

Comparison of home vs gym-based delivery exercise modes of two 8-week supervised aerobic training regimes on cardiorespiratory fitness and arterial stiffness in adults with Intellectual and Developmental Disability

Dissertação elaborada com vista à obtenção do Grau de Mestre em Exercício e Saúde

Orientador: Pedro Xavier Melo Fernandes Castanheira

Júri:

Presidente:

Doutora Maria Helena Santa Clara Pombo Rodrigues, investigadora auxiliar da Faculdade de Medicina da Universidade de Lisboa

Vogais:

Doutora Maria Rita da Silva Alexandre Pinto, investigadora auxiliar da Faculdade de Medicina da Universidade de Lisboa

Doutor Guillermo Ruben Oviedo, professor auxiliar Facultad de Psicología, Ciencias de la Educación y del Deporte Blanquerna-Universitat Ramon Llull

Doutor Pedro Xavier Melo Fernandes Castanheira, professor adjunto convidado da Escola Superior de Desporto de Rio Maior do Instituto Politécnico de Santarém

Bruno Rodrigues Simão

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## *Resumo*

As doenças cardiovasculares (DCV) são uma das principais causas de morte em pessoas com dificuldade intelectual e de desenvolvimento (DID). Fatores de risco tradicionais e emergentes estão associados ao desenvolvimento de DCV. A atividade física é considerada uma estratégia universal para a redução do risco de DCV. No entanto, o confinamento domiciliário apenas permite aplicar intervenções domiciliárias e até ao momento, a eficácia deste tipo de intervenção na redução de fatores de risco em pessoas com DID permanece esclarecer.

O objetivo do estudo foi comparar contextos de exercício, domiciliário vs presencial, durante 8 semanas de dois regimes de treino aeróbio supervisionados na rigidez arterial e na aptidão cardiorrespiratória em adultos com DID. A intervenção incluí-o 17 adultos com DID que foram divididos em dois regimes: treino intervalado em sprints (SIT) e treino contínuo (CAET). Os treinos foram realizados 3 vezes por semana durante 60 minutos. A intervenção presencial melhorou a aptidão cardiorrespiratória e ambos os contextos resultaram em melhorias semelhantes na rigidez arterial.

Concluindo, uma intervenção domiciliária consegue minimizar alguns efeitos fisiológicos deletérios de um confinamento obrigatório em vários fatores de risco, no entanto não corresponde aos benefícios de uma intervenção presencial, independentemente do regime de treino aeróbio.

**Palavras-chave:** aptidão cardiorrespiratória, rigidez arterial, doenças cardiovasculares, dificuldade intelectual e de desenvolvimento, exercício físico, domiciliário, presencial, regime, fatores de risco tradicionais, fatores de risco emergentes.

## *Abstract*

Cardiovascular diseases (CVD) are a leading cause of death in people with intellectual and developmental disability (IDD). Traditional and emergent risk factors such as cardiorespiratory fitness and arterial stiffness are associated with the development of CVD. Physical activity has been appointed as an essential universal strategy for reducing the risk of CVD. However, during the mandatory lockdown home-based interventions are the only alternative to reduce risk factors, and the efficacy of these interventions needs to be confirmed in people with IDD.

The present study aims to compare home vs gym-based delivery exercise modes of two 8-week supervised aerobic training regimes on cardiorespiratory fitness and arterial stiffness in adults with IDD. The intervention included 17 adults with IDD and participants were divided into two regimes: sprint interval training (SIT) and continuous aerobic exercise training (CAET). Training for both regimes was performed 3 times a week for 60 minutes. Only the gym-based intervention improved cardiorespiratory fitness and both contexts had similar results on arterial stiffness.

In conclusion, a home-based intervention may minimize the deleterious physiological effects of a mandatory lockdown on several risk factors but does not match the benefits of a gym-based intervention, regardless of exercise regime.

**Keywords:** cardiorespiratory fitness, arterial stiffness, cardiovascular disease, intellectual and developmental difficulties, physical exercise, home-based, gym-based, regime, traditional risk factors, emergent risk factors

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### III. List of Abbreviations

<b>Abbreviature</b>	<b>Meaning</b>
bDBP	Brachial diastolic blood pressure
bMAP	Brachial mean arterial pressure
BMI	Body mass index
Bpm	Beats per minute
bPP	Brachial pulse pressure
bSBP	Brachial systolic blood pressure
CAET	Continuous aerobic exercise training
cIMT	Carotid intima-media thickness
CO <sub>2</sub>	Carbon dioxide
COVID-19	Corona virus 19
cSBP	Central systolic blood pressure
CV	Coefficient of variation
DBP	Diastolic blood pressure
DS	Down syndrome
GCP	Ginásio Clube Português
HIIT	High intensity interval training
HR	Heart rate
HR max	Heart rate maximum
HRR	Heart rate reserve
IDD	Intellectual and developmental disability
IPAQ	International Physical Activity Questionnaire
Ln	Natural logarithm
MAP	Mean arterial pressure
MET	Metabolic equivalent of task
MVPA	Moderate-vigorous physical activity
O <sub>2</sub>	Oxygen
OMNI-RES	OMNI- Resistance Exercise Scale
PAR-Q+	Physical Activity Readiness Questionnaire for Everyone
PGC-1 $\alpha$	Peroxisomal proliferator activator receptor-gamma coactivator-1alpha
PWV	Pulse wave velocity



RPE	Rate of perceived exertion
SBP	Systolic blood pressure
SD	Standard deviation
SIT	Sprint interval training
VO <sub>2</sub> max	Maximum oxygen uptake
VO <sub>2</sub> peak	Peak oxygen uptake
β	Stiffness index
ε	Elastic modulus
η <sup>2</sup>	Partial eta square

## Introduction

The global coronavirus disease 2019 (COVID-19) pandemic has moved swiftly across the globe infecting millions and testing the health care systems of countries (Theis et al., 2021). As a result of this unprecedented challenge, governments around the world have imposed limitations to assist reduce the rate of infection, limiting involvement in typical everyday activities, travel, and access to a variety of forms of exercise are just a few examples (e.g., gyms were closed, group gatherings were banned, and increased social distancing was recommended) (Hossain et al., 2020). During the pandemic, the vulnerabilities of some groups of people, such as the elderly, pregnant women, and the homeless, have been highlighted (Kirby, 2020; Qiao, 2020; WHO, 2020). The predicament of people with intellectual and developmental disability (IDD), who face a variety of challenges such as health issues, mental illnesses, and social disadvantage, has received less attention (Emerson & Hatton, 2008). Before the pandemic, physical inactivity, low cardiorespiratory fitness, and obesity were already highly prevalent cardiovascular risk factors in adults with IDD (Gawlik et al., 2017; Melville et al., 2017), that just got aggravated during the pandemic (Theis et al., 2021). These and other traditional modifiable cardiovascular risk factors, such as carotid intima-media thickness (cIMT) and arterial stiffness, are linked to adverse structural and functional alterations in the blood vessels. Arterial wall stiffening precedes isolated systolic hypertension and causally contributes to target organ damage (Kaess et al., 2012). As a result, arterial stiffness is a key component of a vicious cycle of hemodynamic dysfunction marked by excessive pulsatility, which leads to heart failure, decreased coronary perfusion, chronic kidney disease, cerebrovascular disease, and other chronic diseases. Measures of large artery stiffness independently predict the risk of incident cardiovascular events in both clinical and community-based cohorts, confirming the key role of arterial stiffness in cardiovascular function (Ben-Shlomo et al., 2014; Chirinos et al., 2014), independent of traditional risk factors (Chirinos et al., 2019).

Regular exercise training and physical activity have been shown to improve both traditional and emergent cardiovascular risk factors in adults with IDD, but this evidence derives from studies on laboratorial and gym-based interventions (Boer & Moss, 2016; Boer et al., 2014; Calders et al., 2011; Melo et al., 2021; Oviedo et al., 2014). Some authors suggest that the magnitude is dependent on the aerobic regime on cardiorespiratory fitness (Boer et al., 2014) and arterial stiffness (Melo et al., 2021), however this is not a universal finding. It remains unknown whether home-based interventions including different aerobic regimes in adults with IDD promotes similar effects to lab/gym-based interventions in adults with IDD. This is important as COVID-19 will not be the last pandemic in our lifetime. Scientists have warned that zoonoses, infectious diseases that transfer from animals to humans, are on the rise and the risk of a new pandemic is higher than ever before (Smith, 2021).

In the present master thesis, we aim to provide further insight on this question through 7 main chapters: 1) a Literature Review on the effects of the COVID-19 pandemic on cardiovascular risk, where the prevalence of traditional and emergent cardiovascular risk factors and the effectiveness of different context and regimes of physical activity and exercise interventions at controlling cardiovascular risk factors are presented; 2) a Methodology section where participants recruitment, study design, exercise interventions, assessment of the outcome variables and statistical analysis are described; 3) a Results section where the study intervention outcomes are presented; 4) a Discussion section where the outcomes of the present study are discussed in comparison to the available data; 5) Limitations and Future Directions where the present study limitations are presented together with recommendations for future studies; 6) and finally, the Conclusion and practical applications found with the present study intervention.

## 1. Literature Review

### I. The SARS-CoV-2 Pandemic

In late December 2019, the SARS-CoV-2 was first identified in Wuhan, Republic of China. This novel coronavirus usually causes minor infections, but it can progress to a serious and even fatal communicable disease known as COVID-19 (Chtourou et al., 2020). COVID-19 is characterized by a human-to-human transmission that occurs rapidly and at a high frequency resulting in a virus that quickly spread globally, putting people's health at risk, and changing drastically the way people used to live their life (Chtourou et al., 2020). The World Health Organization declared this fast and harmful spread of COVID-19 a global pandemic in March 2020. To combat COVID-19 propagation, various public health measures and interventions were introduced, including isolation of confirmed diagnosed cases (Jiang et al., 2020), social distancing, self-isolation, and community lockdowns that limited participation in normal daily activities, travel, and access to many forms of exercise (Chtourou et al., 2020). Even though these COVID-19 mitigation strategies were demonstrated to be effective at attenuating the spread of COVID-19, there are also negative effects associated.

COVID-19 has imposed unprecedented restrictions, significantly affecting society's most vulnerable groups, such as the elderly, pregnant women and the homeless, that have been highlighted during the outbreak (Kirby, 2020; Qiao, 2020; WHO, 2020). The predicament of people with intellectual disabilities, who are vulnerable to a variety of factors such as health issues, mental disorders, and social deprivation, has received less attention (Emerson & Hatton, 2008). The stress associated with the fear of contracting the disease, and the impact of reduced physical activity opportunities are likely to profoundly affect physical activity and mental health in people with IDD (Fitzgerald et al., 2020).

### II. COVID-19 and People with Intellectual Disability: Impact of the Pandemic

COVID-19 pandemic impacts all groups in society, but people with IDD are particularly vulnerable to the pandemic's physical, mental, and social consequences, in part due to their health problems, social circumstances, and cognitive impairments that can limit the understanding of information, resulting in the dependency on their caregivers to be vigilant for them, and leaving people with IDD at a higher risk of infection since most of them rely completely on others to keep them safe (Grier et al., 2020). The high quantity and frequency of information about COVID-19 might overly concern people with IDD, leading to states of anxiety and paranoid thinking that reduces their ability to follow the imposed measures (Courtenay & Perera, 2020). Furthermore, the high incidence of physical health issues, as well as social circumstances and understanding barriers, create ideal settings for people with IDD to experience more severe symptoms (Courtenay & Perera, 2020).

People with IDD were particularly affected by the COVID-19 restrictions as recommendations to meet the physical activity requirements for optimal mental and physical health were harder to accomplish (Fitzgerald et al., 2020). Even if several reasonable adjustments for people with IDD have been made across Europe, including exemptions on face masks use in public and allowing increased daily exercise during lockdown periods, this does not seem to be sufficient to account for the effects of COVID-19 in this population (Oakley et al., 2021). This is worrisome as people with IDD already had low levels of physical activity (Melville et al., 2017) and high prevalence of modifiable cardiovascular risk factors such as hypertension, obesity (Hsieh et al., 2014) and low cardiorespiratory fitness (Gawlik et al., 2017) before the pandemic. Autonomic dysfunction presented as sudomotor

dysfunction, impaired cardiac baroreflex sensitivity and systolic blood pressure variability might partly explain the high prevalence of cardiovascular risk factors in people with IDD (Mussalo et al., 2002; Skrapari et al., 2006; Yang et al., 2013; Zwack et al., 2021). In people with Down Syndrome, chronotropic incompetence was explained by reduced catecholamines responsiveness and blunted parasympathetic withdrawal during exercise and found to be an important determinant for low cardiorespiratory fitness levels (Fernhall et al., 2009; Figueroa et al., 2005).

As physical inactivity levels in people with IDD increased with the COVID-19 restrictions, the risk for cardiovascular diseases during the pandemic likely increased proportionally (Patterson et al., 2018). These represent one of the most important causes of death among people with IDD (O'Leary et al., 2018), and are also the main cause of premature death (Vancampfort et al., 2020). People with IDD already experience an excess mortality rate two to four times higher than people without IDD (Zaal-Schuller et al., 2015), and the death rate by cardiovascular diseases seems not to be decreasing over time (Janicki et al., 1999), specially during the aftermath of the COVID pandemic.

Over 80% of the prevalence of cardiovascular diseases can be attributed to blood vessel pathology such as coronary artery disease, stroke, hypertension (Laurent et al., 2001; Tanaka, 2015). Systemic conduit arteries are expected to provide a robust cushioning effect, allowing for practically constant flow in the microvasculature. However, the stiffening of large conduit arteries impairs this cushioning role, resulting in an increased risk for cardiovascular events (Chirinos et al., 2019). Stiffening of the arteries is characterized by a change in extracellular matrix composition and architecture that involves fragmentation of elastin fibers, deposition of stiff collagen fibers, and cross-linking of collagen molecules by advanced glycation end-products (Palombo & Kozakova, 2016). It leads to an increased energetic demand on the heart and transfer pulsatile energy to the systemic circulation, which consequently damages target organs in the body (Townsend et al., 2015). Thus, arterial stiffness, in particular, aortic pulse wave velocity, is now considered an early marker of cardiovascular pathology (Hansen et al., 2006; Cavalcante et al., 2011), independent of traditional risk factors (Laurent et al., 2001). Structural changes in conduit arteries may also result in increase in cIMT. cIMT represents subclinical atherosclerosis (Centurión, 2016) and has been shown to predict cardiovascular risk (Naqvi & Lee, 2014) even after traditional risk factors for cardiovascular events have been taken into consideration (O'Leary et al., 1999). An increased cIMT is an intermediate stage in the continuum of atherosclerosis, which significantly correlates with coronary and cerebrovascular disease (Chambless et al., 1997; O'Leary et al., 1999). To our knowledge, arterial structure and stiffness have been rarely evaluated in people with IDD. This is surprising attending to the high prevalence of modifiable risk factors (de Winter et al., 2009, 2012; Hsieh et al., 2014) and the association between risk factors and structural and functional changes in arteries (Cernes et al., 2008). Early findings showed that arterial stiffness was similar in people with or without IDD (Rodrigues et al., 2011). Draheim et al., (2010) demonstrated that the cIMT of people with IDD was significantly lower compared to adults without IDD, suggesting that people with IDD might have inherent vascular protection. However, these studies were performed in people with down syndrome and not intellectual disabilities in general, challenging the transfer of the screening results to improvements in cardiovascular risk stratification of people with IDD in general, due to all the syndrome-specific conditions of people with down syndrome (DS) (i.e., congenital heart disease, hypotonia, hypotension, ligament laxity) (Weterings et al., 2019).

#### IV. Physical Activity and Exercise as a Universal Strategy

Physical activity and exercise are a universal strategy that improves not only traditional risk factors but also emergent risk factors (Durstine et al., 2013; Fiuza-Luces et al., 2018), but people with IDD are still not meeting recommended guidelines for physical activity (Hassan et al., 2019). Various studies with people with IDD demonstrated the beneficial effects of aerobic training in traditional risk factors (Boer & Moss, 2016; Boer et al., 2014; Calders et al., 2011; Kim, 2017; Melo et al., 2021; Oviedo et al., 2014). Interventions with aerobic exercise in people with IDD improved cardiorespiratory fitness (+2 to +6 mL/kg/min) (Boer & Moss, 2016; Boer et al., 2014; Calders et al., 2011; S.-S. Kim, 2017; Melo et al., 2021; Oviedo et al., 2014) and blood pressure (-6 to -15 mmHg on brachial systolic blood pressure; -11 mmHg on brachial mean arterial pressure) (Boer et al., 2014; Calders et al., 2011; Melo et al., 2021; Oviedo et al., 2014) with interventions lasting 12 weeks to 3 months, using various aerobic regimes, including continuous aerobic exercise training (CAET), high intensity interval training (HIIT) and combined aerobic and resistance training. HIIT is characterized by high intensity aerobic bouts that targets near-maximal intensities ( $\approx 80\%$  to 100% of maximal heart rate), alternated with periods of active rest or passive rest (Moniz et al., 2020), whereas CAET is characterized by a continuous effort without rest normally performed at a moderate intensity (40% to 60% of heart rate reserve (HRR)) (Riebe et al., 2018; Wewege et al., 2017). Interventions with aerobic exercise in people with IDD often fail to improve body composition (Andriolo et al., 2011; Calders et al., 2011; Carmeli et al., 2005; Melo et al., 2021; Millar et al., 1993), although a few exceptions exist (-2.5 to -4.3 cm on waist circumference; -1 to -5% on fat mass; -0.8 kg/m<sup>2</sup> on body mass index) (Boer & Moss, 2016; Boer et al., 2014; S.-S. Kim, 2017; Oviedo et al., 2014). A few studies have also examined the effects of aerobic training in emergent risk factors such as cIMT and arterial stiffness (S.-S. Kim, 2017; Melo et al., 2021). Melo et al., (2021) with 12 months of CAET and 3 additional months of HIIT in people with IDD showed no changes on cIMT. As for arterial stiffness, Kim, (2017) and Melo et al., (2021) demonstrated significant improvements (-0.8 m/s on aortic pulse wave velocity (PWV); -0.8 a -1.1 m/s on lower limb PWV; -0.1 m/sec/height on PWV) with aerobic exercise interventions ranging between 12 weeks and 15 months including HIIT and CAET regimes. Exercise intensity may play a role in the magnitude of the effects (Karlsen et al., 2017; MacInnis & Gibala, 2017; Wisløff et al., 2007; Wu et al., 2021). It is suggested that HIIT regime results in similar to greater improvements on traditional (Batacan et al., 2017; Campbell et al., 2019; Korman et al., 2020; Wu et al., 2021) and emergent risk factors (Kolmos et al., 2016; Ramos et al., 2015; Samaneh et al., 2020). HIIT permits to accumulate a greater volume of higher exercise intensity during one exercise session compared to CAET (Ross et al., 2016). HIIT produces similar improvements on cardiorespiratory fitness, on peripheral vascular structure and function despite of weekly lower training volume and lower time commitment compared with CAET (Gibala & Jones, 2013; Rakobowchuk et al., 2008). Peroxisome proliferator-activated receptor gamma coactivator 1 $\alpha$  (PGC-1 $\alpha$ ), the “master regulator” of mitochondrial biogenesis, whose expression is intensity-dependent might play a role in the benefits derived from HIIT (Egan et al., 2010; Nordsborg et al., 2010; Skovgaard et al., 2016).

A more intense version of HIIT is sprint interval training (SIT), and this has been gaining interest over the last years as a time-efficient alternative to implement in a program training for people with IDD who are not motivated to exercise continuously at a moderate intensity. It is characterized by peak efforts performed at intensities  $\geq 100\%$  of peak aerobic capacity and includes maximum short or supramaximal efforts (5–30 s) interspersed with periods of active or passive recovery (Sultana et al., 2019). The hypothesis behind the use of interval training is that the vigorous activity segments might promote greater adaptations due to increased cellular stress, while its shorter length and the recovery intervals compared to

CAET allow even untrained people to work at higher intensities than they would be able to if training at a steady-state (Kessler et al., 2012). Beyond that, acute exercise bouts characteristic of interval training provokes repeated rises in laminar shear stress that result in long-term adaptations in arterial function and structure (Green et al., 2017). SIT is a type of exercise that is feasible and well-tolerated by adolescents and young adults with IDD (Boer et al., 2014). HIIT is in fact as feasible as CAET (Korman et al., 2020). Research studies reported that both regimes (SIT and CAET) induced similar improvements in structure and peripheral vascular function (Rakobowchuk et al., 2013), in arterial stiffness (Cocks et al., 2013), in peak oxygen uptake (VO<sub>2</sub> peak) (Gist et al., 2014), and in muscle oxidative capacity (Gibala et al., 2006).

Still, the beneficial effects of aerobic exercise in people with IDD are derived from supervised gym or lab-based interventions, that were forbidden during the COVID-19 mandatory lockdown (Chtourou et al., 2020). In this critical situation, home-based interventions are the only alternative to reduce traditional and emergent risk factors for people with IDD.

## V. Feasibility of Home-Based Exercise

The effects of home-based exercise in people with IDD have been studied (Buono et al., 2021; Simacek et al., 2017). Overall, a high level of satisfaction, particularly in terms of the potential of receiving specialized counseling, continuous assistance, and travel expense savings have been reported (Buono et al., 2021). However, these remote interventions aimed exclusively at improving communication skills and to provide psychological support, not including a focus on the reduction of cardiovascular risk factors through a web-based supervised aerobic exercise training program. To the best of our knowledge, a protocol of exercise training in a home confinement setting has not yet been proposed. This is important as scientists have warned that, infectious diseases that transfer from animals to humans, are on the rise and the risk of a new pandemic is higher than ever before (Smith, 2021).

The beneficial effects of different aerobic exercise regimes and supervision levels of home-based interventions on physical and psychological health have been reported in populations without IDD (Aioke et al., 2018; J. Y. Kim et al., 2019; Kis et al., 2019; Latham et al., 2004; Ochi et al., 2022; van der Kolk et al., 2019; Yakut et al., 2022), including during the COVID-19 outbreak (Borrega-Mouquinho et al., 2021; Vitale et al., 2020). Several of these studies did not evaluate the effects of home-based exercise on cardiovascular risk factors (Borrega-Mouquinho et al., 2021; Kis et al., 2019; Latham et al., 2004), or reported no benefits (Latham et al., 2004; Vitale et al., 2020). However, Aioke et al., (2018), Ochi et al., (2022) and van der Kolk et al., (2019) found beneficial effects on cardiorespiratory fitness (+1 to 3 mL/kg/min) following a home-based HIIT or CAET regime lasting 12 to 24 weeks in adults with chronic kidney disease, breast cancer survivors and Parkinson disease, respectively. Aioke et al., (2018) and Yakut et al., (2022) also found improvements on SBP (-12 to -14 mmHg) and DBP (-5 to -6 mmHg) following a home-based MICT or HIIT regime lasting 12 to 24 weeks in adults with chronic kidney disease and myocardial infarction, respectively. Kim et al., (2019) reported improvements on moderate-vigorous physical activity (MVPA) (+236 min) after a 12 week non-supervised, combined aerobic and resistance regime in cancer survivors. Thus, these benefits are of similar magnitude to those reported previously in on-site settings, suggesting that home-based interventions are effective at reducing barriers to physical exercise while promoting similar benefits in physical activity and health as on-site interventions (Aioke et al., 2018; Ciccolo et al., 2008; Feng et al., 2019; Joseph et al., 2014; van der Kolk et al., 2019). In addition, home-based interventions also represent

a cost-effective method of promoting physical activity because they have the potential to reach a larger number of people at a lower cost (Joseph et al., 2014). However, the comparison of benefits from different exercise delivery modes in adults with IDD is yet to be performed.

The inclusion of inclusion of HIIT in home-based settings has been attempted before (Ochi et al., 2022; Yakut et al., 2022). These interventions were performed with body weight exercises for 12 weeks and reported beneficial effects on peripheral blood pressure (Yakut et al., 2022) and on cardiorespiratory fitness (Ochi et al., 2022). Overall, these findings suggest that the pragmatism of home-based exercise interventions may show to be successful for mitigating barriers to the engagement in physical activity and exercise resulting in positive benefits to health. However, the effect of different aerobic exercise regimes in a home-based exercise delivery setting in adults with IDD is yet to be determined.

## Purpose

Therefore, this dissertation aims to compare home vs gym-based delivery exercise modes of two 8-week supervised aerobic training regimes on cardiorespiratory fitness and arterial stiffness in adults with IDD. Secondary to the main outcomes, hemodynamics, body composition, and physical activity were also analyzed.

## 2. Methodology

### I. Participants

A total of 40 participants from the project SPORTS4ALL by Ginásio Clube Português (GCP), in which over 150 people with IDD attend educational and therapeutic intervention, offered in individualized formats, representation classes, or integrated training in fitness classes at GCP, were recruited to participate in randomized controlled trial aimed to determine the effect of two types of exercise programs, CAET vs SIT on health-related physical fitness, cardiovascular parameters and quality of life (QoL). Study advertising took place through a direct invitation by the research team and rehabilitation technicians. The time frame for recruitment of participants took approximately 1 month. Thirty-six participants met the following inclusion criteria:  $\geq 18$  years and  $\leq 55$  years; diagnosed with mild to moderate IDD; exercising at least  $1d.wk^{-1}$  in the last 2 months; able to participate on group exercise activities with  $\geq 8$  people; able to walk independently; and able to understand and perform all physical fitness assessments. Four participants were excluded because they had of the following criteria: any form of cardiovascular disease, significant respiratory disorder, metabolic disease, atlanto-axial instability, severe or profound IDD, smoking, and/or use of heart rate (HR) and blood pressure altering or non-steroidal anti-inflammatory medications, inability to comply with guidelines for participation in exercise testing and training (Riebe et al., 2018). IDD is defined as a disorder with onset during the developmental period (before the age of 22) that includes both intellectual and adaptive functioning deficits in conceptual, social and practical domains and the following 3 criteria must be met: deficits in intellectual functions confirmed by both clinical assessment and individualized, standardized intelligence testing; deficits in adaptive functioning that result in failure to meet developmental and sociocultural standards for personal independence and social responsibility; and onset of intellectual and adaptive deficits during the developmental period (American Psychiatric Association, 2013; Schalock et al., 2021). Eligible volunteers were enrolled in the study as and when they volunteered. These were invited to an initial meeting with their families/legal guardians, exercise physiologists, and rehabilitation technicians. During this meeting, the procedures of the trial, testing procedures, benefits,

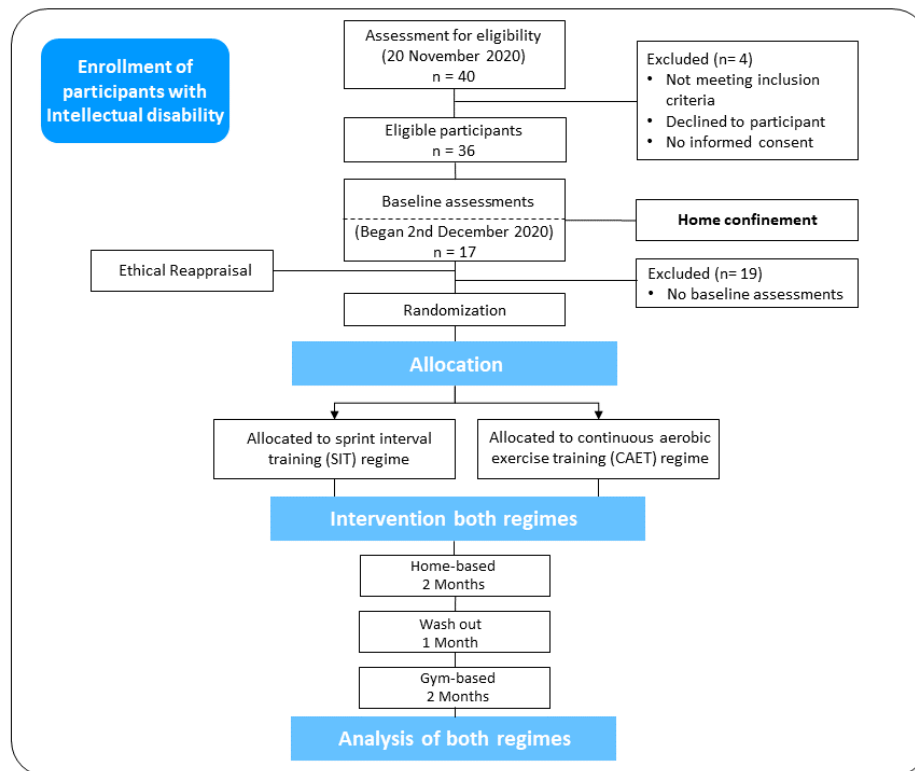
risks, and the time required for the study were explained. In addition, an information sheet about the research and an informed consent form for participants and parent(s)/ legal guardian(s), in accordance with the approval by the Ethical Committee of Faculdade de Motricidade Humana – Universidade de Lisboa, was distributed. Informed written consent was signed by participants and parent(s)/ legal guardian(s) before allocation. After signing the informed consent, participants or parents/legal guardians were asked to answer the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) questionnaire, to assess their readiness to increase their levels of physical activity; the International Physical Activity Questionnaire (IPAQ) questionnaire, to assess the level of physical activity of the participants; and a sociodemographic data questionnaire. During a second visit, all volunteers participated in familiarization sessions before baseline testing at the laboratory. The number of familiarization sessions was repeated until the researchers observed that the participants were confident and able to perform all assessments correctly (1-2 sessions). Of the 36 participants recruited, by the time the mandatory COVID-19 home confinement was declared by the Portuguese government, only 17 participants had complete laboratorial exercise testing.

## II. Design

This study was a randomized controlled trial (**Figure 1**), where a convenience group of 17 who had complete laboratorial exercise testing, were centrally randomized on a 1:1 ratio to either a SIT or CAET by using a random-block randomization scheme (<https://www.randomizer.org/>). Participants in both regimes received a 16-week supervised exercise program performed 3 times a week for 60 min each session. The intervention started with 8 weeks of online training via Google Meets at their homes followed by 1 month of detraining with no exercise sessions besides those made available habitually by the SPORTS4ALL program, and another 8 weeks of on-site training at GCP. During the intervention, monitoring of and adherence to the protocols was assessed with an exercise diary. Schedule of enrolment, intervention, and assessments for the duration of the study are displayed in **Table 1**. Assessments were conducted on 4 occasions over a 20-week period: before (M1) and after (M2) the home-based intervention; and before (M3) and after (M4) the gym-based intervention (**Table 1**). During M1, assessments, personal information regarding age; sex; IDD level; IDD etiology; living arrangement; education; medication, smoking, and alcohol habits, was obtained. All tests were conducted by the same researchers during the morning at a room temperature of 22–24°C and relative physical humidity between 55–65%. Only those researchers with required cognitive and practical skills to competently supervise cardiopulmonary exercise tests (Myers et al., 2014), and/or evaluate arterial structure (Touboul et al., 2007), and stiffness (Townsend, 2016), and/or evaluate body composition, while exhibiting good to excellent (Koo & Li, 2016) inter- and intra- day reproducibility measurements, as assessed by intraclass correlation coefficients and coefficients of variation (CV), participated in the evaluations. Participants were asked to fast from solids for at least 3 h, refrain from alcohol for 24 h, caffeine for 8 h, and vigorous exercise for 48 h prior to the data collection (Van Bortel et al., 2012). All evaluations were performed on a single day of testing at each measurement round. On this day, participants had their (1) body composition measured and then rest quietly for at least 15 min in the supine position prior to data collection in the following order: (2) brachial arterial pressure, (3) cIMT, (4) stiffness indices by carotid vascular ultrasonography, (5) regional arterial stiffness by applanation tonometry, (6) an incremental test to exhaustion, and (7) the IPAQ.



Figure 1 - UPSIDE DOWNS' proposed participant flow chart



### III. Exercise Interventions

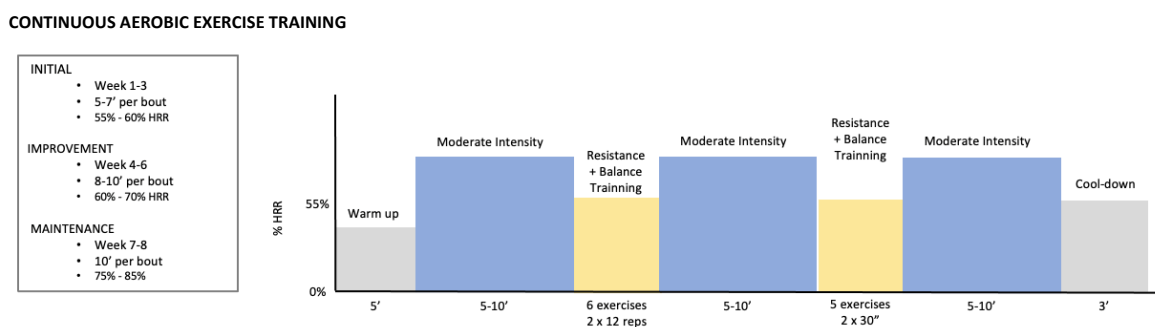
The exercise regimes were delivered at participants' homes for 8 weeks via Google Meets and at GCP during an identical period. All sessions were designed by experienced Exercise Physiologists together with Rehabilitation Technicians, following the American College of Sports Medicine (ACSM) (Riebe et al., 2018) and the National Strength and Conditioning Association (NSCA) guidelines (Haff et al., 2016). The Exercise Physiologists in charge of delivering the interventions underwent a standardized training to ensure that the sessions offered were comparable, and a 2-month familiarization period where they observed the exercise sessions from the project SPORTS4ALL by GCP, got to know the participants, and led exercise activities, while under the supervision of the responsible Rehabilitation Technicians of the project SPORTS4ALL. During this period, the rating of perceived exertion was reinforced using the OMNI scale (Stanish & Aucoin, 2007). The multi-component exercise programs included aerobic, resistance, balance, and flexibility training. Both SIT and CAET regimes were divided into 2 groups: 8-9 participants/group and the participant-Exercise Physiologist ratio of 3:1, partnered with at least 1 Rehabilitation Technician in each exercise session. Both programs were divided into 3 phases adapted from Oviedo et al., (2020): initial phase (week 1-3); improvement phase (week 4-6); and maintenance phase (week 7-8). Sessions for both regimes were matched for the total duration as well. All sessions included 5 min for standardized warm-up exercises and cool-down exercises. The warm-up was implemented to gradually increase the HR, body temperature, joint mobility and prepare the body of the participants to the exercises of the conditioning phase. After the conditioning phase, cool-down exercises were performed followed by stretching exercise. During the washout period, 14 participants performed 3 sessions representing each phase of the home-based intervention wearing heart rate monitors so that we could have a proxy of the exercise intensity in each phase of the home-based intervention. The resistance training included a total of 6 exercises: 3 for upper limbs

(seated biceps curl, triceps extension, and frontal shoulder raise); 2 for the torso (1 for back: seated row and 1 for abdominals: side bend); and 1 for lower limbs (chair squats) (see **Appendix 1**). All exercises were performed with 2-4 kg dumbbells, or participants' body weight. To control the intensity of the strength training, we used the 0-10 points Rate of Perceived Exertion OMNI- Resistance Exercise Scale (RPE OMNI-RES) validated for resistance training (Gearhart et al., 2009). The intensity of the resistance training was kept constant at 2 x 12 rep at RPE OMNI-RES 8, throughout the study period. Balance training was designed to challenge central and peripheral mechanisms involved in the control of movement and stability (vestibular; visual and somatosensory) (see **Appendix 1**). Flexibility exercises were executed after the cool-down period of each session. We used sustained stretches for each major muscle group targeted during the session. Active and passive static stretching exercises were used, holding the position for 10–30 s at a point of tightness or slight discomfort (Riebe et al., 2018).

### IIIa. CAET

CAET was based on a combination of aerobic, resistance, balance, and flexibility exercises (**Figure 2**). During the home-based intervention, aerobic training was performed using body weight exercises such as low impact jumping jacks, slow standing box, slow side shift with floor touch, slow high knees, half burpee (without jump), and hook box (see **Appendix 1**) (Borrega-Mouquinho et al., 2021). During the gym-based intervention, aerobic training was performed on cycle ergometers (Star Trac Spinner Blade ION 7220, Vancouver, WA). The exercise on the cycle ergometer started with 5-min of warm-up followed by 3 bouts of continuous cycling at a steady-state intensity. The length of the bouts (5-10 min) and intensity (55-85% HRR) were progressively increased across each phase. To ensure that the participants were exercising at the appropriate intensity, the OMNI scale 4-6 (Stanish & Aucoin, 2007) was used during the home-based intervention, and an HR chest band (H10 Polar, Electro, Kempele, Finland) was worn during the gym-based intervention.

Figure 2 - Sample of CAET intervention per session



### IIIb. SIT

The SIT consisted of a combination of aerobic, resistance, balance, and flexibility exercises (**Figure 3**). During the home-based intervention, aerobic training was performed using body weight exercises such as jumping jacks, standing box, side shift with floor touch, high knees, half burpee, and hook box (see **Appendix 1**) (Borrega-Mouquinho et al., 2021). During the gym-based intervention, aerobic training was performed on cycle ergometers (Star Trac Spinner Blade ION 7220, Vancouver, WA). Exercise started with 5 min of warm-up followed by bouts of 5-10 min of exercise consisting of 5-20 s all-out sprints followed by 15-45 s of

low cadence recovery (1:3-1:2 work-rest ratio). The duration of the sprints and the active recovery were modified throughout the program. To ensure that the participants were exercising at the appropriate intensity, the OMNI scale 8-10 (Stanish & Aucoin, 2007) was used during the home-based intervention, and an HR chest band (H10 Polar, Electro, Kempele, Finland) was applied during the gym-based intervention.

Figure 3 - Sample of SIT intervention per session

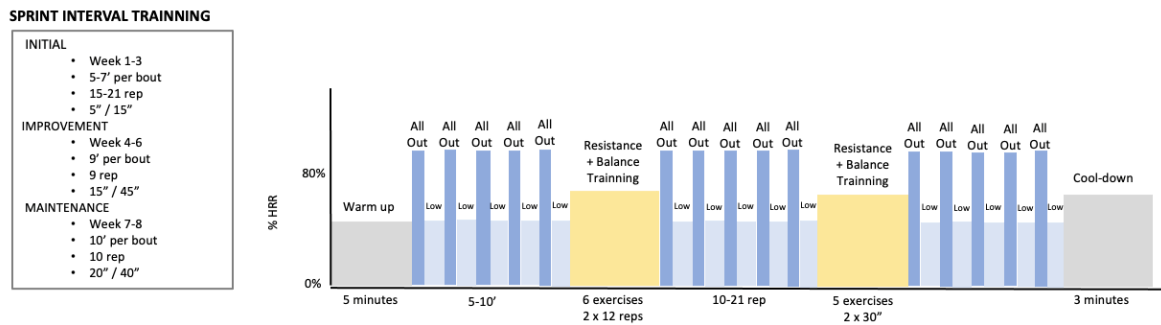


Table 1 - Schedule of enrolment, intervention, and assessments for the duration of the study

	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation				Analysis	
			Home-Based	Wash Out	Gym-Based			
TIMEPOINT	November 2020	December 2020	January 2021	March 2021	April 2021	May 2021	July 2021	August 2021
			M1	M2		M3	M4	
<b>ENROLMENT</b>								
Eligibility screen	X							
Informed consent	X							
PAR-Q+	X							
Demographics			X					
Online Meeting	X							
Random Allocation		X						
<b>INTERVENTIONS</b>								
SIT			X	X		X	X	
CAET			X	X		X	X	

<b>ASSESSMENTS</b>								
<i>Cardiorespiratory Fitness</i>			X	X		X	X	
<i>Arterial Stiffness &amp; Structure</i>			X	X		X	X	
<i>Hemodynamics</i>			X	X		X	X	
<i>Anthropometry/ Body composition</i>			X	X		X	X	
<i>Physical Activity</i>			X	X		X	X	
<b>REPORTS</b>					X			X

#### IV. Outcome measures

##### Cardiopulmonary Exercise Test (CPET)

Each participant performed a ramp incremental cycle ergometer test to exhaustion on a calibrated electronically braked cycle ergometer (Monark 839 E, Ergomedic; Monark, Vansbro, Sweden) at a pedal cadence of 70-75 rev.min<sup>-1</sup>. Initial and incremental workloads were 10-20 watts. The seat was adjusted so that the participant's legs could be at near full extension during each pedal revolution. Inspired and expired gases were continuously analyzed, with mixing-chamber gas exchange measurements through a portable gas analyzer (K5, Cosmed, Rome, Italy). Before each test, the O<sub>2</sub> and CO<sub>2</sub> analyzers were calibrated using ambient air and standard calibration gases of known concentration (16.7% O<sub>2</sub> and 5.7% CO<sub>2</sub>). The calibration of the turbine flowmeter of the K5 was performed using a 3 L syringe (Quinton Instruments, Seattle, Wash., USA) according to the manufacturer's instructions. Heart rate was continuously monitored (Garmin, US) and the participants did not carry the gas analyzer. Data were evaluated in 10 s averages, and peak VO<sub>2</sub> was defined as the highest 20-second value attained in the last minute of effort provided 2 of the following criteria are met: (1) Attaining ~90% of predicted maximal HR [IDD: 210 - 0.56 (age) - 15.5 (DS) (Fernhall et al., 2001); (2) Plateau in VO<sub>2</sub> with an increase in workload (<2.0 mL.kg<sup>-1</sup>.min<sup>-1</sup>); (3) Respiratory exchange ratio ≥ 1.1; and/or (4) subjective judgment by the observer that the participant could no longer continue, even after encouragement. Relative values were compared to cardiorespiratory fitness classifications by age and sex (Pescatello et al., 2014). Chronotropic response to exercise was calculated as: HR Reserve/ (predicted/maximal HR - HR at rest) \*100 (Azarbal et al., 2004). Chronotropic incompetence was defined as a failure to reach 80% of chronotropic response (Brubaker & Kitzman, 2011). HR recovery was calculated as the difference in HR after 1 min of recovery in relation to peak HR. An abnormal HR recovery was defined as a decline in HR inferior to 12 beats per minute (bpm) (Cole et al., 1999).

## Regional Arterial Stiffness and Blood Pressure

Arterial stiffness as measured by PWV from piezoelectric pressure mechanotransducers placed in the carotid, femoral and distal posterior tibial arteries on the right side of the body. The distance between the carotid and femoral and distal posterior tibial arteries was measured directly and entered the Complior Analyse software (ALAM Medical, Paris, France). Right brachial blood pressure was measured twice and entered the Complior Analyse software, and then signal acquisition is launched. The operator positioned the carotid sensor with the help of its specific holder and manually held the femoral sensor on the femoral artery and the distal sensor in the distal posterior tibial artery. When the operator observed 10 carotid pulse waveforms of sufficient quality (>90%), simultaneous carotid and femoral, and distal posterior tibial pressure curves were recorded for 10 pulse waveforms. The time delay (transit time) between the two pulse waveforms was then calculated automatically. Values obtained from the carotid to femoral artery and carotid to distal posterior tibial artery were taken as indices of central/aortic, and lower limbs arterial stiffness, respectively. The inter-day CV for carotid-femoral PWV and carotid-distal PWV were 1.12% and 3.02%, respectively. Operators had at least 3 months of regular training (> 100 hours).

Carotid systolic blood pressure (SBP) was also assessed by the piezoelectric pressure mechanotransducers placed in the carotid artery (Complior Analyse). The waveforms were averaged, and the mean values were extracted from 15 s window of acquisition. The carotid waveforms were calibrated from mean arterial pressure (MAP), measured immediately before the acquisition.

## Local Arterial Stiffness and Blood Pressure

The right common carotid artery was scanned with an Arietta V60 ultrasound machine (Hitachi Aloka Medical Ltd, Mitaka-shi, Tokyo, Japan) using a 7.5-MHz linear array probe incorporating a 5-MHz Doppler transducer. In longitudinal view, the probe was manipulated so that the intima of the artery was imaged clearly from both the anterior and posterior walls, and a single scan line was aligned perpendicularly to the vessel walls at a site 20 mm proximal to the carotid bulb. On-screen cursors were then placed on the anterior and posterior intima-media borders to enable tracking of both walls. The corresponding displacement waveforms and diameter curve were thus calculated using high-resolution online wall tracking ("E-track" technology), with a sampling rate of 1 kHz. Arterial pressure waveforms were obtained automatically in real time by calibrating peak and bottom values with central SBP and diastolic blood pressure (DBP) measured with the Complior Analyse software (ALAM Medical, Paris, France). A pulse wave Doppler ultrasound beam was aligned to the vessel walls at the site of acquisition of the diameter waveform, to simultaneously acquire velocity data (Swampillai et al., 2006). Arterial diameter and velocity were recorded continuously for 20 s. After completing the acquisition, all data were displayed and any individual beats with noisy or unrepresentative waveforms were rejected; all other beats (typically about 20) were selected and signal-averaged to give single waveforms of diameter and velocity (Rakebrandt et al., 2009). Common carotid diameter values and diameter-derived pressure data were used to calculate established indices of local arterial stiffness, such as elastic modulus ( $\epsilon$ ) and stiffness index ( $\beta$ ), according to published algorithms (O'Rourke et al., 2002), in all measurement rounds.

$$\epsilon = (SBP - DBP) / [(Ds - Dd) / Dd],$$

and

$$\beta = \ln(SBP/DBP)/[(Ds - Dd)/ Dd],$$

where Ds and Dd are the maximum and minimum arterial diameters, respectively, measured by wall tracking of the intima-media borders of the carotid artery.

The inter-day CV in our laboratory for intima-media thickness, beta stiffness, PWV beta, and carotid diastolic diameter was 0.11%, 7.10%, 1.75%, and 1.76%, respectively.

## Arterial Structure

cIMT measurements were recorded using high-resolution, non-invasive, semi-automated B-Mode ultrasound (Arietta V60; Aloka/Hitachi Medical Systems). The diameter was measured in M-Mode (Arietta V60; Aloka/Hitachi Medical Systems) with a high-frequency linear array probe (7.5 MHz). cIMT was measured twice on the far wall of the common carotid artery, 1 cm proximal to the bulb at the end-diastolic moment (R-wave), when cIMT is thickest (Touboul et al., 2007). The vascular diameter was measured at the same location as cIMT. The average minimum diameter value of the right common carotid artery, which corresponds with end-diastolic cIMT, was recorded from at least 5 heart cycles (Touboul et al., 2007).

## Body Composition

Height, waist circumference at the iliac crest and body weight were measured to the nearest 0.1 cm and nearest 0.1 kg, respectively, on a scale with an attached stadiometer (model 770, Seca; Hamburg, Deutschland). Body composition was also measured with a seca mBCA 515 using four pairs of electrodes (eight electrodes in total) positioned at each hand and foot. The 8-electrode technique enables segmental impedance measurement of the arms and legs. By this means, impedance was measured with a current of 100  $\mu$ A at frequencies between 1 and 1 000 kHz.

## Physical Activity

The level of physical activity and the sedentary lifestyle of the participants was assessed through the IPAQ long version (Campaniço, 2016). IPAQ measures physical activity over a broad range of activities domains such as leisure-time physical activity, domestic and gardening (yard) activities, work-related physical activity, and transport-related physical activity. To calculate the minutes per week of MVPA all moderate and vigorous sub-domains were included multiplying the minutes by the days of each sub-domain alone ultimately adding all the results to obtain the final answer. Time spent in sedentary activities per day was obtained by multiplying the week sedentary time by 5 plus multiplying the week-end sedentary time by 2 and the final result was this sum divided by seven, corresponding to the 7 days of a week. Compliance with physical activity recommendations was assessed according to the World Health Organization (150 min.week<sup>-1</sup> of moderate-to-vigorous physical activity, defined as  $\geq 21.4$  min.day<sup>-1</sup>) commonly used and validated for people with IDD (Bull et al., 2020).

### 3. Statistical Analyses

We performed an intention-to-treat analysis using all randomized participants. The data are presented as mean and standard deviation. The Shapiro-Wilk and Levene tests, as well as plot inspection, were used to verify normality and homoscedasticity assumptions. To compare individual characteristics independent-samples t-tests were employed.

The coefficient of variation for all variables was calculated using 2 evaluations moments of the same participant done on 2 different days. At least 10 distinct participants were used to calculate the CV as  $CV = \frac{SD}{AVG} \times 100\%$ , where SD stands for standard deviation and AVG for average. The changes in the dependent variables were examined using linear mixed models fitted with restricted maximum likelihood and applying Satterthwaite's method for approximating degrees of freedom for the F test from the R lmerTest package (Kuznetsova et al., 2017). The fixed effects were time and regime, whereas the random intercept was each participant. Using the R sjstats package (Lüdtke et al., 2020), partial eta squares ( $\eta^2$ ) were calculated for each main effect and interaction and interpreted using the rough benchmarks suggested by Cohen (1988) defining small ( $\eta^2 < 0.05$ ), medium ( $\eta^2 < 0.25$ ), and large ( $\eta^2 > 0.25$ ) effects sizes. In the occurrence of significant differences in main effects and interactions, post-hoc comparisons using Tukey's HSD test were performed using the R emmeans package (Lenth R, 2020). All statistical analyses were performed with a significant level ( $\alpha$ ) of  $< 0.05$  using R software (R core Team 2020).

## 4. Results

### I. Characterization of the Exercise Training Programs

The characteristics of the participants are presented in **Table 1**. The overall attendance rate of the home-based intervention was 81% (SIT = 92% and CAET = 69%) with a mean of 19 sessions (SIT = 22 sessions and CAET = 17 sessions) attended in a total of 24 training sessions offered. Only 4 participants of the CAET regime and 1 participant of the SIT regime participated in less than 75% (Pinto et al., 2019) of the home-based sessions (13%, 42%, 46%, 71%, and 71%). The overall attendance rate of the gym-based intervention was 79% (SIT = 77% and CAET = 80%) with a mean of 19 sessions (SIT = 19 and CAET = 19) attended in a total of 24 training sessions offered. Only 3 participants of the SIT regime participated in less than 75% of the gym-based intervention (38%, 63%, and 71%). The reported reasons behind the insufficient attendance rates included lesions (that were not developed during or caused by the exercise sessions, (n=1), schedule mismatch (n=5), and technical issues in the home-based sessions (n=2).

Table 2 - Participants characteristics by regime, pre intervention.

Pre-home-based intervention			
Variables	SIT (n=8) Moment 1	CAET (n=9) Moment 1	Regime differences (p-value)
<b>Characteristics</b>			
Age	26±8	29±13	p = 0.46
Sex (male/female)	6/2	5/4	p = 0.43
Resting heart rate (bpm)	80±11	79±14	p = 0.88
<b>Etiology</b>			
ASD	3	0	p = 0.04
DS	2	3	p = 0.33
GDD	1	4	p = 0.17
ID	2	1	p = 0.48
WS	0	1	p = 0.36

Data are presented as mean ± standard deviation. Abbreviations: ASD = autism spectrum disorder; DS = down syndrome; GDD = global development delay; ID = intellectual disability; WS = williams syndrome; SIT = sprint interval training; CAET = continuous aerobic exercise training.

The physiological demands of home-based and gym-based exercise interventions are displayed in **Table 3**. Average HR and %HRR during SIT and CAET in the home-based intervention did not differ (p = 0.11, p = 0.71, respectively). In the gym-based intervention, HR, but not %HRR, was higher during SIT compared to CAET (p = 0.02, p = 0.64, respectively). There were no differences in HR and %HRR between home-based and gym-based.

Table 3 – Comparison of attained and targeted HRR among delivery exercise modes and aerobic training regimes

Home-based					
		HRR (%)	HRR target (%)	HR (bpm)	HR target (bpm)
Phase 1	SIT	81%±4	≥100%	124±7	156 - 165



	CAET	72%±5	55% - 60%	117±1	116 - 119
Phase 2	SIT	82%±2	≥100%	128±8	156 - 165
	CAET	71%±11	60% - 70%	105±22	119 - 126
Phase 3	SIT	84%±11	≥100%	126±13	156 - 165
	CAET	67%±11	75% - 85%	92±22	130 - 137
<b>Gym-based</b>					
		<b>HRR (%)</b>	<b>HRR target (%)</b>	<b>HR (bpm)</b>	<b>HR target (bpm)</b>
Phase 1	SIT	83%±6	≥100%	129±12	156 - 165
	CAET	75%±9	55% - 60%	105±22	116 - 119
Phase 2	SIT	76%±10	≥100%	124±15	156 - 165
	CAET	72%±9	60% - 70%	96±14	119 - 126
Phase 3	SIT	80%±12	≥100%	129±16	156 - 165
	CAET	72%±8	75% - 85%	100±16	130 - 137

Data are presented as mean ± standard deviation. Abbreviations: HR = heart rate; HRR = heart rate reserve; SIT = sprint interval training; CAET = continuous aerobic exercise training.

## II. Cardiorespiratory Fitness

No differences were observed between regimes at M1 in the selected cardiorespiratory fitness indices ( $p = 0.11$ ;  $\eta^2 = 0.16$ ; **Table 4**). All participants remained classified as unfit (below average, poor, and very poor) from M1 to M4 (Pescatello et al., 2014). Abnormal HR recovery and chronotropic incompetence were present in 24% and 18% of the participants, respectively, throughout the study period. Overall, all the CPETs realized by the participants of the SIT regime were maximal, whereas the participants of the CAET regime only 6 CPETs were maximal. An effect of time was observed for  $\text{VO}_2$  peak ( $p < 0.01$ ;  $\eta^2 = 0.26$ ), suggesting a decrease from M1 to M2 ( $d = -1.8$ ; 95% CI: -0.2 to -3.4 mL/kg/min), and an increase from M2 to M4 ( $d = 2.1$ ; 95% CI: 0.4 to 3.8 mL/kg/min) (**Figure 4**), independent of age, sex, and fat mass. A main effect of time was also observed power output and for time to exhaustion during the CPET, suggesting that power output decreased from M1 to M2 ( $d = -27$ ; 95% CI: -49 to 5 W), but that it increased ( $d = 26$ ; 95% CI: 3 to 50) from M2 to M4 together with exercise duration ( $d = 104$ ; 95% CI: 14 to 194 s). No significant regime main effects or interaction effects were observed.

Table 4 - Comparison of indices of cardiorespiratory fitness among delivery exercise modes and aerobic training regimes

Cardiorespiratory fitness	SIT	CAET	Main effect of time (p-value; partial eta square)	Main effect of aerobic regime (p-value; partial eta square)	Interaction (p-value; partial eta square)
Time to peak power (s)			( $p = 0.02$ ; $\eta^2 = 0.21$ )	( $p = 0.19$ ; $\eta^2 = 0.13$ )	( $p = 0.98$ ; $\eta^2 = 0$ )
	<b>M1</b>	557±132	625±193	-	-
	<b>M2</b>	497±75	553±92	M2 < M4	-
	<b>M3</b>	540±79	623±90	-	-
	<b>M4</b>	595±176	663±72	-	-
Peak Power (W)			( $p < 0.01$ ; $\eta^2 = 0.29$ )	( $p = 0.71$ ; $\eta^2 = 0$ )	( $p = 0.71$ ; $\eta^2 = 0.04$ )
	<b>M1</b>	205±25	192±39	M1 > M2	-
	<b>M2</b>	168±25	174±26	M2 < M4	-
	<b>M3</b>	184±20	177±35	-	-

	<b>M4</b>	200±24	195±45	-	-	-
Heart rate max				(p = 0.03; $\eta^2$ = 0.19)	(p = 0.10; $\eta^2$ = 0.17)	(p = 0.44; $\eta^2$ = 0.07)
(bpm)	<b>M1</b>	159±13	151±29	-	-	-
	<b>M2</b>	158±17	143±26	-	-	-
	<b>M3</b>	146±21	139±19	-	-	-
	<b>M4</b>	143±19	143±24	-	-	-
RER				(p = 0.18; $\eta^2$ = 0.12)	(p = 0.10; $\eta^2$ = 0.17)	(p = 0.46; $\eta^2$ = 0.06)
	<b>M1</b>	1.16±0.14	1.00±0.10	-	-	-
	<b>M2</b>	1.11±0.16	1.07±0.10	-	-	-
	<b>M3</b>	1.11±0.14	1.05±0.09	-	-	-
	<b>M4</b>	1.12±0.18	1.00±0.10	-	-	-
Heart rate recovery				(p = 0.48; $\eta^2$ = 0.06)	(p = 0.83; $\eta^2$ = 0)	(p = 0.57; $\eta^2$ = 0.05)
1 <sup>st</sup> Minute						
(bpm)	<b>M1</b>	19±11	18±6	-	-	-
	<b>M2</b>	21±8	24±8	-	-	-
	<b>M3</b>	22±8	18±5	-	-	-
	<b>M4</b>	22±9	20±11	-	-	-

Data are presented as mean  $\pm$  standard deviation. Abbreviations: RER = respiratory exchange ratio; SIT = sprint interval training; CAET = continuous aerobic exercise training; M = moment.

\*  $p < 0.05$  regime effect significant different.

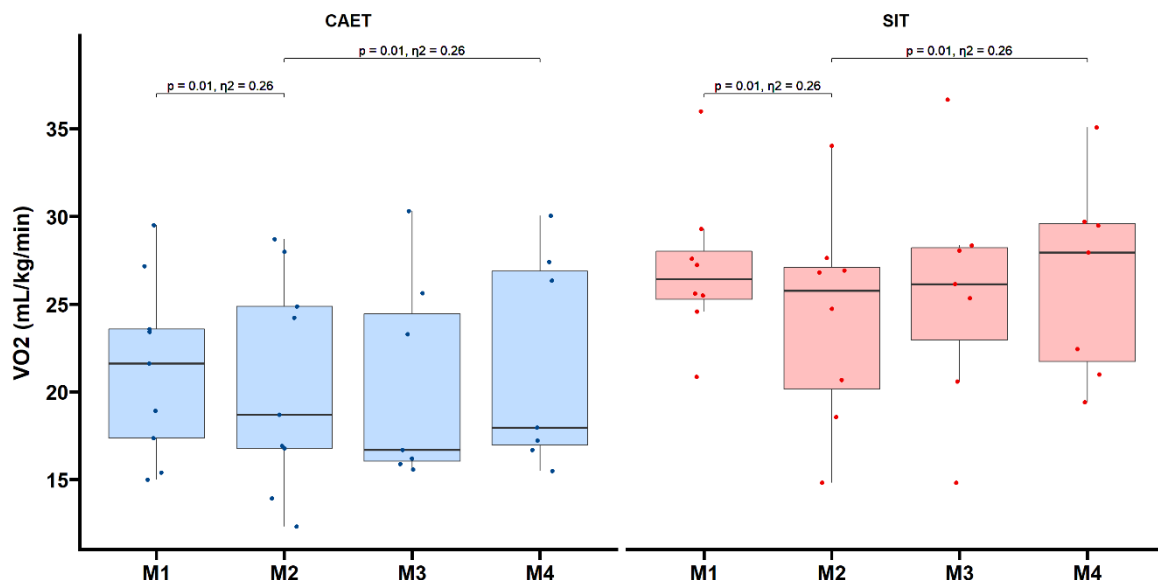


Figure 4 - Comparison of VO<sub>2</sub> peak among delivery exercise modes and aerobic training regimes.

### III. Arterial Stiffness and Structure

No significant differences were observed between regimes in regional or local indices of arterial stiffness. The incidence of aortic PWV above +2SD of the age- and blood pressure-specific mean reference values was 24% at M1, 12% at M2, 7% at M3 and 0% at M4 (The Reference Values for Arterial Stiffness' Collaboration, 2010). Significant main effects of time were observed for regional PWV ( $p < 0.05$ ;  $\eta^2 = 0.20-0.26$ ), suggesting a decrease in aortic PWV between M1 and M2 ( $d = -0.61$ ; 95% CI: -1.1 to -0.1 m/s), and in both aortic PWV ( $d = -0.63$ ; 95% CI: -1.1 to -0.1 m/s) and lower Limbs PWV ( $d = -0.72$ ; 95% CI: -1.4 to -0.1 m/s; Fig. 5) between M1 to M4 in. Changes in aortic PWV, but not in lower limb PWV, remained

significant after adjustment for bMAP, peak  $\text{VO}_2$ , height, fat mass, and age. No significant effects of time or regime were observed in elastic modulus, PWV- $\beta$ , and  $\beta$ -Stiffness between delivery modes or aerobic training regimes (see **Table 5**).

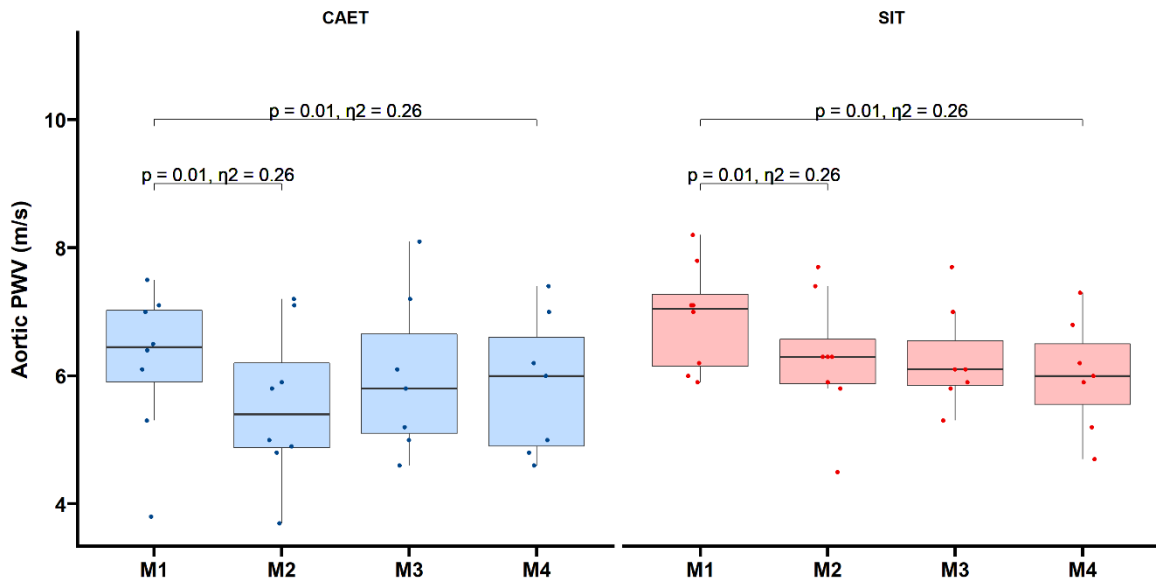


Figure 5 – Comparison of aortic PWV among delivery exercise modes and aerobic training regimes.

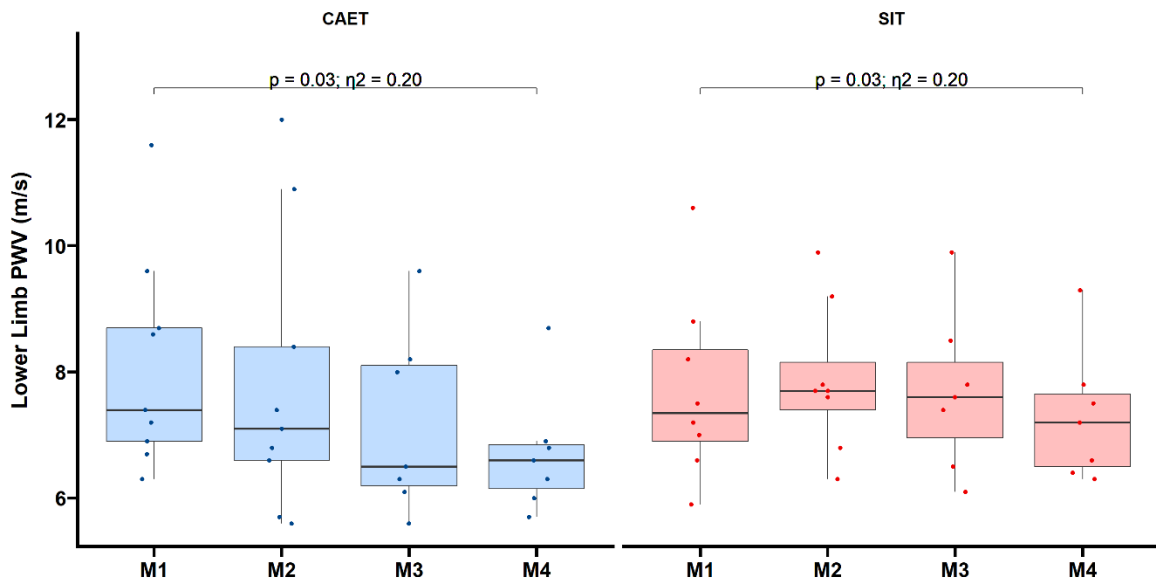


Figure 6 – Comparison of lower limb PWV among delivery exercise modes and aerobic training regimes.

The incidence of carotid intima-media thickness above the 75th age- and sex-specific percentile throughout the study period was 53% ( $p = 0.07$ ) (Engelen et al., 2013). A significant regime by time interaction effect was observed in the carotid diameter ( $p = 0.02$ ), driven by a decrease in carotid diameter from M1 to M4 ( $d = -0.51$ ; 95% CI:  $-0.92$  to  $-0.09$  mm).

Table 5 - Comparison of indices of arterial stiffness and structure among delivery exercise modes and aerobic training regimes

		SIT	CAET	Main effect of time (p-value; partial eta square)	Main effect of aerobic regime (p-value; partial eta square)	Interaction (p-value; partial eta square)
<b>Local Arterial Stiffness</b>						
$\epsilon$				(p = 0.32; $\eta^2$ = 0.09)	(p = 0.87; $\eta^2$ = 0)	(p = 0.26; $\eta^2$ = 0.10)
(mmHg)	<b>M1</b>	59±34	45±18	-	-	-
	<b>M2</b>	61±25	59±31	-	-	-
	<b>M3</b>	57±29	62±12	-	-	-
	<b>M4</b>	52±23	56±10	-	-	-
PWV- $\beta$				(p = 0.25; $\eta^2$ = 0.10)	(p = 0.95; $\eta^2$ = 0)	(p = 0.32; $\eta^2$ = 0.09)
(m/s)	<b>M1</b>	4.5±1.1	4.1±0.9	-	-	-
	<b>M2</b>	4.6±0.7	4.6±1.1	-	-	-
	<b>M3</b>	4.5±1.0	4.8±0.5	-	-	-
	<b>M4</b>	4.3±0.8	4.5±0.4	-	-	-
$\beta$ -Stiffness				(p = 0.20; $\eta^2$ = 0.11)	(p = 0.91; $\eta^2$ = 0)	(p = 0.28; $\eta^2$ = 0.10)
(AU)	<b>M1</b>	4.3±2.0	3.4±1.2	-	-	-
	<b>M2</b>	4.6±1.3	4.4±1.6	-	-	-
	<b>M3</b>	4.3±1.9	4.9±0.8	-	-	-
	<b>M4</b>	4.2±1.5	4.4±0.8	-	-	-
<b>Arterial Structure</b>						
Carotid diastolic diameter				(p = 0.02; $\eta^2$ = 0.21)	(p = 0.56; $\eta^2$ = 0.02)	(p = 0.01; $\eta^2$ = 0.25)
(mm)	<b>M1</b>	5.88±0.53	6.74±1.18	-	-	-
	<b>M2</b>	5.89±0.36	6.05±0.81	-	-	M2 < M1 <sup>†</sup>
	<b>M3</b>	6.16±0.38	6.04±1.10	-	-	M3 < M1 <sup>†</sup>
	<b>M4</b>	5.88±0.32	5.80±1.13	M4 < M1	-	M4 < M1 <sup>†</sup>
Carotid IMT avg				(p = 0.07; $\eta^2$ = 0.16)	(p = 0.13; $\eta^2$ = 0.14)	(p = 0.60; $\eta^2$ = 0.05)
(mm)	<b>M1</b>	0.48±0.08	0.56±0.15	-	-	-
	<b>M2</b>	0.44±0.07	0.54±0.19	-	-	-
	<b>M3</b>	0.47±0.07	0.57±0.13	-	-	-
	<b>M4</b>	0.47±0.08	0.59±0.13	-	-	-

Data are presented as mean  $\pm$  standard deviation. Abbreviations:  $\epsilon$  = elastic modulus; IMT = intima-media thickness; avg = average; SIT = sprint interval training; CAET = continuous aerobic exercise training; M = moment.

<sup>†</sup> p<0.05 interaction (regime x moment) significant difference in the CAET regime

#### IV. Hemodynamics

No significant differences were observed between aerobic regimes in hemodynamic parameters. The incidence of elevated brachial systolic blood pressure (bSBP) decreased from 65% at M1, to 47% at M2 (p = 0.69), 43% at M3, and 36% at M4 (p = 0.66) (Casey et al., 2019). Still, no significant differences were observed in bSBP throughout the study period (**Table 6**). A main effect of time was observed for bDBP and bMAP, suggesting a decrease from M1 to M4 (bDBP: d= -6; 95% CI: -2 to -10 mmHg; bMAP: (d= -6; 95% CI: -2 to -10 mmHg), from M2 and M4 (bDBP: d= -5; 95% CI: -0.4 to -9 mmHg; bMAP: d= -4; 95% CI: -0.4 to -9 mmHg), independently of age, sex, PWV aortic, VO<sub>2</sub> peak, and fat mass. A significant regime by time interaction effect was observed for central systolic blood pressure

(cSBP), suggesting a decrease ( $d = -6$ ; 95% CI:  $-5$  to  $-17$  mmHg) from M1 to M2 in SIT, independently of age, sex and  $VO_2$  peak, but not aortic PWV and fat mass.

Table 6 - Comparison of hemodynamics indices among delivery exercise modes and aerobic training regimes

Hemodynamics	SIT	CAET	Main effect of time (p-value; partial eta square)	Main effect of aerobic regime (p-value; partial eta square)	Interaction (p-value; partial eta square)
bSBP			( $p = 0.23$ ; $\eta^2 = 0.11$ )	( $p = 0.81$ ; $\eta^2 = 0$ )	( $p = 0.19$ ; $\eta^2 = 0.11$ )
(mmHg)	<b>M1</b>	125±13	122±19	-	-
	<b>M2</b>	122±12	124±18	-	-
	<b>M3</b>	120±13	121±11	-	-
	<b>M4</b>	115±12	123±7	-	-
bDBP			( $p < 0.01$ ; $\eta^2 = 0.29$ )	( $p = 0.82$ ; $\eta^2 = 0$ )	( $p = 0.28$ ; $\eta^2 = 0.09$ )
(mmHg)	<b>M1</b>	76±4	80±12	M1 > M4	-
	<b>M2</b>	80±5	77±12	M2 > M4	-
	<b>M3</b>	76±8	74±7	-	-
	<b>M4</b>	71±8	72±5	-	-
bMAP			( $p < 0.01$ ; $\eta^2 = 0.29$ )	( $p = 0.80$ ; $\eta^2 = 0$ )	( $p = 0.45$ ; $\eta^2 = 0.06$ )
(mmHg)	<b>M1</b>	92±5	94±13	M1 > M4	-
	<b>M2</b>	91±7	92±13	M2 > M4	-
	<b>M3</b>	91±8	89±7	-	-
	<b>M4</b>	85±9	89±5	-	-
bPP			( $p = 0.87$ ; $\eta^2 = 0.02$ )	( $p = 0.94$ ; $\eta^2 = 0$ )	( $p = 0.09$ ; $\eta^2 = 0.15$ )
(mmHg)	<b>M1</b>	49±13	42±14	-	-
	<b>M2</b>	46±9	47±13	-	-
	<b>M3</b>	44±11	46±11	-	-
	<b>M4</b>	45±8	50±7	-	-
cSBP			( $p = 0.36$ ; $\eta^2 = 0.08$ )	( $p = 0.39$ ; $\eta^2 = 0.05$ )	( $p = 0.04$ ; $\eta^2 = 0.18$ )
(mmHg)	<b>M1</b>	140±30	118±20	-	M1 > M2 <sup>†</sup>
	<b>M2</b>	123±21	123±15	-	-
	<b>M3</b>	131±30	121±12	-	-
	<b>M4</b>	124±32	120±8	-	-

Data are presented as mean ± standard deviation. Abbreviations: bSBP = brachial systolic blood pressure; bDBP = brachial diastolic blood pressure; bMAP = brachial mean arterial pressure; bPP = brachial pulse pressure; cSBP = central systolic blood pressure; SIT = sprint interval training; CAET = continuous aerobic exercise training; M = moment.

<sup>†</sup>  $p < 0.05$  interaction (regime x moment) significant difference in the SIT regime.

## V. Body Composition

No significant differences were observed between aerobic regimes at M1. According to body mass index (BMI) (Connor & Arif, 2021), 53% of the participants were classified as overweight (41%) or obese (12%) at M1, and 43% (overweight: 29%; obese: 14%) at M3 ( $p > 0.005$ ). According to waist circumference (World Health Organization, 2011), 65% of the participants were classified as elevated at M1, and 50% at M3. According to fat mass (Peine et al., 2013), 24% of the participants were above the 75th percentile at M1, and 29% at M3. A significant main effect of time was observed for fat mass, suggesting that fat mass decreased ( $d = -2$ ; 95% CI:  $-3$  to  $-0.2\%$ ) from M2 to M4, independently of age, sex, aortic PWV, bSBP, and  $VO_2$  peak but not MVPA or total physical activity (Table 7).

Table 7 - Comparison of body composition variables among delivery exercise modes and aerobic training regimes

Anthropometry		SIT	CAET	Main effect of time (p-value; partial eta square)	Main effect of aerobic regime (p-value; partial eta square)	Interaction (p-value; partial eta square)
Weight				(p = 0.20; $\eta^2$ = 0.11)	(p = 0.76; $\eta^2$ = 0)	(p = 0.40; $\eta^2$ = 0.07)
(kg)	<b>M1</b>	68.6±16.5	71.3±14.2	-	-	-
	<b>M2</b>	69.0±17.3	71.8±15.2	-	-	-
	<b>M3</b>	68.0±18.8	70.9±17.6	-	-	-
	<b>M4</b>	68.8±18.2	70.1±17.9	-	-	-
BMI				(p = 0.23; $\eta^2$ = 0.10)	(p = 0.85; $\eta^2$ = 0)	(p = 0.58; $\eta^2$ = 0.05)
(kg/m <sup>2</sup> )	<b>M1</b>	26±4	27±6	-	-	-
	<b>M2</b>	27±5	27±6	-	-	-
	<b>M3</b>	26±5	27±7	-	-	-
	<b>M4</b>	27±5	27±8	-	-	-
WC				(p = 0.13; $\eta^2$ = 0.08)	(p = 0.87; $\eta^2$ = 0)	(p = 0.07; $\eta^2$ = 0.16)
(cm)	<b>M1</b>	0.89±0.10	0.93±0.12	-	-	-
	<b>M2</b>	0.92±0.17	0.99±0.22	-	-	-
	<b>M3</b>	0.91±0.18	0.92±0.15	-	-	-
	<b>M4</b>	0.92±0.17	0.75±0.32	-	-	-
Fat-Free Mass				(p = 0.37; $\eta^2$ = 0.02)	(p = 0.59; $\eta^2$ = 0.02)	(p = 0.62; $\eta^2$ = 0.04)
(kg)	<b>M1</b>	48.9±8.9	46.8±6.9	-	-	-
	<b>M2</b>	48.6±8.7	46.8±7.3	-	-	-
	<b>M3</b>	48.7±9.0	47±8.0	-	-	-
	<b>M4</b>	49.7±9.3	47±8.7	-	-	-
Fat mass				(p = 0.02; $\eta^2$ = 0.23)	(p = 0.44; $\eta^2$ = 0.04)	(p = 0.83; $\eta^2$ = 0.02)
(kg)	<b>M1</b>	19.7±9.8	24.6±8.3	-	-	-
	<b>M2</b>	20.3±10.6	25.1±9.5	M2 > M4	-	-
	<b>M3</b>	19.3±11.2	23.8±12.4	-	-	-
	<b>M4</b>	19.1±11.7	23.1±12.9	-	-	-

Data are presented as mean ± standard deviation. Abbreviations: BMI = body mass index; WC = waist circumference; SIT = sprint interval training; CAET = continuous aerobic exercise training; M = moment.

## VI. Physical Activity

According to the IPAQ-long form, 82% of the participants were physically active, and no significant differences were observed between regimes in physical activity and sedentary time at M1 (p = 0.24; **Table 8**). There was a significant time effect for sedentary time as values decreased from M1 to M2 (d= -75; 95% CI: -148 to -3 minutes per day) and between M1 and M3 (d= -117; 95% CI: -213 to -20 minutes per day). No significant interaction effects with regime were observed.

Table 8 - Comparison of physical activity levels and sedentary time among delivery exercise modes and aerobic training regimes

Physical Activity	SIT	CAET	Main effect of time (p-value; partial eta square)	Main effect of aerobic regime (p-value; partial eta square)	Interaction (p-value; partial eta square)	
IPAQ total			(p = 0.19; $\eta^2 = 0$ )	(p = 0.90; $\eta^2 = 0.11$ )	(p = 0.96; $\eta^2 = 0$ )	
(min/week)	<b>M1</b>	499±735	360±314	-	-	-
	<b>M2</b>	615±470	560±932	-	-	-
	<b>M3</b>	445±902	1050±1266	-	-	-
	<b>M4</b>	457±656	577±734	-	-	-
MVPA			(p = 0.20; $\eta^2 = 0.04$ )	(p = 0.22; $\eta^2 = 0.11$ )	(p = 0.31; $\eta^2 = 0.08$ )	
(min/week)	<b>M1</b>	275±814	300±345	-	-	-
	<b>M2</b>	300±398	330±330	-	-	-
	<b>M3</b>	390±319	785±275	-	-	-
	<b>M4</b>	330±165	600±215	-	-	-
Sedentary Time			(p < 0.01; $\eta^2 = 0.37$ )	(p = 0.66; $\eta^2 = 0.01$ )	(p = 0.11; $\eta^2 = 0.20$ )	
(min/day)	<b>M1</b>	330±129	360±180	-	-	-
	<b>M2</b>	210±118	326±180	M2 < M1	-	-
	<b>M3</b>	261±184	176±36	M3 < M1	-	-
	<b>M4</b>	154±129	189±90	-	-	-

Data are presented as median ± interquartile range. Abbreviations: IPAQ = international physical activity questionnaire; MVPA = moderate-vigorous physical activity; SIT = sprint interval training; CAET = continuous aerobic exercise training; M = Moment.

## 5. Discussion

This is the first study to compare home- vs gym- based delivery modes of two 8-week supervised aerobic training regimes on cardiorespiratory fitness and arterial stiffness in adults with IDD. We found that home-based and gym-based delivery modes were equally effective in reducing aortic PWV, whereas improvements in lower limb PWV, cardiorespiratory fitness, mean arterial blood pressure, and fat mass were only observed following the gym-based intervention. We also found that both SIT and CAET regimes increased cardiorespiratory fitness and reduced aortic PWV and lower limbs PWV in adults with IDD. However, cSBP was only reduced following the SIT regime. Thus, although the home-based exercise intervention seems to have minimized the deleterious effects of the confinement due to COVID-19 on arterial health, a gym-based exercise intervention provided superior cardiovascular benefits in adults with IDD, regardless of the aerobic regime.

### I. Cardiorespiratory Fitness

The effectiveness of aerobic training to improve cardiorespiratory fitness has been demonstrated in adults and older adults with (Boer & Moss, 2016; Boer et al., 2014; Melo et al., 2021) and without IDD (Bouaziz et al., 2020; Milanović et al., 2015; Wen et al., 2019). However, when volume of exercise is controlled, higher intensities of aerobic exercise are more effective for improving cardiorespiratory fitness than lower intensities (Martin-Smith et al., 2020). Boer et al., (2014) for example, examined the effects of SIT and CAET during 15-weeks in adolescents and young adults with IDD and found that both regimes improved VO<sub>2</sub> peak, but gains were superior in SIT (100-110% ventilatory threshold). These findings were later replicated in adults with DS (Boer & Moss, 2016). Recently, Melo et al., (2021) found that the cardiorespiratory fitness non-response rate to 12-months of CAET in adults

with IDD was 60%, and it was reduced to 20% when 3 months of HIIT were added. However, this is not a universal finding. Arboleda-Serna et al., 2019 and Gist et al., 2014 did not observe differences in cardiorespiratory fitness following HIIT and CAET in apparently healthy adults, nor did Roy et al., 2018 and Wewege et al., 2017 in overweight and obese adults, in interventions ranging from 2-10 weeks. In the present study, changes on cardiorespiratory fitness were also independent of the aerobic regime. This discrepant findings may be related to the duration of intervention and exercise intensity.

We found that a home-based intervention did not prevent the deleterious effects of an 8 week mandatory home-confinement. Physical inactivity is the most plausible candidate to explain these results. Although participants reported a maintenance of physical activity levels, and a decreased in sedentary time following the home-based intervention, this is likely biased (Fitzgerald et al., 2020). Bed-rest physical inactivity trials suggest that  $VO_2$  peak is expected to be reduced by 7-15% (0.5-1.1%/day) after 2 weeks of bed rest (Pišot et al., 2016; Schwendinger & Pocecco, 2020). The mandatory home confinement in the present study lasted for 8 weeks and resulted in a decrease of  $\approx 7\%$  of  $VO_2$  peak (- 1.7 mL/kg/min) equivalent to a 0.5 metabolic equivalent of task (MET) decrease, which is similar to the results found in 2 weeks of bed-rest studies. This suggests that the home-based exercise intervention might have slowed down the expected deterioration rate in cardiorespiratory fitness (Schwendinger & Pocecco, 2020). A 1 MET reduction in maximum oxygen uptake ( $VO_2$  max) is associated with an 18% increase in risk of cardiovascular diseases and a 15% reduction in survival (Kodama et al., 2009). Thus, the decrease in  $VO_2$  peak during the mandatory home confinement is expected to have resulted in a 9% increase in risk of cardiovascular disease and an 8% reduction in survival. This is in line with the results from a recent study on the effects of physical inactivity during the COVID-19 outbreak on a 55-year-old male, wherein a decrease in  $VO_2$  max by 0.2% per day was reported, resulting in a 1.2 MET decrease after 8 weeks which corresponds to a 22% increased risk of cardiovascular disease and an 18% increase in all-cause mortality (Schwendinger & Pocecco, 2020). The lack of objective control of exercise intensity during this period may also partially explain these results. It is difficult to precisely define the minimum threshold of intensity needed to improve cardiorespiratory fitness, since it varies depending on the people current cardiorespiratory fitness level, age, health status, physiological differences, genetics, habitual physical activity, and social and psychological factors (Garber et al., 2011). However, it seems that clinical meaningful improvements on cardiorespiratory fitness depends on vigorous intensity (60 – 89% HRR) (Anton et al., 2011; Riebe et al., 2018).

On the other side, the gym-based exercise resulted in an increase of  $\approx 8\%$  of  $VO_2$  peak (+ 2 mL/kg/min), and this adaptation is suggested to be equivalent to a reduction  $\geq 9\%$  in risk for all-cause mortality and  $\geq 11\%$  in cardiovascular mortality (Lee et al., 2011). Changes in  $VO_2$  peak were associated with changes in fat mass, but not sedentary time or arterial stiffness. This suggests that the gym-based aerobic exercise intervention using cycle ergometers may have induced superior energy expenditure compared to the home-based aerobic training intervention using body weight dynamic exercises (Ainsworth et al., 2000). Beyond that, the ability to monitor HR in the gym-based intervention might as well contributed to a higher energy expenditure.

## II. Arterial Stiffness and Structure

Previous studies including adults with (S. Kim, 2017; Melo et al., 2021) and without IDD (Ashor et al., 2014; Huang et al., 2016; Zhang et al., 2018) reported an intensity (HIIT)- and total duration (>10 weeks)- dependent effect of aerobic exercise training on aortic and lower



limb PWV, in particular in those with stiffer arteries. However, our findings suggest that this may not be a universal finding, as both SIT and CAET were equally effective in reducing regional PWV, in line with other studies in adults with (S. Kim, 2017) or without IDD (Hasegawa et al., 2018; Way et al., 2019). Discrepancies may be related to the duration of the exercises intervention and to the similar exercise intensity in both aerobic exercise regimes in the present study (60 – 89% HRR) (Riebe et al., 2018).

In the present study, home- and gym- based delivery modes were effective in reducing aortic PWV, but lower limb PWV was only reduced following the gym-based intervention. This suggests that remote aerobic exercise interventions using body weight, even without objective control of the intensity, are not only effective in controlling traditional cardiovascular risk factors (Rawstorn et al., 2016), but can also deliver vascular benefits (Staiano et al., 2018). The home-based training resulted in a 7% decrease in aortic PWV, and this is likely to reduce the hazard for cardiovascular events (Vlachopoulos et al., 2014). Still, our findings are also in line with those suggesting that stiffness of the peripheral arteries might be harder to change in short aerobic exercise interventions ( $\leq 16$  weeks) (Hayashi et al., 2005). Changes in aortic PWV and lower limbs PWV were associated with changes in MAP. This is not the first time that decreases in regional PWV were associated with blood pressure, since high blood pressure promotes matrix synthesis that consequently causes increases in vascular thickness and structural stiffening. However, increases in nitric oxide availability, improvement of vascular smooth muscle cells function, reduced oxidative stress and inflammation, higher conduit artery elastin content, decreased concentration of vasoconstrictor agents (i.e., endothelin), (Donley et al., 2014; Higashi & Yoshizumi, 2004; Kasapis & Thompson, 2005; Liu et al., 2021; Rush et al., 2005; Zhang et al., 2018) may also explain the changes observed in regional PWV. On the other hand, neither the home- nor the gym-based interventions decreased local arterial stiffness or cIMT. Melo et al., (2021) reported similar results following 15 months of aerobic exercise in adults with IDD, and a systematic review and meta-analysis of randomized controlled trials by Huang et al., (2016) for which IMT was the outcome, concluded that changes in cIMT did not reach statistical significance, also suggesting it might require a longer intervention to change cIMT (Choo et al., 2014).

### III. Hemodynamics

Various studies reported beneficial outcomes on blood pressure following aerobic training in people with IDD, although some suggest that the magnitude is dependent on the aerobic regime. Oviedo et al., (2014) found improvements in both bSBP and bDBP (6/7 mmHg) after 14 weeks of CAET. Calders et al., (2011) found improvements of greater magnitude (15 mmHg) only when a resistance training program was added to CAET. However, Boer et al., (2014) and Melo et al., (2021) found intensity to be a main determinant of hemodynamic adaptations as improvements in bSBP (11 mmHg) and bMAP (11 mmHg) were only observed in SIT and HIIT interventions. However, these are not a universal findings (Boer & Moss, 2016). Not only the discrepancies may be explained by differences in the intensity set for CAET (e.g. Melo X: 50-69% maximum heart rate (HR max), present study: 72% HRR), as by other confounding variables such as the studied populations (IDD vs DS), and the total duration of the intervention (15 weeks to 60 weeks).

Although studies have shown the efficacy of home-based intervention in decreasing peripheral blood pressure (de Tarso et al., 2005; Farinatti et al., 2016; Hua et al., 2009; Turk-Adawi & Grace, 2014), in the present study bDBP and bMAP only decreased after the gym-based intervention. This decrease is likely of clinical significance (Miura et al., 2004), but according to the literature, a decrease in both bSBP (-3 to -11) and bDBP (-2 to -5) was

also expected following the home-based intervention (Hua et al., 2009; Turk-Adawi & Grace, 2014). However, this literature does not reflect the effects of home-based interventions under a mandatory home-confinement. COVID-19 home-confinement restrictions induced higher level of physical inactivity (Fitzgerald et al., 2020) and higher energy intake from poorer dietary control (Khot et al., 2021) and increased caloric/salty food intake (Rolland et al., 2020).

Still, the home-based intervention, particularly the SIT regime, was effective in reducing cSBP (mmHg). This is important as cSBP is a predictor of cardiovascular disease, such as a 10 mmHg increase in cSBP in adults (30-79 years old) is associated with a 1.30 adjusted hazard ratio risk for cardiovascular diseases (Wang et al., 2009). Thus, the 17 mmHg decrease in cSBP observed in the present study is of clinical relevance (Cheng et al., 2013). Mechanistically, this suggests improvements in the timing of the superimposition of the forward and backward waves at the aortic level, lasting the whole diastolic phase (Salvi, 2017). There were no associations between changes in  $VO_2$  peak and changes in peripheral or central blood pressure. However, changes in fat mass were associated with changes in central and peripheral DBP. This was expected (Park et al., 2019; Wyszńska et al., 2020), as increased fat mass is associated with increased sympathetic nervous system and renin-angiotensin-aldosterone system activity, leading to renal sodium reabsorption and renin release (Hall et al., 2021). Weight loss is likely to have caused the reversal of these mechanisms, strengthening its strategic role in the reduction of overall cardiovascular risk (Hall et al., 2021).

#### IV. Body Composition

Studies examining the effects of aerobic training in people with IDD often show no significant changes in body composition (Andriolo et al., 2011; Calders et al., 2011; Melo et al., 2021; Millar et al., 1993), although a few exceptions exist (Boer & Moss, 2016; Boer et al., 2014). In the present study, fat mass decreased  $\approx 10\%$  following the gym-based training but contrary to Boer et al., (2014), we did not find these changes to be dependent on the aerobic exercise regime. These changes in fat mass were associated with the increments in  $VO_2$  peak, MVPA and total physical activity per week, suggesting that even small, statistically non-significant increases in physical activity can benefit body composition. During the home-based intervention, the exercise sessions may have not induced a caloric deficit to result in a clinically relevant body fat decrease (Swift et al., 2018), and offset the likely increase in caloric consumption during the lockdown (Rolland et al., 2020).

#### V. Physical Activity

The majority of exercise intervention studies in IDD were not effective in decreasing physical inactivity (Hassan et al., 2019) or sedentary time (Melville et al., 2015; Ptomey et al., 2021), regardless of the aerobic exercise regime. Only 3 out of 9 studies reviewed reported positive effects on physical activity (Bergström et al., 2013; Shields et al., 2013; van Schijndel-Speet et al., 2017). These were mainly multicomponent (diet, exercise, and physical activity interventions) and used longer durations (8 to 16 months) compared to the present study. In the general population, public health measures to combat the spread of the COVID-19 have resulted in a 48% decrease in physical activity (Schwendinger & Pocecco, 2020) and a 4-6 hours increase in sedentary time (Theis et al., 2021). In the present study we were able to mitigate the expected increase in physical inactivity and sedentary time (Fitzgerald et al., 2020; Theis et al., 2021). However, we recognize this data may be biased since it

relies heavily on the participants' memory and recall with tendency to overreport the duration of activities (Matthews et al., 2011; Shephard, 2003).

## 6. Limitations and Future Directions

This study is not without limitations. We used a convenience group that may have lacked statistical power to support our results. Based upon a sample size of 17 and an obtained effect size of 0.26 for  $\text{VO}_2$  peak, 0.29 for aortic PWV and 0.20 for lower limb PWV, a posteriori achieved power analysis was of 0.68, 0.78 and 0.44, respectively (G-Power Version 3.1.9.3). We are unable to determine causality in the interpretation of the observed exercise-induced improvements in indices of cardiorespiratory fitness and arterial stiffness because we lack a true control group that did not exercised. Aerobic power was determined using a cycle ergometer which may not have any transfer to the activities commonly prescribed to this population. It was not possible to objectively monitor exercise intensity during the home-based intervention. However, we were still able to characterize exercise intensity based on the HR recordings from 3 sessions representing each phase of the home-based intervention as displayed in **Table 3**. Participants in the SIT regime did not attain the target intensity during both delivery modes. CAET and SIT regimes were not isocaloric, instead, they were time-matched. This challenges effective comparisons, as one regime could induce a higher energy expenditure than the other impacting. The home-based intervention occurred during home confinement with extreme restrictive measures, with obvious impact on participants' daily life compared to the gym-based intervention that, although still in the midst of a pandemic, occurred with less restrictive measures. This could result in lower physical activity levels of the participants in the home-based intervention compared to the gym-based intervention. Physical activity levels and sedentary behavior were estimated via questionnaire, that shows limited reliability and validity and that relies heavily on the participants' memory and recall with a tendency to overreport the duration of activities (Matthews et al., 2011; Shephard, 2003). Increased caloric intake during lockdown may have impacted study outcomes. Unfortunately, we were unable to control for energy intake. We only included people with IDD that were somehow familiarized with exercise training, which challenges the overreach of the results of the present study to the high prevalence of people with IDD that do not exercise at all.

## 7. Conclusion

A home-based exercise intervention may minimize the deleterious physiological effects of a mandatory lockdown on aortic arterial stiffness and blood pressure, but does not match the benefits in cardiorespiratory fitness, peripheral arterial stiffness and fat mass from an iso-temporal gym-based intervention, regardless of the aerobic exercise regime.

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Appendix 1

Aerobic training - Phase 1 – SIT Regime

 <p data-bbox="411 831 612 864">Jumping Jacks</p>	 <p data-bbox="986 831 1166 864">Standing Box</p>
 <p data-bbox="336 1267 692 1301">Side Shift with Floor Touch</p>	 <p data-bbox="995 1267 1150 1301">High Knees</p>
 <p data-bbox="708 1715 868 1749">Half Burpee</p>	

Aerobic training - Phase 1 – CAET Regime

 <p>Low impact Jumping Jacks</p>	 <p>Slow Standing Box</p>
 <p>Slow Side Shift with Floor Touch</p>	 <p>Slow High Knees</p>
 <p>Half Burpee (without jump)</p>	

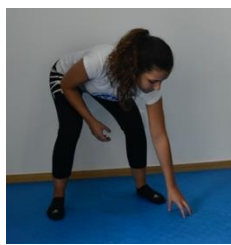
Aerobic training - Phase 2 and 3 – SIT Regime



Jumping Jacks



Standing Box



Side Shift with Floor Touch



High Knees



Half Burpee





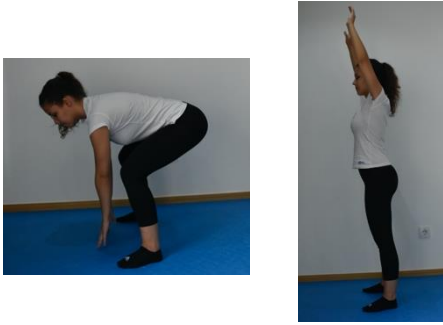



Upside Standing Box



Jumping Jacks (sagittal plane)

Aerobic training - Phase 2 and 3 – CAET Regime

 <p>Low impact Jumping Jacks</p>	 <p>Slow Standing Box</p>
 <p>Slow Side Shift with Floor Touch</p>	 <p>Slow High Knees</p>
 <p>Half Burpee (without jump)</p>	 <p>Hook Box</p>



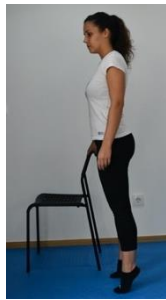
Balance Training – Phase 1 – Both Regimes



One leg stance



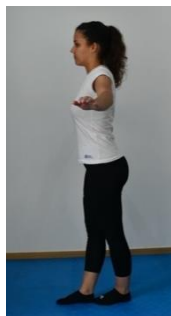
One leg stance



Dynamic plantar flexion



Dynamic dorsal flexion



Tandem front walk

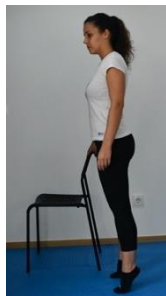
Balance Training – Phase 2 – Both Regimes



One leg stance (front, side, back)



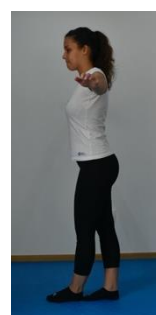
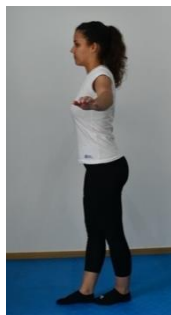
One leg stance (front, side, back)



Static plantar flexion



Static dorsal flexion



Tandem front and back walk

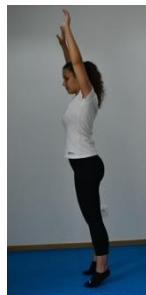
Balance Training – Phase 3 – Both Regimes



One leg stance (eyes closed)



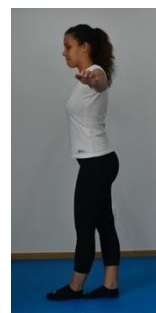
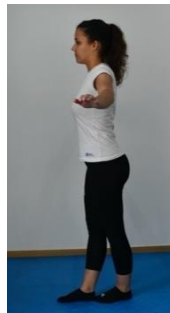
One leg stance (eyes closed)



Static plantar flexion with upper limbs abduction





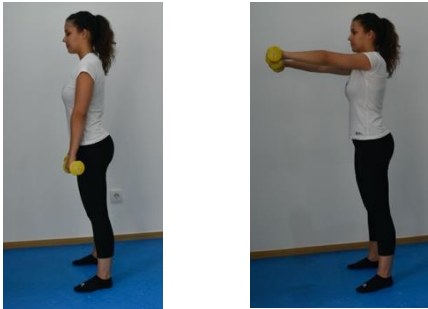



Static dorsal flexion



Tandem front and back walk

Resistance Training – Phase 1, 2, and 3 – Both Regimes

 <p>Chair squat</p>	 <p>Seated Row</p>
 <p>Seated bicep curl</p>	 <p>Tricep extension</p>
 <p>Shoulder flexion</p>	 <p>Side bend</p>