr>
</tbody>
</table>

*JHS is diagnosed if the patient presents with two major criteria; one major and two minor criteria; or four minor criteria. Two minor criteria will suffice if there is an unequivocally affected first-degree relative. Major 1 and Minor 1 criteria are mutually exclusive, as are Major 2 and Minor 2. JHS is excluded by the presence of Marfan’s syndrome or EDS (other than the Ehlers-Danlos hypermobility type [formerly EDS type III]) as defined by the Ghent 1996 and the Villefranche 1998 criteria, respectively (14).
Regarding the epidemiology and demographics of JHS, varied prevalence has been recorded. Thus far, predisposing factors that have been accepted by most include being female and of Asian or African ethnicity as opposed to European decent (3). Bridges and Larsson et al. reported prevalence in children and also the decrease of hypermobility with age (18). In 1983 Biro et al. estimated hypermobility to be 10% to 25% in children with prevalence being more with girls (18, 19). Various geographic incidences have been reported through the years. Data from a West London rheumatology clinic was investigated by Hakim and Graham in 2003. They reported the JHS phenotype to be present in 58% of females and 29% of males in the sample (20). Adult incidences of hypermobility have been recorded to vary from 5% in the USA (21) and 43% in the Noruba tribe in Nigeria (22). These results confirmed the importance of demographic considerations in predicting normative values for different sample populations in JHS research. The terms JHS and BJHS have been used interchangeably since 2000 (13). JHS is defined as being benign when hypermobility and musculoskeletal symptoms occur without the presence of systematic rheumatologic diseases (23). Although in recent years, due to BJHS’s close (seemingly identical) resemblance to EDS type III, some leaders in the field have begun to question whether BJHS could really be considered benign (24).

2.2.4 All joint laxity does not equate to JHS

It is important to discern the varying factors that could cause joints to be lax. Several factors that are structural, biomechanical and hormonal of nature, influence joint laxity. The multitude of causative factors, thusly incited rheumatologists and researchers such as the Special Interest Group on Heritable Disorders of Connective Tissue (developers of the 1998 Brighton criteria) and others, to devise normative models for JHS, which did not solely rely on joint laxity (3). These changes in criterion were crucial to ensure that the classification of syndromes based on heritability, not exclusively rely on non-genetic factors. In literature the most prevalent genetic factor linked with hypermobility syndromes, is the mutation of collagen and collagen sub-type ratios (25). These causative constituents of JHS will be discussed in depth when we examine the pathophysiology of hypermobility.
In 1996, Cross defined in biomechanical terms, that passive laxity is a measure of joint movement within the constraints of capsules, ligaments and cartilage when an external force is applied to the joint during muscular relaxation (26). In their review on applicable models for measuring knee joint laxity, Küpper et al. discuss several of the factors that influence passive joint laxity. One such premise describes the role that the bony surfaces play in the mechanical behavior of the joint’s soft tissue structures. Cartilages and ligamentous supports such as joint capsules and menisci, significantly improve the bony fit between incongruent joint surfaces (27). When considering the passive flexibility of joints, context of the specific joints are of utmost importance, due to the inherent stability of certain joints. A case and point would be the sacroiliac joint, where laxity could hardly be assessed by quantification of joint motion. On the contrary the glenohumeral joint of the human shoulder is a lax joint that relies entirely on ligaments for stability due to minimal contributions by the loose joint capsule (27, 28). In this joint increased R.O.M is considered advantageous, thus Küpper et al. make a strong case for contextually interpreting joints according to function e.g. supporting weight, functional reaching and grasping (27).

Important distinction needs to be made between a state of muscle relaxation (when passive laxity can be measured) and joint motion present in functional activities, as this would imply active/functional laxity (27). Snyder-Mackler reported on this clinically significant distinction when finding that some patients with passive laxity do not demonstrate functional laxity (29). Agreeably, Aalbersberg et al. stated that well timed muscle contraction or co-contraction of applicable magnitude could assist in controlled dynamic joint function by preventing exaggerated joint laxity (30).

Another interesting factor that can be added to the list of external aspects influencing joint laxity, are hormones. In 2004, Jansson et al. revealed in their sex based study on GJL in 1845 Swedish school children that GJL peaks in adolescent girls around age 15 (31). They promoted that this occurs due to the hormonal changes that takes place during puberty (31, 32). Other studies have found that GJL can be more complex in mature females as changes in joint laxity have been reported to occur during the menstrual cycle (27, 33). Belanger et al. in 2004, have however deemed this point as
controversial on the basis of obscurity regarding biologically different populations and/or methodological differences that might have confounded findings (27, 34).

In several sports where suppleness is deemed advantageous, intense stretching regimes are applied in order to increase flexibility. Aesthetic sports such as gymnastics and ballet demand utmost ranges of motion about joints to ensure fluidity of movement and graceful execution (35). It is common knowledge in sports and athletic training literature, that stretching exercises are essential if flexibility is to be increased or maintained (36). Stretching exercises promote flexibility by positively effecting the plasticity (tendency to assume new and greater length after passive stretching) of connective tissue (36). Coincidentally these are the same connective tissue structures (tendons, facial sheaths, ligaments and joint capsules) that form the structural support backbone for joints that underlie some of the diagnostic criteria for JHS (28).

In this, it is evident that there exists an inherent problem; Constituents that are determinant of syndromes which are widely perceived to originate from heritable genetic factors (i.e. BJHS, EDS) can be biomechanically induced (8). One case and point being the forward trunk flexion that is common practice in stretching exercise regiments (36). This maneuver performed to the extent of being able to place the hands flat on the floor by bending forward with knees fully extended, accounts for one awarded point in the Beighton nine-point scoring system to identify JH (15). The application of stretching routines to increase flexibility are also not isolated to athletes. It is considered a fundamental prerequisite to general wellness (37). Thus confounding this predicament to a broader spectrum of the general population. Un-astoundingly, Cameron et al. reported in their 2010 study on the association of GJH with a history of glenohumeral joint instability, that the dominating Beighton nine-point maneuver to be scored, was the forward trunk flexion. This sign was observed in 14.1% of men and 46.4% of women in a sample population of 1050 participants (38).
2.2.5 Classifications of BJHS

Considering the discrepancies regarding factors that potentially play a role in joint laxity, it is unsurprising that several classification criteria have been developed and modified through the years. On their meta-analysis on GJH and the risk of lower limb joint injury during sport, Pacey et al. reported seven different measures of GJH. Table 2.3 derived from their 2010 systematic review, summarizes the most common diagnostic criteria found in literature (39).

Table 2.3: Objective measures of hypermobility (39).

<table>
<thead>
<tr>
<th>Objective Measures</th>
<th>Description of Measure (Including Variations)</th>
<th>Cut-off Point Indicating Hypermobility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Beighton nine-point (15).</td>
<td>• 5th finger MCP dorsiflexion ≥90˚ (passively extend fingers parallel to forearm)</td>
<td>≥ 3</td>
</tr>
<tr>
<td></td>
<td>• Passive thumb to forearm</td>
<td>≥ 4</td>
</tr>
<tr>
<td></td>
<td>• Hyperextension of elbows ≥10˚</td>
<td>≥ 5</td>
</tr>
<tr>
<td></td>
<td>• Hyperextension of knees ≥10˚</td>
<td>(variation in literature)</td>
</tr>
<tr>
<td></td>
<td>• Palms flat on the floor</td>
<td></td>
</tr>
<tr>
<td>Modified 6-point Beighton and Horan (40).</td>
<td>• Passive 5th finger MCP joint extension ≥90˚</td>
<td>No cut-off used,</td>
</tr>
<tr>
<td></td>
<td>• Thumb to forearm passively</td>
<td>implemented as continuous scale.</td>
</tr>
<tr>
<td></td>
<td>• Elbow hyperextension ≥10˚</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Knee hyperextension ≥10˚</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ankle hyperextension ≥45˚</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Palms to floor with knees straight</td>
<td></td>
</tr>
<tr>
<td>Modified 5-point Carter and Wilkinson (41).</td>
<td>• Passive dorsiflexion of 5th finger ≥90˚</td>
<td>≥ 2</td>
</tr>
<tr>
<td></td>
<td>• Passive hyperextension of the fingers parallel to the forearm</td>
<td>≥ 3</td>
</tr>
<tr>
<td></td>
<td>• Thumb to forearm</td>
<td>(variation in literature)</td>
</tr>
<tr>
<td></td>
<td>• Hyperextension of elbow</td>
<td></td>
</tr>
</tbody>
</table>
| 10-point Carter and Wilkinson (42). | - Hyperextension of knee
- Palms on floor (femoral anteversion) |
|-------------------------------------|------------------------------------------|
| 9-point Nicholas (43).               | - Passive hyperextension of fingers to parallel with forearm
- Passive thumb to forearm flexor aspect
- Elbow hyperextension ≥10°
- Knee hyperextension ≥10°
- Dorsiflexion of ankle ≥30° |
| 8-point Wynne and Davies (44).       | - Thumb to volar aspect of forearm
- 5th MCP hyperextension ≥90°
- Elbow hyperextension
- Knee hyperextension |

≥ 5

≥ 1

≥ 3 (variation in literature)
In light of the fact that no laboratory or radiologic criteria exist, current diagnosis is based on generalized laxity and specific joint involvement (45). Carter, Wilkinson, Beighton, Bulbena and Rotes have since identified and developed the Brighton’s criteria that has generally been accepted as the gold standard in diagnosis of BJHS (14). Regarding the classification of individuals into either hypermobile or non-hypermobile, several studies have reported on the good test-retest reliability of the Beighton nine-point scoring system. These studies report substantial agreement between assessors, with k-value within the range of 0.60 – 0.79 (46, 47). The issue of cut-off scores in the Beighton criteria have however led to much obscurity in hypermobility literature, with no universal consensus on a JH threshold. Research has been published using cut-off scores of 4, 5/9, 6/9 as well as modified scores of 3/5 (48, 49). This study will follow suit with the most prevalent cut-off score of 4 or greater denoting hypermobility. This cut-off score correlates with the criteria utilized in the Revised 1998 Brighton criteria (13, 48).

2.3 The Physiology of hypermobility

2.3.1 Musculoskeletal and Connective Tissue

As the classifications and criteria have been discussed, it is glaringly evident that the majority of physiological issues that play a role in hypermobility constitute musculoskeletal or connective tissue factors. As Rodney Grahame so eloquently put it, when commenting on the benefit of enhanced ROM to the performing arts, “The biological price for this enhanced flexibility is tissue fragility, which underlies the musculoskeletal elements of JHS” (8). The majority of tissues in the musculoskeletal system (i.e. bone, tendons, ligaments, skin and cartilage) owe their physical integrity and extensive tensile strength to their considerable collagen component (8, 32). This marked reliance on the structural integrity of collagen for sound movement mechanics, inevitably challenges those with hypermobility severely. This is due to the fact that the foremost causative factor of hypermobility is genetically debilitated collagen formation (8, 11). Table 2.4 summarizes several connective tissue related predispositions that all those with JHS, as commonly listed in literature.
Table 2.4: Musculoskeletal and connective tissue predispositions of hypermobility.

<table>
<thead>
<tr>
<th>Listed predispositions of hypermobility in literature</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>24. Susceptibility to soft-tissue injury</td>
<td></td>
</tr>
<tr>
<td>25. Impaired healing (collagen component of scar tissue)</td>
<td></td>
</tr>
<tr>
<td>26. Poor formation of superficial scarring (i.e. thin, shiny and often sunken below skin surface)</td>
<td></td>
</tr>
<tr>
<td>27. Tendency to sprains</td>
<td></td>
</tr>
<tr>
<td>28. Muscle tears</td>
<td>(8)</td>
</tr>
<tr>
<td>29. Tendon-bone attachment traction lesions</td>
<td></td>
</tr>
<tr>
<td>30. Meniscus tears</td>
<td></td>
</tr>
<tr>
<td>31. Stress fractures</td>
<td></td>
</tr>
<tr>
<td>32. Overuse lesions (work and performance related upper limb disorders)</td>
<td>(11)</td>
</tr>
<tr>
<td>33. Non-inflammatory spinal and joint pain</td>
<td></td>
</tr>
<tr>
<td>34. Varying degrees of degenerative joint disease</td>
<td></td>
</tr>
<tr>
<td>35. Tendency for joint “lock” at end range</td>
<td>(50)</td>
</tr>
<tr>
<td>36. Poor postural habits</td>
<td></td>
</tr>
<tr>
<td>37. Propensity to STR (tendinitis, bursitis, fasciitis and fibromyalgia)</td>
<td></td>
</tr>
<tr>
<td>38. Extensive skin laxity, striae and papyraceous scarring</td>
<td>(48)</td>
</tr>
<tr>
<td>39. Hallux Valgus (bunions) due to increased medial foot loading</td>
<td>(51)</td>
</tr>
<tr>
<td>40. Altered muscle activation pattern</td>
<td>(52)</td>
</tr>
</tbody>
</table>

Presentations in Adolescence

<table>
<thead>
<tr>
<th>Presentations in Adolescence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>41. Motor delay</td>
<td>(8) (53)</td>
</tr>
<tr>
<td>42. Ankle instability</td>
<td></td>
</tr>
<tr>
<td>43. Flat feet</td>
<td></td>
</tr>
<tr>
<td>44. Clumsiness</td>
<td></td>
</tr>
<tr>
<td>45. Fidgetiness</td>
<td></td>
</tr>
<tr>
<td>46. Development coordination disorder (dyspraxia)</td>
<td></td>
</tr>
</tbody>
</table>
In order to fully understand the role of connective tissue, it is imperative that one understands the physiological and biochemical structure of its components, and with its link to hypermobility, in particular, collagen. Collagen is a particularly tough fiber that has a white appearance and is resistive to stretching. Under high magnification the fibers are longitudinally arranged parallel fibrils. Each fibril is subdivided into microfibrils that consist of collagen molecules, also with longitudinal parallel arrangement (54). Each collagen molecule consists of a tri-stranded helix polypeptide chain, with the most prevalent polypeptides being proline, glycine, hydroxyproline and hydroxylysine (54). Thus far, no less than 12 types of collagen have been identified with the first four identifiable types being the most common. Collagen fibers, being flexible though inelastic, exhibits strength per unit weight that supersedes that of steel (32). In the various tissues (bone, ligaments, skin, tendons, muscles) that it is found, collagen can be remodeled from several types of cells that secrete procollagen molecules i.e. fibroblasts, chondroblasts and osteoblasts (54). The different types of connective tissue are composed from different types of cells, ground substance and protein fibers, within which the amount and arrangement of collagen fibers essentially determines the mechanical properties (32).

With this foreknowledge, we can begin to understand how genetic mutation in the formation of collagen could influence joint laxity. The exact mechanism at work in BJHS has not been established although it can be linked to the same pathogenic process that causes hypermobility in patients suffering from osteogenesis imperfecta, where the deficiency arises from the substitution of the amino acid glycine to bulkier amino acids in the triple helix structure of collagen. This exchange causes the larger amino acid side-chains to create steric hindrances that create a "bulge" in the collagen complex, which compromises both the molecular nano-mechanics as well as the interaction between the molecules (55). This results in the joints, muscles, tendons and ligaments being laxer and more fragile than is the case in the general population (12, 56).
The “bulging” creates more distance between molecules in the tri-strand helix, thus weakening the covalent peptide bonds which then compromises the rigidity of the collagen (57). In 2006, Malfait et al. gathered evidence from tissue biopsies, that supported the notion of interference with processing on the N-propeptide of either α-chains (α-1 ; α-2) of the triple helix of specifically Type-I collagen. In addition they reported Type-V collagen mutations to be present in hypermobility (48, 58). Figure 2.3 depicts the triple helix structure with the central glycine protein (59). It has also been suggested that similar to HDCT’s, genetic encoding that effect the constitution of connective tissue matrix factors i.e. fibrillins, collagens, elastins and proteoglycans results in hypermobile presentations (48, 49).

Another predisposing factor to JHS has been suggested by Schalkwijk et al. They propose mutation in the non-collagenous tenascin-X molecule to be plausible cause. Tenascin-X is a connective tissue ground matrix glycoprotein that presents with anti-adhesive properties (60). A causative factor commonly referenced in literature is a hypothesis by Russek that suggests an abnormal ratio of Type-I vs Type-III collagen decreases tissue stiffness in JHS. He proposes that this is due to over-representation of the thinner, more elastic Type-III collagen within the soft tissue matrix (48, 49). In review, all these studies point to the same leading cause of JH, namely the compromised structural integrity of connective tissue.
2.3.2 Neurologic, proprioceptive and algesic features of hypermobility

It is clearly observable that hypermobility is a multifaceted and multisystemic occurrence, though the complexity of it is commonly overlooked. In recent years, it has become apparent that central and peripheral nervous system abnormalities could be linked with JHS. One of the most common neurologic features linked with hypermobility is diminished joint proprioceptive acuity (8). In their 2009 study, measuring knee proprioception and muscle torque in children with HMS, Fatoye et al. reported that children with HMS, tested significantly poorer joint kinaesthesia (JK) and joint position sense (JPS) that their healthier counterparts. Additionally, muscle torque for knee flexion and extension was also significantly less in the test group of HMS children when compared to the control group (35). These findings were consistent to observations made by Malik et al. in a study on proprioceptive acuity in adults with HMS (61). Several factors linked to impaired joint proprioception such as poor coordination, clumsiness, poor motor development and reduced muscle development have in some instances been believed to be simultaneously causative and symptomatic (35). The strongest case for instigating factors of diminished proprioception in HMS, has been made against abated muscle spindle activation (62).

The muscle spindles are the mechnano-sensors that are responsible for information regarding fiber length and tension. Along with the golgi-tendon apparatus, pascinian corpuscles and joint receptors, they are known as proprioceptors. These end organs relay information on muscular dynamics and limb movement, on an almost instantaneous rate to the CNS (63). Muscle spindles in particular, primarily responds to muscle stretch. The muscle spindles are fusiform and aligned parallel to the extrafusal fibers of the muscle, thus causing a simultaneous stretch in the spindle when muscle stretch occurs (63). The spindles consist of connective tissue capsules that encloses groups of small muscle fibers, these bundles are known as intrafusal fibers. These fibers consist of a non-contractile central region and contractile ends, each region with their own innervation. The central regions, lacking in myofibrils are wrapped with tonically active sensory neurons that project to the CNS and synapse directly with alpha-motor neurons that innervate the extrafusal fibers of the particular muscle. Referent Gamma-motor neurons innervate the contractile ends of the
intrafusal fibers. When a muscle reflex is set in motion by the firing of the alpha-motor neurons to contract the extrafusal muscle fibers, Gamma-motor neurons fire simultaneously in the contractile ends of the muscle spindle, thus maintaining a stretch on the non-contractile central region, regardless of the muscle length. This process known as Alpha-Gamma coactivation, ensures that central region afferent sensors remain responsive, and thus muscle tone can be maintained (32, 63).

From literature it appears that the link between proprioceptive deficit and hypermobility is very much a progressive “cause vs symptom” closed cycle. It has been well documented that children with generalized joint laxity are prone to delayed/poor motor development. In various ways, aspects including joint laxity, poor coordination and weak muscle development then causes abnormal joint mechanics (35). These initial congenital biomechanical deficits have been attributed as the start of the impaired proprioception cascade in hypermobile individuals. Malik et al. has theorized that the altered joint biomechanics lead to repetitive stresses that damage the joint receptors (61). Damage to the articular mechanoreceptors then leads to distorted afferent information. These same sensory fibers synapse with gamma-motor neurons of the muscle spindles, in the spinal cord. Thus, articular mechanoreceptor damage inhibits sensory input that decreases gamma-motor neuron excitability (62). As a result (considering the governance of muscle spindle functioning by the gamma-motor neurons) muscle spindle sensitivity is decreased and consequently proprioceptive acuity diminishes (35, 62). In this closed cycle of “causative vs symptomatic” factors, as displayed in Figure 2.4, diminished proprioception plays its part by in turn influencing the initial causative factor i.e. abnormal articular biomechanics (11, 35).
A primary complaint in JHS is joint pain. It is present in various representations of hypermobility linked syndromes and is also a deciding factor in whether a state of hypermobility can be considered benign (11). Although all joints can be affected, the knees, spine, shoulders and feet are most commonly symptomatic. Activities in which the individual participates, can also influence which joints are affected (11). The stresses and strains put on the joints of hypermobile individuals by the “diminished joint proprioception cycle” as discussed previously, also produces fatigue and pain. Pain then inhibits the use of the joint, which could in turn lead to weakness in surrounding muscles (11). In a similar “cause vs symptom” cycle to proprioception, the weakened muscles lead to decreased stability and control, that potentially causes strain and further aggravating pain (11).
Joint pain was a major presenting complaint in children diagnosed with HMS. In 125 cases, scrutinized by Adib et al. pain was present in 92 children (74%) (35). In 2009, Grahame reported that in 700 JHS patients that attended his hypermobility clinic at University College Hospital (London, UK), 26% claimed their pain was of “life dominating” proportions (8). Though it now appears obvious in literature, the link between JHS and pain was only discovered in the early two-thousands (13). Chronic pain related to JHS, usually has a subtle onset, superimposing on previous widespread musculoskeletal pain. This chronic form of pain distinguishes itself from acute pain in several ways. Chronic pain diffusely distributes itself without being reliably traceable to specific injury. It may distribute to the whole body, half body or quadrants. It is often associated with dysesthesia, allodynia (tender points) or hyperesthesia (8). In cases of JHS, any type of body movement can aggravate pain. This causes individuals to resort to altered movement patterns as a strategy of pain avoidance. This strategy has been termed kinesiophobia (64).

The effects of kinesiophobia on joint biomechanics and muscle deconditioning, again plunges the individual into the downwards spiral of joint degeneration (8). Grahame reports that the onset of JHS related chronic pain is rarely spontaneous. He claims factors like lifestyle changes (new jobs, new physical activities), sudden traumatic events or injury could trigger this unfortunate occurrence. The diagram in Figure 2.5, derived from Grahame’s paper on Joint Hypermobility Syndrome Pain, describes the pathogenesis of chronic pain syndrome in JHS (8).
Figure 2.5: The Pathogenesis of chronic pain syndrome in JHS (8).

2.3.3 Postural Adaptations

Another aspect where hypermobile individuals are disadvantaged by chronic pain and the accompanied kinesiophobia, regards posture control (11). Posture is defined as an individual’s position of sitting, walking or standing. Various intrinsic and extrinsic factors influence one’s posture. Postural control demands coordination of various systems i.e. sensory input from vestibular, visual and proprioceptive sensors as well as CNS and musculoskeletal correspondence (65). Kendall et al. described good posture as “the state of muscular and skeletal balance which protects the supporting structures of the body against injury and progressive deformity” (66). Keer et al. have reported that patients with recurrent lower back pain (similar to chronic pain syndrome
in JHS) have been shown to alter postural strategy, whereby deep postural stability muscle activation is delayed, this leaves the spine susceptible to perturbation (11).

The process of postural or movement alteration as found in fear avoidance or kinesiophobia has been found to occur in individuals who are pain-free, but were experimentally induced to anticipate pain on movement (67). Fortunately, for patients with JHS it has been shown that the changes of representation of affected muscles on the somatosensory cortex, along with other neuroplastic changes are reversible by motor skill training (68).

2.3.4 Neuropathological features associated with hypermobility

2.3.4.1 Carpal Tunnel Syndrome (CTS)

Suspicion that peripheral nerves could be at risk in JH, due to increased traction and movement of joint structures have long been of concern. This was accentuated by reports of correlation between CTS and JH (8). CTS occurs due to median nerve compression in the carpal tunnel. This is a common neuropathy in the general population with physical factors such as repetitiveness, personal risk factors and various medical conditions i.e. diabetes and thyroid disease being part of the etiology (69). Along with CTS, other entrapment neuropathies such as sciatica have been linked with BJHS. Although the origin of entrapment neuropathies have not been widely published or established with certainty, it is believed that the link lies with the decrepit nature of connective tissue in BJHS (69).

A strong association between CTS and JHS was confirmed in a study by Aktas et al., where a significant correlation was found between JHS (Brighton criteria) and electrophysiological proven CTS in 55 patients (8, 69). Pathophysiologically, the injury to the median nerve within the carpal tunnel due to ischemic damage and mechanical compression, whether chronically or intermittently, eventually leads to altered

© University of Pretoria
myelination followed by axonal loss (69, 70). In a study by Hassan et al. they found that among BJHS patients 45.6% presented with a clinical diagnosis of carpal and/or tarsal tunnel syndromes (69, 71). Due to these strong correlations, researchers have suggested that BJHS could be a predisposing factor to CTS and similarly those with CTS could be predisposed to BJHS (8, 69).

2.3.4.2 Chronic Fatigue Syndrome (CFS)

Researchers in the field of CFS have also noticed associations with JH. From an initial, uncontrolled study, Nijs et al. observed that in at least a sub-group, (11/44; 25%) of CFS adult patients, presented with proof of JH (72). The main feature of CFS is debilitating fatigue present for a duration of no less than 6 months. This occurrence is often accompanied with other symptoms i.e. headaches, painful lymph nodes, myalgia and arthralgia, sleep disturbance and neurocognitive complaints (46). Such has been the association between fatigue and musculoskeletal pain that suggestions have been made to classify CFS with the presentation of widespread muscle and joint pain as an important CFS sub-class. The well discussed factor of impaired proprioception has again been marked as a primary cause in linking CFS and JHS. Researchers have hoped to use this link, in searching for possible management strategies to relieve the symptoms of CFS (46).

In an Interesting study on this point, Nijs et al. hypothesized that impaired joint proprioception accounts in part for JH in CFS patients. Additionally, they assumed that if indeed this was the case, there would be solid rationale in using proprioceptive training as a treatment strategy for hypermobility in CFS patients. Their study yielded several interesting results, in that they found GJH to be more common in CFS adults, than in healthy control subjects, yet within the CFS group, no associations were found between GJH and knee proprioception. Neither did there appear to be any significant correlation between JH and musculoskeletal pain in CFS patients (46).
This suggests that the majority of debilitating musculoskeletal factors and pain in CFS, might tie with other neuropathological mechanisms. Nijs et al. concluded that although an increased prevalence of GJH presented in CFS (nearly 60% in their study), no evidence supported the clinical importance of hypermobility in CFS patients (46).

**2.3.4.3 Psychological and Cephalalgia factors in hypermobility**

Though not yet confirmed, some association with hypermobility and certain psychiatric states including phobic states and panic disorders have been reported. This affiliation has been attributed to a chromosomal link involving a genomic duplication in chromosome 15, that occurs in cases of JHS as well as these psychiatric disorders (8) (73). In cases where JHS is accompanied by fatigue, anxiety and depression, the social functioning of patients is impacted negatively to the extent of negating the individual’s quality of life (74). It has to be mentioned that studies on the association of psychiatric disorders and JHS are not in abundance, and some reports lack confirmation (8, 73).

Headaches are a symptom related to hypermobile patients that have gained research interest over the last two decades. The most prevalent being headaches that are of a cervicogenic nature. One of the most profound studies that shed light on the pathogenesis of headaches in hypermobile individuals, and more so, the role of the cervical spine therein, was done by Rozen et al. in 2006. Their study reported that in 11/12 patients who complained of assiduous daily headaches, excessive intersegmental motility of the cervical vertebra was prevalent (75). These 12 patients were evaluated for hypermobility by means of the Beighton nine-point scale. The conclusion formed from this study, was that cervical spine hypermobility could play a critical role in the pathogenesis of recurrent daily headaches (75). Another type of cephalalgie presentation that is becoming increasingly recognized, is the occurrence of orthostatic headaches. This condition is reported to occur, due to sporadic intracranial hypotension, with the presumed pathogenic mechanism being cerebrospinal fluid leakage from the subarachnoid space. In a prospective study by Scievink et al. 38% of patients presenting with recurrent orthostatic headaches, manifested with signs of connective tissue disorders and types of EDS. (76). The
authors of the study suggested that if linked to connective tissue instability, the inherent fragility of the dural membranes, may result in cerebrospinal fluid leakage (76).

2.3.5 Other extra-articular features associated with JHS

Considering the insurmountable evidence pointing to the role of connective tissue deficiency in the pathophysiology of JHS, it is unsurprising that several extra-articular features regarding connective tissue integrity arise in JHS. Some of these manifestations specifically associated with skin fragility, include ocular ptosis (drooping eyelids), varicose veins and bruising (3). In their study on some of the extra-articular features of BJHS, Mishra et al. studied 58 patients and 30 controls in order to clarify the phenotype of BJHS patients. In an elaborate investigation, they examined several factors: rheumatologic and ophthalmic results, hypermobility scores, echocardiographs, bone mineral density, as well as skin thickness, - elasticity and – light transmissibility. Although more cases of MVP was recorded in patients with BJHS than with the control subjects, neither aortic diameter nor MVP showed correlation with hypermobility. Bone mass density also didn’t show any significant reduction. Skin related measures did however indicate connective tissue relation factors. Ophthalmic examination indicated upper-eyelid laxity in 41% of patients. Also, in skin measures, significant correlation was found between hypermobility and skin stretchiness, as well as light transmissibility of the skin (3, 77).

On the point of extra-articular features of JHS and the role of connective tissue, Farmer et al. asked a highly relevant question in their study titled; “Unexplained gastro-intestinal symptoms and JH: is connective tissue the missing link ?”. In their study, they evaluated 129 referrals to a neuro-gastroenterology clinic, where they found that 63 (49%) patients indicated GJH. They also found that an unclear etiology for GI-symptoms, was significantly more frequent in GJH patients, when compared to those without GJH. Some of the symptoms experienced by patients with co-existent BJHS and GI-symptoms include: bloating (57%), abdominal pain (81%), reflux symptoms (48%), nausea (57%), vomiting (43%), constipation (38%) and also diarrhea (14%) (78). In search of explanations for functional gastro-intestinal disorder (FGID), Farmer
et al. made the intriguing statement that most extra-intestinal features of FGID are also common features of BJHS. Some associated features they tabulated include (78):

- Chronic episodic pain
- Fibromyalgia
- CFS
- Psychological co-morbidity (Incidences of anxiety and depression)
- Autonomic nervous system dysfunction
- Panic disorders
- Migraine
- Sleep disturbance
- Allergy

This symptomatic co-existence lead to the investigation of common cause. Although not substantiated by experimental evidence, Farmer et al. hypothesized that the key to a connective tissue link, might lie with the complex connective tissue matrix confined within the gut wall. This has a significant contribution in the mechanical properties of the gut. Cellular mechano-receptors like intramuscular arrays, the interstitial cells of Cajal and intra-ganglionic laminar endings embedded in the muscularis externa react to mechanical shear and pressure force to influence gastric motility (32, 78). For the sake of hypothesis, it suffices to say that changes in the connective tissue of the muscularis externa are probable to influence sensory functioning (78). In substantiation of this notion, Meier-Ruge described hypo-peristalsis associated with colonic dismosis, as a state with reduced or absent connective tissue within the myenteric plexus and/or the longitudinal or circular muscle layers (79).

The same mechanism of action that compromises the connective tissue matrix has evidently also been shown to cause weakness in other visceral supporting structures. Within isolated case studies, an occurrence of abdominal-wall hernias were found to be prevalent in hypermobile patients. Similarly, excessive laxity of the pelvic floor supporting structures have been identified in JHS patients, that predispose these individuals to genital prolapse, with the highest frequency being uterine prolapse in female patients (8, 80).
2.3.6 Endocrine factors in hypermobility

Sufficient research has been done to declare the multi-systemic physiology involved in hypermobility and its symptomatic presentations. Nevertheless, it seems surprising to find substantial amounts of literature regarding endocrinological influence on hypermobility. The most confounding of which, regards sex based occurrences of hypermobility, pertaining to gonadotropic hormones. One study in particular begged to answer questions regarding the influence of hormones on knee joint mechanics in healthy females, following their statement “ACL tears were between two to eight times more likely in females” (81, 82). The study built forth on the premise of Bowling et al. in 1989, which suggested that hormonally influenced joint laxity was a strong potential factor in the high frequency of female ACL injuries. Park et al. constructed their study to test serum estradiol and progesterone levels, knee joint laxity, lower joint kinetics and electromyography (EMG) measures at three intervals during the menstrual cycle, these being; follicular phase, ovulation and luteal phase. In concurrence with common physiological knowledge they reported progesterone and estradiol levels lowest during follicular phase, with higher levels of both hormones recorded during luteal phase (32, 81). Multiple regression analysis on their data, reported that estradiol and progesterone explained 80.1% of maximum knee laxity. This study concluded that increased knee joint laxity occurred during the ovulation phase and also that there was a reduced peak knee rotational moment during this phase, which they premised might be due to a protective mechanism because of the increased laxity in the joint (81).

This topic is however a minefield of contradicting findings, with multiple studies having reported on female ACL injuries during different phases of the menstrual cycle (83). In a retrospective study, Wojtys et al. found a higher than expected rate of non-contact ACL injuries in 28 females, during the estrogen peak period of ovulation, which concurs with the findings of Park et al (81, 84). In contrast, a study by Slauterbeck et al. that made use of salivary sex hormone levels, correlated ACL injuries with the follicular phase of the menstrual cycle (85). In addition to the inconcurrency of the topic, an examination of the proposition that hormonal laxity predisposes to injury, Karageanes et al. found no significant differences in KT-1000 measures between the three prominent menstrual phases in 26 female athletes over an 8 week period (86).
Other varying factors that can be found in these studies that could play a role include oral contraceptive usage and ACL tissue sourcing.

A certainty that does however arise from these studies, is that hormonal attribution to ligament laxity does exist. The prime example from which most studies stem, is certainly the associated increased extensibility of the pelvic region soft tissues and the interosseous ligament of the pubic symphysis with concurrent levels of estradiol and relaxin that occur during pregnancy (32, 83). Little is actually known about the exact physiological mechanism of action by which hormones influence joint laxity, although some telling propositions have been made.

Due to its prominent role during pregnancy the mechanisms of relaxin has been most abundantly found in literature. Current knowledge suggests that relaxin affects collagen turnover by stimulating collagenase expression, and by attuning collagen secretion and synthesis in human dermal fibroblasts (87). In rat studies relaxin has been shown to reduce collagen fiber density and organization, as well as length and degree of interdigitation of elastin (83). As with most hormones the action of relaxin, prerequisites the expression of relaxin receptor proteins. Most relevant to the field of endocrinologically induced ligament laxity in humans, is the fact that relaxin receptors have been identified in the human ACL (88).

As is the case with relaxin, estradiol receptors have been identified in the human ACL fibroblasts, suggesting that estradiol identifies the ACL as target tissue and may affect its structure and composition (89). Controversy does however remain regarding the role of estradiol in inhibition of ACL procollagen and fibroblast proliferation and synthesis (83). Several studies have yielded contradicting results, suggesting that the effects of exogenous estradiol depends heavily on concentration and the species tested. In the comprehensive study by Faryniarz et al., they found similar levels of estrogen receptors in males and female ACL cells. This study suggests that sex based functional implication may lie with circulating estrogen, although the synovial fluid levels of estrogen remains unknown. Interestingly, they also reported that estrogen receptors are activated not only by estrogen, but also by growth factors. These results
concur with cited studies, suggesting that estrogen alone might not influence sex differences in ACL injuries (83).

Dose dependency also seems to play a major part, with studies indicating that supraphysiological levels of 17-B-estradiol administered to rabbit ACL cultured fibroblasts had a 40-50% reduction in collagen synthesis (89). On the contrary, when Seneviratni et al. exposed cultured ovine fibroblasts to physiologic levels of 17-B-estradiol (2.2 to 250 pg. /ml), no effect was observed in collagen synthesis and fibroblast proliferation (90). When presenting dose and time dependent results, Yu et al. saw a decrease in fibroblast propagation with increasing 17-B-estradiol concentration on the first and third day of exposure, yet by days seven and fourteen, the dose dependent effects dwindled. A similar pattern was exhibited in procollagen-1 (83, 91). These studies indicating dose dependent variation, along with their own studies, brought Yu et al. to the conclusion that rhythmic variations in estradiol during a menstrual cycle, might influence ACL fibroblast metabolism (91).

In certainly one of the most extensive studies concerned with sex-steroid mechanisms underlying non-contact knee injuries in females, Dehghen et al. aimed to investigate the effects of sex-steroids on relaxin receptor iso-forms (RXFP-1; RXFP-2) and its presentation in knee ligaments and tendons (92). Relaxin effectively “loosens” connective tissue through various workings. Relaxin affects extracellular matrix components such as collagen, water and hyaluronan, which is a non-sulfated glycosaminoglycan and macro-component of connective, epithelial and neural tissue (32, 92). By up-regulating the expression of hyaluronic acid synthase, relaxin increases cervical hyaluronan content, which effectively loosens the dense collagen fiber network, due to the imposing size of these molecules (93). Other mechanisms of relaxin include anti-fibrotic action by down regulating fibroblast activity, up-regulation of collagenase synthesis as well as increasing matrix metalloproteinases (MMP). MMP’s are extracellular proteases that hamper matrix remodeling by degrading extracellular matrix components, such as collagen (92).
Apart from the known presentation of collagen receptors on the ACL, Dehghan et al. researched the expression of these receptors on other important structural supports of the knee, including the patellar tendon and lateral collateral ligament. In what is likely one of the most profound findings in favor of sex-steroid influence on connective tissue, Dehghan et al. reported that the expression of RXFP-1 protein and mRNA in the patellar tendon and lateral collateral ligament is up-regulated by estrogen and progesterone, and conversely down regulated by testosterone. Interestingly, no significant changes in RXFP-2 expression was noted (92). While this study provided novel evidence on how steroid-hormones up- and down-regulate relaxin receptor expression in connective tissue, that may help to provide a basis for the underlying increase in female non-contact knee injuries, the authors precaution against readily extrapolating this evidence to humans, seeing as the study was conducted on knee ligament samples of WKY rats (92). Nevertheless, this study provides firm insight into hormonal mechanisms of interaction on connective tissue and joint laxity.

2.4 Hypermobility and injury

In understanding the pathophysiology of how generalized hypermobility destabilizes the supporting structures of joints, it should come as no surprise that the incidence of hypermobility and MSI is greatly represented in literature. A study by Bin Abd Razak et al. very directly asked the question, whether generalized ligamentous laxity (GLL) may be a predisposing factor for musculoskeletal injuries (7). GLL has been implicated in various injuries such as cruciate ligament injuries, ankle sprains and shoulder instability. Bin Abd Razak et al. hypothesized in their prospective age-and sex matched case control study, that GLL would be common occurrence in individuals with musculoskeletal injuries, when compared to a control population. Despite this hypothesis concurring with known reviews such as the Pacey et al. meta-analysis of 2010, they found that with several other systematic reviews unable to determine definite difference in risk of injury with GLL, further investigation was warranted (7, 39).

In their study, one hundred individuals aged between 18 and 25 who reported to a primary military health care facility with signs of musculoskeletal injuries, were examined for GLL using the Beighton nine-point scoring system with cut-off at ≥4. An equal number of age and sex matched individuals without complaints of MSI made up the control group. The results indicated that GLL was present in 12% of cases,
compared to 4% in the control group. With lower body injuries being more prevalent, this study showed that individuals with musculoskeletal injuries were 3.35 times more likely to have GLL. Thus, they concluded that GLL may be a predisposing factor to musculoskeletal injuries (7).

When considering the implication of these findings, one can extrapolate that it would carry most importance for subgroups that have the highest frequency of musculoskeletal injuries. From the award winning review of Pacey et al. it is evident that two groups are used exclusively more than others in this field of research due to their high prevalence of injuries (39). Of the 4841 studies considered by Pacey et al. the 18 studies that met the inclusion criteria all used participant groups that were either specific to sports or the military (39).

### 2.4.1 GLL and injury in military subgroups

Musculoskeletal injuries, whether it sprains, strains, soft tissue injuries or dislocations are practically synonymous with physically active populations. Hence the fact that military academies and populations have been the sample catchment for various studies in the field of MSI research, providing significant subject numbers that undergo physical activity in controlled environments. The amount of research done on military populations is also deemed necessary and beneficial to the institutions themselves. In their article entitled “The burden and management of sports-related musculoskeletal injuries and conditions within the US military”, Cameron and Owens states that musculoskeletal injuries significantly burdens military service personnel, as well as the military health system. It is deemed a leading cause of disability discharge (94). Sports and PT related injuries accounts for much lost duty time and also causes several non-battle related medical evacuations. They also found that these injuries were consistent with those commonly associated with athletic populations (94).

In a study by Lauder et al. examining sports and PT related hospitalization in US army personnel, they found that most injuries affected the lower extremities, with the site distribution indicating the knee to be most affected, then the ankle, followed by the heel, foot and lower leg. The types of injuries most common were, bone fractures
(33%), strains and sprains (29%), joint dislocations (15%) and concussions (5%). In military men, injury associated activities ranking from most prevalent were basketball, football, softball and PT. In service woman, activities ranked PT, basketball, softball followed by skiing (95).

A very interesting statistic regarding deployed soldiers by Hauret et al. states that despite the volumes of media focus on battle related injuries in the recent Iraq and Afghanistan conflicts, US soldiers were 2-4 times as likely to be evacuated from the conflict zone due to non-battle injuries, with the number one factor being sports and PT related injuries. Hauret et al. classified more than 80% of the non-battle injuries they examined as being acute traumatic or musculoskeletal related. The injuries they found most common, ranked from most to least prevalent were:

- Fractures
- Overuse Injury (pain and inflammation)
- Joint dislocation
- Strains and sprains
- Internal joint derangement (i.e. ACL ruptures, articular cartilage lesions, meniscus tears) (94, 96).

The evidence of these studies suggest that musculoskeletal injuries have a significant impact on military personnel readiness, whether at base or during deployment (94). With the link between GJL and musculoskeletal injuries being well established, one can especially see the need to factor in incidences of JH in military populations in order to better understand its causative impact and to investigate possible preventative measures.

One study in particular that has definitively done so was conducted by Mullick et al. in their clinical profiling of BJHS from a tertiary care military hospital in India. The participants of their study consisted of 45 males and 39 females that were diagnosed with BJHS according to the Beighton nine-point scoring system at the rheumatology clinic of the Army hospital, Delhi. The patients had a mean age of 30 ± 3.71 years, with most being military personnel. All had joint pain with some having evidence of degenerative changes. The patients had a median Beighton score of 6/9. Despite the
presence of known features of BJHS that presented in this study i.e. STR, joint pain, skin laxity and CTS, one incidental finding stood out. Their results indicated that 9 out of 18 patients with Beighton scores $\geq 7$, indicated lateral head tilt, when frontally observed (97). They concluded that this interesting observation might be considered a clue to BJHS.

The diverse nature of physical activity that is engaged in by military populations, makes it theoretically impossible to relate all studies on GLL and injury incidence in military subgroups. Thus it is imperative to search for common denominators. The most common of these found in reviews of literature is that near all military personnel participate in physical fitness training regimes and sports. “On the fields of friendly strife are sown the seeds that on other fields, on other days, will bear the fruits of victory”, this quote by General Douglas McArthur underlines the philosophy and importance of why sports participation plays an integral part in military recruitment development (44). It implies that the challenging nature of sports and physical exertion is an imperative tool in preparing for the challenging environment of the battlefield.

A concise and general explanation of the physical activity undergone by military recruits can be assumed when looking at the guidelines employed by the United States Military Academy (USMA). PT are mandatory sessions conducted 3-5 times per week, with a duration of approximately one hour. These sessions generally consist of any of the following focus areas:

- Running
- Muscular strength training
- Endurance training
- Speed and Agility training
- Calisthenics (BW exercises) (94).

Along with the compulsory PT training, military servicemen spend a significant amount of time participating in sports. The types of sports differ significantly between military institutions. Within the USM some of the sports that are most commonly participated in and that frequently leads to injuries include basketball, football, flag football, softball
and weightlifting (94). Concurrently, Uhorchak et al. reported that Department of Physical Education classes for USMA cadets include basketball, skiing, close-quarters combat and challenging obstacle courses. Further mandatory military training also include activities such as helicopter-repelling and parachuting as well as simulated war-games (44). USMA cadets are required to engage in intramural, club or varsity sports through all, bar two, of their semesters at the academy. The sports most often participated in, include football, soccer, rugby, touch football, and basketball. Strikingly, all of these activities require high exertions of either cutting, jumping or both, often performed under high levels of fatigue which undoubtedly predisposes military servicemen to greater than average risk of contact and noncontact injuries (44).

2.4.2 GLL and Injury in Sport

Since the relationship between hypermobility and joint mechanics has been established, a flurry occurred among researchers to answer questions regarding hypermobility and its influence on sports. The prevalent theme of these studies can be summarized into two questions, 1. Does GJL increase risk of injury in a particular sport? 2. How does hypermobility influence performance in a particular sport? These questions have been applied to an abundant number of sports codes each with their own concerns regarding the matter. Some of the sports referenced in articles reviewed by Pacey et al. include: Lacrosse, soccer, field hockey, rugby union, ballet and dance, netball, American football, baseball, basketball, cross country, gymnastics, wrestling (39).

In order to draw meaningful conclusions from these diverse populations, the activities were grouped according to the American Academy of Pediatrics system for the data extraction of the review. Sports were batched as contact or collision sports, limited contact sports and noncontact sports (98). There were however sports that transcended more than one classification, and was labeled as mixed sports (39). From all included studies, the researchers decided to specify three categories of lower limb injuries i.e. all lower limb joint injuries, knee joint injuries and ankle join injuries. Various factors influenced the results of this meta-analysis. With the concise conclusion being that individuals with GJH carry a significantly higher risk of injury to the knee joint.
during contact sports participation, although on the other hand, the ankle joint carries no extra risk of injury regardless of the type of sport engaged in (39).

Although literature reviews are helpful in asserting an overview on the influence of hypermobility on injury in sport, one cannot negate the diverse specificity in the movement patterns of different sports and how these impact the probability of injury in specific joints. A case and point being the study of Stewart et al. on GLL and the incidence of injury in seasonal first division club rugby players. At p=0.034 they indicated a significantly higher incidence of injury in hypermobile players. The results of the injuries (to knees, shoulders, hips, ankles, wrists and hands) as measured in injuries/1000 exposure hours can be perused in Figure 2.6 (99).

![Figure 2.6: Injury rate in 1000 exposure hours by hypermobility status (99).](image)

On the contrary, in a study by Decoster et al. researching hypermobility related injury patterns in Lacrosse players, no difference in overall injury was indicated between hypermobile athletes and their non-hypermobile peers (100). Similarly in English professional football (soccer), Collinge et al. found injury risk to be very much the same between hypermobile and non-hypermobile football players. Interestingly, though not statistically significant, they did however point out that once injured, hypermobile players took longer to return to training and competition. They also made mention that
when comparing athletic populations, the accuracy is highly dependent on the Beighton cut-off score selection (48).

While there might be sufficient evidence to suggest that excessive JH might be an advantageous performance factor in aesthetic sports such as ballet and gymnastics, an injury like glenohumeral joint dislocation due to excessive laxity would be severely detrimental in contact sports or combat (8). The link with injury is certainly, among others, a major driving factor behind hypermobility research. Due to differences in study methods and measurements, as well as having to deal with a vast range of sports and activities, it is a field riddled by ambiguous answers (39).
2.5 References


Chapter 3: Sex differences in the Beighton nine-point hypermobility test scores

3.1 Key focus of the study

The aim of this study was to clarify the discrepancies in the comparison of males and females concerning the incidence of JH indicative of BJHS in a randomized selection of the generalised population in a South African context.

3.2 Background of the study

It is generally accepted that there is predominance in females towards hypermobility. It should be considered that many of these studies were not done in recent years, had seemingly small sample groups and were not particularly representative of the general population as the sample groups consisted of children, individuals diagnosed with hypermobility related syndromes and old-aged sufferers of rheumatism (1).

By making use of a basic research approach, in collecting of quantitative data this study set out to elucidate sex discrepancies in hypermobility. Thus, we hoped to deliver research that was more concurrent and representative of a broader spectrum of the population by testing four hundred and eighty individuals, from four geographically widespread areas of South Africa, for indicated hypermobility according to the Beighton nine-point hypermobility score.

3.3 Research objectives

Objective 1:

To find a comparable reference in the difference between male and female incidences of hypermobility in a sample group representative of the general population.

Objective 2:

If significant difference was found, to clarify the possible reasons for this occurrence.
3.4 Review of literature

In literature, hypermobility has been shown to present with varied prevalence according to epidemiological and demographic factors such as age, sex and ethnicity. Thus far, predisposing factors that have been accepted by most, include being female and of Asian or African ethnicity as opposed to European decent (2). Bridges and Larsson et al reported prevalence in children and also the decrease of hypermobility with age (3). In 1983 Biro and colleagues estimated hypermobility to be 10% to 25% in children, with prevalence being more with girls (3, 4). Various epidemiological incidences have been reported through the years. Data from a West London rheumatology clinic was investigated by Hakim and Graham in 2003. They reported the JHS phenotype to be present in 58% of females and 29% of males in the sample (5). Adult incidences of hypermobility have been recorded to vary from 5% in the USA to 43% in the Noruba tribe in Nigeria (6, 7).

In a study which queried a military medical database in the United States of America, it was found that the prevalent race and sex associated with hypermobility was white females compared to black and “other” (8). These findings substantially contradict a study done in India, where a sample group of eight hundred and twenty nine Indian children between ages 3-19 were tested according to the Beighton nine-point protocol. They reported a 58.7% incidence of JH, and a near equal sex incidence (9).

Conclusive explanation of the higher female tendency have eluded researches, although reports that also link to the higher prevalence of female non-contact ACL injuries, suggest that cause might be found in female specific endocrine markers, or more specifically influence of gonadotropic hormones relaxin and estradiol, as well as the influence of female specific joint angles (10, 11).
3.5 Research design and methods

3.5.1 Research approach

This study was conducted as basic research, making use of qualitative data to further understanding regarding demographic patterns in this field. A cross sectional approach was chosen for this study in order to observe the prevalence of JH in the sample group with correlation analysis describing the epidemiology between males and females.

3.5.2 Ethical considerations

The research protocol was submitted to and approved by A) the Ethics board of the participants and, B) the Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria. Ethical approval for the data collected from the SANDF recruits was granted by the 1 Military Hospital Research Ethics Committee (1MHREC) with the document added as Appendix A. Orientation and screening sessions were held at all testing venues, were all procedures were explained to the participants, followed by the signing of informed consent forms (Appendix B). All the participants were encouraged to ask questions and to accustom themselves with the impeding procedures.

3.5.3 Participants

The total sample population for this study consisted of four hundred and eighty individuals. This was a randomized population that were tested at four wide-spread geographical areas throughout the Republic of South Africa. The four groups that participated consisted of three populations (total of three hundred recruits) that were representing three different law enforcement academies (TP 1, TP 2, TP 3) and the last group consisted of one hundred and eighty second year university students.

The total sample population comprised of 45% males and 55% females.
3.5.3.1 Inclusion/Exclusion criteria

The inclusion criteria in all groups required the participants to sign informed consent to voluntary participation in the study and completion of a PAR-Q form. The main exclusion criteria entailed any history of osteological or rheumatologic diseases, as to exclude any cases where the occurrence of hypermobility could be symptomatic of these syndromes, as the purpose of the study was to only identify BJHS. Further exclusion criteria entailed:

- Refusal to give written informed consent.
- Medical exclusion from physical exercise.
- Failure to adhere to test procedures

3.5.3.2 Participant screening and informed consent

An initial orientation and screening session was organized, where potential participants was screened to ensure compliance with the criteria listed above. It included:

- An explanation of the study purpose, procedures and risks.
- Screening for the criteria mentioned above through written completion of the pre-test questionnaire on health.
- Provision and discussion of the pre-test instructions.
- Opportunity for participants to ask questions regarding the study and their involvement.
- Informed Consent Forms (Appendix B) was supplied to participants who met the inclusion criteria outlined above.

3.5.3.3 Discontinuation criteria

After the study has commenced, individual participants was eliminated from the study in the event of:

- Failure to comply or finish with the testing procedure.
- Voluntary discontinuation by participant.
3.6 General Procedures and Measurements

3.6.1 Biographical data and questionnaires

Biographical data was collected and considered in order to determine the demographic distribution of the sample population as well as to cross reference any outliers that might occur. The personal and family history questionnaire was examined to assert whether participants comply with the pre-requisites for participation in the study as set out in the inclusion/exclusion criteria. The state of physical activity of the participants was asserted with the use of the lifestyle evaluation, physical activity questionnaire and the frequency intensity time (FIT) index of Kasari. Hypermobility has been reported to influence and be influenced by physical activity (12). Though not represented in the results due to special constraint, these questionnaires were used in cross referencing outlying test results and screening criteria. The following questionnaires were applied in this study along with the data sheet presented as Appendix C:

**Personal and Biographical Information**

This questionnaire provides the basic information on the participant regarding demographical and biographical factors, such as age, sex, ethnicity etc.

**Family and Personal History**

Information obtained from this questionnaire pertains to personal and family medical history. This helps identify and highlight possible risk factors and predispositions to hereditary disease that the participant might have. The answers to this section were important to assure compliance with inclusion criteria and to prevent possible injury or exposure to risk factors.

**Lifestyle Evaluation**

The lifestyle evaluation consists of seven sub-categories, namely: exercise/fitness, nutrition, tobacco use, alcohol and drugs, emotional health, safety, and disease prevention. This questionnaire serves as an evaluation of the overall lifestyle of the individual, thus highlighting high risk behavioural choices resulting in deteriorated health which possibly predispose the individual to various medical complications.
Lifestyle and modifiable risk behaviours has proven to be important factors affecting physical health and can be directly correlated with an individual’s current state of wellbeing (13). The questionnaire data was converted into scores that categorized the individuals into low, medium or high risk as a component of wellness.

**Physical Activity Questionnaire**

The Paffenbarger Physical Activity Questionnaire was used in order to further assess general health/lifestyle, but more specifically, it was used to gauge leisure- and work-time physical activity levels in order to evaluate the overall physical activity index. Statements are given to which individuals give an answer which best suites their behaviour frequency. In addition, information on leisure time activity is requested through questions concerning frequency of exercise (hours per week). The questionnaire data was converted into scores that defined the individual’s physical fitness state into low, medium or high risk. Scores were allocated to the various questions and the estimated energy expenditure was calculated by means of kilocalorie scores (14).

**Fit index of Kasari**

The FIT index of Kasari serves as a further evaluation of a person’s level of physical activity (15). The questionnaire uses 3 parameters, namely (1) frequency of exercise (2) intensity of exercise and (3) time spent on workout. The FIT index is then calculated using the following formula:

FIT index = (points for frequency) * (points for intensity) * (points for time).

A person can obtain a minimum score of 1 and a maximum score of 100. The higher the score the more physically active the person is considered to be, therefore this evaluation is not based on energy expenditure, but rather on the three important parameters involved during exercise regimes. The questionnaire was able to provide an additional fitness score to supplement the previous questionnaire. The questionnaire data was also converted into scores that define the individual’s physical fitness state into low, medium or high risk.
3.6.2 Beighton nine-point scale testing

Several methods and criteria for testing HMS has been developed and re-evaluated over the years of study in this field. For this study subjects were tested according to the Beighton 9-point scoring system. This is a modification of the Carter and Wilkinson scoring system and has been in use for many years to identify widespread hypermobility (16).

The Beighton nine-point scale method of diagnosing hypermobility requires the participant to complete manoeuvres that entails attempted hyper-extension around 9 specific joints. The researcher will then judge whether these manoeuvres were successfully accomplished. In order for the subjects to perform the movements correctly, the researcher illustrates the required action and then judges the range of motion achieved by the subject and awards scores accordingly. A single point is awarded if the hyper-extension meets the criteria for each specific joint. Table 3.1 and Figure 3.1 set out the criteria for the nine manoeuvres.

**Table 3.1: Beighton nine-point hypermobility test (17).**

<table>
<thead>
<tr>
<th>Joint</th>
<th>Set point limit criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>left little (fifth) finger</td>
<td>passive dorsiflexion beyond 90°</td>
<td>1</td>
</tr>
<tr>
<td>right little (fifth) finger</td>
<td>passive dorsiflexion beyond 90°</td>
<td>1</td>
</tr>
<tr>
<td>left thumb</td>
<td>passive dorsiflexion to the flexor aspect of the forearm</td>
<td>1</td>
</tr>
<tr>
<td>right thumb</td>
<td>passive dorsiflexion to the flexor aspect of the forearm</td>
<td>1</td>
</tr>
<tr>
<td>left elbow</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>right elbow</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>left knee</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
</tbody>
</table>
right knee | hyperextend beyond 10° | 1
---|---|---
forward flexion of trunk with knees full extended | palms and hands can rest flat on the floor | 1

Figure 3.1: Maneuvers of the Beighton nine-point hypermobility test (17).

For diagnostic purposes, the Beighton criteria states that a score of 4/9 or greater indicates the probability of BJHS (16). The method is accurate and concise, and it is ideal for processing data from large sample populations. This method is also one of the major criteria used in the revised Brighton diagnostic criteria for BJHS, which consists of a system combining major and minor indicators like the occurrence of arthralgia, varicose veins, STR, abnormal skin and re-occurring dislocation and sublocation of joints (18).

3.6.3 Anthropometric testing

General anthropometric tests were done to ensure the sample group were of homogenous physical attributes. This carried great importance regarding the fact that the second research objective stated that the study had to be reflective of a general population. The following procedures were performed in order to gather the anthropometric data:

**Weight and height**

- Weight was measured in Kilograms using a Seca™ electronic scale
- Height was measured in Meters by means of a Leicester Height Measure MKII™
Body Mass index (BMI)

Calculating BMI:

- Square the height measurement by using the following formula:
  \[\text{Height in metres} \times \text{height in metres} = \text{height in metres}^2\]
- BMI equals BW in kilograms divided by height in metres squared (kg/m\(^2\))
  \[\text{BW in kg ÷ height in m}^2 = \text{BMI in kg/m}^2\]
- Measure height in metres (m) and weight in kilograms (kg) and record the results.

Body fat percentage

Body fat percentage was calculated by using the Yuhasz 6-Skinfold method for males and females (19)

Equipment:
- Skinfold callipers, Body Logic©
- Partner to take measurements
- Marking pen (optional)

Instructions:

The following areas must be measured using a skinfold calliper:

- **Abdominal**: Vertical fold, 2.5 cm to the right of navel
- **Supra-iliac**: Diagonal fold, directly above iliac crest
- **Thigh**: Vertical fold, midway between knee cap and top of thigh
- **Calf**: Vertical fold, inside of leg on largest part of calf
- **Sub-scapular**: Diagonal fold, directly below shoulder blade
- **Triceps**: Vertical fold, midway between elbow and shoulder

Determining percentage body fat:

- **Men**: 6 skinfolds x 0.1051 + 2.585
- **Women**: 6 skinfolds x 0.1548 + 3.58

Body fat % values for males and females are summarized in tables 3.2 and 3.3.
Table 3.2: Body fat recommendation Table for men (19).

Percentage body fat (%)

<table>
<thead>
<tr>
<th>Men</th>
<th>20 - 39 years</th>
<th>40 - 59 years</th>
<th>60 - 79 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>3 – 5</td>
<td>3 – 5</td>
<td>3 – 5</td>
</tr>
<tr>
<td>Low/ athletic</td>
<td>6 – 7</td>
<td>6 – 10</td>
<td>6 – 12</td>
</tr>
<tr>
<td>Recommended</td>
<td>8 – 19</td>
<td>11 – 21</td>
<td>13 – 24</td>
</tr>
<tr>
<td>Overweight</td>
<td>20 – 24</td>
<td>22 – 27</td>
<td>25 – 29</td>
</tr>
<tr>
<td>Obese</td>
<td>≥ 25</td>
<td>≥ 28</td>
<td>≥ 30</td>
</tr>
</tbody>
</table>

Table 3.3: Body fat recommendation Table for women (19).

Percentage body fat (%)

<table>
<thead>
<tr>
<th>Women</th>
<th>20 - 39 years</th>
<th>40 - 59 years</th>
<th>60 - 79 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential</td>
<td>8 – 12</td>
<td>8 – 12</td>
<td>8 – 12</td>
</tr>
<tr>
<td>Low/ athletic</td>
<td>13 – 20</td>
<td>13 – 22</td>
<td>13 – 23</td>
</tr>
<tr>
<td>Recommended</td>
<td>21 – 32</td>
<td>23 – 33</td>
<td>24 – 35</td>
</tr>
<tr>
<td>Overweight</td>
<td>33 – 38</td>
<td>34 – 39</td>
<td>36 – 41</td>
</tr>
<tr>
<td>Obese</td>
<td>≥ 39</td>
<td>≥ 40</td>
<td>≥ 42</td>
</tr>
</tbody>
</table>

3.7 Data processing and statistical analysis

The data analysis consisted of descriptive statistics that correlated the prevalence of BJHS between the males and females in the sample population. The statistics were calculated by means of the NCSS™ statistical analysis software program.
3.8 Results

The results of the study indicated that 26.19% of all subjects tested were hypermobile (Table 3.4). When comparing the incidence of BJHS between males (♂) and females (♀) in Table 3.5, it was seen that data recorded from all four sample groups indicated higher percentages for females than males. Sex specific totals showed 36.41% incidence for females compared to 13.96% for males.

Table 3.4: Hypermobility incidence of sample populations.

<table>
<thead>
<tr>
<th>Population</th>
<th>2nd Years</th>
<th>TP 1</th>
<th>TP 2</th>
<th>TP 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>% HM &gt; = 4</td>
<td>36.42</td>
<td>17.31</td>
<td>6.25</td>
<td>14.35</td>
<td>18.79</td>
</tr>
<tr>
<td>% HM &gt; = 6</td>
<td>16.05</td>
<td>5.13</td>
<td>1.56</td>
<td>3.04</td>
<td>6.36</td>
</tr>
<tr>
<td>% HM = 9</td>
<td>3.09</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>1.04</td>
</tr>
<tr>
<td>% Total population hypermobility &gt; = 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>26.19</td>
</tr>
</tbody>
</table>

Table 3.5: Sex specific incidence of hypermobility of sample populations.

<table>
<thead>
<tr>
<th>Population</th>
<th>2nd Years</th>
<th>SAPD HK</th>
<th>SAPD D</th>
<th>SANDF</th>
<th>Total population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>♂</td>
<td>♀</td>
<td>♂</td>
<td>♀</td>
<td>♂</td>
</tr>
<tr>
<td>% HM &gt; = 4</td>
<td>27.27</td>
<td>38.76</td>
<td>10.96</td>
<td>22.89</td>
<td>2.77</td>
</tr>
<tr>
<td>% HM &gt; = 6</td>
<td>9.09</td>
<td>17.83</td>
<td>2.74</td>
<td>7.23</td>
<td>0.00</td>
</tr>
<tr>
<td>% HM = 9</td>
<td>3.03</td>
<td>3.10</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Sex specific totals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The descriptive statistics, represented as means indicated ($\mu = 2.27 \pm 2.21$ SD) for females and ($\mu = 1.14 \pm 1.66$ SD). In the two-sample test report for independence, equal variances were rejected by the modified Levene test for equal variances. Normal distribution was rejected at $\alpha = 0.05$. Figure 3.2 shows a box plot distribution of the mean average scores for males (Total M) and females (Total F). A p-value of 0.0001 was reported for the correlation between these two values.
After statistical analysis no significant correlation between the occurrence of hypermobility and BMI or hypermobility and body fat percentages could be reported from this study. Interestingly, individuals who presented with Beighton scores of nine, which indicated hypermobility in all the joints tested, were only found amongst the second year students and the SANDF recruits. Both these groups consisted of populations aged between 18 and 25, as opposed to the SAPD HK and SAPD D groups, which consisted of a broader spectrum of adult aged individuals between ages 18 and 65.

3.9 Discussion

This study delivered clear and concise results that are comparable to previous studies due to the standardised method of testing and diagnostic protocol that was used. Statistically, a significant difference was reported in the occurrence of JH between males and females according to the Beighton nine-point hypermobility score. By using a cut-off score of four or greater as indicative of JH, as commonly prescribed in literature, this study reported JH in 26.19% of a general adult population, with
prevalence indicated as 36.41% in females as opposed to 13.93% in males. With a p-value of 0.0001 reported for the two-sample correlation between these two groups, the difference between sexes in this study, was deemed to be statistically significant.

In an interesting observation from our study, full scores of nine joints tested were only found amongst younger adult aged populations, aged 18 to 25. These finding seem to support the notions of earlier research by Grahame et al., suggesting that hypermobility decreases with age (17).

The results of this study confirm findings in literature and some related current research. A study that purposed to link glenohumeral joint instability to hypermobility also reported a prevalence of female hypermobility. It is interesting to note that a general prevalence of only 1.5% was reported by the researchers, even though the tests were also conducted using the Beighton nine-point scale scoring system for scores of 4 and greater (20). Another study comprising of 660 subjects from a music school that were tested for the frequency of incidence and nature of their hypermobility, also concurred with the premise of female predominance (3). What is noticed when comparing the most current results are the discrepancies regarding the reported rates and magnitudes of incidences.

If current trends suggest that BJHS is caused by genetic predisposition (16), and taking into consideration the reported female prevalence, it begs to ask the question, what causes this genetic defect to favour females if it is generally accepted that there is no significant difference in the structural composition of connective tissue proteins between males and females?

An explanation could be found when looking at hormonal differences between men and women. The hormone relaxin is well known for its function of increasing laxity of the pubic symphysis and cervix prior to labour (21). The hormone is secreted by pregnant and non-pregnant women and its mechanism is believed to be the inhibition
of collagen synthesis. Researchers found that the hormone increases laxity in the ACL, and they confirmed the presence of relaxin receptors in this ligament (21). In a similar study the presence of estrogen and progesterone receptors in the ACL were validated, when knee laxity was measured during various stages of the menstrual cycles of participants. Laxity of the knee increased at menstrual stages with varied secretion of these hormones (10).

Several contradicting finds have also been presented, especially regarding the phases off the menstrual cycle that leads to increased joint laxity (22). Never the less, there is substantial evidence to suggest that general joint laxity due to hormonal influence may play a major part in the hypermobility predominance in females. An ulterior explanation was proposed by Liu et al. who suggested that female specific joint angles might also influence joint laxity, especially in the lower extremities (10, 11). These finding have however also not yet been conclusively verified. It is clear that further research is warranted in order to fully understand the prevalence of JH in females.

### 3.10 Conclusion

The findings of this study suggests that in a generalized, multi-ethnic South African adult population, Beighton nine-point hypermobility scores are greater in females than in males, thus being indicative of higher probability of wide spread JH or BJHS amongst women. Some indicators in this study also concur with prior research showing that hypermobility decreases with age. The reason for female prevalence of JH is still unclear, with the most prominent hypotheses suggesting that the influence of female specific hormones on connective tissue as well as female joint biomechanics could be the underlying effectors.
3.11 Suggestions for future research

Considering the prominently reported correlation between hypermobility and injury, and seeing as this study indicates a one in four likelihood of JH in the general population, findings propose that screening for hypermobility could be important in physically active populations. The significant prevalence amongst females, could also warrant further research into sex specific diagnostic criteria for BJHS.
3.12 References


Chapter 4: Comparison of the Beighton nine-point hypermobility scores between males and females with relation to altered muscular component

4.1 Key focus of the study
Investigate possible differences in Beighton nine-point hypermobility scores between males and females (age 18-25) with relation to altered muscular component.

4.2 Background of the study
Non-contact musculoskeletal and joint injuries have gained much attention in military academies. Studies suggest that musculoskeletal injuries have a significant impact on military personnel readiness, whether at base or during deployment as well as costing military institutions millions of dollars (1). US soldiers in the recent Afghanistan engagement were 2-4 times as likely to be evacuated from the conflict zone due to non-battle injuries, with the number one factor being sports and PT related injuries (2). Coincidently the role that hypermobility might play in musculoskeletal and joint injuries, have also been in the research spotlight over recent years. Various studies have reported contradictory results on the influence of hypermobility on musculoskeletal injuries, with most concluding that the impact is very much dependent on movement patterns, and joint angles specific to the physical activity.

Incidence of hypermobility has been reported to be as common as 36% in females and 14% in males (3). Due to the high numbers of personnel in military institutions participating in various types of physical activity on a frequent basis, hypermobility and musculoskeletal or joint injuries are bound to coincide. Military personnel do however formally engage in regular exercise and various resistance training programs which have been shown to increase proprioception and muscle torque deficits as well as decrease muscle deconditioning in hypermobile individuals (4).

Considering this information and reviewed literature, it could be hypothesized that where physical activity/sports/exercise might lead to greater probability of MSI in hypermobile individuals, it could also concurrently lessen the degree of hypermobility in these individuals. To our knowledge, no studies have been done to investigate the
interplay of physical activity and hypermobility in a military setting. This study attempted to quantify the interaction of a set military basic training exercise regime on the states of hypermobility, with relation to altered muscular component.

4.3 Research objectives

OBJECTIVE 1:

Monitor and determine the changes in altered muscular component expressed as LBM, during 20 weeks of a military basic training program, and scrutinize the efficacy of the military basic training program to bring about changes in LBM

OBJECTIVE 2:

Screen baseline and concurrent Beighton nine-point hypermobility scores of military recruits during an intervention period of 20 weeks basic training, and correlate results to changes in muscular component

4.4 Review of literature

In a study which queried a military medical database in the United States of America, it was found that the prevalent race and sex associated with hypermobility was white females compared to black and “other” (5). These findings substantially contradict a study done in India, where a sample group of 829 Indian children between ages 3-19 were tested according to the Beighton nine-point protocol. They reported a 58.7% incidence of JH, and a near equal sex incidence (6). Another study on a paediatric sample found children with HMS to have markedly lower JK and JPS measures (4). Although it is relatively conclusive that females and children in general are more susceptible to BJHS, it can be noted that there are still questions to be answered regarding sex, age, race and incidence of BJHS in general populations.
In light of this study, it is imperative to give thought to all possible factors of hypermobility that could markedly influence physical activity and subjection to an intense training regime. It has been suggested that hypermobile individuals may be predisposed to Soft-tissue rheumatism (STR - tendinitis, bursitis, fasciitis and fibromyalgia) and subsequent musculoskeletal pain (7). Another study that aimed to assess the prevalence of Generalized Soft Tissue Rheumatism (GSTR) in a student sample (age 20.23 SD 1.56.) found Hypermobility to be the main contributor, amongst other factors such as fibromyalgia, myofascial pain syndrome and CFS (8). In 2008 a study done in Turkey suggested BJHS to be a predisposing factor to Carpel Tunnel Syndrome (CTS) and possibly other entrapment neuropathies (9).

Engaging in physical activity or exercise is of utmost importance in order to improve overall health and wellness. Several chronic lifestyle diseases correlate highly with a sedentary lifestyle (10). Exercise prevents chronic diseases such as obesity, hypertension, oncogenesis, high cholesterol, cardiovascular and cardio respiratory health conditions (11). Greater margins of the general population are actively engaging in exercise and physical activities due the positive effects on health and wellness (12). The health benefits for sedentary people that engage in moderate exercise such as brisk walking is tremendous. Physically active people reduce their colon and breast cancer risk with up to 40% and the risk of having a stroke or suffering from high blood pressure are reduced with 30%. High stress levels are reduced or replaced with improved sleep, flexibility, fitness, a healthier body composition, muscle strength and endurance (11). Exercise or physical activity is the main activator of musculoskeletal adaptation (11).

Several studies have been done on sport specific sample groups to correlate the incidence of injury and adverse training effects in hypermobile individuals. Due to ever increasing participation in physical activity and exercise for the sake of increased health and fitness, it has become imperative to form a conclusive understanding of all factors that could influence hypermobile individuals from a general population that engage in moderate to intense physical activity. Consider the results of a study done in 2004 in which a home-exercise regime showed remarkable effect in increasing proprioception and ameliorating symptoms in 16 of 18 participants with JHS (13).
Few studies in hypermobility have touched on the influence that LBM might have on joint laxity. LBM is defined as the mass component that the body equates to, once the estimated mass of fat is subtracted. This fat-less body mass, comprises the combined mass of the skeleton, organs, blood and fluid components of the body, muscle, connective tissue and skin (14). LBM can be measured in various ways, though the most contemporary method used involves determining body fat percentage by use of skinfold measures and subtracting the converted mass from BW: \( \text{LBM} = \text{Body Mass} - (\text{Body Mass} - \text{Body Fat} \%) \) (15). One study in particular that considered the association of hypermobility with body composition was done by Shultz and colleagues. In their attempt to identify multiplanar knee laxity profiles that associate with physical characteristics, they observed BMI (BMI) amongst their populations as a body composition determinant (16). BMI measured as Kg/m\(^2\) is calculated by dividing body mass by the square of body height, and is commonly used as a soft tissue quantifier (muscle and fat mass), as well as an obesity calculator (15).

An interesting find by Shultz and colleagues, showed that clusters with greater magnitudes of varus valgus and internal/external rotational knee laxity, were positively associated with being younger, with a smaller Q-angle, of shorter femur length, less thigh strength and have lower BMI. When they considered quadriceps strength, every 1-SD increase in quadriceps strength and BMI decreased the odds of being in the moderate (0.26 BMI & 0.86 Strength) or high (0.02 BMI & 0.29 Strength) clusters for knee laxity. Seeing as higher BMI can denote greater lean mass in males and larger fat mass in females, and keeping in mind the well reported positive correlation between lean mass and strength, they concluded that lean mass could to some extent explain sex differences in knee laxity values. They did however concede that more accurate measures of LBM and control of other confounding sex factors are needed to confirm underlying sex aspects in laxity profiles.

Considering the aim of this study to focus on the muscle component of body composition, BMI scores were deemed an inadequate measure of body composition as it fails to distinguish between muscular component and fat mass. The root of this study to investigate altered muscular component in hypermobility is largely founded
on previous research such as the work done by Ferrell and colleagues that reported improved proprioception and greater muscle strength in adult HMS patients, following a closed kinetic exercise program of 8 weeks (13). Similarly, positive results in hamstring and quadriceps muscle strength gains by means of strength training, deems it probable that muscle torque and proprioceptive acuity can also be improved in children with HMS (4). While the bulk of research considering exercise prescription, specifically in rheumatologic hypermobility patients have focussed on the positive effects of proprioceptive training regimes, mention has been made of the ability of exercise to counteract muscle deconditioning and muscle torque deficits in hypermobility. This is however a field that warrants further research (4, 17).

4.5 Research design and methods

4.5.1 Research approach

This study, conducted in the setting of a military base was approached according to a repeated-measures design. The longitudinal nature of the study allowed for data to be collected at three different observational intervals, producing the researchers with paired data for within group comparison. In this design each participant acts as their own control, producing dependant observations, which can easily be statistically tried using paired test protocols. This design accurately measures the change induced by the intervention over time due to the fact that the paired design controls for extraneous variation among the observations (18).

4.5.2 Ethical considerations

The research protocol was submitted to and approved by A) the Ethics board of the participants and, B) the Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria. Ethical approval for the data collected from the SANDF recruits was granted by the 1 Military Hospital Research Ethics Committee (1MHREC) with the ethical approval document attached as Appendix A. Orientation and screening sessions were held at the testing venue, where all procedures were explained to the
participants, followed by the acknowledgement of informed consent (Appendix B). All the participants were encouraged to ask questions and to accustom themselves with the impeding procedures.

4.5.3 Participants

The sample population for this study consisted of two hundred and thirty four SANDF recruits enrolled for basic training at the SANDF’s Lephalale base located in the Limpopo province of South Africa. The participants were between the ages of eighteen and twenty five. The total sample population comprised of 57% males and 43% females.

4.5.3.1 Inclusion/Exclusion criteria

The inclusion criteria required the participants to be between the ages eighteen to twenty five. Participation was subject to having signed informed consent to voluntary participation in the study and completion of a PAR-Q form. The main exclusion criteria entailed any history of osteological or rheumatologic diseases, as to exclude any cases where the occurrence of hypermobility could be symptomatic of these syndromes. Further exclusion criteria entailed:

- Refusal to give written informed consent.
- Medical exclusion from physical exercise.
- Failure to adhere to test procedures

4.5.3.2 Discontinuation criteria

After the study has commenced, individual participants was eliminated from the study in the event of:

- Failure to comply or finish with the testing procedure.
- Voluntary discontinuation by participant.
4.5.4 Data collection timeframe

Data for this study was collected at three instances. The baseline testing was done at commencement of the intervention. This will be referred to in the text as Week 1. An interim data collection occurred at Week 12 of the basic training period. Final data collection occurred at cessation of the basic training intervention period at 20 weeks.

4.6 General Procedures and Measurements

4.6.1 Biographical data and questionnaires

Biographical data was collected and considered in order to determine the demographic distribution of the sample population as well as to cross reference any outliers that might occur. The personal and family history questionnaire was examined to assert whether participants comply with the pre-requisites for participation in the study as set out in the inclusion/exclusion criteria. The state of physical activity of the participants was asserted with the use of the lifestyle evaluation, physical activity questionnaire and the FIT index of Kasari. The personal and biographical data sheets and questionnaires that were applied in this study are available as Appendix C.

4.6.2 Beighton nine-point scale testing

Several methods and criteria for testing HMS has been developed and re-evaluated over the years of study in this field. For this study subjects were tested according to the Beighton 9-point scoring system. This is a modification of the Carter and Wilkinson scoring system and has been in use for many years to identify widespread hypermobility (18).

The Beighton nine-point score method of diagnosing hypermobility requires the participant to complete manoeuvres that entails attempted hyper-extension around 9 specific joints. The researcher will then judge whether these manoeuvres were successfully accomplished. In order for the subjects to perform the movements correctly, the researcher illustrates the required action and then judges the ROM
achieved by the subject and awards scores accordingly. A single point is awarded if the hyper-extension meets the criteria for each specific joint. Table 4.1 and Figure 4.1 sets out the criteria for the nine manoeuvres.

Table 4.1: Beighton nine-point hypermobility test (19).

<table>
<thead>
<tr>
<th>Joint</th>
<th>Set point limit criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>left little (fifth) finger</td>
<td>passive dorsiflexion beyond 90°</td>
<td>1</td>
</tr>
<tr>
<td>right little (fifth) finger</td>
<td>passive dorsiflexion beyond 90°</td>
<td>1</td>
</tr>
<tr>
<td>left thumb</td>
<td>passive dorsiflexion to the flexor aspect of the forearm</td>
<td>1</td>
</tr>
<tr>
<td>right thumb</td>
<td>passive dorsiflexion to the flexor aspect of the forearm</td>
<td>1</td>
</tr>
<tr>
<td>left elbow</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>right elbow</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>left knee</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>right knee</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>forward flexion of trunk with knees full extended</td>
<td>palms and hands can rest flat on the floor</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure 4.1: Maneuvers of the Beighton nine-point hypermobility test (19).
For diagnostic purposes, the Beighton criteria states that a score of 4/9 or greater indicates the probability of BJHS (18). The method is accurate and concise, and it is ideal for processing data from large sample populations. This method is also one of the major criteria used in the revised Brighton diagnostic criteria for BJHS, which consists of a system combining major and minor indicators like the occurrence of arthralgia, varicose veins, STR, abnormal skin and re-occurring dislocation and sublocation of joints (20).

4.6.3 Anthropometric measures

The following procedures were performed in order to gather the anthropometric data:

**Weight and height**

- Weight was measured in Kilograms using a Seca™ electronic scale
- Height was measured in Meters by means of a Leicester Height Measure MKII™

**Body fat percentage**

Body fat percentage was calculated by using the Yuhasz 6-Skinfold method for males and females (14).

Equipment: Skinfold callipers, Body Logic

The following areas must be measured using a skinfold calliper:

- **Abdominal**: Vertical fold, 2.5 cm to the right of navel
- **Supra-iliac**: Diagonal fold, directly above iliac crest
- **Thigh**: Vertical fold, midway between knee cap and top of thigh
- **Calf**: Vertical fold, inside of leg on largest part of calf
- **Sub-scapular**: Diagonal fold, directly below shoulder blade
- **Triceps**: Vertical fold, midway between elbow and shoulder
Determining percentage body fat:

- Men: $6 \times 0.1051 + 2.585$
- Women: $6 \times 0.1548 + 3.58$

**LBM / Muscular Component**

LBM was measured by determining body fat percentage using skinfold measures and subtracting the converted mass from BW:

- LBM = Body Mass – (Body Mass – Body Fat %) (15).

Due to this method readily deducting fat mass, for the purpose of this study muscular component was deemed the only constituent of LBM to be susceptible to any substantial changes in mass over a period of 20 weeks of exercise intervention. Thus, any changes that might’ve occurred in the combined mass of the skeleton, organs, skin, connective tissue, blood and fluid component were considered negligible (14, 21).

**4.6.4 Intervention protocol**

The intervention protocol was supervised and implemented by the superior officers of the recruits, including PT instructors and Medical officers. The participants were exposed to 20 weeks of basic training. The component of basic training that characteristically contributes the most to muscular strength, endurance and cardiovascular adaptations in the form of structured exercises, are PT sessions. These sessions typically commenced with a warm up period aimed at increasing heart rate, intramuscular temperature and range of movement. The greater part of the sessions consisted of various sets of upper body, lower body and core endurance exercises as well as intervals of BW and external weight resistance exercises and running. The outline of the PT program is set out in Table 4.2. Other physically challenging components of basic training that are lesser specificity towards muscular adaptation goals, though they contribute greatly to LBM adaptations, included: Drilling, route marches with combat kit (8km & 14km), field craft, musketry and combat training. For the purpose of further studies, injury data for the intervention period was also recorded.
Table 4.2: Outline of the military PT intervention (22).

<table>
<thead>
<tr>
<th>Training component</th>
<th>Resistance modality</th>
<th>Time (minutes) allocated</th>
<th>Exercises completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm up</td>
<td>None</td>
<td>322</td>
<td>x</td>
</tr>
<tr>
<td>Upper body</td>
<td>BW</td>
<td>x</td>
<td>28 *</td>
</tr>
<tr>
<td>Endurance exercises</td>
<td>BW + 20kg external</td>
<td>x</td>
<td>64 **</td>
</tr>
<tr>
<td>Core endurance</td>
<td>BW</td>
<td>x</td>
<td>28*</td>
</tr>
<tr>
<td>exercises</td>
<td>BW + 20kg external</td>
<td>x</td>
<td>64 **</td>
</tr>
<tr>
<td>Lower body</td>
<td>BW</td>
<td>x</td>
<td>28*</td>
</tr>
<tr>
<td>endurance exercises</td>
<td>BW + 20kg external</td>
<td>x</td>
<td>64 **</td>
</tr>
<tr>
<td>Running</td>
<td>None</td>
<td>950</td>
<td>x</td>
</tr>
<tr>
<td>High intensity</td>
<td>None</td>
<td>213</td>
<td>x</td>
</tr>
<tr>
<td>interval</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>training (HIIT)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*From week 1 completed three sets of 10–12 repetitions of exercises performed by muscle groups in this body region and from weeks 1–2 completed two sets of 10–12 repetitions, progressing to three sets of 10–12 repetitions in weeks 3–4 of exercises performed by muscle groups in this body region.

**From weeks 5 to 12 completed all exercises with 20 kg wooden poles in pairs performed by muscle groups in this body region, starting with two sets of 10–12 repetitions and progressing to three sets of 10–15 repetitions.

4.7 Data processing and statistical analysis

Statistics for the three collection time frames were calculated by means of the NCSS™ statistical analysis software program. Due to the large sample group with n = 221, there was great certainty in assuming a normal distribution, thus the parametric paired T-test was used to correlate findings in hypermobility and LBM respectively. Linear regressions were performed to identify significance between the two modalities within the three timeframes.
4.8 Results

Initial sex results were concurrent with a previous study that indicated hypermobility was more prevalent in females than in males (16). Baseline hypermobility results indicated mean Beighton scores of 1.69 +/- 1.92 for females and 1.24 +/- 1.64 for males. Beighton scores for both groups increased at the week 12 interval to 2.77 +/- 2.2 for females and 1.74 +/- 1.85 for males respectively. Coincidentally after the full extent of the intervention period at week 20, the means for both male and female subject groups indicted a decrease in hypermobility scores to 2.13 +/- 1.99 for female participants and 1.26 +/- 1.56 for males. The means for the hypermobility scores are summarized in Figure 4.3.

LBM scores before the onset of the intervention were recorded as 45.95 +/- 5 for females and 54.98 +/- 5.96 for males. The LBM scores were represented in kilograms. Week 12 data showed a steady incline from baseline weights in both groups as the female participant mean increased to 50.02 +/- 5.24. This increase of 4.07 kilograms was comparable with the male group who increased with 3.21 mean kilograms over the same timeframe. Final measurements for LBM at week 20 indicated a negligibly small increase from week 12 to 50.26 +/- 5.41. Measures for the male participants at termination of the intervention period also indicated only a slight increase in LBM with the final mean recorded as 58.75 +/- 5.89. The abridged results for LBM can be seen in Figure 4.4.

Parametric T-tests were used to process correlations within group for the respective measure assessment timeframes. For all hypermobility correlations the null hypothesis stated that no difference existed between data collections. Correlation of the first instances indicated week 1 hypermobility scores to be less than those measured in week 12. This was the case in both, male and female groups. Statistically the p-value in both correlations were less than 0.05 and the null hypothesis was rejected, thus these differences were deemed significant. When comparing the baseline data with the final data, both sexes indicated week 1 hypermobility scores to be less than week 20, although these differences were not significant. Week 12
comparisons with the final scores showed hypermobility scores recorded at the week 12 interval to be significantly greater. Again, this was true for male as well as female sample groups. These hypermobility comparisons are summarized in Table 4.3 and depicted as a bar chart in Figure 4.3.

Similar to the hypothesis for hypermobility correlations, the null hypothesis for LBM also assumed no differences to exist between testing intervals. As one can observe from the data in Table 4.4, LBM scores increased from initial testing compared to week 12 in both sexes. The null hypothesis in both cases were rejected, thus indicating significant LBM increase towards week 12. When baseline data was compared to final LBM results, the significant increase was again evident in both sexes. Comparisons of the latter part of the intervention period between week 12 and week 20 again indicated a slight increase in LBM, although the null hypothesis was only rejected in the male sample group. Hence, the slight increase in LBM for the female group for the period week 12 to week 20 was statistically insignificant. The increases in LBM for the two groups can be observed in Figure 4.4.

Table 4.3: Paired T-test results for hypermobility correlation.

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th></th>
<th>Males</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Null Hypothesis</td>
<td>Paired group findings</td>
<td>P-value</td>
<td>Statistical significance</td>
</tr>
<tr>
<td>-----</td>
<td>-------------------</td>
<td>-----------------------</td>
<td>---------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Week 1 = Week 12</td>
<td>Week 1 &lt; Week 12</td>
<td>p &lt; 0.05</td>
<td>Reject Ho</td>
<td></td>
</tr>
<tr>
<td>Week 1 = Week 20</td>
<td>Week 1 &lt; Week 20</td>
<td>p &gt; 0.05</td>
<td>Cannot reject Ho</td>
<td></td>
</tr>
<tr>
<td>Week 12 = Week 20</td>
<td>Week 12 &gt; Week 20</td>
<td>p &lt; 0.05</td>
<td>Reject Ho</td>
<td></td>
</tr>
</tbody>
</table>
Table 4.4: Paired T-test results for LBM correlation.

<table>
<thead>
<tr>
<th>Null Hypothesis</th>
<th>Paired group findings</th>
<th>P-value</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1 = Week 12</td>
<td>Week 1 &lt; Week 12</td>
<td>p &lt; 0.05</td>
<td>Reject Ho</td>
</tr>
<tr>
<td>Week 1 = Week 20</td>
<td>Week 1 &lt; Week 20</td>
<td>p &lt; 0.05</td>
<td>Reject Ho</td>
</tr>
<tr>
<td>Week 12 = Week 20</td>
<td>Week 12 = Week 20</td>
<td>p &gt; 0.05</td>
<td>Cannot reject Ho</td>
</tr>
</tbody>
</table>

Linear regressions were performed to determine whether a significant relationship existed between hypermobility and LBM variations, thus, whether changes in LBM could be explained by changes in hypermobility and visa-versa. The slope, the estimated change in week 1 hypermobility per unit change in week 1 LBM, was -0.0373 with a standard error of 0.0164. The significance level of the t-test was 0.0241. Since 0.0241 < 0.0500, the hypothesis that the slope is zero was rejected. The slope for week 12 hypermobility vs LBM was -0.0364 with a standard error of 0.0194, with a t-test significance level at 0.0617, the hypothesis of a slope at zero was not rejected. Overall change in hypermobility to LBM after 20 weeks, indicated a slope of -0.0460 with a standard error of 0.0164, with a significance level of 0.0055, thus rejecting zero slope assumptions.
4.9 Discussion

As set out in the first objective of this study, in scrutiny of the efficacy of a military basic training program to bring about changes in lean muscular component, the constituent and duration of the program applied was deemed to be successful as increases in LBM was reported for both sexes over the 20 week duration, as can be observed in Table 6. An interesting find in the results as graphed in Figure 4.2, indicated that the intervention was equally effective in increasing lean muscular component for individuals initially classified as hypermobile by having a Beighton nine-point score of >4 and their non-hypermobile counterparts.

![Estimated Marginal Means of LeanBodyMass](image)

**Figure 4.2:** LBM adaptation between hypermobile and non-hypermobile participants.
As is evident in the changes from baseline to week 12, the initial effects of intense physical activity seemed to significantly elevate the state of hypermobility, whilst during the same timeframe statistically significant increases in lean muscle component occurred. Interestingly during the week 12 to week 20 timeframe, as LBM increased, though not significantly, hypermobility scores decreased with statistical significance to near baseline levels in both female and male test groups. Thus it seems that initial increases in hypermobility “normalized” after a prolonged period of physical activity even though lean muscle component showed slight further increases. This notion is further strengthened by the fact that for both sexes, as well as the whole participant group combined, the changes in Beighton nine-point scores over the 20 week period was not statistically significant.

![Changes in Hypermobility](image-url)

**Figure 4.3:** Bar chart representing changes in hypermobility.
A major point of discussion of this study would then be to clarify the rise in hypermobility scores after twelve weeks of intense PT. Numerous studies in exercise science have shown that initial effects of anaerobic and resistance exercise, are neural adaptations. Neural adaptations that occur due to resistance exercise, which are of particular importance to joint extensibility are; improved synchronized reciprocal inhibition in muscles (agonist – antagonist coordination) and increased neural stretch tolerance by means of supra-spinal inhibitory signal disinhibition (23, 24). These adaptations along with others, inadvertently cause the nervous system to be more permissive to greater stretch and ROM in muscle tendon structures. It has also long been reported that resistance training, and activity in itself increases flexibility and ROM (12).

We propose that the initial incline in nine point Beighton hypermobility scores could be attributed to an increase in general joint mobility or flexibility and increased ROM which are the early effects of physical activity in a primarily sedentary sample. However, at the end of the 20 week exercise intervention, Beighton scores for both sexes reverted
back to near base line, thus reporting that changes in hypermobility during this period was statistically insignificant. The notion is put forth that the increases in muscle-tendon extensibility which occurred as initial adaptations to the training program was counteracted by other physiological training adaptations, which may be of slower onset. Particularly the effect of high intensity exercise and resistance training on the proliferation of the strength and structure of connective tissues by increasing collagen fibril number, diameter and density, could possibly decrease generalized flexibility, at advanced training adaptation stages. Muscle hypertrophy has long been reported to negate generalized flexibility and ROM, though it is unlikely to be the effector during weeks 12 to 20, seeing as no significant LBM gains were indicated during this period (12). Warranting the evidence, connective tissue proliferation is the most likely effector of decreasing hypermobility scores leading up to the final data collection, although further studies will be needed to conclusively assert this assumption.

Regardless of the fact that Beighton nine-point scores reverted close to base line levels, linear regression analysis indicated significant correlations with LBM at baseline and final data collection, thus indicating that increases in LBM are associated with decreased Beighton nine-point scores, suggesting that the “hypermobility peak” leading up to week 12 can be clarified by initial training induced generalized flexibility, hormonal changes to anaerobic exercise or other factors yet to be investigated. These are however suggested explanations, and the findings of this study warrants further research to clarify, initial adaptations of intense training on nine-point hypermobility scores.

4.10 Conclusion
The military basic training regime, employed in this study was equally effective in bringing about increases in LBM in hypermobile and non-hypermobile participants alike. This intervention also brought about significant changes in Beighton nine-point hypermobility scores. It is evident that intense exercise might bring about an initial “peak” in Beighton nine-point scores, the cause of which warrants further research. Linear regression analysis in this study, indicated that increased LBM is significantly
associated with lower Beighton nine-point hypermobility scores. These findings suggest that the adaptations brought about by prolonged intense exercise training and increased LBM, might stabilize joints to oppose JH.

4.11 Suggestions for future research

It is common knowledge in sports and athletic training literature, that stretching exercises are essential if flexibility is to be increased or maintained (12). Stretching exercises promote flexibility by positively effecting the plasticity (tendency to assume new and greater length after passive stretching) of connective tissue (12). Coincidentally these are the same connective tissue structures (tendons, facial sheaths, ligaments and joint capsules) that form the structural support backbone for joints that underlie some of the diagnostic criteria for the Beighton nine-point score (25). In this lies an inherent problem; Constituents that are determinant of syndromes which are widely perceived to originate from heritable genetic factors (i.e. BJHS, EDS) can be biomechanically induced when applying the Beighton nine-point score (26). One case and point being the forward trunk flexion that is common practice in stretching exercise regiments (12). This maneuver performed to the extent of being able to place the hands flat on the floor by bending forward with knees fully extended, accounts for one awarded point in the Beighton nine-point scoring system to identify JH (27). The application of stretching routines to increase flexibility are also not isolated to athletes. It is considered a fundamental prerequisite to general wellness (11). Thus confounding this predicament to a broader spectrum of the general population. Un-astoundingly, Cameron et al. reported in their 2010 study on the association of GJH with a history of glenohumeral joint instability, that the dominating Beighton nine-point maneuver to be scored, was the forward trunk flexion. This sign was observed in 14.1% of men and 46.4% of women in a sample population of 1050 participants (28).

Though the Beighton nine-point score is only an indicator of JH, we suggest that future studies focus on refining the diagnostic criteria (as done in the case of the revised Brighton criteria), for BJHS and GJH to compensate for factors such as generalized joint elasticity and flexibility, whilst also distinguishing sex specific cut-off scores (19).
Considering the outcome of this study we also propose follow on studies as to the reasons behind initial exercise induced increases in Beighton nine-point hypermobility scores, as well as further investigations into body composition associations with hypermobility, especially the impact of total body mass on joint loading biomechanics in hypermobile individuals.
4.12 References


Chapter 5: Correlation between joint hypermobility and incidence of MSI in a training population

5.1 Key focus of the study

Investigate the possible association between JH and incidences of MSI of defense force recruits undergoing 20 weeks of basic training.

5.2 Background of the study

It is glaringly evident from literature that the majority of physiological issues that play a role in hypermobility constitute musculoskeletal or connective tissue factors. As Rodney Grahame so eloquently put it, when commenting on the benefit of enhanced ROM to the performing arts, “The biological price for this enhanced flexibility is tissue fragility, which underlies the musculoskeletal elements of JHS” (1). The majority of tissues in the musculoskeletal system (i.e. bone, tendons, ligaments, skin and cartilage) owe their physical integrity and extensive tensile strength to their considerable collagen component (1, 2). This marked reliance on the structural integrity of collagen for sound movement mechanics, inevitably challenges those with hypermobility severely. This is due to the fact that the foremost causative factor of hypermobility is genetically debilitated collagen formation (1, 3).

Add to this the extensive external forces exerted on the musculoskeletal structure by the various physical demands of military basic training, and one can easily compute that there exists an apparent risk for MSI. MSI, whether it be sprains, strains, soft tissue injuries or dislocations are practically synonymous with physically active populations. Hence the fact that military academies and populations have been the sample catchment for various studies in the field of MSI research, providing significant subject numbers that undergo physical activity in controlled environments. The amount of research done on military populations is also deemed necessary and beneficial to the institutions themselves. In their article entitled “The burden and management of sports-related musculoskeletal injuries and conditions within the US military”, Cameron and Owens states that musculoskeletal injuries significantly burdens military
service personnel, as well as the military health system. It is deemed a leading cause of disability discharge (4). Sports and PT related injuries accounts for much lost duty time and also causes several non-battle related medical evacuations. They also found that these injuries were consistent with those commonly associated with athletic populations (4).

This being the case, there is an apparent need for research to clarify as many possible risk factors of MSI in military as well as physically active populations. Since the relationship between hypermobility and joint mechanics has been established, questions regarding the association of JH and musculoskeletal injuries also arose. Some studies that directly begged to ask the question whether GLL may be a predisposing factor for musculoskeletal injuries, have conclusively found this to be the case, yet their findings did not concur with several other systematic reviews (5).

This study, consisting of an ample numbered sample group, aimed to shed light on the possible association between JH and MSI in a population burdened with the physiological stresses of an intense training program. The resultant conclusions of this study was intended to be of use to military institutions and physical populations in determining the need for possible precautionary measures for participants with JH.

5.3 Research objectives

**OBJECTIVE 1:**

Screen baseline and concurrent Beighton nine-point hypermobility scores of military recruits during a period of 20 weeks basic training and diagnose indicated JH according to a greater than four cut-off score.
OBJECTIVE 2:

Analyse MSI occurrences as recorded by military medical personnel and compare injury observation ratios between participants with indicated JH (hypermobile group) and control counterparts (non-hypermobile group). Establish odds ratios between hypermobile and non-hypermobile for MSI and test hypothesis of independence between groups:

$H_0$: JH and MSI are independent.

$H_1$: JH and MSI are not independent.

OBJECTIVE 3:

Utilize injury data to prospectively analyse the localized distribution of MSI as documented by the military medical staff, in order to draw comparisons between hypermobile and non-hypermobile groups.

5.4 Review of literature

The inquiring rationale of this study begs to ask the question: Does hypermobile participants have a greater risk of injury when engaged in moderate to intense physical activity? In an attempted answer, scientists have shown that the hypermobile population tend to have weaker proprioceptive ability (6). This decreased sense of joint position, which in itself is a strong indicator to greater risk of injury, may also be a factor in accelerated degeneration of joints in these individuals (7). Also, it has been reported that those with HMS are more susceptible to osteoarthritis (8). Increased nerve compression disorders (9), MVP (10), chondromalacia patellae, excessive anterior mandibular movement (11), uterine prolapse and varicose veins are some conditions that are also more widespread in hypermobile individuals (12). The presence of MVP has severe effects on physical exercise due to the regurgitation of blood through the mitral valve that in turn has degenerative effects on cardiac output.

Regarding the physical injury prevalence in those with BJHS, studies on professional footballers have shown no difference in the incidence of injury frequency of athletes
with BJHS in correlation to those without, though it was interesting to note that players with BJHS took longer to recover from injuries (13). On the contrary a study done on first division club rugby players found the incidence of injury to be significantly higher in participants who indicated JH. Interestingly, this study indicated no significant differences in peak strength between the hypermobile and tight groups (14). Studies done on hypermobility in professional ballet dancers have also confirmed prolonged recovery time for dancers with BJHS (15).

Along with the compulsory PT training, military servicemen spend a significant amount of time participating in sports. The types of sports differ significantly between military institutions. Within the USM some of the sports that are most commonly participated in and that frequently leads to injuries include basketball, football, flag football, softball and weightlifting (4). Concurrently, Uhorchak et al. reported that Department of Physical Education classes for USMA cadets include basketball, skiing, close-quarters combat and challenging obstacle courses. Further mandatory military training also include activities such as helicopter-repelling and parachuting as well as simulated war-games (16). Strikingly, all of these activities require high exertions of either cutting, jumping or both, often performed under high levels of fatigue which undoubtedly predisposes military servicemen to greater than average risk of contact and noncontact injuries (16).

With the link between BJHS and musculoskeletal injuries being well established, one can especially see the need to factor in incidences of JH in military populations in order to better understand its causative impact and to investigate possible preventative measures. One study in particular that has definitively done so was conducted by Mullick et al. in their clinical profiling of BJHS from a tertiary care military hospital in India. The participants of their study consisted of 45 males and 39 females that were diagnosed with BJHS according to the Beighton nine-point scoring system at the rheumatology clinic of the Army hospital, Delhi. The patients had a mean age of 30 ± 3.71 years, with most being military personnel. All had joint pain with some having evidence of degenerative changes. The patients had a median Beighton score of 6/9.
5.5 Research design and methods

5.5.1 Research approach

This study followed a prospective cohort approach in that baseline data was collected, and subjects were grouped according to the presence or absence of a specific risk factor. An observational time period ensued, after which information about the outcome of interest was collected and analysed. This presented the researchers with ample independent data from which two-group comparisons could be drawn in order to ascertain the effects of the predetermined risk factor. This study may closely resemble a non-randomized clinical trial, if the 20 weeks of basic training is considered as an “intervention” period. This is however not the case, seeing as the basic training component was a mandatory preparation period for the sample population and not an applied intervention to induce a specific outcome i.e. MSI. For this reason, this study design resembles a prospective cohort rather than a clinical trial. In literature, intense PT has however been correlated with high occurrence rates of MSI (4). Clear distinction should be made between 1; intervention to induce outcome and 2; physical activity with associated risk. The latter being the case, this distinction is key to the research approach and design of this study.

5.5.2 Ethical considerations

The research protocol was submitted to and approved by A) the ethics board of the participating institution and, B) the Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria. Ethical approval for the data collected from the SANDF recruits was granted by the 1 Military Hospital Research Ethics Committee. (1MHREC)(Appendix A). Orientation and screening sessions were held at the testing venue, where all procedures were explained to the participants, followed by the acknowledgement of informed consent (Appendix B). All the participants were encouraged to ask questions and to accustom themselves with the impeding procedures.
5.5.3 Participants

The sample population for this study consisted of two hundred and thirty four SANDF recruits enrolled for basic training at the SANDF’s Lephalale base located in the Limpopo province of South Africa. The participants were between the ages of eighteen and twenty five. The total sample population comprised of 57% males and 43% females.

5.5.3.1 Inclusion/Exclusion criteria

The inclusion criteria required the participants to be between the ages eighteen to twenty five. Participation was subject to having signed informed consent to voluntary participation in the study and completion of a PAR-Q form. The main exclusion criteria entailed any history of osteological or rheumatologic diseases, as to exclude any cases where the occurrence of hypermobility could be symptomatic of these syndromes. Further exclusion criteria entailed:

- Refusal to give written informed consent.
- Medical exclusion from physical exercise.
- Failure to adhere to test procedures

5.5.3.2 Discontinuation criteria

After the study has commenced, individual participants was eliminated from the study in the event of:

- Failure to comply or finish with the testing procedure.
- Voluntary discontinuation by participant.

5.5.4 Data collection timeframe

Data for this study was collected at three instances. Baseline testing was done at commencement of basic training. This will be referred to in the text as Week 1. An interim data collection occurred at Week 12 of the basic training period. Final data
collection occurred at cessation of the basic training period at 20 weeks. A complete injury database was compiled at the end of the 20 week period.

5.6 General Procedures and Measurements

5.6.1 Biographical data and questionnaires

Biographical data was collected and considered in order to determine the demographic distribution of the sample population as well as to cross reference any outliers that might occur. The personal and family history questionnaire was examined to assert whether participants comply with the pre-requisites for participation in the study as set out in the inclusion/exclusion criteria. The state of physical activity of the participants was asserted with the use of the lifestyle evaluation, physical activity questionnaire and the FIT index of Kasari. The personal and biographical data sheets and questionnaires that were applied in this study are available as Appendix C.

5.6.2 Beighton nine-point scale testing

Several methods and criteria for testing HMS have been developed and re-evaluated over years of study in this field. For this study, subjects were tested according to the Beighton 9-point scoring system. This is a modification of the Carter and Wilkinson scoring system and has been in use for many years to identify widespread hypermobility (17).

The Beighton nine-point score method of diagnosing hypermobility requires the participant to complete manoeuvres that entails attempted hyper-extension around 9 specific joints. The researcher will then judge whether these manoeuvres were successfully accomplished. In order for the subjects to perform the movements correctly, the researcher illustrates the required action and then judges the range of motion achieved by the subject and awards scores accordingly. A single point is awarded if the hyper-extension meets the criteria for each specific joint. Table 5.1 sets out the criteria for the 9 manoeuvres.
Table 5.1: Beighton nine-point hypermobility test (18).

<table>
<thead>
<tr>
<th>Joint</th>
<th>Set point limit criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>left little (fifth) finger</td>
<td>passive dorsiflexion beyond 90°</td>
<td>1</td>
</tr>
<tr>
<td>right little (fifth) finger</td>
<td>passive dorsiflexion beyond 90°</td>
<td>1</td>
</tr>
<tr>
<td>left thumb</td>
<td>passive dorsiflexion to the flexor aspect of the forearm</td>
<td>1</td>
</tr>
<tr>
<td>right thumb</td>
<td>passive dorsiflexion to the flexor aspect of the forearm</td>
<td>1</td>
</tr>
<tr>
<td>left elbow</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>right elbow</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>left knee</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>right knee</td>
<td>hyperextend beyond 10°</td>
<td>1</td>
</tr>
<tr>
<td>forward flexion of trunk with</td>
<td>palms and hands can rest flat on the floor</td>
<td>1</td>
</tr>
<tr>
<td>knees full extended</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 5.1: Illustrated maneuvers of the Beighton nine-point hypermobility test (18).

For diagnostic purposes, the Beighton criteria states that a score of 4/9 or greater indicates the probability of BJHS or JH (17). The method is accurate and concise, and it is ideal for processing data from large sample populations. This method is also one of the major criteria used in the revised Brighton diagnostic criteria for BJHS, which consists of a system combining major and minor indicators like the occurrence of
arthralgia, varicose veins, STR, abnormal skin and re-occurring dislocation and sub-location of joints (19).

5.7 SANDF Basic training

The basic training protocol was supervised and implemented by the superior officers of the recruits, including PT instructors and medical officers. The participants were exposed to 20 weeks of intense physical activity in accordance with SANDF protocols. The component of basic training that characteristically contributes the most to muscular strength, endurance and cardiovascular adaptations in the form of structured exercises, are PT sessions. These sessions typically commenced with a warm up period aimed at increasing heart rate, intramuscular temperature and range of movement. The greater part of the sessions consisted of various sets of upper body, lower body and core endurance exercises as well as intervals of BW and external weight resistance exercises and running. The outline of the PT program is set out in Table 5.2. Other physically challenging components of basic training that are of lesser specificity towards muscular adaptation goals included: Drilling, route marches with combat kit (8km & 14km), field craft, musketry and combat training. Injury data for the full physical activity training period was recorded.

**Table 5.2: Outline of the military PT intervention (20).**

<table>
<thead>
<tr>
<th>Training component</th>
<th>Resistance modality</th>
<th>Time (minutes) allocated</th>
<th>Exercises completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm up</td>
<td>None</td>
<td>322</td>
<td>x</td>
</tr>
<tr>
<td>Upper body Endurance exercises</td>
<td>BW</td>
<td>x</td>
<td>28 *</td>
</tr>
<tr>
<td></td>
<td>BW + 20kg external resistance</td>
<td>x</td>
<td>64 **</td>
</tr>
<tr>
<td>Core endurance exercises</td>
<td>BW</td>
<td>x</td>
<td>28 *</td>
</tr>
<tr>
<td></td>
<td>BW + 20kg external resistance</td>
<td>x</td>
<td>64 **</td>
</tr>
<tr>
<td></td>
<td>BW</td>
<td>x</td>
<td>28 *</td>
</tr>
<tr>
<td>Exercise</td>
<td>Resistance</td>
<td>Reps</td>
<td>Weeks</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-----------------------------</td>
<td>------</td>
<td>-------------</td>
</tr>
<tr>
<td>Lower body endurance exercises</td>
<td>BW + 20kg external resistance</td>
<td>x</td>
<td>64**</td>
</tr>
<tr>
<td>Running</td>
<td>None</td>
<td>950</td>
<td>x</td>
</tr>
<tr>
<td>High intensity interval training (HIIT)</td>
<td>None</td>
<td>213</td>
<td>x</td>
</tr>
</tbody>
</table>

\(BW = \text{body weight.}\)

*From week 1 completed three sets of 10–12 repetitions of exercises performed by muscle groups in this body region and from weeks 1–2 completed two sets of 10–12 repetitions, progressing to three sets of 10–12 repetitions in weeks 3–4 of exercises performed by muscle groups in this body region.

**From weeks 5 to 12 completed all exercises with 20 kg wooden poles in pairs performed by muscle groups in this body region, starting with two sets of 10–12 repetitions and progressing to three sets of 10–15 repetitions.

5.8 Injury data collection and analysis

A complete injury database was compiled by the military medical personnel of the SANDF. Relevant information in the database included the participant identification numbers, the diagnosis of the injury, treatment received and the time off due to injury. Participant identification numbers were used in cross reference with the Beighton nine-point hypermobility scores. Data was also presented and analyzed as graphs indicating the distribution of injuries along with the phase of training. A participant’s first occurrence of MSI was deemed an observation for statistical purposes. Multiple occurrences were disregarded, thus creating a nominal binary scale of observations in recruits, in order to avoid statistical errors through the recount of chronic and recurring injuries.

5.9 Data processing and statistical analysis

Data from this study was analysed with the use of the NCSS™ statistical analysis software program. The Beighton nine-point hypermobility scores were recorded and participants indicating a score of greater and equal to four at any one of three
observational periods were grouped as having indicated JH. The groups are referenced in text as 1; Hypermobile and 2; Non-hypermobile. With two distinct groups being established, observations of MSI were correlated to individuals in either groups in terms of binary nominal accounts, thus causing the data to be presentable in a 2x2 contingency Table. In this study, hypermobility assumes the role of the risk factor for which odds ratios were calculated. In order to test for association between JH and MSI, the Chi square distribution was used to test the hypothesis of independence between proportions. As indicated by the use of a 2x2 contingency Table, at 1 degree of freedom the critical value of $\alpha = 0.05$ was 3.841. As per the second objective of this study, the hypotheses were stated as:

$H_0$: JH and MSI are independent.

$H_1$: JH and MSI are not independent.

In accordance with the third objective of this study, the observations regarding the distribution in sites of MSI was counted and presented for comparison in the form group percentages histograms.

5.10 Results

Beighton nine-point scores indicated that 73 of the 234 participants (31%) in the study could be grouped as having indicated JH with the applied cut-off score at $> 4$ (17). The hypermobility group consisted of 42 females and 31 males (58% Females, 42% males). The remaining 161 participants were grouped as non-hypermobile. This group consisted of 57 females and 104 males (35% females and 65% males). Regarding the counting of MSI incidences, a participant’s first occurrence of MSI was deemed as an observation for statistical purposes. In order to avoid statistical errors through the recount of chronic and recurring injuries, multiple occurrences were disregarded, thus creating a nominal binary scale of observations in recruits. The results of this injury observation protocol indicated that within the hypermobile participants, 66% had incidences of MSI during the 20 week period. Coincidentally, within the non-hypermobile group, 52% of individuals had incidences of MSI.
Ratios within these groups showed that among the hypermobile participants, individuals were 1.92 times more likely to incur a MSI as opposed to remaining injury free. Within the non-hypermobile group, this likelihood declined to a ratio of 1.06. The odds ratio implemented to compute risk in a general population indicated that an individual with JH is 1.8 times more at risk of MSI when participating in intense physical activity. Table 5.3 shows the observational data from which the cross product ratios were derived.

Table 5.3: Contingency Table of MSI observation between hypermobile and non-hypermobile groups.

<table>
<thead>
<tr>
<th></th>
<th>MSI</th>
<th>Non-MSI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypermobile</td>
<td>48</td>
<td>25</td>
<td>73</td>
</tr>
<tr>
<td>Non-Hypermobile</td>
<td>83</td>
<td>78</td>
<td>161</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>131</td>
<td>103</td>
<td>N = 234</td>
</tr>
</tbody>
</table>

An interesting result regarding within-group sex distributions indicated substantially increased incidences of MSI for females in both hypermobile and non-hypermobile groups. In the hypermobile group 81% of females and 45% of males had MSI occurrences and concurrently 74% of females and 39% of males from the remaining non-hypermobile individuals had recorded incidences of MSI. In the sample population as a whole this translates into a ratio of 3.3 for the occurrence of MSI in females and 0.69 in men. The presentation of MSI is substantially higher amongst females undergoing intense PT in the sample population, a cross-product ratio between sexes in this sample suggests that females are 4.81 times more at risk of MSI when undergoing intense physical activity, than their male counterparts.

The Chi-square distribution was used to test the hypothesis of independence between proportions. As indicated by the use of a 2x2 contingency Table, at 1 degree of freedom the critical value at α = 0.05 was 3.841. As per the second objective, to
estimate a correlation in the incidences of MSI between the hypermobile and non-hypermobile group, the null hypothesis stated that JH and MSI are independent. The results of the test indicated a Chi-square observational value of 4.11 ($X^2 = 4.11$). In accepting a critical value of 3.841 with $\alpha = 0.05$, and $4.11 > 3.841$, we reject the null hypothesis of independence and conclude that a relationship exists between JH and MSI in individuals participating in an intense PT program.

As per the third objective, the localization of the musculoskeletal injuries incurred by the two groups were recorded and analysed in order to validate prospective studies. This data was expressed in terms of within-group observations at 8 joint regions, and 1 non-specific category, i.e. soft tissue. Observations in this category were generally muscular pain and strains. Table 5.4 and Table 5.5 display these distribution results as bars of group percentages. The results indicated near similar injury distribution frequencies between groups, with no significant differences.

**Table 5.4: Localization of MSI in the hypermobility group.**

![MSI localization percentage chart](image_url)
5.11 Discussion

The first objective of this study, which aimed to screen participants for JH according to the Beighton nine-point scale with a ≥4 diagnostic criteria, produced hypermobility rates that corresponds with contemporary research, where the same diagnostic criteria was applied (8, 21). In finding a 31% incidence of indicated JH, the researchers were afforded ample numbered sample groups in order to correlate JH and MSI incidences. Observational percentages and odds ratios indicated higher incidences of MSI amongst the hypermobility group. These findings concur with the age and sex matched case control studies done by Bin Abd Razak et al. who hypothesized GLL to be conjoint with musculoskeletal injuries (5). This was also the conclusions of the meta-analysis by Pacey et al. which established that individuals with GJH carry a significantly higher risk of injury during contact sports participation (22). It needs to be taken into account that due to various factors, not all findings regarding MSI incidences in literature are comparable, with the principal reason being the discrepant nature of the physical activities undertaken by sample populations. To the best of our
knowledge, no other studies have been undertaken to research MSI incidence in relation to hypermobility within military groups exposed to physically intense basic training protocols. This serves as an important contextual foundation for the outcome of this study.

The initial prevalence of MSI occurrences as indicated by the resultant odds ratio of 1.8, was reinforced by the rejection of the null hypothesis of independence, as per the $X^2$ test. In considering the $X^2$ observed value being only marginally greater than the critical value ($4.11 > 3.841, \alpha=0.05$) and this study not being experimental in nature, it cannot be said that hypermobility is causative of MSI, only that these two are related.

In considering the contextual nature of the PT which the recruits were exposed to as set out in Table 2, one should notice in broad overview that external resistance was limited to 20kg, with the bulk of the training being body-weight exercises, apart from combat training phases which included full combat kit of unspecified weight. The undefinable forces exerted by this training regime leads to further research questions, in which one can debate whether greater external resistance forces would not exponentially increase the occurrence of MSI, and thusly cause a greater divergent distribution between groups seeing as a correlation between JH and MSI, however slight, does exist. This train of thought hypothesises that the difference in MSI between hypermobile and non-hypermobile groups could be load dependant.

Some remarkable results that were not originally objectified, appeared in the statistical analysis. Within-group sex analysis indicated significantly higher MSI incidence rates for females in both groups. In the sample population as a whole this translated into an odds ratio which suggested that females are 4.81 times more at risk of MSI when undergoing intense physical activity, than their male counterparts.

The third objective of this study was aimed at observing the anatomical locational incidences of MSI, in order to prospectively identify whether certain musculoskeletal locations are more at risk of injury in hypermobile populations. As can be seen from the bar charts (Table 5.4 and Table 5.5), these results indicated near similar distributions among the two groups, with the four highest percentages in both groups
being in the Knee, Soft tissue, Ankle and Groin categories. The remaining five categories had equally low distributions among both groups, all indicating incidence rates of <10%, excluding only the groin localized occurrences in the hypermobility group, at 13%. These findings do not substantiate the findings of Pacey et al. who found higher risk of knee joint injury amongst hypermobile groups in meta-analyzed studies (22).

Comparisons for studies of this nature are challenging due to the lack of concurrent locational injury distribution criteria. This study made use of 8 generalized joint sites along with a ninth soft tissue category, whereas Pacey et al. decided to specify three categories of lower limb injuries i.e. all lower limb joint injuries, knee joint injuries and ankle join injuries (22). In the study by Stewart et al. reporting on injury rates per exposure hours in hypermobile rugby players, the researchers used a 6 – site criteria (knees, shoulders, hips, ankles, wrists and hands) (14). Thus, it is apparent that in order to clarify results regarding injury distributions, this research field is in dire need of a contemporary gold-standard localization classification to be employed in future studies.

5.12 Conclusion

JH screening in this study indicated that hypermobility is common occurrence amongst a general African population aged between 18 and 25. In the sample population as a whole it was clear that all individuals participating in intense physical activity as demanding as military basic training are greatly at risk of sustaining MSI. Individuals that indicate with JH according to the Beighton nine-point score, are marginally more at risk of MSI, although no specific difference in the anatomical site distribution of injury was found between hypermobile and non-hypermobile groups. Sex differences did however indicate that females are significantly more at risk of MSI, when confronted with the physical demands of military basic training. In searching for comparative research it is clear that the investigation of MSI in physically active populations necessitates load/force appropriation categories, as well as a concurrently applied classification of MSI location.
5.13 Study limitations and suggestions for future research

Investigations into literature applicable to this study revealed several discrepancies preventing parallel research to be adequately comparative. Prospective features to be researched, should include development of a comprehensive criteria which causes mechanical load and force on joints during different PT protocols to be quantified and comparable. Whilst protocols such as the FIT index are adequate in comparing workload, joint load quantifications should be introduced in physical activity studies that aim to examine MSI occurrences. New technologies should be utilized to advance the field of MSI brought about by the mechanical loads and forces that are induced by intense PT. One newly developed technology that should be explored, is the use of force measuring insoles inserted into the footwear of participants. These devices could well give insight into the loads and forces experienced particularly in the joints of the lower body, during training regimes such as, and similar to, a military basic training regime.

Furthermore, in studies wanting to monitor the anatomical localization of MSI distributions, the development of a homogenous site criteria would allow researchers to optimize the use of associated studies for comparisons. Thus, allowing for more accurate meta-analysis and refined conclusions. This would also greatly advance attempts to statistically associate specific types of physical activities with exactly located musculoskeletal injuries.
5.14 References


Chapter 6: Integrated discussion and conclusion

It is evident from this exposition and the research which precedes it, that JH in its various forms are in many ways misconstrued and misrepresented. Hypermobility as a symptom of HDCT is well known, whilst understanding around JH as a stand-alone non-symptomatic occurrence is vague at best (1). In research history, comprehension was often sought in descriptive nomenclature of the various hypermobility occurrences, as discussed in chapter 2 of this study (2). Several attempts to gain understanding from hypermobility definitions might be considered hapless, as in many cases terminology does not expressly differ in terms of the attributes of the hypermobility condition, but merely in minor features, thus causing perceptiveness to be lost in ambiguity. Nevertheless, one measure that seems prevalent throughout literature is the inclusion of the Beighton nine-point hypermobility score as a diagnostic criteria for the various JH conditions. By employing this measure we attempted to underline the commonality and frequent occurrence of JH in a general population. Our findings regarding hypermobility incidence aligned with several relevant publications, as we reported GJH to be as common as 29% in males and 36% in females.

This dissertation also aimed to shed light on the importance of the distinguishable elements of hypermobility that occur outside of HDCT’s. A primary facet of non-symptomatic hypermobility, was the hypermobility related connective tissue linkage to the musculoskeletal system. Literature also reiterated that all joint laxity does not equate to JH as we explored several non-genetic factors of joint laxity such as stretching induced flexibility and hormonal effects on joint laxity. Our study discussed several extra-articular facets of hypermobility, some of which were neuropathological, cephalalgic and endocrine in nature. These aspects related to hypermobility which were often scarcely researched and classed as secondary symptoms of HDCT’s, provided significant understandings into the genetic nano-mechanics of hypermobility (3, 4).

Undoubtedly, the leading question regarding hypermobility and its influence on human movement, is whether the hyper extensibility of joints brought about by hypermobility
increases susceptibility to MSI. In addressing this broad inquiry we explored the physiological adaptation to training effects on hypermobility in chapter 4’s repeated measures study, by focussing on the influence of LBM changes brought about by an intense PT program.

From a literary standpoint we gained vast insights into the physiological pathways by which hypermobility might influence the structural integrity of connective tissues and its collagen compounds (1, 5). These insights along with substantive evidence on how hypermobility influences proprioception, lead us to postulate the “cause vs. symptom” closed cycle of diminished joint proprioception in Figure 6.1 which causes abnormal joint biomechanics in congenital forms of excessive joint laxity.

![Figure 6.1: Cycle of causative factors regarding diminished joint proprioception in hypermobile individuals.](image)

* Adapted from information in chapter 2.
In attempting to directly address the questions regarding musculoskeletal injury, the prospective cohort study of chapter 5, meticulously recorded and analysed incidences of MSI between hypermobile and non-hypermobile groups subjected to a military basic training program. Even though several studies have been conducted which focus on the association of hypermobility and injury in physically active populations, various factors influence the comparability of results yielded from these studies. This is evident from reviews such as the study by Pacey et al from which only 18 of 4841 hypermobility and injury related studies met the inclusion criteria for their meta-analysis (6). The most prolific hindrance to reaching comprehensive conclusions in this field is the variance in load and force demands between physical activities. As is the case with the chapter 5 study in which the Injury data yielded decisive outcomes, an apparent lack of concurrent studies with similar contextual basis, condenses attempts at a comparative analysis. Nonetheless, our studies questioned conventions and generated conclusive results in an intense training military population, thus providing us with significant insights and various grounds on which to base future research.

6.1 Discussion on Study 1

The first study from this exposition as set out in chapter 3, endeavored to shed light on the epidemiology of non-symptomatic JH in a randomized selection of the generalized South African context. The primary objective sought to elucidate sex discrepancies in hypermobility. From literary history it is evident that the incidence of hypermobility differs according to the geographic and ethic demographics of the sample population. Establishing sex specific prevalence rates in a South African general population would prove vital, as recent literature is increasingly proposing association between hypermobility and injury.

A cross-sectional research approach was implemented with an ample numbered sample population of 480 individuals from four wide-spread geographical areas. Individuals were tested for JH according to the Beighton nine-point hypermobility score with a diagnostic criteria of 4/9 or greater (7). Results indicated a 26.19% overall incidence of JH, with sex specific totals showing a 36.41% incidence for females
compared to 13.96% for males. Two sample T-test correlations deemed the sex difference in hypermobility incidence to be statistically significant.

Our findings concur with several contemporary studies also indicating increased female predisposition to GJH, although there are still notable discrepancies regarding the reported rates and presentations of JH in literature (8). Some indicators in this study also concur with prior research showing that hypermobility decreases with age. The reason for female prevalence of JH is still unclear, with the most prominent hypotheses suggesting that the influence of female specific hormones on connective tissue as well as female joint bio-mechanics could be the underlying effectors.

6.2 Discussion on Study 2

Non-contact musculoskeletal and joint injuries have gained much attention in military academies, with studies suggesting a significant impact on military personnel readiness, costing military institutions millions of dollars (9). Coincidently the role that hypermobility might play in musculoskeletal and joint injuries, have also been in the research spotlight over recent years. Military personnel engage in regular exercise and various resistance training programs which have been shown to increase proprioception and muscle torque deficits as well as decrease muscle deconditioning in hypermobile individuals (10). Considering these findings, the second study discoursed in chapter 4 attempted to quantify the interaction of a set military basic training exercise regime on the states of hypermobility, in particular with relation to altered muscular component.

The repeated measures design of the study with data collected at three observational intervals produced paired data for within group comparisons. JH was determined according to the Beighton nine-point hypermobility score with a diagnostic criteria of 4/9 or greater (7). Muscular component was measured as LBM by using the formula: 

$$LBM = Body\ Mass - (Body\ Mass - Body\ Fat\ %)$$

(11). With the equation readily deducting fat mass, muscular component was deemed the only constituent of LBM to
be susceptible to any substantial changes in mass over a period of 20 weeks of exercise intervention (12, 13). The military exercise protocol consisted of varied components of bodyweight and externally resisted muscle endurance exercises, high intensity interval training, distance running, combat training and route marches.

Results indicated that the exercise intervention was successful in bringing about equally significant increases in LBM in both groups. From baseline to week 12, the initial effects of intense physical activity seemed to significantly elevate the state of hypermobility, whilst during the same timeframe statistically significant increases in lean muscle component occurred. Interestingly during the week 12 to week 20 timeframe, as LBM increased, though not significantly, hypermobility scores decreased with statistical significance to near baseline levels in both female and male test groups. Thus it seems that initial increases in hypermobility “normalized” after a prolonged period of physical activity even though lean muscle component showed slight further increases.

Linear regressions indicated a significant correlation between increased LBM and associated decreases in hypermobility. We propose that the “hypermobility peak” leading up to week 12 can be clarified by initial training induced generalized flexibility, neural adaptation of exercise which increases ROM or other factors yet to be investigated (14, 15). These findings suggest that the adaptations brought about by prolonged intense exercise training and increased LBM, might stabilize joints to oppose JH. Finally, this study also lead us to suggest further research into diagnostic criteria for JH which distinguishes constituents of joint elasticity and general flexibility from hypermobility indicators.

6.3 Discussion on Study 3

Our third study as put forth in chapter 5, sets out to clarify one of the most prevalent discussions in hypermobility research i.e. the association between JH and MSI. The majority of physiological issues that play a role in hypermobility constitute the
musculoskeletal or connective tissue structures. These structures need to withstand the extensive external forces exerted on them by the various physical demands of intense exercise encountered in military basic training. Sports and PT related injuries accounts for much lost duty time and also causes several non-battle related medical evacuations. Prevalent injuries in military training academies were found to be consistent with those commonly associated with athletic populations (9). Since the relationship between hypermobility and altered joint mechanics has been established, there exists an apparent need to clarify this occurrence as a possible risk factor of MSI in the military and other physically active populations.

This study was diversified into several objectives. The first of which was to determine Beighton nine-point hypermobility scores and diagnose indicated JH incidences. From these findings 31% of participants were grouped as hypermobile, consisting of a 58% female and 42% male distribution, thus producing an ample numbered sample group of hypermobile participants (n = 73) for the central aim of the investigation. The main objective pursued, involved comparing MSI occurrences as recorded over the 20 week training period between the hypermobile group and their non-hypermobile counterparts. Resultant ratios within these groups showed that among the hypermobile participants, individuals were 1.92 times more likely to incur a MSI as opposed to remaining injury free. Within the non-hypermobile group, this likelihood declined to a ratio of 1.06. The odds ratio implemented to compute risk in a general population indicated that an individual with JH is 1.8 times more at risk of MSI when participating in intense physical activity. In ascertaining whether the resultant observations carried significance, the Chi-square test indicated an observational value of 4.11 which is greater than the critical value of 3.84 at α = 0.05, thus indicating an association between JH and MSI.

Lastly a prospective analysis was done on the localized distribution of the MSI’s which occurred during the training period. The results indicated near similar injury distribution frequencies between groups, with no significant differences. Interestingly, within-group sex distributions indicated that females are 4.81 times more at risk of MSI when undergoing intense physical activity.
Along with highlighting the fact that intense physical activity is associated with high incidences of MSI, this study provided several insights into the relationship between MSI and JH. In indicating that individuals with JH are marginally more at risk of sustaining MSI we found that contextually comparative research is scarce, especially due to dissimilar load and force appropriations amongst physically active sample populations. From this study we also propose that successful reviews of injury site distributions in future studies, necessitate a concurrently applied classification system on the localization of MSI.

6.4 Closing remarks

The culmination of this research paper, produces several key insights into the associations between JH and the general population. The foremost finding to take note of is the high prevalence of JH amongst the South African population. The importance of fully understanding the mechanisms surrounding JH is apparent when considering that incidence ratios approximate to one in three individuals.

The connective tissue association between JH and physical activity was discussed in depth, emphasizing the symptomatic as well as causative role through which congenital hypermobility could potentiate MSI in physically active populations. In investigating this occurrence, we looked at physiological adaptations to intense exercise that could potentially reverse the destabilization of hypermobile joints. In postulating that increases in muscular component could influence hypermobile joint stabilization, we reported that increased LBM is significantly associated with lower Beighton nine-point hypermobility scores following 20 weeks of intense PT. While this linearity was negated during the early stages of the training regime, we suggested that concurrent adaptations in flexibility, conceivably could influence Beighton nine-point hypermobility scores. In scrutinizing the diagnostic criteria and distinguishing factors of JH, this, amongst other discrepancies and limitations were discussed in all three of the distinct studies.
Certainly the most notable research question incorporated in this study is the influence of hypermobility on MSI. Our results conclusively signified that individuals with JH are more at risk of sustaining MSI when subjected to intense PT. No distinguishing differences in the localized site presentation of injuries were indicated between hypermobile and non-hypermobile groups, while distinctly different sex incidence rates were observed. These findings should encourage further research into possible preventative measures for hypermobile individuals participating in strenuous activities.

6.5 Conclusion

In considering all our findings we conclude that JH is an underdiagnosed common occurrence in the South African general population. The congenital influences on connective tissue development in hypermobile individuals sufficiently undermines musculoskeletal integrity to the extent where they are susceptible to increased risk of injury when participating in intense physical activity. These mechanisms can however be counteracted by the implementation of specific exercises promoting joint stabilization, proprioceptive acuity and increased muscular component.
6.6 References


Appendix A – 1MHREC

CLINICAL TRIAL APPROVAL: “THE INFLUENCE OF A BASIC TRAINING PROGRAM ON SOUTH AFRICAN MILITARY RECRUITS.”

1. The 1 Military Hospital Research Ethics Committee (1MHREC), comprised of the following members, and adhering to OCP/ICH and SA Clinical Trial guidelines, evaluated the above-mentioned protocol and additional documents:
   a. Lt Col M. Baker: Neurologist, male, chairman 1MHREC.
   b. Col H. du Plessis: Surgeon, male, member 1MHREC.
   c. Ls Col C. Duvenage: Specialist Physician, female, member 1MHREC.
   d. Lt. Col. D. Mahapa: Dermatologist, female, member 1MHREC.
   e. Lt. Col. L. Hofmeyr: Otorhinolaryngologist, male, member 1MHREC (non-voting on this study).
   f. Ms C. Juterson: Layperson, independent of the organization, female, member 1MHREC.

2. The following study protocol was evaluated “The Influence of a Basic Training Program on South African Military Recruits.”

   Documentation submitted included the protocol description and covering letter.
CONFIDENTIAL

3. The recommendations are:

The study was ethically approved on 19 October 2009. The principal investigator will be Lt Col E. Törblanche. Report backs are to be made to the MHI REC six months, in the event of any serious adverse events and on completion or termination of the study.

(M.K. Baker)
CHAIRMAN MILITARY HOSPITAL RESEARCH ETHICS COMMITTEE: LT COL
DIST
For Info:
Lt Col E. Törblanche
PARTICIPANT INFORMATION AND

INFORMED CONSENT FORM

Faculty of Health Sciences
Department of Physiology
PO Box 2034, Pretoria, 0001 (R9-8, BMS-Building)
Tel: (012) 319-2138 Fax: (012) 321-1679

Investigator

Henri – Charl Terblanche
Department of Physiology
University of Pretoria
Tel: 082 454 4463
Email: henri.terblanche@up.ac.za

Supervisor

Dr PJ du Toit
Department of Physiology
University of Pretoria
Tel: (012) 420 2536
Email: peet.dutoit@up.ac.za

TITLE:

The influence of an intense training program on hypermobility and correlation between hypermobility and incidence of injury

INTRODUCTION

You are invited to volunteer for a research study. This information leaflet will help you to decide if you would like to participate. Before you agree to take part in this study you should fully understand what is involved. If you have any questions, which are not fully explained in this leaflet, do not hesitate to ask the investigator. You should not agree to take part unless you are completely happy about all the procedures involved.
WHAT IS THE PURPOSE OF THIS STUDY

The aim of the PT program is to develop the physical fitness of the recruit and we would like to research if this training has an effect on the hypermobility (double jointed state) of males and females over a period of 20 weeks. The study will help us understand the effects of intense PT on the hypermobile individuals and the occurrence of any possible injuries that might be related to hypermobility.

WHAT IS THE DURATION OF THIS STUDY?

If you decide to take part you will be one of possibly 480 participating recruits. The physical program will last 20 weeks where you will be subject to testing on week 1, 12 and 20.

EXPLANATION OF PROCEDURES TO BE FOLLOWED

The study will commence with an information session, where all the processes and information of this study will be explained to you. After you have been fully informed of what the study entails and what will be required of you, should you choose to participate, you will be asked to sign a form stating your written consent to voluntary participation in this study. Once you have given your consent to voluntary participation you will be asked to complete several questionnaires applicable to the study, a short explanation of what each questionnaire entails is provided below:

Please note: The Information and Questionnaire session will only occur once at the onset of the study and should take approximately 3 hours. You will be guided throughout the process with a researcher nearby to answer all questions you might have.

- Questionnaires
  - Personal and Biographical Information
    These are questions regarding your age, ethnicity, sex etc.
  - Family and Personal Medical History
    These are medical history questions to ascertain that you are in a good state of health for safe participation in this study.
  - Personal Stress Inventory (PSI)
    This questionnaire regards your general perception of the emotional and psychological stresses that you incur each day. Your score will be screened to ensure that the
physical nature of the study will not add any stress that could be detrimental to your health

- **Nutritional Assessment**
  *In this questionnaire you will answer questions regarding your nutritional state to assure that your nutritional state is conducive to physical performance*

- **Lifestyle Evaluation**
  *This questionnaire serves as an overall evaluation of your lifestyle choices to highlight any predispositions to medical complications*

- **Paffenbarger Physical Activity Questionnaire**
  *This questionnaire calculates leisure and work time physical activity levels*

- **FIT Index of kasari**
  *The Kasari index regards the frequency, intensity and time regarding your physical activities to ascertain a baseline of fitness*

- **Profile of Mood State Questionnaire (POMS)**
  *The POMS is used to assess your mood states, this is of importance because it influences your cardiovascular system.*

- **State Trait Personal Inventory (STPI)**
  *The STPI will assess variations in your emotional state which is indicative of your mental health.*

Further testing that will be done at week 1, 12 and 20
- Physical health measurements
- Physical performance tests
- Hypermobility testing

It is important that you let the investigator know of any medicines (either prescriptions or over-the-counter medicines), alcohol or other substances that you are currently taking.

**HAS THE STUDY RECEIVED ETHICAL APPROVAL?**

This research study protocol was submitted to the faculty of Health Science research Ethics Committee, University of Pretoria and written approval has been granted by that committee.

**WHAT ARE YOUR RIGHTS AS A PARTICIPANT IN THIS STUDY?**

Your participation in this trial is entirely voluntary and you can refuse to participate or stop at any time without stating a reason. Your withdrawal will not affect your access to other medical
care or your career at your organisation. The investigator retains the right to withdraw you from the study if it is considered to be in your best interest. If it is detected that you did not give an accurate history you may be withdrawn from the study at any time.

MAY ANY OF THESE STUDY PROCEDURES RESULT IN DISCOMFORT OR INVOLVE ANY SORT OF RISKS?

The only discomfort may be the fitness tests and these are part of your set basic training program. The discomfort that might be experienced during the physical fitness tests are short periods of heavy breathing (shortness of breath), perspiration and heat discomfort associated with physical activity. Tiredness or post-exercise fatigue may also set in. No blood will be drawn. Participants in this study do not bear any extra risk apart from the normal risk experienced as part of the basic training program.

CONFIDENTIALITY

All information obtained during the course of this study is strictly confidential. Data that may be reported will not include any information which identifies you as a participant. In connection with this research, it might be important to the Faculty of Health Science Research Ethics Committee, the section Sports Medicine, University of Pretoria, as well as your organisational doctor, to be able to review your medical records.

Any information uncovered regarding your tests result or state of health as a result of your participation in this research study will be held in strict confidence. You will be informed of any finding of importance to your health or continued participation in this study but this information will not be disclosed to any third party in addition to the ones mentioned above without your written permission. The only exception to this rule will be cases in which a law exists compelling us to report individuals infected with communicable diseases. In this case, you will be informed of our intent to disclose such information to the authorized state agency.

INFORMED CONSENT

I hereby confirm that I have been informed by the investigator, HC Terblanche about the nature, conduct, benefits and risks of the research study. I have also received, read and understood the above written information (Patient Information Leaflet and Informed Consent) regarding the research study.
I am aware that the results of this study, including personal details regarding my sex, age, date of birth, initials, health and performance will be anonymously processed into a study report.

I may, at any stage, without prejudice, withdraw my consent and participation in the study. I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in this study.

Participant’s name

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

(Please print)

Patient's signature...................................................................................................

Date......................................................................................................................

I, HC Terblanche herewith confirm that the above participation has been informed fully about the nature, conduct and risks of the above study.

Investigators name: Henri-Charl Terblanche

(Please print)

Investigator’s signature.........................................................................................

Date......................................................................................................................

Witness’s name*..................................................................................................
Witness’s signature……………………..Date………………………..

(Please print)

*Consent procedure should be witnessed whenever possible.
Appendix C – Data Sheet

DATA CAPTURE FORM (1)

<table>
<thead>
<tr>
<th>Participant number:</th>
<th>Number</th>
<th>Date:</th>
<th>DD</th>
<th>MM</th>
<th>YEAR</th>
</tr>
</thead>
</table>

**BODY MASS**

<table>
<thead>
<tr>
<th>Measure</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

**CIRCUMFERENCES**

<table>
<thead>
<tr>
<th>Measure</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder (cm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Arm (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest (cm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Forearm (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist (cm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdomnl (cm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prox Thigh(cm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Mid Thigh (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distl Knee (cm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Knee (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calf (cm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Ankle (cm)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SUB-CUTANEOUS FAT**

<table>
<thead>
<tr>
<th>Measure</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biceps (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triceps (mm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Sub-scap (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdomnl (mm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Suprailiac(mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thigh (mm)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Calve (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supraspn (mm)</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
HEART RATE VARIABILITY

Vent Rate (bpm): ____________  PR int. (ms): ____________

QRS Dur. (ms): ____________  QT/QTc int. (ms): ____________

P/QRA/T axis: ____________

RV5/SV1 amp.: ____________  RV5+SV1 amp.: ____________

VI-PORT

CSI (%): ____________  HR (bpm): ____________

Rhythm (Y/N): ____________  QRS Dur. (ms): ____________

RRSD (ms): ____________

BLOOD PRESSURE

Syst (mmHG): ____________  Diast (mmHg): ____________

FITNESS

*Sit and Reach:  Thigh  Shins  Toes

* Use sit and reach box and do modified sit and reach test

**Push-ups (#/1 min): ____________  Type of push-up: ____________

* All men do full push-up and all women do half push-up

Sit-ups (#/1 min): ____________

3-Min Step test (pulse/15 sec): ____________