DELFT UNIVERSITY OF TECHNOLOGY

LIVING WITH MARFAN SYNDROME: AMBULATORY BLOOD PRESSURE MEASUREMENT DURING LIFTING AND CARRYING INFANTS

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Abstract

This study investigated the effects of lifting and carrying activities on ambulatory blood pressure (BP) responses in healthy adults. Participants performed simulated infant carrying tasks with different weight loads (0kg, 5kg and 10kg) using two lifting techniques (stoop and flat). Continuous BP was measured using the Finapres NOVA ambulatory BP monitor. The indicative results showed increases in peak systolic BP during lifting (5 kg: stoop +44.0 mmHg & flat +41.1 mmHg) and average SBP during carrying phases (5 kg: stoop +12.96 mmHg & flat +12.04 mmHg) compared to unloaded situations, with greater BP elevations observed for heavier loads (lifting 10 kg: stoop +56.9 mmHg & flat +43.2 mmHg; carrying 10 kg: stoop +19.87 mmHg & flat +14.11 mmHg). The lifting technique also impacted BP responses, as stoop lifting produced higher systolic BP peaks than flat lifting (+5.9 mmHg, +8.8 mmHg & +19.6 mmHg for 0 kg, 5 kg & 10 kg respectively). Detailed analyses were conducted by defining quantitative parameters such as baseline BP, peak BP during lifting, start BP after lifting, and end BP before lowering. The findings from this study have implications for developing guidelines on safe lifting and carrying practices for individuals with conditions like Marfan syndrome, which are prone to aortic complications from elevated BP.

Abbreviations

Table 1: List of abbreviations.

Abbreviation	Definition
ABPM	Ambulatory Blood Pressure measurement
BP	Blood Pressure
DBP	Diastolic Blood Pressure
HR	Heart Rate
LTPA	Leisure Time Physical Activity
MAP	Mean Arterial Pressure
NIOSH	National Institute of Occupational Safety and Health
OL	Occupational Lifting
OPA	Occupational Physical Activity
OSHA	Occupational Safety and Health Administration
PPG	Photoplethysmography
PA	Physical Activity
SBP	Systolic Blood Pressure

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Preface

Marfan Syndrome is a genetic disorder that transferred to me from my parents. I have always had it and it is noticeable; I am 1.97 meters tall, slender build, have long digits, flat feet and have scoliosis. I have always played waterpolo at a competitive level, where swimming is recommended for people with scoliosis. However, I knew that I should not carry "heavy" stuff and the doctor recommended a maximum of 5 kg. This was a loose guideline at the time. Last year, during my Master in Biomedical Engineering at the age of 25, I had an annual aorta checkup at the hospital during which they noticed a dissection in my vertebral artery (an artery to the brain). Because of this, Dr. Kauling of the Erasmus Medical Centre in Rotterdam, my practicing cardiologist, recommended to me to quit playing waterpolo and to strictly keep the (previously loose) guideline of 5 kg. This, at the time, was devastating news for me.

When talking about this news to my supervisor Dr. A. H. A. Stienen, he mentioned that not lifting heavy and not doing your own sport is not the end of the world, but the concept of not being able to lift your children seemed terrible to him. Then a critical question came up: "what does this limit of 5 kg mean?". This 5 kg limit is set for everyone with Marfan Syndrome that has progressed to a certain level: young and old, man and woman, physically active and not physically active, in shape and obese. I imagine that there is a difference between an old obese woman and a young (previously) sporty man. After research and an interview with Dr. Kauling it became evident that these questions had no evidence based answers. Then I decided to dedicate my Master thesis to finding out if the 5 kg limit should apply to me, and more specifically, at what weight should I not lift my possible future children anymore?

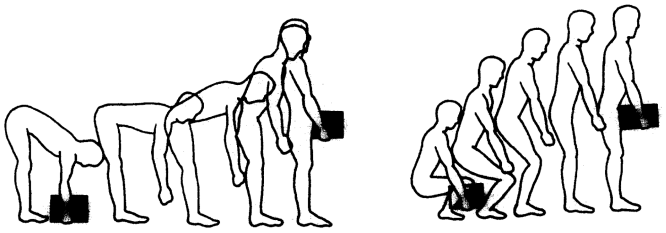
1 | Introduction

Marfan syndrome is a genetic disorder that affects the connective tissue, which provides strength and flexibility to structures like blood vessels, ligaments and bones. People with Marfan syndrome often have tall, thin builds with long arms, legs, fingers and toes. They may also experience vision problems, lung complications, and heart issues like aortic aneurysms or mitral valve prolapse[5]. One of the main concerns for individuals with Marfan syndrome is monitoring and managing their blood pressure (BP). Elevated BP can be especially dangerous for those with Marfan syndrome, as it increases the risk of aortic dissection or rupture, see Figure 2.1[6]. Surgical aortic replacement is necessary when the aortic diameter exceeds 50 mm, but this procedure carries significant risks. Therefore, preventing aortic dilation and careful regulation of BP are crucial for people with Marfan syndrome[7].

Physical activity can have a significant impact on BP, and it is essential for individuals with Marfan syndrome to understand how different types of physical exertion affect their BP. Participating in physical activities like sports or lifting heavy objects acutely increase BP and heart rate (HR) due to various factors. HR increases because muscles require more oxygen, leading to constriction of adjacent vessels[8]. Additionally, the pressor reflex causes peripheral arteries to constrict, increasing peripheral resistance and consequently BP[2, 8, 9].

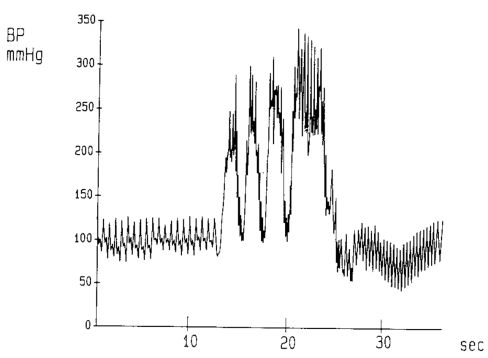
Existing research highlights the importance of tailored advise for individuals with Marfan syndrome. This is particularly true for physical activity and lifting activities[5]. While general recommendations suggest avoiding intensive physical activity and heavy lifting, evidence-based strategies specific to Marfan syndrome are lacking. Consequently, there is a pressing need for further research to establish evidence-based guidelines tailored to the unique needs of individuals with Marfan syndrome, particularly concerning BP management during physical activity[5]. For example, there is a general consensus that lifting with a parallel stance/flat-back lift (Figure 1.1b) is the preferred lifting technique over the stoop lift (Figure 1.1a) with regards to the force exerted on the body[1] and with developing chronic lower back pain[1, 10, 11]. This is specifically relevant for people with a lot of occupational lifting or physically demanding jobs[8]. These researches are not primarily focused on BP and therefor these recommendations are not tailored for people with Marfan Syndrome. Additional information of the existing lifting recommendations can be found in Section 2.5.

This leaves questions on what to precisely advise to people with Marfan Syndrome. For example, Palatini et al. measured acute intra-arterial BP during near-maximal weight squatting, showing a tremendous BP increase[12], see Figure 1.2a. Based on research like this it is correctly deduced that Marfan Syndrome patients should omit heavy lifting, which is simply detrimental for individuals

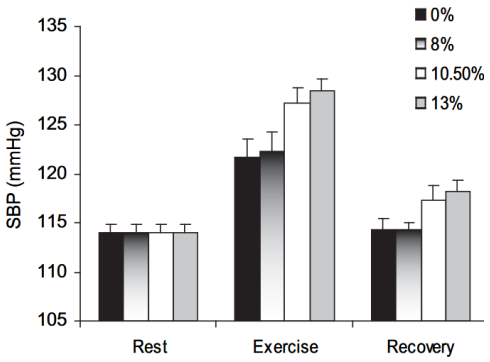


(a) Stoop lift. (b) Parallel stance/flat-back lift.

Figure 1.1: The two lifting techniques[1].



(a) Intra-arterial BP changes during weight-lifting (squatting) at near-maximum capacity. Four repetitions to exhaustion were accomplished by Palatini et al. [12].



(b) Adolescents SBP compared during walking with weighted backpack for 15 minutes. The weight was represented in percentage of body weight, by Daneshmandi et al. [14].

Figure 1.2: Lifting at near-maximum capacity in short time period(a) and lifting a weighted backpack for a prolonged period of time(b). In the case of Marfan Syndrome both should be kept to a minimum.

with Marfan Syndrome[5]. Integrating insights from existing studies that examined BP responses to lifting and carrying loads can enhance our understanding of how exactly different activities impact individuals with Marfan syndrome. These insights inform recommendations on safe lifting practices and physical activities to mitigate the risk of aortic complications while promoting overall well-being.

Firstly, Mbada et al. compared different infant-carrying techniques to find the most mother-friendly method[13]. They compared frontal, back and hip carrying techniques using a 10 kg load (which is the average weight of a 9 month old infant) during a 6 minute treadmill walk at 1.1 m/s. Mbada et al. found no significant difference in systolic BP (SBP) between carrying a 10 kg load and no load after a rest period of 3-5 minutes. Assuming that Marfan Syndrome patients have the same BP response as the healthy subjects in the study of Mbada et al. would mean that the carrying technique does not have a prolongued impact on BP response[13]. The experimental setup by Mbada et al. cannot account for the acute BP as it measures the BP 3-5 minutes after the 6 minute treadmill walk. Additionally, Mbada et al. found that frontal infant-carrying, though more fatiguing, did not significantly affect SBP compared to back infant-carrying[13] meaning that looking at backpack carrying experiments will provide additional insight into carrying.

Daneshmandi et al. studied the effect of carrying school backpacks on adolescent students since backpack use has been causing increased concern associated to musculoskeletal problems with school children[14]. They mentioned that backpack carrying is the preferred way of carrying a load close to the spine, symmetrically while maintaining balance. Daneshmandi et al. used a backpack with different loads (0, 8, 10.5 and 13% body weight) and let 370 adolescent boys walk a treadmill for 15 minutes at 1.1 m/s. They found that SBP significantly increased with loads corresponding to 10.5% and 13% of body weight compared no load, but did not significantly increase for a load of 8% (Figure 1.2b)[14]. Increasing the load from 8% to 10.5% initiated an increase in SBP, implying that carrying a load significantly increases SBP at a certain percentage of body weight[14] between 8 and 10.5%. The opposite idea, that SBP does not significantly increase when carrying under a certain percentage of body weight, is hopeful for people with Marfan Syndrome. This hypothesized *BP carrying limit* needs to be further researched for adults with Marfan Syndrome, since the study by Daneshmandi et al. was performed on 12.5 year old boys with no cardiovascular complications the results are likely different with this different subject group[14].

In another research Bhambhani et al. performed a similar experiment with healthy adults using weights that were held with both hands[15]. They used 11 healthy men (age, height and weight (SD): 25.1 (3.0) years, 1.79 (0.06) m, 78.2 (10.5) kg respectively) and compared unloaded, 15 kg and 20 kg loads while walking on a treadmill at a personally preferred pace for 4 minutes. The loads of 15 kg and 20 kg equate to 19.2% and 25.6% average body weight using the provided average subject weight. Similar to the 10.5% load in the research by Daneshmandi et al. there was a significant increase in SBP when the men had to carry a load compared to walking unloaded. Interestingly, there was no

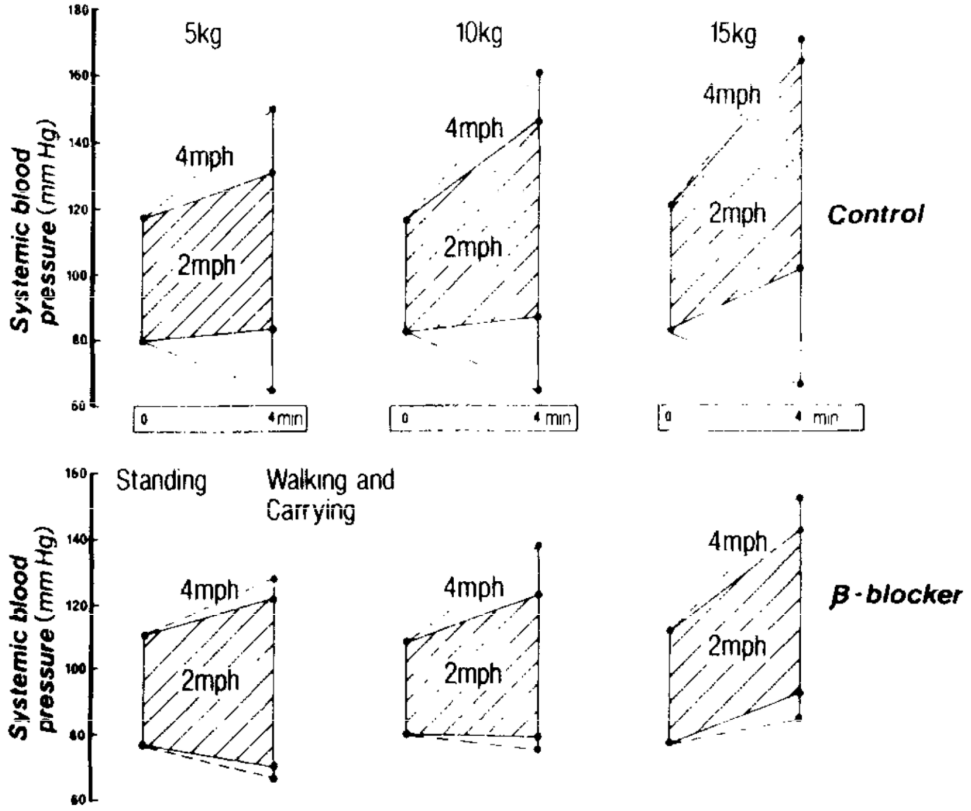


Figure 1.3: Circulatory effects of lifting and carrying a suitcase in healthy adult men and the influence of beta-adrenoceptors blockade. Upper and lower data points refer to SBP and DBP respectively; continuous and interrupted plots to 2 and 4 mph data respectively[2].

significant difference in SBP between a load of 15 kg and 20 kg[15] just as there was a small but significant difference (1.3 mmHg) in SBP between carrying 10.5 and 13% body weight in the research by Daneshmandi et al. [14].

Finally, Silke et al. evaluated the circulatory effect of β blockers on lifting and carrying a suitcases next to the body on 6 healthy men aged 21-31 years. They compared the different weights (5, 10 and 15 kg) as well as walking speeds of 2 and 4 mph (0.89 and 1.78 m/s) on a treadmill for 4 minutes and found that the systolic pressor response was speed and weight related[2]. The SBP increased significantly as the speed increased as well as when the weight increased, see Figure 1.3. After administering the β blockers the SBP increased less for all but the slowest speed and lowest weight (2 mph and 5 kg) compared to without the β blockers. Assuming that these results are transferable to Marfan Syndrome patients, this study implies that walking slowly with an infant is preferred for Marfan Syndrome patients, since it increases the BP less compared to walking at a higher pace. Additionally, using β blockers greatly reduces SBP as well as the increase in SBP when partaking in physical activity. A false assumption would be that Marfan Syndrome patients should not participate in physical activity at all, since their BP would stay low. It is important to note that leisure time physical activity (LTPA) has long-term benefits on BP[16, 17]. Aerobic exercises like walking, swimming, and cycling are recommended, especially for individuals with Marfan Syndrome[18], as they help manage BP. Such exercises can lead to significant reductions in BP for up to 24 hours after a workout[9]. Consequently, daily aerobic exercise can cause systematically reduced BP.

Combining the previously mentioned works by Palatini et al.[12], Mbada et al.[13], Daneshmandi et al.[14], Bhambhani et al.[15] and Silke et al.[2] creates an understanding of the circulatory response on healthy subjects. Presently, the advice for Marfan Syndrome patients is to avoid intensive physical activity, heavy lifting and exercises that require a forced expiration against a closed airway (the Valsalva Maneuver[19]); this in order to keep the BP as low as possible and to mitigate a large dP/dt[5]. In the Erasmus Medical Centre in Rotterdam the advise is to lift a maximum of 5 kg. The gap in the literature concerning the exact influence of increased weight compared to the increase in BP

leaves medical practitioners to give advise by "Consensus of Expert opinion based on clinical experience" and not based on evidence[5].

The daily trade-off that Marfan Syndrome patients currently have to make on "do" or "not do" with objects around 5 kg can influence their quality of life. Most of the activities of daily living can be replaced with alternative lifting or carrying technology, but specifically lifting and carrying infants is important for both infant and the parent. The advantages of infant carrying include promotion of the physical, emotional and mental development of the infant as well as increasing the phychosocial bond between infant and parent[13] (bare in mind it is also practical and fun).

1.1 Hypothesis

Based on the existing advice for lifting it is expected to see an increase in peak SBP for increased weights. Finding the difference between lifting 5 kg and 10 kg is especially interesting, because of the limit of 5 kg and infants quickly outgrow 5 kg. Idem for carrying 5 kg compared to carrying 10 kg for 5 minutes. Additionally, there is no differentiation for lifting techniques when posing the limit of 5 kg, where different techniques possibly have different results in SBP increases. The hypothesis is firstly that lifting 10 kg will increase the peak SBP at least 5 mmHg compared to the 5 kg conditions. Secondly, carrying 10 kg will increase the SBP at least 5 mmHg compared to a 5kg load. Finally, stoop lifting increases the BP at least 5 mmHg more than the flat lift.

1.2 Goal

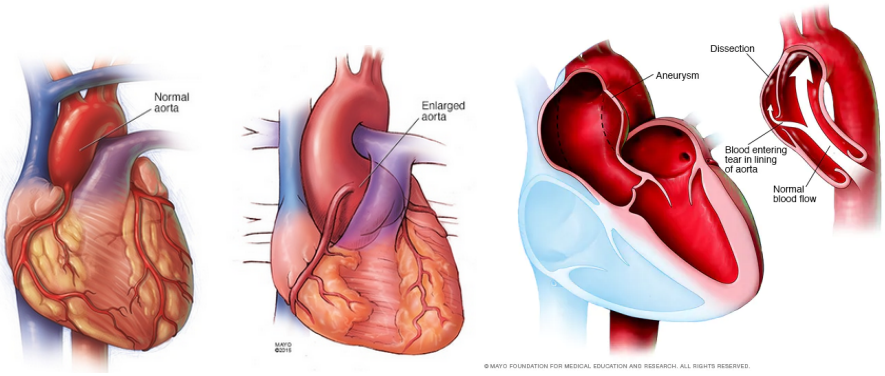
The goal of this indicative study is to contribute to the growing body of research on the relationship between physical activity and BP for individuals with Marfan syndrome, presently by researching healthy individuals. This is paramount for cardiologists when advising people with cardiovascular problems like Marfan Syndrome on the limit of weight they should lift and carry. This limit is to protect the Marfan patients but at the same time puts a limit on the ability to interact with infants. A first step is to find out whether or not the current 5 kg limitation put onto people with Marfan Syndrome is valid, by performing an indicative experiment comparing 5 kg and 10 kg loads during lifting and carrying infants.

2 | Background

2.1 Marfan Syndrome

BP is an important parameter to monitor for people with different diseases including Marfan syndrome[7]. The main focus of this research is Marfan Syndrome, which is a genetic disease that affects the connective tissue. Mutations in the FNB1 gene that encode the extracellular matrix protein, fibrillin-1, classically causes Marfan Syndrome[3]. Mortality in Marfan Syndromw patients is closely associated with the progressive dilation of the aorta, underscoring the critical importance of timely surgical interventions to prevent fatal outcomes [7, 20]. Aortic dilation occurs most often in the wall of the aortic root [21] (see Figure 2.1). Clinical management of Marfan Syndrome includes preventive aortic replacement surgery, guided by specific threshold values for aortic diameters to mitigate the risk of aortic dissection and rupture. Over the past decades, this aggressive surgical approach has significantly improved the life expectancy of individuals with Marfan Syndrome[21]. Still prevention is preferred due to the high risk associated with this treatment [5].

To prevent aortic dilation, it is essential to understand why dilation occurs. Normal hemodynamic stressors are outwardly directed forces of wall strain, twisting forces of torsion, intrinsic wall stress, and endothelial shear forces. These stressors are causing damage to arterial cells, regardless of underlying tissue abnormalities. Additionally, mechanotransduction of hemodynamic stress results in activation of endothelial and medial growth factors and secondary messengers. The intrinsic tissue abnormalities of the Marfan aortic root—wall thinning, aortic dilation, and loss of distensibility—increase wall stress further and increase hemodynamic stress[3]. This is likely a reason for dilation but the true reason is still a topic of debate and there is not a widely accepted consensus according to Dr. R. M. Kauling, cardiologist at the Erasmus Medical Centre in Rotterdam. However, all experts agree that BP typically is to be kept at a minimum to prevent a negative spiral of aortic dilation and possible catastrophic aortic rupture[3]. It was found that reduction in the rate of increase in aortic BP over time (dP/dt) was more effective at lowering risk of aortic dissection than could be explained by reduction of BP alone[22], implicating that both the static SBP level and the increase rate should be managed. The next section discusses the considerations Marfan Syndrome patients should take when doing physical activity to prevent aortic dilation.



(a) Normal and dilated aortic root[6]. (b) Dissection in aortic root[23].

Figure 2.1: The aortic root is a typical place for dilation and dissection for Marfan Syndrome patients[3].

2.2 Aortic BP

Monitoring aortic BP is crucial for individuals with Marfan syndrome due to the high risk of aortic complications associated with the condition[7, 20]. Marfan syndrome is characterized by aortic dilation, which can lead to life-threatening events like aortic rupture if not managed promptly[7]. Aortic distensibility, measured through aortic BP, serves as a potential predictor of aortic events in Marfan syndrome patients, aiding in the timely identification of individuals at risk for complications[21]. Regular monitoring allows healthcare providers to track changes in aortic distensibility and detect abnormalities early, enabling proactive interventions to prevent aortic dissections and other severe outcomes in individuals with Marfan syndrome[21].

Aortic BP can be measured using various techniques. One method involves utilizing applanation tonometry to derive central aortic pressures from peripheral pulse wave analysis, providing valuable insights into cardiovascular health and predicting outcomes[19, 24], more on that in section 2.4. Additionally, the oscillometric technique, which records pressure oscillations during cuff deflation, indirectly estimates mean intra-arterial pressure and can be used in ambulatory and home monitoring settings [25]. Another approach involves assessing aortic distensibility through image analysis software and calculating distensibility values based on cine MRI and non-invasively measured BP during cardiac magnetic resonance imaging[7].

Aortic BP can be estimated using a generalized transfer function, which involves noninvasive techniques like applanation tonometry to calculate aortic BP from peripheral signals[25]. This method utilizes transcutaneous pressure transducers to obtain pressure waveforms, mimicking intra-arterial measurements, and is applicable to radial, carotid, or femoral arteries. By analyzing the radial, carotid or femoral pulses and applying mathematical models (generalized transfer function) to derive aortic waveforms, central SBP, diastolic BP, and pulse pressure (PP). Additionally, indices of arterial stiffness such as augmentation index and pulse wave velocity (PWV) can be estimated, providing valuable insights into cardiovascular health and predicting cardiovascular events[26]. This approach offers a noninvasive and practical way to assess aortic BP and its implications for cardiovascular outcomes.

2.3 Generalized transfer function

The generalized transfer function (GTF) is the most established and widely used method for noninvasively deriving aortic BP from peripheral pressure waveforms[27]. It assumes the relationship between central and peripheral pressure waveforms is constant across subjects or a set of subjects with similar characteristics. This relationship is modeled using a GTF to reconstruct the central pressure waveform from the peripheral waveform. The GTF acts as a low-pass filter that compensates for the boost in high frequency components as the pressure wave travels from the aorta to the periphery[27]. It provides a quantitative aortic pressure waveform for further cardiovascular analysis[27].

However, central arterial stiffness (or distensibility) differs for Marfan patients compared to healthy patients as well as with aging, hypertension, exercise, etc. which changes the central-peripheral pressure relationship. To counter this variability adaptive transfer function (ATF) methods try to tune the GTF to derive more reliable aortic pressure estimates for each individual. One approach uses regression formulas to determine an optimal peak resonance frequency for tuning the GTF based on brachial SBP[27]. Individualized transfer function (ITF) methods focus on individualizing the pulse transit time, the main determinant of the aorta-brachial and aorta-radial model, to account for inter-subject and intra-subject variability not captured by the GTF[27]. However, ITF methods are not yet fully validated by invasive data and rarely used clinically.

In summary, while the GTF is the most established method, its generalizability has been questioned. Adaptive and individualized approaches aim to improve accuracy by accounting for subject-specific factors, but require further validation[25].

2.4 Measuring peripheral BP

Monitoring BP accurately is crucial for detecting and managing cardiovascular problems like Marfan Syndrome and hypertension[28] where it has been demonstrated that the SBP is of greater importance than the diastolic and mean BP[29]. In addition to appalation tonometry and the standard sphygmomanometer other noninvasive technologies like photoplethysmography (PPG) have become popular for estimating BP due to their ease of use and ability to provide continuous monitoring. PPG measures blood volume changes in a microvascular bed of the skin based on optical properties, such as absorption, scattering, and transmission properties of human body composition under a specific light wavelength. PPG is a compound word that consists of "photo" meaning light; "plethysmo" meaning volume; and "graphy" meaning recording[30]. Single-site PPG is the most popular wearable cuffless BP monitoring device[4] and it is mostly used on the finger, see Figure 2.2.

An interesting method was first developed by Penaz and works on the principle of the "unloaded arterial wall." Arterial pulsation in a finger is detected by a photoplethysmograph under a pressure cuff. The output of the plethysmograph is used to drive a servo-loop, which rapidly changes the cuff pressure to keep the output constant, so that the artery is held in a partially opened state. The oscillations of pressure in the cuff are measured and have been found to resemble the intra-arterial pressure wave in most subjects[19]. The Finapress is a commercially available device that uses this principle[19, 31].

However, by combining PPG with other biosignals such as electrocardiogram (ECG), it is possible improve the accuracy of BP estimation. This is because additional measures derived from ECG, like pulse wave velocity (PWV), are inversely correlated with BP. PWV reflects the speed at which pressure waves travel through the arteries, while pulse transit time (PTT) measures the time it takes for arterial pressure waves to propagate[4, 28]. Recent research has focused on developing PPG-based multimodal biosignal systems to estimate BP accurately and evaluate hypertension. These studies have shown promising results, demonstrating high measurement accuracies and effective combinations of technologies. By integrating multiple biosignals, these systems provide a more comprehensive understanding of cardiovascular health and enable continuous monitoring, which is essential for effective Marfan Syndrome management[4].

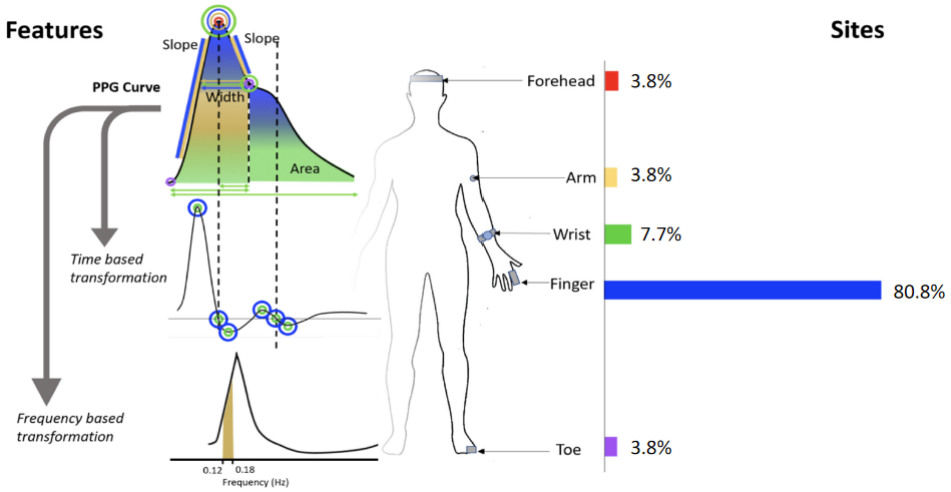


Figure 2.2: Single-site PPG features and measurement sites[4]

2.5 Existing lifting recommendations

The American Occupational Safety and Health Act was established in 1970 and created both the Occupational Safety and Health Administration (OSHA) in the Department of Labor, as well as the National Institute of Occupational Safety and Health (NIOSH) in the Department of Health and Human Services[32]. In a complex partnership they address the safety of workers with regards to occupational conditions and activities like lifting[32], similar to the Working Conditions Act (ARBO)

in the Netherlands. The NIOSH has composed an elaborate Lifting Equation with guidelines for occupational lifting[11], contributing greatly to the prevention work-related lower back disorders. This lifting equation calculates the Recommended Weight Limit (RWL) by applying multipliers for six task variables: load constant, horizontal location, vertical location, distance, asymmetry, and coupling. The RWL represents the weight limit that nearly all healthy workers can perform over a substantial period of time without an increased risk of developing lifting-related low back pain[11].

The equation is defined by the following formula: RWL = LC x HM x VM x DM x AM x FM x CM
Where:

- LC = Load Constant (23 kg)
- HM = Horizontal Multiplier (25/H)
- VM = Vertical Multiplier (1 - 0.003 | V-75 |)
- DM = Distance Multiplier (0.82 + 4.5/D)
- AM = Asymmetric Multiplier (1 - 0.0032A)
- FM = Frequency Multiplier (from conversion table)
- CM = Coupling Multiplier (from conversion table)

And where: Horizontal location of the load (H), Vertical location of the load (V), Vertical travel distance of the load (D), Asymmetry angle of the lift (A), Lifting frequency (F) and Quality of hand/object coupling (C)[11]. Each multiplier serves to decrease the recommended weight limit from the ideal 23 kg based on the specific conditions of the lifting task[11]. The equation is limited to two-handed manual lifting tasks that meet the underlying conditions and criteria.

Example: Assuming that this lifting equation can account for the unpredictable nature of lifting a live load, such as sudden movements or shifts in an infant's center of mass, it is possible to estimate the RWL. Assume a two handed squat lift with the following task variables: Vertical distance (D): 1.5 meters (for cradle position), Asymmetry angle (A): 0 degrees (no twisting), Lifting frequency: 1 lift per 10 minutes, Horizontal distance (H): 30 cm and Quality of hand/object coupling: Poor (holding an infant) gives a recommended weight limit of 15 kg.

The example is not representative for all interactions with infants and serves as an indication of RWL for lifting an infant from the ground. The Lifting Equation by the NOISH is specifically developed for healthy workers excluding Marfan Syndrome patients, since they have altered connective tissue. Marfan Syndrome patients have a lower RWL compared to healthy workers[11]. Additionally, and more importantly, this Lifting Equation was constructed to prevent work-related lower back disorders and does not take into account BP[11], therefor it cannot be provide a RWL for Marfan Syndrome patients when mitigating aortic dilation.

2.6 Physical activity paradox

The *Physical activity paradox* states that occupational physical activity (OPA) (including occupational lifting) is detrimental and leisure time physical activity (LTPA) improves your health[8]. According to Holtermann et al. there are 6 reasons for this paradox where most reasons are due to insufficient recovery time and prolonged mild activity compared to short high intensity exercise[16].

1. The intensity and duration of OPA and LTPA are vastly different. Where improvement of cardiorespiratory fitness requires high phisical activity for a short period of time, OPA often have 8 hour sessions of 30-35% of aerobic capacity which may actually impair cardiovascular health.
2. OPA over a long period of time show increased HR for up to 24 hours, where LTPA actually decreases HR. Prolonged increase HR can cause cardiovascular disease.
3. Occupational lifting (OL) elevates BP in the same way as HR for 24 hours. LTPA can also involve heavy lifting, but for a shorter period of time and does not result in increased BP.
4. Insufficient recovery time for OPA can cause fatigue and exhaustion, where LTPA often have more recovery time.

5. The environment of OPA is often not in the control of the person, think of climate, shade, hydration and access to rest. Where LTPA is often performed under self regulated conditions.
6. Markers of inflammation remain in the body until the body has recovered from the PA. OPA for consecutive days without sufficient rest can cause sustained inflammation. Where with LTPA people often take enough rest.

3 | Materials and method

To prove the hypothesis an indicative experiment was proposed: monitor SBP during lifting and carrying by using a non invasive ambulatory BP measurement (ABPM) device on the upper extremity (UE). Real life scenarios were simulated by lifting an infant from the ground, carrying it for 5 minutes and lowering it, to find its influence on SBP. Three different weights were used to see if there is a difference when the load is increased. Additionally, two different lifting techniques (Figure 1.1) were compared to find if there is a difference in SBP response, see Figure 3.1. The subjects were connected to a Finapres Nova[31] (ABPM device). The experiment was conducted in The Erasmus Medical Centre in Rotterdam in February 2024. The experiment was approved by the Human Research Ethics Committee of TU Delft. Statistical analysis was done using a t-test.

3.1 Protocol

When the subjects had entered the room and had given consent they were connected to the ambulatory BP measurement device. The subjects performed the experiment following an initial rest period of 5 minutes to get the rest HR. The experiment entailed 6 conditions in a randomized order. A single condition was as follows (see Figure 3.1): The subject stood up an positioned themselves onto the treadmill, where they had 1 minute rest to separate the effect of standing up on BP from the effect of lifting. Then the subject lifted the infant using either the stoop or the flat lift and held the infant in cradle position. Then the treadmill started and increased to a speed of 1.1 m/s where the subject carried the infant for 5 minutes. After 5 minutes of carrying, the treadmill stopped and the subject lowered the infant using the same technique as used for lifting. Then the subject had 4 minutes of seated rest. Resulting in 10 minutes per condition.

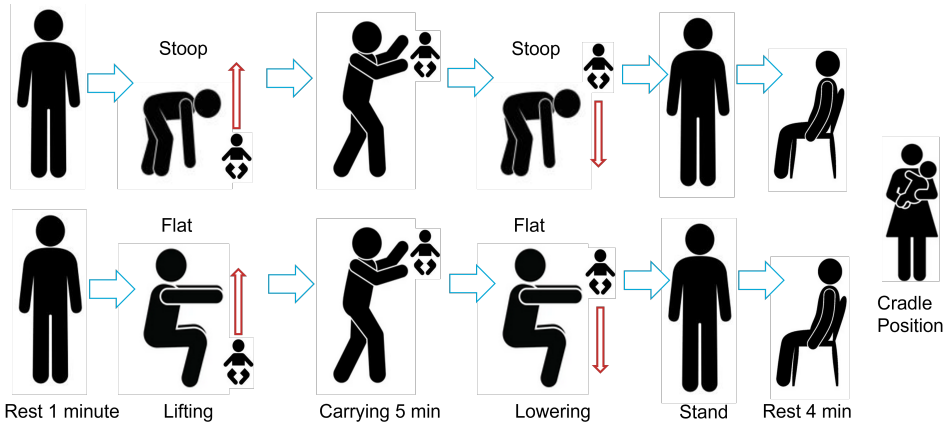


Figure 3.1: The protocol of the experiment where the subjects performed either the stoop lift or the flat lift, carried the infant for 5 minutes and then lowered the baby with the same technique while connected to a ABPM device. 4 minutes of seated rest followed. The infant was held in cradle position (right).

The 2 techniques and 3 different weights result in 6 different conditions, see Figure 3.2:

- SL0: Weight of 0 kg; Stoop lift, carrying, lowering and rest
- FL0: Weight of 0 kg; Flat lift, carrying, lowering and rest
- SL5: Weight of 5 kg; Stoop lift, carrying, lowering and rest
- FL5: Weight of 5 kg; Flat lift, carrying, lowering and rest
- SL10: Weight of 10 kg; Stoop lift, carrying, lowering and rest
- FL10: Weight of 10 kg; Flat lift, carrying, lowering and rest

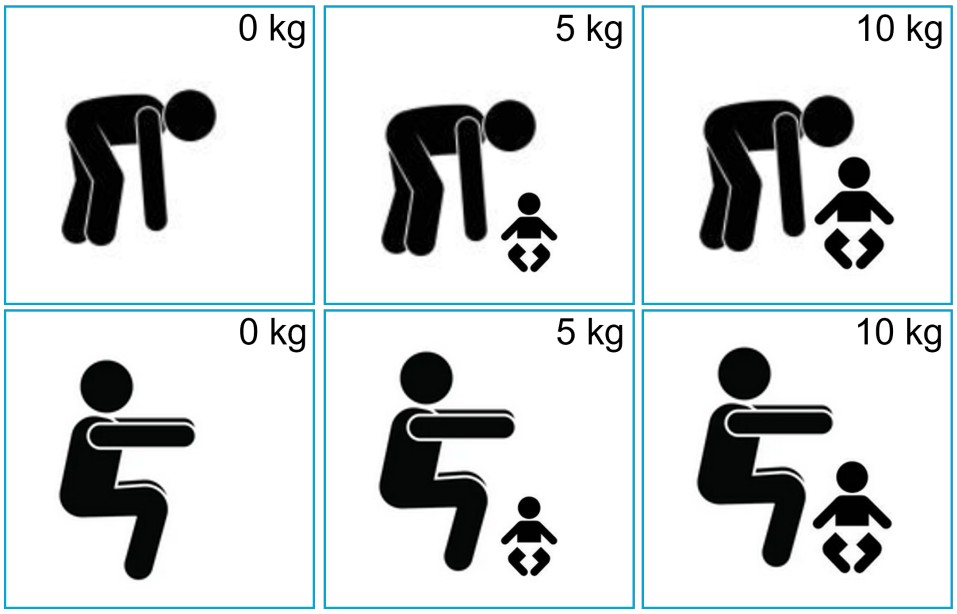


Figure 3.2: The different lifting conditions: top is stoop lift, bottom is flat lift. From left to right: 0 kg, 5 kg and 10 kg.

3.2 Subjects

The subjects were healthy white men and women with no medical history concerning cardiovascular problems. The subjects were aged 24 to 28 years old. The subjects were not overweight nor underweight. 5 men and 5 women were included in the experiment. See table 3.1. Marfan Syndrome subjects would be preferred for this indicative study since the circulatory response is dependant on the subjects physiology. Since the long term risks of this experiment on Marfan Syndrome patients were not known it would have been beyond the scope of this indicative research to to provide an ethically correct experiment with Marfan Syndrome subjects.

Table 3.1: Subject information.

Data	Mean (SD)
Age (years)	25.4 (1.77)
Height (cm)	180.9 (8.97)
Weight (kg)	74.7 (9.96)
BMI (kg/m^2)	22.8 (1.78)
Physical activity per week	4.3 (1.63)

3.3 Measurements and equipment

Measuring the BP in the aorta would be ideal for this experiment, but currently there is no non invasive way to measure this aortic BP directly[4]. PPG on the brachial artery will be used as a surrogate for the aortic BP[33] since this is the only available methodology at the Erasmus Medical Centre in Rotterdam. The Finapres NOVA[31] is used as ABPM device. Using a Generalized Transfer Function (GTF) it is possible to do an estimation of the aortic BP from the brachial artery using a non invasive method[27, 29, 34], however because of the remaining uncertainty in the GTF it was not applied in this research.

The Finapres NOVA (FMS) was used to continuously measure the BP of the subjects. The Finapres measured the BP in the right hand index finger and reconstructed the brachial arterial pressure using an arm cuff on the left arm[31], see Figure 3.3a. The Finapres included a height correction unit that was connected to the sternum of the subjects using medical tape. The subjects walked on a treadmill at a constant speed of 1.1 m/s (typical walking speed)[35], see Figure 3.3b. The custom weights that were used[1] are 0 kg (control), 5 kg (weight of a new-born) and 10 kg (typical weight of a 9 month old infant), see Figure 3.3c. The weights included baby dolls and appropriate lead weights for the purpose of comfortably holding the dolls in cradle position, see Figure 3.3d. The first 9 months of the infant is a period of the growth spurt and the period where the infant is carried most often[13].

(a) Hand & finger module of Finapres. (b) The treadmill with the 5 kg doll. (c) The 10 kg doll that needs to be lifted. (d) Subject walking with Finapres.

Figure 3.3: The equipment that was used to simulate lifting and carrying infants. A 0.126 kg doll was used for 0 kg scenarios.

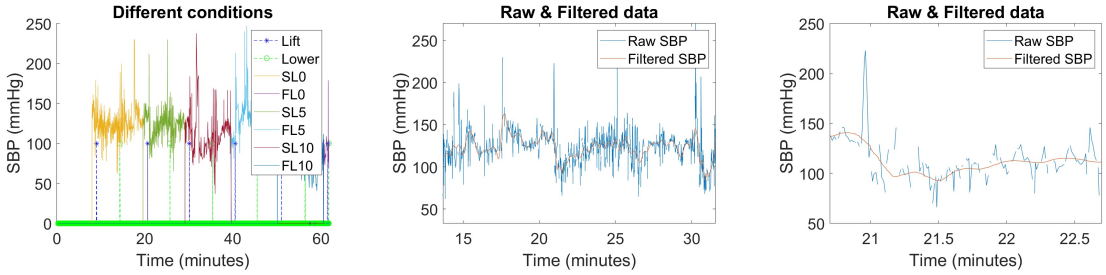
[1] Since using actual infant could be unethical

4 Data analysis

The data was analysed using **Matlab**. The codefiles were explained in the appendix A2. The BP data retrieved from the Finapres NOVA was first reviewed, then the raw BP data was augmented. The augmented data was used for the results in Chapter 5.

4.1 Review the data

The data was marked per condition as can be seen in Figure 4.1a. Then, for visual analysis purposes, the missing data was linearly filled and a 4th order Butterworth filter was used to remove the transient effects of the signals, see Figure 4.1b & 4.1c.



(a) Raw data showing different conditions.

(b) Raw data & filtered data: random sample.

(c) The filter removes the transient effects.

Figure 4.1: Data review.

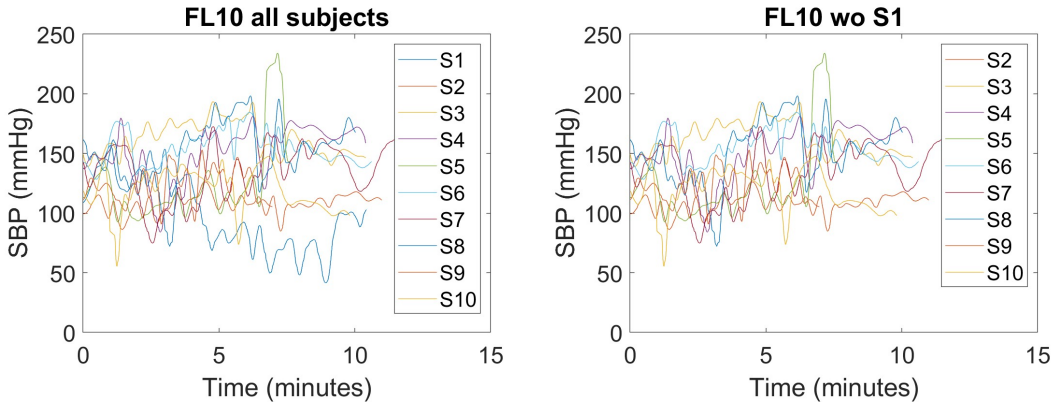
4.1.1 Erroneous data

The filtered version of the data enabled an analysis of the bigger picture. For example, Figure 4.2 shows the SBP for lifting 10 kg with a flat lift (FL10) of all the subjects in one figure. This way irregular behaviour was easily spotted erroneous was omitted from the results. As can be seen in figure 4.2a, subject 1 showed a significant dip in SBP after 4 minutes. The dip went down to <20 mmHg, which was possibly due to equipment failure. This is unrealistic and therefor condition FL10 of subject 1 was excluded from the results. When removing subject 1 in Figure 4.2b it can be seen that subject 5 (green) shows a peak that coincided with the moment where the subject accidentally pressed the finger sensor against a chair, in these instances the pressure sensor did not sense the BP, but rather an external mechanical pressure. Luckily, this peak occurred during the rest period, which was not used in the analysis.

4.1.2 Review condition

By reviewing the overall progression of the data (Figure 4.2b) three different stages were identified during each condition. The lifting stage typically occurred approximately one minute after standing up (t=0), although this timing varied among individuals. The peaks observed at the start of each condition largely align with the act of standing up from a resting position. Following the lifting stage, the carrying stage starts where the SBP steadily increases until approximately 6 minutes when the treadmill stops and the lowering phase starts. Throughout the lowering phase, BP showed large

fluctuations. Around the 7-minute mark, BP reached a stable level, which coincided with the period of seated rest.



(a) All Data for the flat lift with 10 kg condition.

(b) Flat lift with 10 kg without subject 1.

Figure 4.2: Condition FL10 reviewed

Considering the different stages during the conditions it made sense to split the analysis into three subcategories: lifting, carrying (between lifting and lowering) and lowering. Caution was taken when analysing lifting and lowering, since they did not happen at predefined timestamps. The filtered signal, as can be seen in more detail in Figure 4.1c, was not desirable for the complete data analysis, since the peaks were filtered out.

4.1.3 Quality review of conditions

Subjects that have a gap in their data were removed. Gaps of 1 second or larger (if the sample time was greater than 1 second) during/close after the lifting and lowering event resulted in disqualification and were excluded from the results. Figure 4.3 was used as a visual support, here the sampletime was plotted during the various conditions. As an example the different subjects are displayed for stoop lift 10 kg in Figure 4.4.

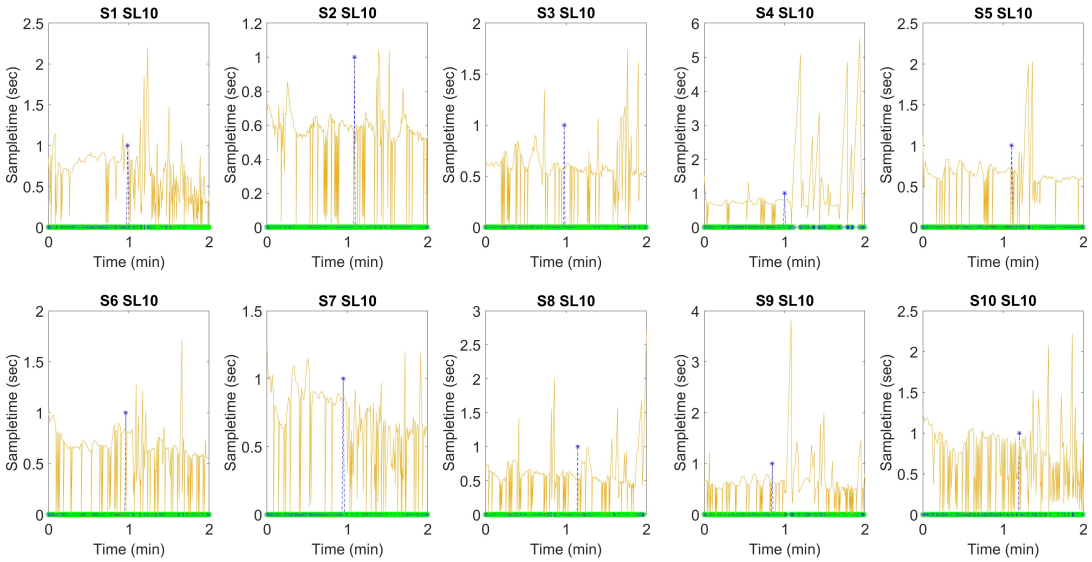


Figure 4.3: Show the sampletime in seconds on the y-axis during stoop lift with 10 kg. Lifting is indicated in blue. Sampletimes larger than 1 second around the lifting action can have a undesired impact on the results.

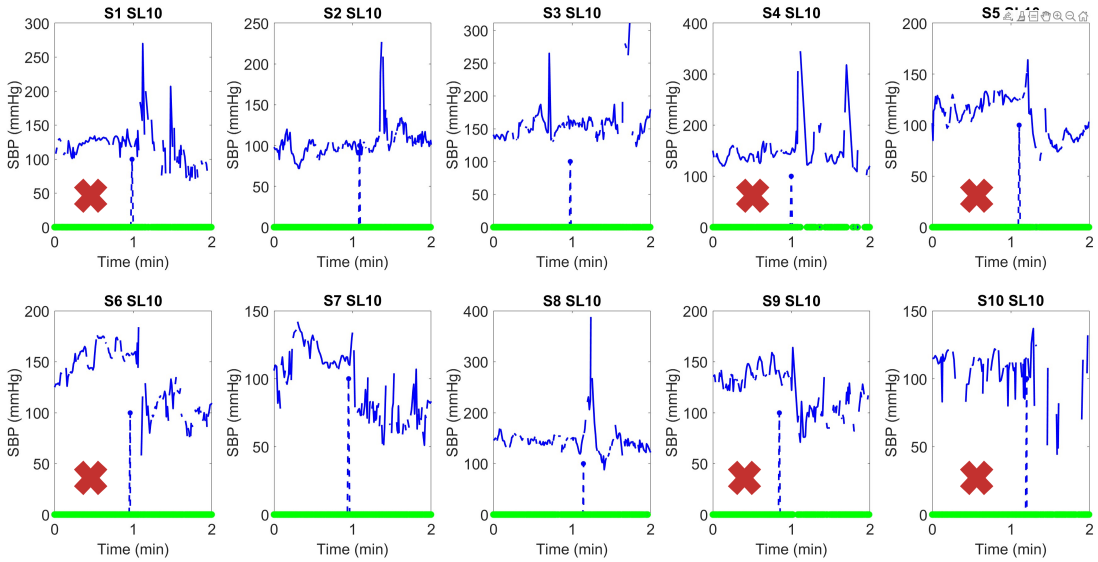
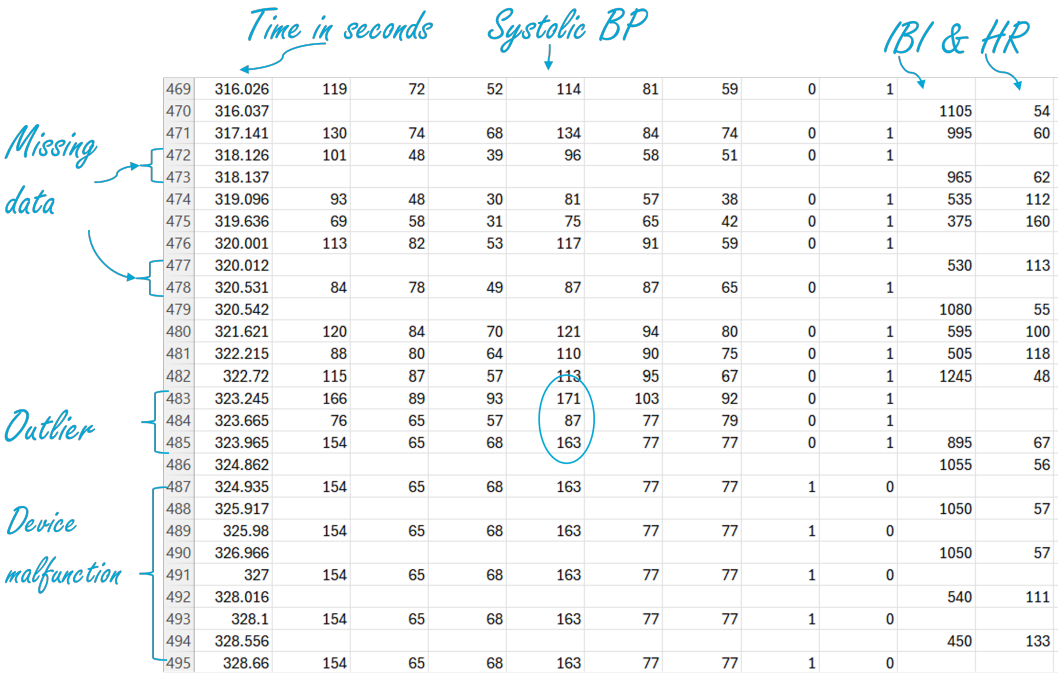


Figure 4.4: Show the raw SBP data for lifting with straight legs with 10 kg. Lifting is indicated with a blue dotted line.

In Figure 4.4 subject 1, 4, 5, 6, 9 & 10 are not eligible and were excluded in the results. This way the quality of the data was managed, however the quantity was halved.

4.2 Augmenting data

In this section that data augmentation is explained step by step. A graphical understanding is formed showing the same example data every step of the way compared to its raw data.



469	316.026	119	72	52	114	81	59	0	1		
470	316.037									1105	54
471	317.141	130	74	68	134	84	74	0	1	995	60
472	318.126	101	48	39	96	58	51	0	1		
473	318.137									965	62
474	319.096	93	48	30	81	57	38	0	1	535	112
475	319.636	69	58	31	75	65	42	0	1	375	160
476	320.001	113	82	53	117	91	59	0	1		
477	320.012									530	113
478	320.531	84	78	49	87	87	65	0	1		
479	320.542									1080	55
480	321.621	120	84	70	121	94	80	0	1	595	100
481	322.215	88	80	64	110	90	75	0	1	505	118
482	322.72	115	87	57	113	95	67	0	1	1245	48
483	323.245	166	89	93	171	103	92	0	1		
484	323.665	76	65	57	87	77	79	0	1		
485	323.965	154	65	68	163	77	77	0	1	895	67
486	324.862									1055	56
487	324.935	154	65	68	163	77	77	1	0		
488	325.917									1050	57
489	325.98	154	65	68	163	77	77	1	0		
490	326.966									1050	57
491	327	154	65	68	163	77	77	1	0		
492	328.016									540	111
493	328.1	154	65	68	163	77	77	1	0		
494	328.556									450	133
495	328.66	154	65	68	163	77	77	1	0		

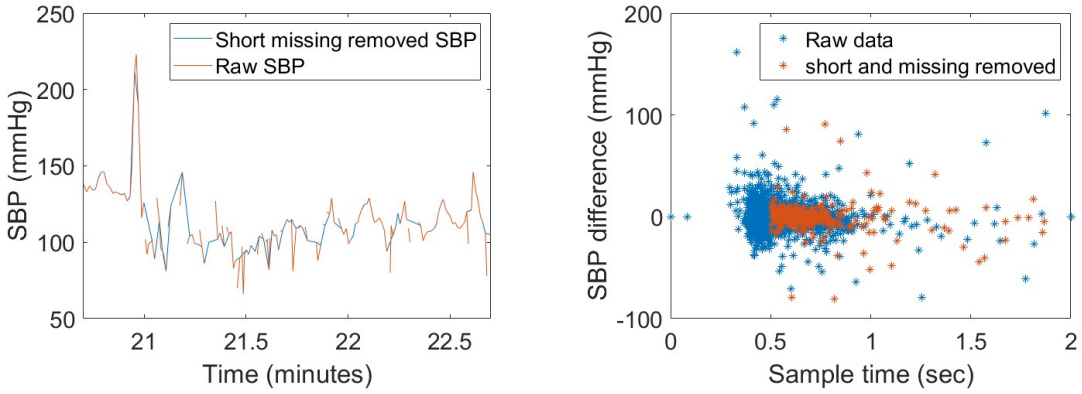
Figure 4.5: Snapshot of sample data (Microsoft Excel), first (left) column is the time in seconds, fifth column is the SBP in the upper arm, the most right columns are the inter beat interval and the heart rate.

4.2.1 Take out missing values and outlier

Firstly, when looking at an example of the raw data (Figure 4.5) the missing values in the sample data showed a pattern. The values were written out to the excel sheet with the two values right hand side values missing (inter beat interval and heart rate). Then after a short interval (Sampletime(s)$<$ 0.02 sec) the two right hand values were filled in with the other columns empty. See for example row 472 and 473. The IBI and HR were not used in this research therefor the samples that miss 4 or more columns were not useful and were removed by the "rmmissing" function in Matlab, see A2.2.1.

Then there were outliers that did not follow the trend of the SBP, possibly due to equipment or due to sampling. See for example row 483, 484 and 485 in Figure 4.5: here the fifth column (SBP) was 171 mmHg, then 0.4 seconds later the SBP was 87 mmHg (a drop of over 50%) and then 0.3 seconds later the SBP was up again to 163 mmHg. Relatively short samples often showed this phenomenon and did not by themselves add value to the data. Leading to the removal of samples that are shorter than 0.5 seconds.

The result of removing the missing values and short values on the data can be seen in Figure 4.6a. Then to get a feeling for what changed in the data Figure 4.6b shows the data with on the y-axis the difference in SBP and on the x-axis the sample time. It can be seen that the raw data has samples with short sample times and with large SBP differences which do not add value and rather add outliers to the signal. The new signal contains the relevant information without the outliers, which is a more accurate representation of the real BP.



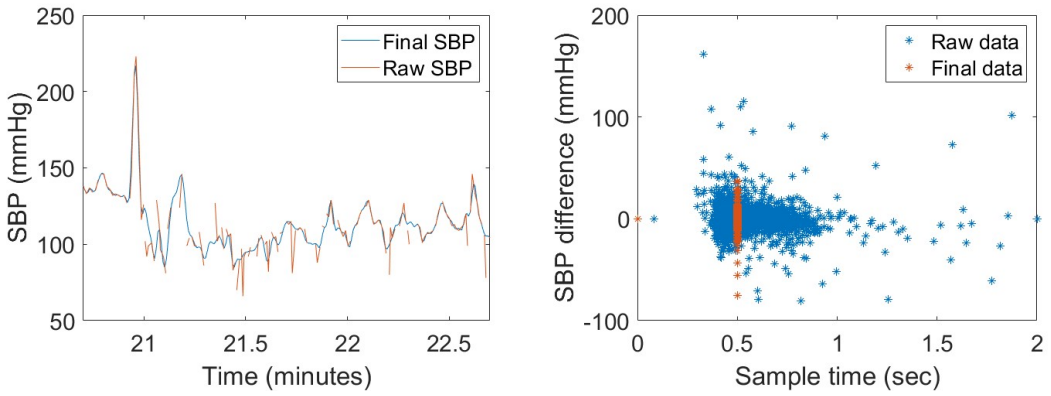
(a) Raw data & SBP over time after removing short and missing samples.

(b) Raw data & SBP differences vs sampletime after removing short and missing samples.

Figure 4.6: The effect of removing short and missing samples on the raw data.

4.2.2 Resampling data

The data was then resampled so that the signal had a sampling frequency of 2 Hz. The resampling meant that some information was lost. This resampling was useful for calculating means while losing a minimal amount of information. Additionally, it was optional to do frequency analysis and to apply a generalized transfer function to get the aortic BP. Figure 4.7a shows the minimal information loss in the resampled data compared to the raw data. Comparing Figure 4.6a and 4.7a showed minimal changes in the data. Additionally, Figure 4.6b shows that all the included samples have a sample time of 0.5 seconds.



(a) Raw data & Data Post Resampling at 2 Hz. (b) Sample Time & SBP difference after Resampling.

Figure 4.7: The effect of resampling after removing short and missing data.

Fast Fourier Transform

A sample frequency of 2 Hz was selected since frequencies greater than 1 Hz (≈resting HR) were assumed to be noise when looking at BP. Therefore, a sampling frequency of 2Hz is enough to induce no aliasing, this was checked by a FFT in Figure 4.8.

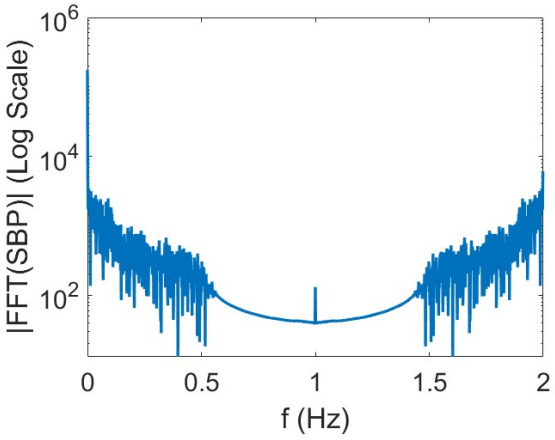


Figure 4.8: FFT of SBP of one random subject showing no aliasing.

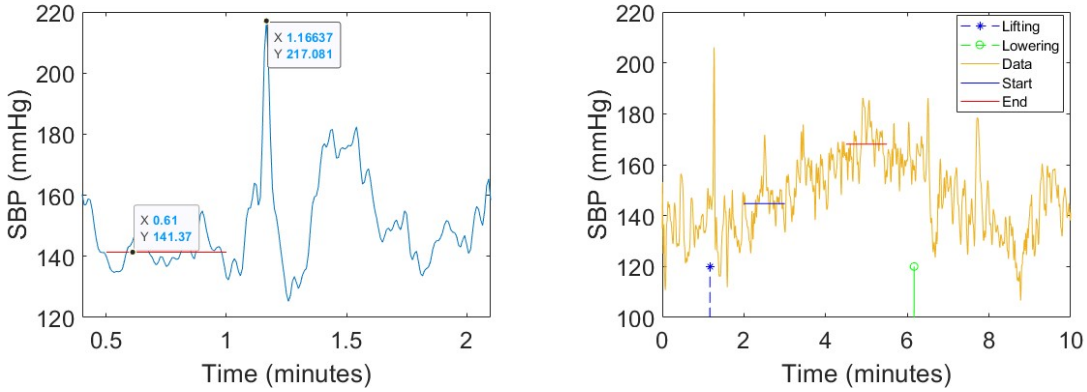
4.3 Conclusion

First the data was reviewed to get an idea of how to interpret, analyse and retrieve eligible data. When reviewing the data it became obvious to separate the analysis into three different stages: lifting (pick up event in code), carrying (trend in code) and lowering (put down event in code). The data was reviewed for eligibility, so that conditions with large gaps of missing data (Sampletime(s)>1) are excluded to keep the quality of this experiment as high as possible. However, this resulted in a smaller sample size.

Then, the raw data was augmented by removing missing data samples, removing outliers by excluding samples that have a short sampling time (Sampletime(s)<0.5) and by resampling the irregularly sampled data to 2 Hz. This is done to improve the quality of the data while mitigating information loss. See the difference between the raw data and the data that is used in the results in Figure 4.7a.

5 | Results

To conduct statistical analysis on the data under various conditions, quantitative parameters were established. Specifically, for lifting and lowering activities, these parameters included the baseline SBP recorded just before the event and the peak SBP observed during the event (see Figure 5.1a). In the case of carrying, the start SBP (after lifting) and end SBP (before lowering) were determined (see Figure 5.1b). The quantitative measures provide the results in Table 5.1.



(a) In this example Baseline (average just before lifting) was 141 mmHg and Peak was at 217 mmHg.

(b) In another example Start (after lifting) was 145 mmHg and End (before lowering) was 170 mmHg.

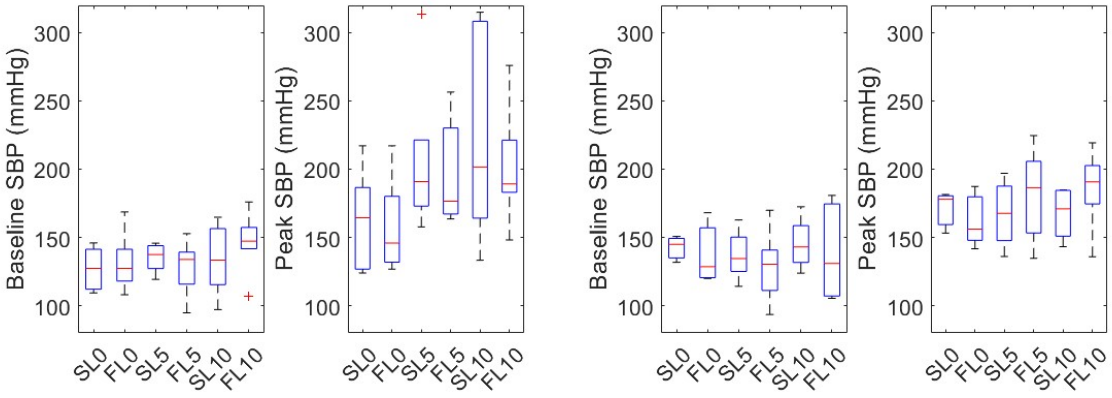
Figure 5.1: The quantitative measures for lifting and lowering: Baseline and Peak. The quantitative measures of carrying: Start and End.

Table 5.1: Results of quantitative measures: Baseline was the average SBP just before lifting; Peak was the highest observed SBP during lifting; Carrying increase the average SBP just before lowering minus the average SBP just after lifting. *significant increase compared to 0 kg condition. Lifting results are displayed in Figure 5.2a and carrying results are displayed in Figure 5.3b.

Data (mmHg)	Stoop (0 kg) (Mean±SD)	Flat (0 kg) (Mean±SD)	Stoop (5 kg) (Mean±SD)	Flat (5 kg) (Mean±SD)	Stoop (10 kg) (Mean±SD)	Flat (10 kg) (Mean±SD)
Baseline SBP	127.2±14.8	131.8±21.2	135.2±10.2	127.5±19.3	133.4±26.0	146.0±22.9
Peak SBP	163.8±36.0	157.9±35.0	207.8±56.7	199.0±37.8	220.7±77.6	201.1±43.6
Carrying incr.	2.7±8.0	2.2±4.7	15.7±11.5*	14.3±8.2*	22.6±11.2*	16.3±8.2*

5.1 Lifting and lowering

The peak SBP was nearly always higher than the baseline SBP for both lifting (Figure 5.2a) and lowering (Figure 5.2b). The baseline SBP for lifting and lowering give similar ranges for all conditions. The peak SBP during lifting seemed to increase with increased loads, where lowering did not increase peak SBP with increased loads, although this is not statistically significant. The peak SBP during lifting for various conditions has been compared in Table 5.2. No significant differences were found. The difference between the mean values were indicated in Table 5.2. The difference between the 0 kg situations and the increased load situations was greater than the difference from 5 kg to 10 kg. Additionally, the difference between the two lifting techniques seemed to increase with increased loads, where the stoop lift had the higher peak SBP.



(a) Lifting. See Table 5.1.

(b) Lowering.

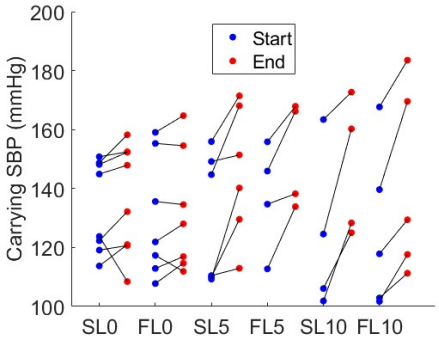
Figure 5.2: Baseline and Peak, with the conditions on the x-axis: SL0 stoop lift 0 kg (n=6), FL0 flat lift 0 kg (n=6), SL5 stoop lift 5 kg (n=6), FL5 flat lift 5 kg (n=7), SL10 stoop lift 10 kg (n=4), FL10 flat lift 10 kg (n=6). No significant differences were found.

Table 5.2: Mean difference (effect size) and p-values when comparing the peaks of different lifting conditions, resulting from a t-test. No statistical difference was found between the stoop and flat lift in every condition, nor was there a significant difference between the control (0 kg) and increased weights. The + indicates that the second argument is larger than the first argument.

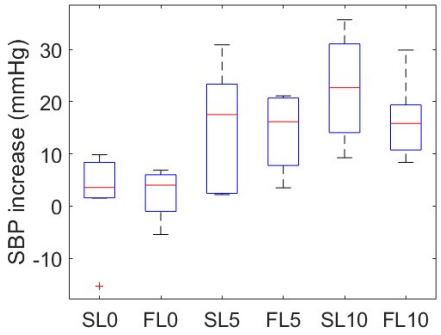
Lift peak comparison	Mean (mmHg)	p-value
Flat (0 kg) vs Stoop (0 kg)	+5.9	0.78
Flat (5 kg) vs Stoop (5 kg)	+8.8	0.74
Flat (10 kg) vs Stoop (10 kg)	+19.6	0.60
Stoop (0 kg) vs Stoop (5 kg)	+44.0	0.14
Stoop (0 kg) vs Stoop (10 kg)	+56.9	0.13
Stoop (5 kg) vs Stoop (10 kg)	+12.9	0.75
Flat (0 kg) vs Flat (5 kg)	+41.1	0.07
Flat (0 kg) vs Flat (10 kg)	+43.2	0.09
Flat (5 kg) vs Flat (10 kg)	+2.1	0.92

5.2 Carrying

The start and end results per subject (as calculated in Figure 5.1b) can be seen in Figure 5.3a. The SBP had a large inter-subject variability for both the start and end values during carrying as can be seen in Figure 4.2b. Consequently, displaying the averages of the SBP did not provide an adequate representation of the effect of carrying an infant (the averages could be similar for all conditions, depending on the included subjects). An increase (End-Start) provided a better representation of the circulatory effect of carrying. The SBP increase (End-Start) per condition can be seen in Figure 5.3b. The SBP elevated for all conditions during carrying, however the increased loads elevated the SBP more compared to the 0 kg conditions. The difference between the means of each condition can be seen in Table 5.3. Carrying a 5 kg load (stoop p=0.012, flat p=0.028) and carrying a 10 kg load (stoop p=0.005, flat p=0.003) significantly increased SBP compared to carrying 0 kg. The elevation the 0 kg situations to the 5 kg situations is greater than the elevation from 5 kg to 10 kg. Additionally, the difference between the two lifting techniques seemed to increase with increased loads, where the stoop lift had a larger SBP increase while carrying.



(a) The start and end of carrying for every subject.



(b) Comparing carrying at the end vs start (End-Start). See Table 5.1.

Figure 5.3: Displaying the increase in SBP due to carrying, the value directly before lowering minus the value directly after lifting. With the conditions on the x-axis: SL0 stoop lift 0 kg (n=8), FL0 flat lift 0 kg (n=7), SL5 stoop lift 5 kg (n=6), FL5 flat lift 5 kg (n=4), SL10 stoop lift 10 kg (n=4), FL10 flat lift 10 kg (n=5).

Table 5.3: Mean difference (effect size) and p-values when comparing the different carrying conditions, resulting from a t-test. * signifies a statistical significance. No statistical difference was found between the stoop and flat lift in every condition. There was a significant difference found between the control and increased weights (p<0.05). There was no significant difference found between the 5 kg and the 10 kg conditions. The + indicates that the second argument is larger than the first argument.

Carrying comparison	Mean (mmHg)	p-value
Flat (0 kg) vs Stoop (0 kg)	+0.5	0.885
Flat (5 kg) vs Stoop (5 kg)	+1.4	0.837
Flat (10 kg) vs Stoop (10 kg)	+6.3	0.364
Stoop (0 kg) vs Stoop (5 kg)*	+13.0	0.028
Stoop (0 kg) vs Stoop (10 kg)*	+19.9	0.005
Stoop (5 kg) vs Stoop (10 kg)	+6.8	0.375
Flat (0 kg) vs Flat (5 kg)*	+12.0	0.012
Flat (0 kg) vs Flat (10 kg)*	+14.1	0.003
Flat (5 kg) vs Flat (10 kg)	+2.1	0.719

6 | Discussions and Conclusions

6.1 Clinical relevance

Presently, the advise given to people with Marfan Syndrome at the Erasmus Medical Centre in Rotterdam is to lift and carry a maximum load of 5 kg, which is based on medical expertise. However, in this research there seemed to be only a small difference (stoop +12.9 mmHg, flat +2.1 mmHg) between lifting 5 kg and lifting 10 kg. Additionally, there seemed to be a small difference (stoop +6.8 mmHg, flat +2.1 mmHg) between carrying 5 kg and carrying 10 kg. These differences were not statistically proven and need further research. A power analysis was done to find the amount of subjects needed in these future researches, see section 6.4.1. Should this indicative study be recreated with sufficient Marfan Syndrome subjects, and hold the same results, then it should be incorporated in recommendations for people with Marfan Syndrome.

6.2 Discussion and future research

The results of this study provide valuable insights into the SBP responses during common physical activities involving infants. By understanding how lifting, carrying and lowering an infant affects SBP, individuals with Marfan syndrome can make informed decisions about their physical activity and take steps to minimize the risks associated with elevated SBP.

This research shows that carrying any load significantly increases SBP compared to walking without load concluding that carrying an infant should be mitigated for people with Marfan Syndrome[5]. However, using a flat lift to lift 10 kg increased the SBP only +2.1 mmHg compared to the 5 kg flat lift. To put this into perspective, SBP is shown to increase with ± 8 mmHg when administering 200-300 mg of caffeine[36] and Silke et al. found that using β blockers reduced the SBP increase during carrying a suitcase of 10 kg at 0.89 m/s with 15 mmHg compared to carrying without β blockers[2].

Additionally, this research shows that lifting increases SBP more than lowering with the same weights. Therefore lowering an infant is preferred over lifting an infant for people with Marfan Syndrome. Interestingly, lowering showed minimal difference in SBP response across all the conditions, implying that once a Marfan Syndrome patient is holding the infant lowering should pose no cardiovascular risk. When comparing the stoop lift and flat lift it is suggested to prefer the flat lift (Figure 1.1b), which (luckily for people with Marfan Syndrome) coincides with advise to prevent chronic lower back pain[1, 10], since the SBP has a smaller increase compared to the stoop lift for all loads. Future research is needed to prove these suggestions. Another interesting finding is that carrying has a slightly lower SBP increase for the flat lift compared to the stoop lift for all 3 the weights, however these results have a large p-value (Table 5.3).

For lifting itself there were relevant differences between lifting without load and with increased load, although not statistically significant in this research. Therefore the load during lifting should be minimized[22]. Interestingly, there seemed to be a small difference (stoop +12.9 mmHg, flat +2.1 mmHg) between lifting 5 kg and lifting 10 kg. Since this difference is not statistically significant, future research will clarify this difference. Should this difference hold true, then an increase of only 2.1 mmHg from 5 to 10 kg is a tremendously small argument to permanently restrict the ability of Marfan Syndrome patients to interact with infants. Which, consequently, reduces the quality of life of both the parent and the infant[13].

The experiment in this research used 0 kg, 5 kg & 10 kg as loads, used a treadmill for 5 minutes and took healthy men and women aged 24-28 years old with an average weight of 74.9 kg. The research by Daneshmandi et al. used body weight equivalent loads[14]. Two other major differences between this research and the research by Daneshmandi et al. is that they used adolescent boys (age (SD): 12.53 (0.5) years), they carried a load for 15 minutes and measured the SBP after 18 minutes (after 3 minutes of rest). Should the two researches be deemed comparable they had conflicting results. Daneshmandi et al. found that carrying an 8% body weight backpack did not increase SBP significantly and 10.5% body weight did (Figure 1.2b). While no significant changes were expected between carrying 0 kg and 5 kg loads, this research interestingly found significant increases in SBP when carrying 5 kg and 10 kg loads (equivalent to ≈6.7% and ≈13.3% body weight respectively). Implying that the proposed *BP carrying limit* is not valid in this case.

Similarly to Daneshmandi et al., a study by Mbada et al. measured the SBP after a 3-5 minutes rest period. Where this research compared the SBP after the start of the activity to the SBP just before the end of the activity to more accurately display its progression (Figure 5.1b). In another research, Bhambhani et al. compared carrying 15 kg to carrying 20 kg using a similar subject group compared to this study, except they used only men[15]. Comparable to this research, they found no significant differences between the SBP when the load was increased with 5 kg.

An interesting future research would be to see how taking care of a infant would experience *the physical activity paradox*. To analyse if taking care of a infant would constitute as OPA or LTPA, therefor be detrimental or beneficial for cardiovascular health.

This experiment only begets more curiosities about the possibilities with Marfan Syndrome: how does the circulatory response change with age and sex, since BP levels are dependant on age and sex[37]? What about different lifting techniques; for example lifting from a table or being handed your infant (since lowering increases SBP less than lifting)? What about different weights or body weight equivalent weights? How does the speed of lifting affect the circulatory response? What about different levels of physical activity or BMI in the subjects? *"These are all things that are not clearly defined in literature regarding Marfan Syndrome, which leaves practitioners to rely on expert guessing instead of evidence based advise."* was mentioned by Dr. R. M. Kauling, cardiologist and head of the Marfan department in the Erasmus Medical Centre in Rotterdam, during an interview. He continues with mentioning that studies like these are *"hyper-relevant"* for people with Marfan Syndrome or other heart diseases. Studies should be more focused on the **living with** heart disease, with day to day activities. Additionally, he reiterates that currently people that are diagnosed with Marfan Syndrome are recommended to lift a maximum of 5 kg, which imposes a comprehensive limitation on everyday life. However this recommendation is based on general Marfan Syndrome expertise and is not based on evidence, nor differentiated for different sexes, ages, levels of physical activity or BMI. Studies like this one provide more insight into these issues.

Dr. Kauling goes on to say: *"Unfortunately, the results of these studies with healthy people should be treated with caution, since the results could not be completely transferable to people with heart disease."* Implying that there is a need for future research like this research using Marfan Syndrome subjects.

6.3 Conclusion

In this research, there were small (statistically insignificant) differences for SBP for lifting and carrying a 10 kg compared to a 5 kg infant. However, there was an indication that SBP increases during lifting and carrying for increased loads. There was no significant difference between any lifting conditions nor was there a significant difference between lowering conditions. Conversely, carrying showed significant differences between the 0 kg and 5 kg as well as between the 0 kg and 10 kg conditions. There was an indication that the flat lifting technique is preferable over the stoop lifting technique due to a lower SBP during lifting and carrying. Further research is needed to prove the indicated differences.

6.4 Limitations

First and foremost, a major limitation when monitoring BP was the location of the sensor. For Marfan Syndrome patients it is paramount to monitor aortic SBP to prevent possible dilation in the aortic root. This irreversible dilation can lead to likely fatal aortic rupture. This research used the left brachial SBP as a surrogate for the aortic SBP (section 2.2), since the experiment required an ABPM device. Although brachial SBP gives an estimation of the aortic SBP[27] it is not the same. Aortic BP measurements are preferred. Future research could use a GTF for their specific subject group or could use an invasive BP monitoring method.

Secondly, there was no dietary restriction posed on caffeine before the experiment. SBP is shown to increase with ± 8 mmHg when administering 200-300 mg of caffeine[36]. This limitation can easily be overcome by requiring the subject to refrain from drinking coffee before the experiment. Additionally, it is possible that the subjects experienced the white coat effect. The white coat effect is where the subject have increased BP in case of medical settings[38]. To prevent this, the experiment should be done with an ABPM device that is invisible to the subjects and the subjects should not actively know that they are being monitored[19].

Thirdly, the subject of this experiment were healthy adults, which will likely give different results to adults with Marfan Syndrome, as mentioned by Dr. Kauling. To find results that are applicable to Marfan Syndrome patients this experiment should be recreated with Marfan Syndrome patients. The amount of subjects needed can be found in section 6.4.1

A limitation of this research lies in the data analysis, where the data was augmented to remove outliers and resample the data. Some information, however small, was lost. For more details see 4.2.

Another limitation is that the pulmonary response of the patients was not monitored during the experiment. Holding your breath can induce pressure in the thorax and reduces the preload to the heart. This reduction in preload triggers the baroreflex and other compensatory reflexes which influence the BP. To analyse this effect scientist often use the Valsalva Maneuver which mimics for example blowing up a balloon or playing saxophone[39]. The 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease mentions that the Valsalva maneuver should be avoided, since it can induce acute increases in SBP to >300 mmHg[5]. This limitation can be overcome using a manometer and properly instructing the subjects.

Measuring the BP in your finger while performing an action using your hands and arms should also be mitigated. The BP spiked when the hand was squeezed and crashed when the tension was released. This phenomenon can be seen in Figure 6.1 where the author squeezed and released a tabletop with his hand for one minute (from minute 4 to 5), then had 1 minute of rest, and then again did one minute of on and off squeezing. These rapid spikes can influence the results gravely, when one participant squeezes and another does not squeeze their hand when lifting a certain weight. A way to prevent this is to use an alternative ABPM device. Measuring BP during activities is not trivial with current non invasive ambulatory techniques, because most cuffing method require a stationary position of the subject during the measurement. Only an intra-arterial method coupled to a Holter technique or a telemetering system can provide BP measurements in unrestricted subjects[9]. Future research should focus on finding noninvasive methods to measure BP in ambulatory situations[4] without using the UE.

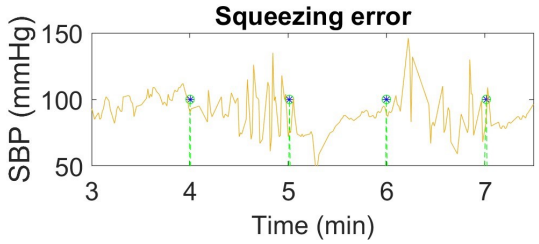


Figure 6.1: Fluctuations due to squeezing. one minute of on and off squeezing, one minute of rest and then again a minute of on and off squeezing.

Additionally, some subjects reported an unpleasant experience when carrying the 10 kg doll in combination with the arm cuff of the Finapres. Changing hold was not permitted since this would influence the measurement. Meanwhile, the blood was cut off to the majority weight lifting left arm during inflation of the arm cuff (calibration). The left arm was selected to be the majority weight lifting arm since the finger module was on the right index finger, which was prone to fluctuations due to applied pressure, see Figure 6.1.

6.4.1 Power analysis

The major limitation of this research was that no statistical differences were found between the different conditions, therefor a power analysis was performed for the peak lifting SBP by looking at Table 5.2 for the standard deviation and at Table 5.3 for the effect size. The results of this analysis will provide the amount of subjects needed to have statistical power should this experiment be replicated. Assuming $\alpha = 0.05$, the power = 0.9. The results are in Figure 6.2.

- **0 kg vs 5 kg:** To detect a significant difference between 0 kg and 5 kg for stoop lift (assuming a standard deviation of 56.7 mmHg and an effect size of 44 mmHg), **18** subjects would be required. Similarly, for the flat lift (with a standard deviation of 37.8 mmHg and an effect size of 41.1 mmHg), **9** subjects would be needed.
- **0 kg vs 10 kg:** When comparing 0 kg and 10 kg for stoop lift (with a standard deviation of 77.6 mmHg and an effect size of 56.9 mmHg), **20** subjects would be necessary. For the flat lift (assuming a standard deviation of 43.6 mmHg and an effect size of 43.2 mmHg), **11** subjects would be needed.
- **5 kg vs 10 kg:** To detect the difference between 5 kg and 10 kg for stoop lift (with a standard deviation of 77.6 mmHg and an effect size of 12.9 mmHg), **384** subjects would be required. For the difference between 5 kg and 10 kg flat lift (with a standard deviation of 77.6 mmHg and an effect size of 2.1 mmHg), **15057** subjects would be needed.
- **Stoop vs Flat:** For stoop (0 kg) and flat (0 kg) lifting techniques, assuming a standard deviation of 36.0 mmHg and an effect size of 5.9 mmHg, **398** subjects would be required. In the indicative experiment, the difference between stoop (10 kg) and flat (10 kg) lifting techniques was found to be 20.6 mmHg. Assuming a standard deviation of 77.6 mmHg and an effect size of 20 mmHg, **159** subjects would be needed to detect this difference.

When comparing carrying: The difference between stoop (10 kg) and flat (10 kg) is 6.3 mmHg. Assuming a Std of 11.2 mmHg and an effect size of 6 mmHg gives: **38** subjects. Comparing Stoop (5 kg) to Stoop (10 kg): Assuming a Std of 11.5 mmHg and an effect size of 6.8 mmHg gives: **31** subjects. Finally, comparing flat (5 kg) to flat (10 kg): Assuming a Std of 8.2 mmHg and an effect size of 2.1 mmHg gives: **175** subjects.

Furthermore, it is recommend to include more subjects than strictly necessary or do multiple repetitions per subject when working with the Finapres, as the missing data might make your data unusable.

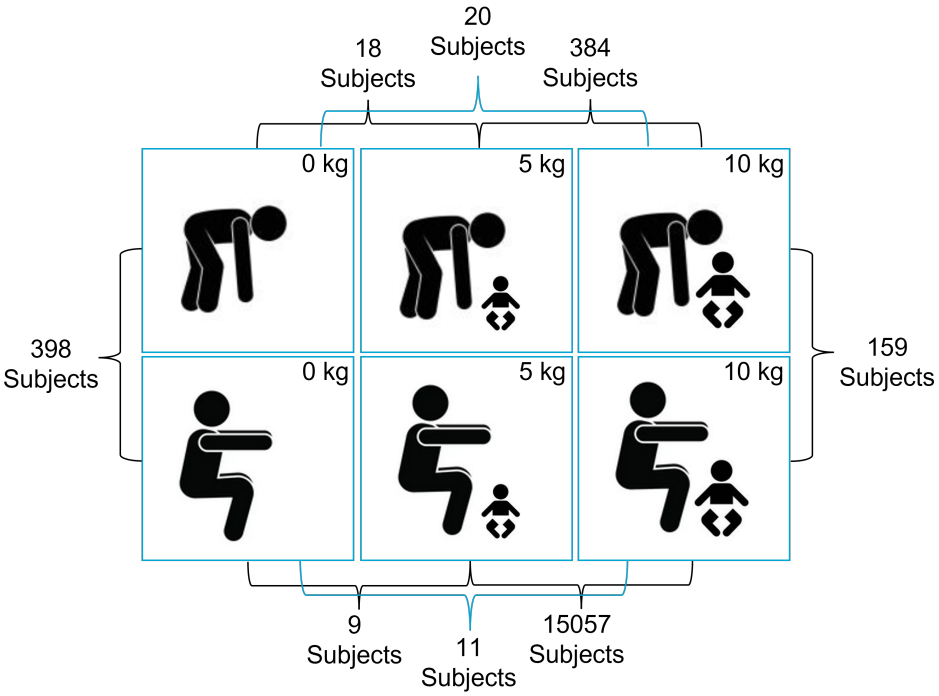


Figure 6.2: Showing the amount of subjects that would be necessary to find statistically significant differences for the peak lifting SBP, based on the results of this indicative study. The top row show the stoop lift and the bottom shows the flat lift. From left to right it is 0 kg, 5 kg and 10 kg. Stoop 0 kg - 5 kg: 18 subjects, stoop 0 kg - 10 kg: 20 subjects, stoop 5 kg - 10 kg: 384 subjects, stoop (0 kg) - flat (0 kg): 398 subjects, stoop (10 kg) - flat (10 kg): 159 subjects, flat 0 kg - 5 kg: 9 subjects, flat 0 kg - 10 kg: 11 subjects, flat 5 kg - 10 kg: 15057 subjects.

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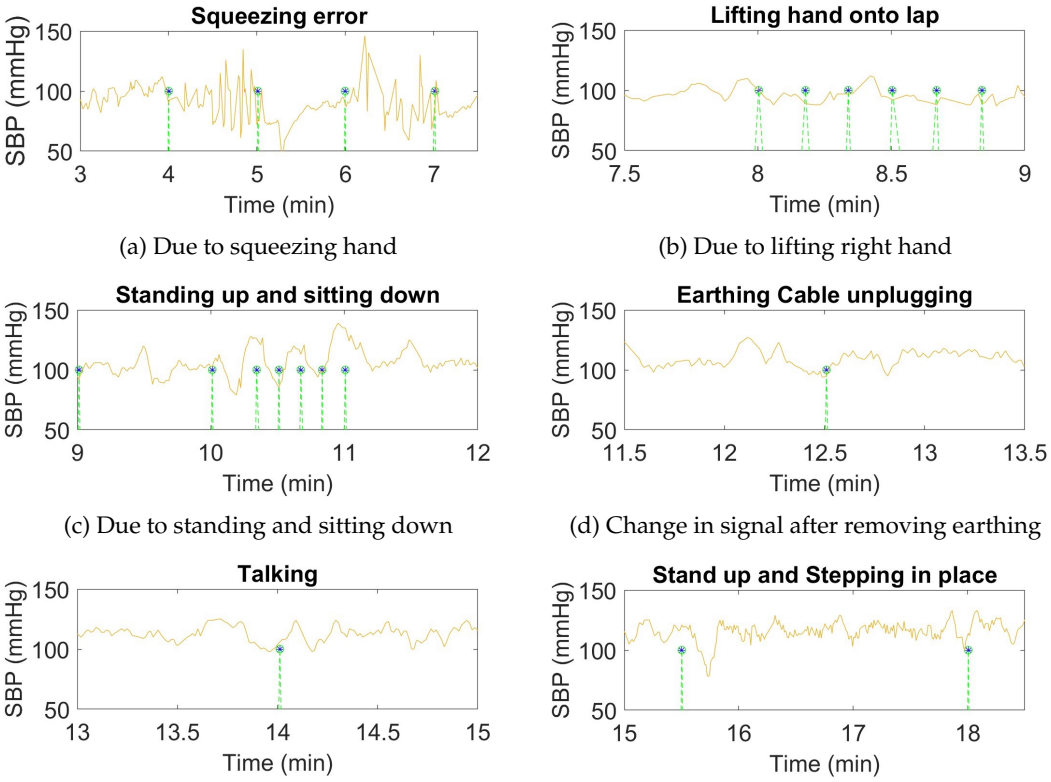
A1 | Appendix 1 - Data fluctuations

Different maneuvers were tested to see if the Finapres presented undesired fluctuations. Firstly, the muscles in the hand are tensed while lifting using the hand. The flexion puts pressure on the vessels in the hand and increase the BP. Consequently, subjects that squeezed the infant doll during the experiment likely had different results to those that did not squeeze the infant doll, as be seen in Figure A1.1a. Secondly, lifting the hand with the sensor onto the lap while sitting down resulted on a small fluctuation in the reading (Figure A1.1b). The height correction unit that was connected to the sternum of the subjects helped with minimizing these fluctuations. Thirdly, the effect of standing up and sitting down was determined by sitting and standing up every 10 seconds for a whole minute (Figure A1.1c). Fourthly, since there was not earthing connection at the experiment location the additional earthing cable only was connected to the metallic cart on which the Finapres was mounted and not to a wall mounted ground connection. The Finapres was tested with its usual correct grounding in Figure A1.1a, A1.1b & A1.1c and was disconnected in Figure A1.1d. Figure A1.1e & A1.1f were executed with the disconnected earthing cable. The difference was not noticeable and the fluctuations in the signal were due to standing up and sitting down at minute 12 and just before minute 13 respectively. Then, the influence of talking (while seated) was tested in Figure A1.1e. Subject were discouraged to talk during the experiment, but it as allowed and did happen. Lastly, standing up and stepping in place (stepping without going forward) was tested and showed a more frantic signal compared to resting like in Figure A1.1e.



(a) Due to squeezing hand

(b) Due to lifting right hand

(c) Due to standing and sitting down

(d) Change in signal after removing earthing

(e) Due to talking

(f) Due to stepping on place

Figure A1.1: Fluctuations in the raw (removed missing) data of the Finapres. Events are indicated in green.

A2 | Appendix 2 - Code Explained

The Matlab code is displayed an explained in this chapter. The Flowchart in Figure A2.1 serves as visual aid in understanding the structure of the code.

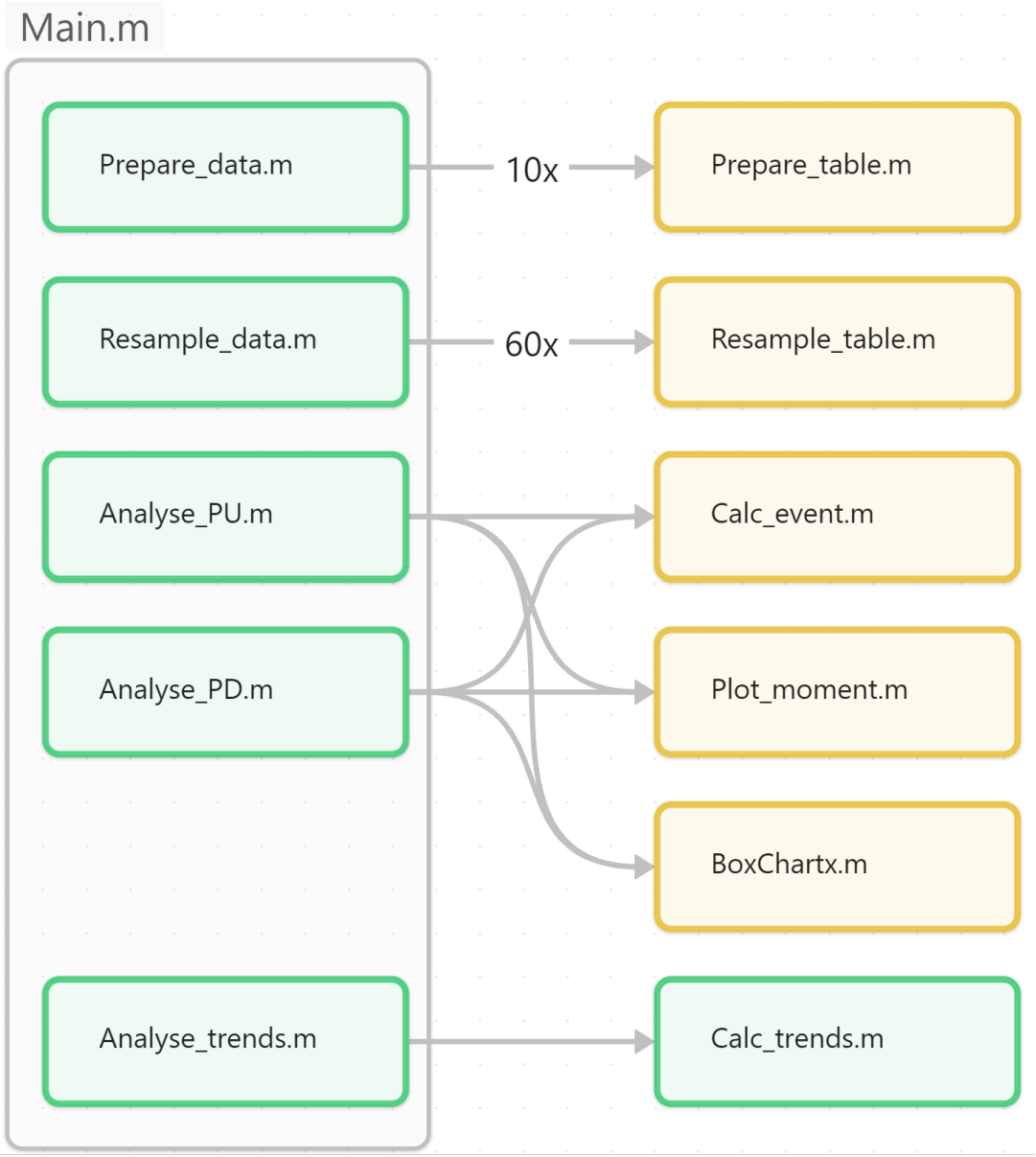


Figure A2.1: Code flowchart, Lifting is referred to as PU(Pick up), and lowering is referred to as PD(Put down), The green boxes are scripts and the yellow boxes are functions.

A2.1 Main.m

Main.m executes the whole code and calls all the other scripts. Additionally here the global variables fs(sampling frequency), ColumnName (the column of interest: SBP or MAP) and XPU & XPD (ranges used in plots for PU and PD) are defined.

```
% Main file
clear; % clear the workspace

%% Import and prepare data
Prepare_data;
%% subject info
Subject_info;
%% Resample data
fs = 2; % Select sampling frequency
Resample_data;

%% Specify what BP will be analysed
columnName = 'reSYS_mmHg_'; % Specify the column name that will be analysed
if columnName == 'reMAP_mmHg_'
    columnNameTitle = 'MAP';
else columnNameTitle = 'SBP';
end

%% Analyse phenomenon Pick up and Put down
XPU = [0 2]; % pick up moment for plots only
XPD = [5 8]; % put down moment for plots only
Analyse_PU; % includes scripts that can plot the PU moments
Analyse_PD; % includes scripts that can plot the PD moments

%% Analyse trends
Analyse_trends;

%% Plot different Situations
%Plott()
%PlotRawVsFiltered
%PlotRawVsShortMissingRemoved;
%PlotDifreMAPVsfiMAP: % Dif between reMAP and fiMAP
%Plot_errors; % Plot the measurement of errors (subject 0)
%Plot_example
%PlotSampletimeVsSysdif;
%PlotFFT(S1C1.reSYS_mmHg_, fs) % FFT, used to check for aliasing

%%
t_test;
Power_analysis;
```

A2.2 Prepare_data.m

After Prepare_data.m all the experimental data is loaded into the Matlab workspace. The Subjects have their complete data stored in a table according to their number, for example S1. Then the data is split into the different conditions and put into their own table, for example S1C1.

```
%% Load in the experimental data
S1 = Prepare_table("S1_2024-02-12_09.06.39 Basic Nova.csv");
S2 = Prepare_table("S2_2024-02-12_10.41.25 Basic Nova.csv");
S3 = Prepare_table("S3_2024-02-12_12.51.44 Basic Nova.csv");
S4 = Prepare_table("S4_2024-02-12_14.08.18 Basic Nova.csv");
S5 = Prepare_table("S5_2024-02-12_16.04.40 Basic Nova.csv");
S6 = Prepare_table("S6_2024-02-19_09.15.11 Basic Nova.csv");
S7 = Prepare_table("S7_2024-02-19_10.39.25 Basic Nova.csv");
S8 = Prepare_table("S8_2024-02-19_12.38.18 Basic Nova.csv");
S9 = Prepare_table("S9_2024-02-19_14.06.35_1 Basic Nova.csv");
S10 = Prepare_table("S10_2024-02-19_16.03.57 Basic Nova.csv");
%% Create conditions
num_conditions = 6; % Define the number of conditions

for subj = 1:10 % Loop over subjects from 1 to 10
    % Load data for the current subject
    subject_data = eval(sprintf('S%d', subj)); % Extract data for the current subject
```

```
18
19      for cond = 1:num_conditions % Loop over conditions for each subject
20          % Extract data for the current condition
21          condition_data = subject_data(subject_data.(['c', num2str(cond), '_bool']) > 0,
    :);
22          % Calculate t0 (time difference from the start)
23          condition_data.t0 = condition_data.Time_min_ - condition_data.Time_min_(1); %
    start at 0
24
25          % Assign the data for the current condition to a new variable
26          eval(sprintf('S%dC%d = condition_data;', subj, cond)); % Create variables like
    S1C1, S1C2, etc.
27      end
28  end
29
30  % Clear temporary variables
31  clear num_conditions cond subject_data condition_data;
```

A2.2.1 Prepare_table.m

Prepare_data.m uses Prepare_table.m to prepare the individual tables. This means: removing missing, removing short samples and creating boolean arrays that help indicate the different conditions. These boolean arrays are used in Prepare_data.m to create the different tables consisting of only the selected condition.

- C1 = SL1: Weight of 0 kg (Control); Stoop lift, walking(5 min), lowering and rest
- C2 = FL2: Weight of 0 kg (Control); Flat lift, walking(5 min), lowering and rest
- C3 = SL5: Weight of 5 kg; Stoop lift, walking(5 min), lowering and rest
- C4 = FL5: Weight of 5 kg; Flat lift, walking(5 min), lowering and rest
- C5 = SL10: Weight of 10 kg; Stoop lift, walking(5 min), lowering and rest
- C6 = SL10: Weight of 10 kg; Flat lift, walking(5 min), lowering and rest

```
1  %% First prepare the data in Excel
2  % Delete the top information and split the data of the semicolons using Excel.
3  % find and replace in Excel: SM1 Skipped; SM2: 'Stand up' to Pick up
4  % find and replace in Excel: SM2 Skipped; SM3: 'Lie down' to Put down
5  % find and replace in Excel: "Stand test x" to the correct "Sty"
6  % ADD Columns 'Time(min)', Sampletime(sec), sysdif
7  function S = Prepare_table(title)
8  %% Then readout the data using readtable
9  %title = "S1_2024-02-12_09.06.39 Basic Nova.csv";
10 S = readtable(title);
11
12 % Remove rows where there are at least 4 values missing
13 S = rmmissing(S,"MinNumMissing",4);
14
15 % use only values where the sample time is large than the limit
16 S = S(S.Sampletime_sec_>0.5,:);
17 S.Sampletime_sec_ = [0; diff(S.Time_sec_)]; %recalibrate sampletime
18 S.MAPdif =[0; diff(S.reMAP_mmHg_)]; %recalibrate MAPdif
19 S.SYSdif =[0; diff(S.reSYS_mmHg_)]; %recalibrate SYSdif
20
21 %% Separate different conditions
22 PU = 'Pick up'; % the pick up happens
23 PD = 'Put down'; % the put down happens
24 S.PU_bool = strcmp(S.Marker, PU); % mark where pick up happens, rest is 0
25 S.PD_bool = strcmp(S.Marker, PD); % mark where put down happens, rest is 0
26
27 % Find different conditions, based on region and string
28 S.c1_bool = strcmp(S.Region, 'St1'); %Boolean that equals 1 when C1
29 S.c2_bool = strcmp(S.Region, 'St2'); %Boolean that equals 1 when C2
30 S.c3_bool = strcmp(S.Region, 'St3'); %Boolean that equals 1 when C3
31 S.c4_bool = strcmp(S.Region, 'St4'); %Boolean that equals 1 when C4
32 S.c5_bool = strcmp(S.Region, 'St5'); %Boolean that equals 1 when C5
33 S.c6_bool = strcmp(S.Region, 'St6'); %Boolean that equals 1 when C6
```

A2.3 Resample_data.m

After Resample_data all the previous tables are overwritten by a resampled version to have a sampling frequency of 2Hz. The sampling frequency(fs) is defined in Main.m, see A2.1. This way the data is usable for mathematical manipulations.

```
%% Experiment data
% Prepare_data has to be done before this script

% Define the number of conditions
num_conditions = 6;

% Loop over subjects from 1 to 10
for subj = 1:10
    % Loop over conditions for each subject
    for cond = 1:num_conditions
        % Load data for the current subject and condition
        subject_condition_data = eval(sprintf('S%dC%d', subj, cond));

        % Resample the table with the given sampling frequency (fs)
        subject_condition_data = Resample_table(subject_condition_data, fs);

        % Add Subject information
        subject_condition_data.Age = ones(height(subject_condition_data),1).*Subjectinfo
    .Age(subj);
        subject_condition_data.Height = ones(height(subject_condition_data),1).*
    Subjectinfo.Height(subj);
        subject_condition_data.Weight = ones(height(subject_condition_data),1).*
    Subjectinfo.Weight(subj);
        subject_condition_data.BMI = ones(height(subject_condition_data),1).*Subjectinfo
    .BMI(subj);
        subject_condition_data.Sex = ones(height(subject_condition_data),1).*Subjectinfo
    .Sex(subj);
        subject_condition_data.PA = ones(height(subject_condition_data),1).*Subjectinfo.
    PA(subj);

        % Assign the resampled data back to the corresponding variable
        eval(sprintf('S%dC%d = subject_condition_data;', subj, cond));
    end
end

% Clear temporary variables
clear num_conditions subj subject_condition_data cond;
```

A2.3.1 Resample_table.m

Resample_data.m uses Resample_table.m to resample the provided tables. This function also uses the fs (sampling frequency).

```
%% function that resamples the data of the given table
function S = Resample_table(ttable, fs)
%ttable = S5C;
%fs = 2; %sample frequency
p = 2; % upsampling factor
q = 1; % downsampling factor
%% resample SYS, MAP, DIA and HR
[reSYS_mmHg_,Time_sec_] = resample(ttable.reSYS_mmHg_,ttable.Time_sec_,fs,p,q);
[reMAP_mmHg_,Time_sec_] = resample(ttable.reMAP_mmHg_,ttable.Time_sec_,fs,p,q);
[reDIA_mmHg_,Time_sec_] = resample(ttable.reDIA_mmHg_,ttable.Time_sec_,fs,p,q);
[HRAP_bpm_,Time_sec_] = resample(ttable.HRAP_bpm_,ttable.Time_sec_,fs,p,q);

Time_min_ = Time_sec_/60;
t0 = Time_sec_- Time_sec_(1); %set t0 time to zero
%round the moment of Pick up and Put down
PU_sec = round(ttable.Time_sec_(ttable.PU_bool)- ttable.Time_sec_(1));
PD_sec = round(ttable.Time_sec_(ttable.PD_bool)- ttable.Time_sec_(1));
PU_bool = t0==PU_sec; %Create boolean array where pick up happens
PD_bool = t0==PD_sec; %create boolean array where put down happens
t0 = t0/60; %get t0 in minutes

% useful for plotting, Not needed
```

```
Sampletime_sec_ = [0; diff(Time_sec_)]; %recalibrate sampletime
SYSdif =[0; diff(reSYS_mmHg_)]; %recalibrate


% return S
S = table(Time_sec_, reSYS_mmHg_, reMAP_mmHg_, reDIA_mmHg_, HRAP_bpm_, Time_min_,
    PU_bool, PD_bool, t0, Sampletime_sec_, SYSdif);
```

A2.4 Analyse_PU.m

Analyse_PU.m uses Calc_event.m that analyses specific events using the columnName (eg MAP, SBP or DBP) and vectors that store the ranges (Baseline and Event) for all the events. The results are stored in appropriately named tables like C1PU for the Pick up moment of Condition 1. The eligible conditions can be plotted using the custom Plot_moment.m function(see A2.4.2).
Then the results of the analysis are plotted using custom BoxChart functions called BoxChart1.m and BoxChart2.m who plot the same data, but using a different layout. Additionally there are BoxChart1r.m and BoxChart2r.m which are functions that display the relative data, this is the absolute data divided by the baseline data.
This is done for the Pick up moments and the Put down moments.

```
%% Analyse_PU
%% Analyse the different PU Conditions MAP
%replaces C1PUaMAP
% Define custom baseline and pickup ranges for each subject
%columnName = 'reMAP_mmHg_'; % Specify the column name
baselineRanges = {{0.5, 1}, {0.5, 1}, {0.5, 1}, {0.5, 1}, {0.5, 1}, {0.5, 1}};
eventRanges = {{1, 1.5}, {1, 1.5}, {1.5, 2}, {1, 1.5}, {1, 1.5}, {1, 1.5}};
% Call the function with custom ranges
C1PU = Calc_event(fs, baselineRanges, eventRanges, columnName,1, S2C1, S4C1, S5C1, S7C1,
    S8C1, S9C1);
%Plot_moment(XPU, ' C1', '',S2C1, S4C1,S5C1, S7C1,S8C1, S9C1);
%Plot_moment(XPU, ' C1', '',columnName ,S1C1, S2C2, S3C1, S4C1,S5C1, S6C1,S7C1,S8C1,S9C1
    ,S10C1); %Plot all

%% C2PUaMAP
baselineRanges = {{0.5, 1.2}, {0.5, 1}, {0.5, 0.9}, {0.5, 0.9}, {0.5, 1}, {0.5, 1}};
eventRanges = {{1.2, 1.5}, {1, 1.4}, {0.9, 1.4}, {0.9, 1.1}, {1, 1.4}, {1, 1.4}};
% Call the function with custom ranges
C2PU = Calc_event(fs, baselineRanges, eventRanges, columnName, 2, S2C2, S5C1, S6C1, S7C1
    ,S8C1, S9C1);
%Plot_moment(XPU, ' Condition 2', ': Straight back with 0kg', columnName,S2C2, S5C2,S6C2
    , S7C2,S8C2, S9C2);

% C3PUaMAP; % for pickup analysis script
baselineRanges = {{0.5, 1}, {0.5, 1}, {0.5, 1.2}, {0.5, 0.8}, {0.5, 1}, {0.5, 1}};
eventRanges = {{1, 1.5}, {1, 1.5}, {1.2, 2}, {1, 1.5}, {1, 1.5}, {1, 1.5}};
% Call the function with custom ranges
C3PU = Calc_event(fs, baselineRanges, eventRanges, columnName, 3, S1C3, S2C3, S3C3, S4C3
    , S5C3, S8C3);
%Plot_moment(XPU, ' Condition 3', ': Straight legs with 5kg', columnName, S1C3, S2C3,
    S3C3, S4C3, S5C3, S8C3);

% C4PUaMAP; % for pickup analysis script
baselineRanges = {{0.5, 0.8}, {0.5, 1}, {0.7, 0.9}, {0.5, 0.9}, {0.9, 1}, {0.5, 0.9},
    {0.5, 0.8}};
eventRanges = {{0.8, 1.5}, {1, 1.5}, {0.7, 2}, {0.9, 1.5}, {0.9, 1.5}, {0.9, 1.5}, {0.8,
     1.5}};
% Call the function with custom ranges
C4PU = Calc_event(fs, baselineRanges, eventRanges, columnName, 4, S2C4, S3C4, S5C4, S7C3
    , S8C4, S9C4, S10C4);
%Plot_moment(XPU, ' C4', ': Straight back with 5kg', columnName, S2C4, S3C4, S5C4, S7C3,
     S8C4, S9C4, S10C4);

% C5PUaMAP; % for pickup analysis script
baselineRanges = {{0.5, 1.1}, {0.5, 1.5}, {0.5, 0.9}, {0.5, 0.9}, {0.5, 0.9}, {0.5, 1}};
eventRanges = {{1.1, 1.5}, {1.5, 2}, {0.9, 1.5}, {0.9, 1.5}, {0.9, 1.3}, {1, 1.5}};
% Call the function with custom ranges
C5PU = Calc_event(fs, baselineRanges, eventRanges, columnName, 5, S2C5, S3C5, S5C5, S6C5
    , S7C5, S8C5);
```

```
%Plot_moment(XPU, ' Condition 5', ': Straight legs with 10kg', columnName, S2C5, S3C5, S5C5, S6C5, S7C5, S8C5);


% C6PUaMAP; % for pickup analysis script
baselineRanges = {{0.5, 0.9}, {0.5, 1}, {0.5, 1.1}, {0.5, 1.2}, {1, 1.5}, {1, 1.5}};
eventRanges = {{0.9, 1.2}, {1, 1.5}, {1.1, 1.5}, {1.2, 1.5}, {1.5, 2}, {1.5, 1.7}};
% Call the function with custom ranges
C6PU = Calc_event(fs, baselineRanges, eventRanges, columnName, 6, S1C6, S2C6, S3C6, S4C6, S6C6, S7C6);
%Plot_moment(XPU, ' Condition 6', ': Straight legs with 10kg', columnName, S1C6, S2C6, S3C6, S4C6, S6C6, S7C6);

%% Plot Data
% BoxChart1({C1PU, C2PU, C3PU, C4PU, C5PU, C6PU}, 40,250, columnNameTitle); % create a BoxchartPU data
% %Set main title above the subplots
% sgtitle([columnNameTitle ' comparison during Pick up']);
%
BoxChart2({C1PU, C2PU, C3PU, C4PU, C5PU, C6PU}, 80,320, columnNameTitle); % create a BoxchartPU data
%Set main title above the subplots
%sgtitle([columnNameTitle ' comparison during Pick up']);
%
%% Relative data: This data has been normalized by the mean.
% % This means that a value of 1.5 = 1.5 x the baseline MAP of that row.
%
% BoxChart1r({C1PU, C2PU, C3PU, C4PU, C5PU, C6PU}, 0.3,2.5, columnNameTitle); % create a BoxchartPU data
% %Set main title above the subplots
% sgtitle('Relative 'columnNameTitle' comparison during Pick up')
%
% BoxChart2r({C1PU, C2PU, C3PU, C4PU, C5PU, C6PU}, 0.3,2.5, columnNameTitle); % create a BoxchartPU data
% % Set main title above the subplots
% sgtitle('Relative 'columnNameTitle' comparison during Pick up');
```

A2.4.1 Calc_event.m

This function calculates the Baseline, Peak, Lowest, Relative Peak and Relative Lowest value of the provided event, using the baseline and event range arguments. The event and baseline happen at inconsistent moments, therefor the range needs to be specified. This data is calculated for all the provided condition tables and returned in a table.

```
function rtable = Calc_event(fs, baselineRanges, EventRanges, columnName,numberCondition, varargin)
    % Define subjects
    subjects = varargin;

    % Initialize arrays
    nSubjects = numel(subjects);
    Baseline = zeros(nSubjects, 1);
    Peak = zeros(nSubjects, 1);
    Lowest = zeros(nSubjects, 1);
    RelativePeak = zeros(nSubjects, 1);
    RelativeLowest = zeros(nSubjects, 1);
    Age = zeros(nSubjects, 1);
    Height = zeros(nSubjects, 1);
    Weight = zeros(nSubjects, 1);
    BMI = zeros(nSubjects, 1);
    Sex = zeros(nSubjects, 1);
    PA = zeros(nSubjects, 1);
    Condition = numberCondition .* ones(nSubjects, 1); % All subjects have the same condition

    % Calculate values for each subject
    for i = 1:nSubjects
        % Extract subject data
        subject = subjects{i};

        % Extract baseline and pickup ranges for the current subject
```

```
        baselineRange = baselineRanges{i};
        eventRange = EventRanges{i};

        % Calculate baseline mean
        Baseline(i) = mean(subject.(columnName)(baselineRange{1}.*60.*fs:baselineRange{2}.*60.*fs));

        % Calculate peak
        Peak(i) = max(subject.(columnName)(eventRange{1}.*60.*fs:eventRange{2}.*60.*fs));

        % Calculate lowest
        Lowest(i) = min(subject.(columnName)(eventRange{1}.*60.*fs:eventRange{2}.*60.*fs));

        % Calculate relative peak (peak divided by baseline)
        RelativePeak(i) = Peak(i) / Baseline(i);

        % Calculate relative lowest (lowest divided by baseline)
        RelativeLowest(i) = Lowest(i) / Baseline(i);

        % Add subject details
        Age(i) = subject.Age(1);
        Height(i) = subject.Height(1);
        Weight(i) = subject.Weight(1);
        BMI(i) = subject.BMI(1);
        Sex(i) = subject.Sex(1);
        PA(i) = subject.PA(1);
    end

    % Create table
    rtable = table(subjects', Baseline, Peak, Lowest, RelativePeak, RelativeLowest, Condition, Age, Height, Weight, BMI, Sex);
end
```

A2.4.2 Plot_moment.m

This function is used to plot a specific timeframe of the provided condition tables. Additionally the title of the subfigures is given as an input argument. This function is mostly used, and tailored for, Analysis in Analyse_PU.m or Analyse_PD.m but is also used in some other occasions. The function uses a for loop to interate through the provided tables and plot the columnName data as well as the PU and PD markers, within the desired x-axis limit.

```
function Plot_moment(xlim_range, subtitle, append_text, columnName, varargin)
    % varargin is a cell array containing the tables
    columnNameTitle = columnName(3:5);
    % Find the number of tables that are passed
    num_tables = nargin - 4; % Subtract 4 for xlim_range, subtitle, append_text, and columnName

    % Create a figure with tiled layout
    figure;
    tiledlayout(2, ceil(num_tables/2));

    % Plot for each table
    for i = 1:num_tables
        nexttile;
        eligible_data = varargin{i}; % Extract subject data from input
        plot(eligible_data.t0, eligible_data.PU_bool .* 100, 'b--*', ...
             eligible_data.t0, eligible_data.PD_bool .* 100, 'g--o', ...
             eligible_data.t0, eligible_data.(columnName));
        title(['S' num2str(i) subtitle append_text]);
        xlabel('Time(min)');
        ylabel([columnNameTitle ' (mmHg)']);
        xlim(xlim_range);
        %legend({'Pick up', 'Put down', ['Subject' num2str(i)]}, 'Location', 'southwest');
    end

    % Adjust the layout
    fontsize(18, 'points');
```

```
end
```

A2.4.3 BoxChart2.m

This custom function is used to create a boxchart on the provided data. The fontsize and the limit of the y-axis are hardcoded into the functions. They use a for loop to iterate through all the data.

```
function BoxChart2(Data,yMin,yMax, columnNameTitle)
    datasets = Data;

    % Initialize arrays to store all pressure data and group labels
    allMeanPressure = [];
    allMaxPressure = [];
    allMinPressure = [];
    groupLabels = [];

    % Define the new x-axis labels
    xLabels = {'SL0', 'FL0', 'SL5', 'FL5', 'SL10', 'FL10'};

    % Concatenate pressure data from all datasets
    for i = 1:length(datasets)
        allMeanPressure = [allMeanPressure; datasets{i}.Baseline];
        allMaxPressure = [allMaxPressure; datasets{i}.Peak];
        allMinPressure = [allMinPressure; datasets{i}.Lowest];
        % Add group labels based on the new x-axis labels
        groupLabels = [groupLabels; repmat(xLabels(i), numel(datasets{i}.Baseline), 1)];
    end

    % Define font size
    fontSize = 16;

    % Create a new figure
    figure;

    % Create subplot for Mean Pressure
    subplot(1, 2, 1, 'Position', [0.1, 0.1, 0.4, 0.8]); % Adjust the position property
    boxplot(allMeanPressure, groupLabels, 'Widths', 0.5);
    ylabel(['Baseline ' columnNameTitle ' (mmHg)']);
    ylim([yMin, yMax]);
    %xlabel('Condition');
    set(gca, 'XTickLabel', xLabels, 'FontSize', fontSize); % Set x-axis labels and font
    size
    set(gca, 'FontSize', fontSize); % Set y-axis font size

    % Create subplot for Max Pressure
    subplot(1, 2, 2, 'Position', [0.55, 0.1, 0.4, 0.8]); % Adjust the position property
    boxplot(allMaxPressure, groupLabels, 'Widths', 0.5);
    ylabel(['Peak ' columnNameTitle ' (mmHg)']);
    ylim([yMin, yMax]);
    %xlabel('Condition');
    set(gca, 'XTickLabel', xLabels, 'FontSize', fontSize); % Set x-axis labels and font
    size
    set(gca, 'FontSize', fontSize); % Set y-axis font size

    % Adjust the layout to avoid overlap
    %tightfig;
end
```

A2.5 Analyse_trends.m

Analyse_trends.m calculates the columnName data just after the Pick up moment happens(Start) and the subject starts walking on the treadmill and the MAP just before the Put down moment(End). This way the effect of walking with a weighted load can be observed. The data is stored in tables corresponding to their condition(eg C1trend). These calculations are done inside the Calc_trends.m file and then the non-eligible data is removed. Then the data is plotted using a custom boxplot.

```
%% Analyse trends
%% Calculate the trends based on columnName (MAP or SYS)
Calc_trends;
```

```
4
5
6  %% plot the trends and take out the non eligible
7  %Plot_moment([0 8], ' C1', ': Straight legs with 0kg', columnName,S1C1,S2C1,S3C1,S4C1,
       S5C1,S6C1,S7C1,S8C1,S9C1,S10C1);
8  % fontsize(15, 'points'); % Adjust the layout of plot
9
10 % delete rows that are not eligible
11 C1trend(10,:) = []; %delete row 10
12 C1trend(7,:) = []; %delete row 7
13
14 %% plot the trends and take out the non eligible
15 %Plot_moment([0 8], ' C2', ': Straight back with 0kg', columnName,S1C2,S2C2,S3C2,S4C2,
       S5C2,S6C2,S7C2,S8C2,S9C2,S10C2);
16 % fontsize(15, 'points'); % Adjust the layout of plot
17
18 % delete rows that are not eligible
19 C2trend(10,:) = []; %delete row 10
20 C2trend(7,:) = []; %delete row 7
21 C2trend(1,:) = []; %delete row 1
22
23 %% plot the trends and take out the non eligible
24 % Plot_moment([0 8], ' C3', ': Straight legs with 5kg', columnName,S1C3,S2C3,S3C3,S4C3,
       S5C3,S6C3,S7C3,S8C3,S9C3,S10C3);
25 % fontsize(15, 'points'); % Adjust the layout of plot
26
27 % delete rows that are not eligible
28 C3trend(10,:) = []; %delete row 10
29 C3trend(9,:) = []; %delete row 9
30 C3trend(6,:) = []; %delete row 6
31 C3trend(5,:) = []; %delete row 5
32
33 %% plot the trends and take out the non eligible
34 % Plot_moment([0 8], ' C4', ': Straight back with 5kg', columnName,S1C4,S2C4,S3C4,S4C4,
       S5C4,S6C4,S7C4,S8C4,S9C4,S10C4);
35 % fontsize(15, 'points'); % Adjust the layout of plot
36
37 % delete rows that are not eligible
38 C4trend(10,:) = []; %delete row 10
39 C4trend(9,:) = []; %delete row 9
40 C4trend(7,:) = []; %delete row 7
41 C4trend(6,:) = []; %delete row 6
42 C4trend(5,:) = []; %delete row 5
43 C4trend(1,:) = []; %delete row 1
44
45 %% plot the trends and take out the non eligible
46 % Plot_moment([0 8], ' C5', ': Straight legs with 10kg', columnName,S1C5,S2C5,S3C5,S4C5,
       S5C5,S6C5,S7C5,S8C5,S9C5,S10C5);
47 %fontsize(15, 'points'); % Adjust the layout of plot
48
49 % delete rows that are not eligible
50 C5trend(10,:) = []; %delete row 10
51 C5trend(9,:) = []; %delete row 9
52 C5trend(8,:) = []; %delete row 8
53 C5trend(6,:) = []; %delete row 6
54 C5trend(2,:) = []; %delete row 2
55 C5trend(1,:) = []; %delete row 1
56
57 %% plot the trends and take out the non eligible
58 %Plot_moment([0 8], ' C6', ': Straight back with 10kg', columnName,S1C6,S2C6,S3C6,S4C6,
       S5C6,S6C6,S7C6,S8C6,S9C6,S10C6);
59 % fontsize(15, 'points'); % Adjust the layout of plot
60
61 % delete rows that are not eligible
62 C6trend(10,:) = []; %delete row 10
63 C6trend(8,:) = []; %delete row 8
64 C6trend(7,:) = []; %delete row 7
65 C6trend(4,:) = []; %delete row 4
66 C6trend(1,:) = []; %delete row 1
67
68 %% plot
69 datasets = {C1trend, C2trend, C3trend, C4trend, C5trend, C6trend};
70
```

```
% Define the x-axis labels
xLabels = {'SL0', 'FL0', 'SL5', 'FL5', 'SL10', 'FL10'};

% Initialize arrays to store all pressure data and group labels
allEndr = [];
groupLabels = [];

% Concatenate data from all datasets
for i = 1:length(datasets)
   allEndr = [allEndr; datasets{i}.Diff];
   groupLabels = [groupLabels; repmat(i, numel(datasets{i}.Subjects), 1)];
end

% Define y-axis limits
yMin = 0.8;
yMax = 1.4;
fontSize = 18;

% Create a new figure
figure;

% Create boxplot
boxplot(allEndr, groupLabels, 'Widths', 0.5);
ylabel(['Relative ' columnNameTitle ' at end'], 'FontSize', fontSize);
%ylim([yMin, yMax]);
%xlabel('Condition', 'FontSize', fontSize);
set(gca, 'XTickLabel', xLabels, 'FontSize', fontSize); % Set x-axis labels and font size


%% Plot all conditions separately
% Define condition labels
conditionLabels = {'SL0', 'FL0', 'SL5', 'FL5', 'SL10', 'FL10'};

% Create a new figure
figure;

% Define the width of each subplot
subplotWidth = 0.4;

for i = 1:length(conditionLabels)
    % Extract data for the current condition
    data = eval(['C' num2str(i) 'trend']);
    Start = data.Start;
    End = data.End;

    % Calculate the number of data points
    numPoints = length(Start);

    % Define x-coordinates for Start and End
    xStart = (i-1)*2 + ones(size(Start));
    xEnd = (i-1)*2 + 2 * ones(size(End));

    % Plot Start data
    scatter(xStart, Start, 'b', 'filled');
    hold on;

    % Plot End data
    scatter(xEnd, End, 'r', 'filled');

    % Connect Start and End data
    for j = 1:numPoints
        line([xStart(j), xEnd(j)], [Start(j), End(j)], 'Color', 'k');
    end
end

% Set x-axis ticks and labels
xticks(1:2:length(conditionLabels)*2);
xticklabels(conditionLabels);
set(gca, 'FontSize', fontSize); % Set x-axis font size

% Set labels and title
ylabel(['Carrying ' columnNameTitle ' (mmHg)'], 'FontSize', fontSize);

```

```
% Add legend
legend({'Start', 'End'}, 'Location', 'best');

% Set grid
%grid on;

% Set xlim to show all conditions
xlim([0, length(conditionLabels)*2 + 1]);

% Clear
clear datasets allEndr groupLabels i yMin yMax

%% Plot example
% eligible_data = S3C3;
% plot(eligible_data.t0, eligible_data.PU_bool .* 120, 'b--*', ...
%              eligible_data.t0, eligible_data.PD_bool .* 120, 'g--o', ...
%              eligible_data.t0, eligible_data.(columnName), ...
%              (2:0.01:3)', ones(101,1).*C3trend.Start(3),'b', ...
%              (4.5:0.01:5.5)', ones(101,1).*C3trend.End(3),'r');
%         %title('');
%  xlabel('Time (minutes)');
%  ylabel([columnNameTitle ' (mmHg)']);
%  ylim([100 220]);
%  xlim([0 10]);
%  legend({'Lifting', 'Lowering', 'Data', 'Start', 'End'}, 'Location', 'best');
```

Analyse_trends.m uses Calc_trends.m to calculate the trends and put them in their correct table.

A2.6 Calc_trends.m

```
%% calculate the trends an their increase
% Define conditions
num_conditions = 6;

% Define Startlim and endlim before the loop
Startlim = 2 * 60 * fs : 3 * 60 * fs;
Endlim = 4.5 * 60 * fs : 5.5 * 60 * fs;

% Loop through each condition
for condition = 1:num_conditions
    % Define Subjects for the current condition
    Subjects = compose("S%dC%d", (1:10)', condition * ones(10, 1));

    % Initialize arrays to store Start, End and Endr values
    Start = zeros(numel(Subjects), 1);
    End = zeros(numel(Subjects), 1);
    Endr = zeros(numel(Subjects), 1);
    Diff = zeros(numel(Subjects), 1);

    % Show condition
    Condition = ones(numel(Subjects), 1) * condition;

    % Check if each subject has sufficient data
    for i = 1:numel(Subjects)
        if length(eval(Subjects(i) + "." + columnName)) > max(Endlim)
            Start(i) = mean(eval(Subjects(i) + "." + columnName + "(Startlim)"));
            End(i) = mean(eval(Subjects(i) + "." + columnName + "(Endlim)"));
            Endr(i) = End(i) ./ Start(i);
            Diff(i) = End(i) - Start(i);
        end
    end

    % Put it in a table
    eval(['C', num2str(condition), 'trend = table(Subjects, Start, End, Condition, Endr,
     Diff);']);
end

% Clear temporary variables
clear Subjects Start End Endr Diff Condition condition i;
```

A2.7 Power_analysis.m

This script provides the power analysis. First put in the right values.

```
% Set parameters
effect_size = 43.2;  % mmHg
alpha = 0.05;  % significance level
power = 0.90;  % desired power level
Std_within = 43.6; % Setting based on expected variability in PU peak

% Calculate total sample size needed for Z-test
total_sample_size_anova = sampsizepwr('z', [effect_size, Std_within], alpha, power);

% Display results
fprintf('Total sample size needed for z-test: %d\n', round(total_sample_size_anova));
```

A2.8 t_test.m

This script provides the t-test. First the mean values and std values are calculated. Then a t-test for lifting (Pick up) was performed followed by a t-test for carrying.

```
%% Calculate values that are put in report
PUBaseline_Std = [1:6];
PUBaseline_Std(1) = std(C1PU.Baseline);
PUBaseline_Std(2) = std(C2PU.Baseline);
PUBaseline_Std(3) = std(C3PU.Baseline);
PUBaseline_Std(4) = std(C4PU.Baseline);
PUBaseline_Std(5) = std(C5PU.Baseline);
PUBaseline_Std(6) = std(C6PU.Baseline);

PUPeak_Std = [1:6];
PUPeak_Std(1) = std(C1PU.Peak);
PUPeak_Std(2) = std(C2PU.Peak);
PUPeak_Std(3) = std(C3PU.Peak);
PUPeak_Std(4) = std(C4PU.Peak);
PUPeak_Std(5) = std(C5PU.Peak);
PUPeak_Std(6) = std(C6PU.Peak);

Trend_Std = [1:6];
Trend_Std(1)= std(C1trend.Diff);
Trend_Std(2)= std(C2trend.Diff);
Trend_Std(3)= std(C3trend.Diff);
Trend_Std(4)= std(C4trend.Diff);
Trend_Std(5)= std(C5trend.Diff);
Trend_Std(6)= std(C6trend.Diff);

PUBaseline_mean = [1:6];
PUBaseline_mean(1) = mean(C1PU.Baseline);
PUBaseline_mean(2) = mean(C2PU.Baseline);
PUBaseline_mean(3) = mean(C3PU.Baseline);
PUBaseline_mean(4) = mean(C4PU.Baseline);
PUBaseline_mean(5) = mean(C5PU.Baseline);
PUBaseline_mean(6) = mean(C6PU.Baseline);

PUPeak_mean = [1:6];
PUPeak_mean(1) = mean(C1PU.Peak);
PUPeak_mean(2) = mean(C2PU.Peak);
PUPeak_mean(3) = mean(C3PU.Peak);
PUPeak_mean(4) = mean(C4PU.Peak);
PUPeak_mean(5) = mean(C5PU.Peak);
PUPeak_mean(6) = mean(C6PU.Peak);

Trend_mean = [1:6];
Trend_mean(1)= mean(C1trend.Diff);
Trend_mean(2)= mean(C2trend.Diff);
Trend_mean(3)= mean(C3trend.Diff);
Trend_mean(4)= mean(C4trend.Diff);
Trend_mean(5)= mean(C5trend.Diff);
Trend_mean(6)= mean(C6trend.Diff);
% These values are put in report

```

```
%% t test for PU
% Store peak data for each condition in a cell array
peak_conditions = {C1PU.Peak, C2PU.Peak, C3PU.Peak, C4PU.Peak, C5PU.Peak, C6PU.Peak};

% Initialize a matrix to store p-values
p_values = zeros(9, 2); % 9 comparisons, 2 columns for condition indices

% Perform pairwise comparisons and store p-values
p_values(1, :) = [1, 2];
p_values(2, :) = [3, 4];
p_values(3, :) = [5, 6];
p_values(4, :) = [1, 3];
p_values(5, :) = [1, 5];
p_values(6, :) = [2, 4];
p_values(7, :) = [2, 6];
p_values(8, :) = [3, 5];
p_values(9, :) = [4, 6];

% Initialize a cell array to store p-values and comparisons
p_table = cell(9, 3); % 9 rows for comparisons, 3 columns for comparison and p-values

% Calculate p-values and populate the table
for i = 1:size(p_values, 1)
    condition1 = peak_conditions{p_values(i, 1)};
    condition2 = peak_conditions{p_values(i, 2)};
    [~, p] = ttest2(condition1, condition2);
    p_table{i, 1} = sprintf('C%d vs C%d', p_values(i, 1), p_values(i, 2));
    p_table{i, 2} = p;
end

% Display the table
disp('Comparison     P-value');
disp(p_table);


%% t test for carrying

% Store Diff data for each condition in a cell array
Diff_conditions = {C1trend.Diff, C2trend.Diff, C3trend.Diff, C4trend.Diff, C5trend.Diff,
     C6trend.Diff};

% Initialize a matrix to store p-values
p_values_Diff = zeros(9, 2); % 9 comparisons, 2 columns for condition indices

% Perform pairwise comparisons and store condition indices
p_values_Diff(1, :) = [1, 2];
p_values_Diff(2, :) = [3, 4];
p_values_Diff(3, :) = [5, 6];
p_values_Diff(4, :) = [1, 3];
p_values_Diff(5, :) = [1, 5];
p_values_Diff(6, :) = [2, 4];
p_values_Diff(7, :) = [2, 6];
p_values_Diff(8, :) = [3, 5];
p_values_Diff(9, :) = [4, 6];

% Initialize a cell array to store p-values and comparisons
p_table_Diff = cell(9, 3); % 9 rows for comparisons, 3 columns for comparison and p-
    values

% Calculate p-values and populate the table
for i = 1:size(p_values_Diff, 1)
    condition1_Diff = Diff_conditions{p_values_Diff(i, 1)};
    condition2_Diff = Diff_conditions{p_values_Diff(i, 2)};
    [~, p_Diff] = ttest2(condition1_Diff, condition2_Diff);
    p_table_Diff{i, 1} = sprintf('C%d vs C%d', p_values_Diff(i, 1), p_values_Diff(i, 2))
    ;
    p_table_Diff{i, 2} = p_Diff;
end

% Display the table
disp('Comparison     P-value');
disp(p_table_Diff);
```