

kinesitherapie

**Masterthesis** 

and Meta-Analysis

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## Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de

The effects of Low- to Low-Moderate Intensity Aerobic Exercise with Blood Flow Restriction on Cardiorespiratory Fitness in Healthy People: A Critical Systematic Review

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

**COPROMOTOR :** Prof. dr. Frank VANDENABEELE



## Faculteit Revalidatiewetenschappen

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**BEGELEIDER :** De heer Sjoerd STEVENS

### Acknowledgement

This master's thesis was written in order to obtain the master's degree in Rehabilitation Sciences and Physiotherapy at the University of Hasselt. We discussed the effects of low- to low-moderate intensity aerobic exercise with blood flow restriction on cardiorespiratory fitness in healthy people. This topic has allowed us to further expand our knowledge.

First of all, we would like to thank our supervisor and co-supervisor, dr. Anouk Agten and Prof. dr. Frank Vandenabeele. They have given us the opportunity to investigate a self-chosen topic, in which we are very interested.

Thanks to the guidance, the feedback and the responsibility they have given us, we were able to successfully complete this master's thesis.

We would also like to thank Prof. dr. Raf Meesen, dr. Caroline Strouwen for their information about statistical procedures, drs. Sjoerd Stevens for his useful recommendations and Prof. dr. Chris Burtin for his help in defining the exercise intensity as selection criterion.

In addition, we would like to thank our parents. They made it possible to study at the University of Hasselt and have been a great support during the writing of our master's thesis.

Finally, we would like to thank each other. Without the great cooperation, we would not have been able to complete this thesis successfully. We were always there for each other and supported each other when necessary.

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#### **Research context**

This master's thesis is an individual study, situated in the musculoskeletal rehabilitation sciences and physiotherapy department at the University of Hasselt (UHasselt). It is a duo master's thesis performed over two years. In the first year a systematic review was done and a research protocol was developed on the reliability and feasibility of the use of threedimensional ultrasonography for volume measurement of skeletal muscles. Initially, an experimental study on this topic was planned to be performed in the second year at REVAL, the study centre for rehabilitation research of the University of Hasselt. Due to our interest in Blood Flow Restriction Training (BFRT) this plan was changed, and we were given the opportunity to perform a systematic review with data-pooling (meta-analysis) on a relevant topic in the research domain of BFRT. Nowadays, BFRT is widely being investigated. However, no research is currently being conducted in Belgium. Therefore, this master's thesis could be of value for further research at REVAL.

Blood Flow Restriction Training is a relatively low intensity and low volume training method whereby the arterial blood inflow to distal muscles is partially restricted, causing inadequate oxygen supply (hypoxia) within muscle tissue (Manini & Clark, 2009), combined with venous blood volume pooling due to complete restriction of veins (Scott, Loenneke, Slattery & Dascombe, 2015). Currently, the evidence about aerobic exercise with BFR is scarce. However, there is some evidence that aerobic exercise with BFR could improve maximal oxygen consumption (VO2max). Maximal oxygen consumption is the maximal amount of oxygen that an individual can utilize during a maximal exercise effort and can be regarded as an indicator of one's current cardiorespiratory fitness. While very low- to low intensity aerobic exercise is not capable of eliciting an adequate stimulus for improvements in VO2max, high intensity to maximal intensity exercise may not be appropriate in some cases such as musculoskeletal injuries, post-operative rehabilitation and frail elderly.

No systematic review with meta-analysis of studies was yet conducted on the comparison between different healthy populations and between types and modalities of exercise. Therefore, we undertook such review. The main research question of this review with metaanalysis was: "What are the effects of low- to low-moderate intensity aerobic exercise with blood flow restriction on cardiorespiratory fitness in healthy people?".

This systematic review with meta-analysis was supervised by the following persons: Dr. Anouk Agten, as supervisor, Prof. Dr. Frank Vandenabeele as co-supervisor and Mr. Sjoerd Stevens,

as mentor. The review was written by Liam Thijs and Mathias Thoelen, both master's students, complementing each other. We received full autonomy to determine our research topic and to perform this master's thesis, as this topic was not part of the research projects of the research unit. After receiving information about aerobic exercise intensities from Prof. dr. Chris Burtin, we were able to determine this as inclusion criterion. Statistical analyses for the meta-analysis could be performed after receiving detailed information and formulas from dr. Carolien Strouwen. We independently performed the selection process, quality assessment and data-extraction. Reflections in the discussion were made together. Consensus was reached in areas of initially diverging views. An even amount of time and effort was invested by both of us.

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#### 1. Abstract

**Background:** While low intensity aerobic exercise is not capable of improving cardiorespiratory fitness (VO2max), high intensity aerobic exercise may not be appropriate in some cases. Therefore, low- to low-moderate intensity aerobic exercise with Blood Flow Restriction (BFR) could offer a solution by providing a low mechanical stimulus and still obtaining improvements in VO2max. The main objective of this systematic review and meta-analysis was to investigate the effects of low- to low-moderate intensity aerobic exercise with BFR on VO2max in healthy people.

**Methods:** The PubMed, Web of Science and Scopus electronic databases were consulted for the identification of studies meeting following criteria: BFR was solely applied to aerobic exercise, the training protocol was at least two weeks and the outcome was chronic effects on VO2max. Quality assessment was based on the revised Cochrane risk-of-bias tool for randomized trials (RoB2). An inverse variance statistical method was used in Review Manager 5.3. Subgroup analyses were conducted on different healthy populations and types and modalities of exercise.

**Results:** The literature search yielded seven studies in total. All were included in the systematic review. Five were included in the meta-analysis. This provided data of 168 and 73 participants, respectively. The final risk of bias was judged as 'some concerns' for all studies. The overall effect of low- to low-moderate intensity aerobic exercise with BFR on VO2max was statistically significant (Z = 7.22; p < 0.00001) with a mean difference of 3.16 ml/kg/min [95% CI = 2.30, 4.01]. Elite athletes, healthy adults and all exercise types and modalities showed a significant improvement in VO2max.

#### **Discussion and conclusion:**

This meta-analysis shows that low- to low-moderate intensity aerobic exercise with BFR can offer a solution to improve VO2max in cases where high intensity exercise is not appropriate. Due to the small amount of studies included, conclusions should be made with caution.

#### Important keywords:

Aerobic exercise, Low- to low-moderate intensity, Blood Flow Restriction, Cardiorespiratory fitness, Healthy people

#### 2. Introduction

Maximal oxygen consumption (VO2max) is the maximal amount of oxygen that an individual can utilize during a maximal exercise effort. On one hand, VO2max is the golden standard to measure an individual's endurance performance (Allen, Seals, Hurley, Ehsani & Hagberg, 1985). On the other hand, VO2max can be regarded as an indicator of one's current cardiorespiratory fitness and is therefore a predictor for the risk of disease-specific mortality and all-cause mortality (Harber et al., 2017). The risk of chronic diseases, disease-specific mortality and all-cause mortality can be decreased by physical activity, as concluded by Kruk (2007) and Harber et al. (2017).

The recommendation for aerobic exercise on a weekly basis is provided by The American College of Sports Medicine (ACSM) (Riebe, Ehrman, Liguori, Magal & American College of Sports Medicine, 2018). They recommend performing at least five days moderate intensity aerobic exercise of 30-60 minutes per day or at least three days vigorous intensity aerobic exercise of 20-60 minutes per day, or a combination of three to five days of moderate and vigorous intensity aerobic exercise to achieve and maintain health/fitness benefits. The ACSM demarcated five exercise intensities as following: 1. very low intensity: <30% of Heart Rate Reserve (%HRR) or Oxygen Uptake Reserve (%VO2R), <57% of Maximum Heart Rate (%HRmax) and <37% of VO2max; 2. low intensity: 30-39% of HRR or VO2R, 57-63% of HRmax and 37-45% of VO2max; 3. moderate intensity: 40-59% of HRR or VO2R, 64-76% of HRmax and 46-63% of VO2max; 4. vigorous or high intensity: 60-89% of HRR or VO2R, 77-95% of HRmax and 64-90% of VO2max and 5. near maximal to maximal intensity: ≥90% of HRR or VO2R, ≥96% of HRmax and ≥91% of VO2max. While very low- to low intensity aerobic exercise is not capable of eliciting an adequate stimulus for improvements in VO2max, high intensity to maximal intensity exercise may not be appropriate in some cases such as musculoskeletal injuries, postoperative rehabilitation and frail elderly. Scribbans, Vecsey, Hankinson, Foster and Gurd (2016) recommend a training intensity above approximately 60% of VO2max, which corresponds to moderate intensity as described by the ACSM, to improve VO2max in healthy adults. They suggest no additional increases in VO2max with an increasing training intensity above approximately 60% of VO2max. A solution to provide a low mechanical stimulus and still obtain results, could be low- to low-moderate intensity aerobic exercise with the most proximal application of Blood Flow Restriction (BFR) by pneumatic compression on both thighs.

Blood Flow Restriction training (BFRT) is a relatively low intensity and low volume training method whereby the arterial blood inflow to distal muscles is partially restricted, causing inadequate oxygen supply (hypoxia) within muscle tissue (Manini & Clark, 2009), combined with venous blood volume pooling due to complete restriction of veins (Scott et al., 2015). This training method has been developed by Dr. Yoshiaki Sato in Japan, since 1966. It was first known as "kaatsu training", meaning "training with added pressure" (Patterson et al., 2019). He developed a pneumatically pressurized cuff system (Kaatsu Master Device) as reported in Sato (2005). Nowadays, kaatsu training is performed all over the world. It is more commonly referred to as "Blood Flow Restriction Training" and does not always require the Kaatsu Master Device (Patterson et al., 2019). Practical Blood Flow Restriction Training (pBFRT) uses elastic wraps or bands to achieve restriction and a perceived tightness of seven out of ten. The current evidence about BFRT, reported in the Position Stand paper of Patterson et al. (2019), suggests that low intensity resistance training with BFR has significant effects in skeletal muscle hypertrophy and strength in healthy young people (Lixandrao et al., 2018), athletes (Cook, Kilduff & Beaven, 2014), elderly (Centner, Wiegel, Gollhofer & König, 2019) and load compromised people in need of rehabilitation (Hughes, Paton, Rosenblatt, Gissane & Patterson, 2017). The effects in skeletal muscle strength are lower compared to high load resistance training, while the effects in skeletal muscle hypertrophy are equally effective as concluded by Patterson et al. (2019).

Currently, the evidence about aerobic exercise with BFR is scarce. However, the systematic reviews with meta-analyses of Slysz, Stultz and Burr (2016) and Centner et al. (2019) suggest that in both young and older people aerobic exercise with BFR can increase skeletal muscle hypertrophy and strength, respectively. Silva et al. (2019) concluded that aerobic exercise with BFR is safe for athletes, healthy young, obese and elderly individuals. Furthermore, there is some evidence that aerobic exercise with BFR could improve VO2max. A possible explanation could be a decline in both oxygen delivery and metabolite clearance during BFRT (Suga et al., 2009).

However, no systematic review with meta-analysis was yet conducted on the comparison between different healthy populations and between types and modalities of exercise (i.e., cycling, rowing or walking; continuous or interval). Therefore, the aim of this systematic review and meta-analysis was to investigate the effects of low- to low-moderate intensity aerobic exercise with blood flow restriction on cardiorespiratory fitness in healthy people.

#### 3. Methods

This systematic review with meta-analysis was performed in accordance with the guidelines provided in the PRISMA Statement (Moher, Liberati, Tetzlaff, & Altman, 2009).

#### 3.1. Research question

What are the effects of low- to low-moderate intensity aerobic exercise with blood flow restriction on cardiorespiratory fitness in healthy people?

#### 3.2. Literature search

The literature search was performed until March 30<sup>th</sup>, 2020. The PubMed, Web of Science and Scopus electronic databases were consulted. Keywords were selected as 'Title-Abstract', 'Title-Abstract-Keyword' and 'Topic' respectively. Two separate subcategories were combined with 'AND'. Keywords within a subcategory were combined with 'OR'. The first subcategory representing the intervention contained the following keywords: 'Blood Flow Restriction', Blood Flow Moderation', 'BFR', 'BFRT', 'Occlusion Training', 'Ischemic Training', 'KAATSU' and 'Vascular Occlusion'. The second subcategory representing the outcome contained the following keywords: 'VO2max', 'VO2peak', 'Maximal Oxygen Uptake', 'Maximal Oxygen Consumption', 'Aerobic Capacity', 'Aerobic Fitness', 'Aerobic Performance', 'Cardiorespiratory Fitness' and 'Physical Endurance'.

#### 3.3. Eligibility criteria

Eligibility of studies was assessed independently by two reviewers (L.T. & M.T.) based on the following criteria. Consensus was reached in areas of initially diverging views.

Experimental studies were included if the exercise intensity was low- to low-moderate, defined as a percentage from 30% to 50% of VO2R, HRR or maximal power (Pmax); a percentage from 37% to 50% of VO2max or a percentage from 57% to 70% of HRmax. This criterion was established based on Riebe et al. (2018) and on a consensus between both reviewers, taking the relevance of this study into account.

Moreover, studies were included if BFR was applied during the exercise; if the duration of the training protocol was at least two weeks, leading to a timespan of at least two weeks between pre- and post-measurement of VO2max or VO2peak; if means and standard deviations of

VO2max or VO2peak were reported or obtained on request to first author and if the population were healthy humans.

Studies were excluded in case of an abstract, protocol, review or case report; if the manuscript was not written in English or Dutch; if the outcome only focused on acute effects on VO2max within a training session; if BFR was only applied pre- or post-exercise and if BFR was not solely imposed on aerobic training in a concurrent training protocol.

In order to maximize the amount of information, no eligibility criteria were established on age, gender distribution, physical level, BFR modality, exercise type (i.e., cycling, rowing or walking) and exercise modality (i.e. continuous or interval).

Studies were excluded from the statistical analyses if there were no data reported and if the authors were not contactable for a request. The data will be specified in 'section 3.6. Statistical analysis'.

#### 3.4. Quality assessment

Selected Studies were assessed on quality in accordance with the items described in the "Revised Cochrane risk-of-bias tool for randomized trials (RoB2)" published by the RoB2 Development Group (Higgins, Savović, Page, Elbers & Sterne, 2019). This tool provides a framework which is divided in five domains: the randomization process, the intervention procedure (comprised of an assignment part and an adherence part), the outcome data, the outcome measurement and the reporting of the result. Items were scored with "yes", "probably yes", "no", "probably not", "no information" or "not applicable". Based on answers and following an algorithm, a judgement about the risk of bias was given for each domain. At the end, a final overall risk of bias judgement was given to all included studies separately. The judgement "low risk of bias" was given if all abovementioned domains were of low risk of bias, "some concerns" if at least one domain had some concerns and "high risk of bias" if at least one domain had some concerns leading to a lower quality. Studies judged "high risk of bias" were to be excluded.

A green or red colour was added to visually display a positive or negative value while a black colour represents an impartial value. Quality assessment was performed independently by two reviewers (L.T. & M.T.). Consensus was reached in areas of initially diverging views.

#### 3.5. Data-extraction

Data were independently extracted from included studies by the two researchers (L.T. & M.T.). Consensus was reached in areas of initially diverging views.

First, study characteristics including intervention duration, session frequency, adjustment of training intensity and control of dietary patterns were obtained. Secondly, participant characteristics including population, mean age, sample size, gender distribution in the intervention and control groups and pre-test Body Mass Index (BMI) of the intervention group were extracted. In case of absence, BMI was calculated using the following formula, weight (kg) / [height (m)]<sup>2</sup>. Furthermore, group characteristics including exercise type, modality, exercise duration, exercise intensity, BFR modality and assessment of limb occlusion pressure (LOP) or arterial occlusion pressure (AOP) were obtained. Outcome characteristics including measurement instrument and primary outcome measure were extracted.

Finally, pre- and post-measurement data of VO2max or VO2peak as means and standard deviations, reported as relative values (ml/kg/min), percentual changes, significance and F-values were extracted. In case of absence of a percentual change, the following formula was used to calculate it: [(MEANpost – MEANpre)/MEANpre] × 100.

#### 3.6. Statistical analyses

A meta-analysis was performed by pooling data via the inverse variance statistical method in Review Manager 5.3 (RevMan V.5.3; Cochrane Collaboration, Oxford, UK). 'Generic inverse variance' was selected as the outcome type and the outcome was named 'VO2max'. A fixed effect model was used. As effect measure, 'mean difference' was selected. Mean difference of pre-test versus post-test (d) and standard error of mean difference (SE) were entered as data. Mean differences could be calculated by subtracting the pre-test value from the posttest value. If SE was not provided in the study, the following calculation had to be made: SE = d/t-value. If a t-value was not provided in the study, it could be calculated with the online tdistribution calculator (STAT TREK) by entering an exact p-value and a value for degrees of freedom (sample size minus one). Alternatively, if an F-value was provided, the t-value could be calculated with the following formula:  $F=t^2$ . Three sub-analyses were performed based on population (elite athletes and healthy adults), exercise type (cycling, treadmill walking and rowing) and exercise modality (continuous and interval). Confidence intervals were set at 95%. Statistical significance was set at a p-value of < 0.05.

#### 4. Results

#### 4.1. Results study selection

The literature search yielded 1383 studies in total, composed of 42 results on Pubmed, 416 results on Web of Science and 925 results on Scopus. Details can be found in Tables 1, 2 and 3. An amount of 282 duplicates was removed. A number of 900 studies were excluded on title and 182 studies on abstract based on abovementioned eligibility criteria. Consequently, 19 studies remained for screening on full text of which six studies were to be included. One study, i.e. the study of Ursprung (2016), was included by hand searching after reviewing the reference lists of the included studies and related systematic reviews, i.e. Bennett and Slattery (2019). The study of Held, Behringer and Donath (2020) was included based on their training intensity below an individual heart rate equivalent to the first lactate threshold. They reported that this intensity was between 65% of HRmax and a blood lactate concentration of 2 mmol/L, which corresponded to the upper limit of our inclusion criterion. The study of Conceição et al. (2019) did not report means and standard deviations of VO2max or VO2peak. These data were obtained on request to the first author. Eventually, seven articles were included in this systematic review. Furthermore, the studies of Abe et al. (2010b), Held et al. (2020) and Kim et al. (2016) did not report SE or values with which we could calculate SE. Only the authors of Held et al. (2020) were contactable for obtaining these data. Eventually, five articles were included in the statistical analyses. The selection process can be found in Figure 1 and Table 4 gives an overview of the excluded studies on abstract and full text.

# Table 1Keywords in PubMed

	Keywords	Hits in November	Hits on March
		2019	30 <sup>th</sup> , 2020
#1	Blood Flow Restriction [Title/Abstract]	530	572
#2	Blood Flow Moderation [Title/Abstract]	22	22
#3	BFR [Title/Abstract]	1.393	1.443
#4	BFRT [Title/Abstract]	41	46
#5	Occlusion Training [Title/Abstract]	58	61
#6	Ischemic Training [Title/Abstract]	17	18
#7	KAATSU [Title/Abstract]	101	106
#8	Vascular Occlusion [Title/Abstract]	4.149	4.206
#9	VO2max [Title/Abstract]	7.274	9.989
#10	VO2peak [Title/Abstract]	1.799	3.269
#11	Maximal Oxygen Uptake [Title/Abstract]	4.635	4.704
#12	Maximal Oxygen Consumption	2.712	2.742
	[Title/Abstract]		
#13	Aerobic Capacity [Title/Abstract]	5.083	5.185
#14	Aerobic Fitness [Title/Abstract]	3.041	3.120
#15	Aerobic Performance [Title/Abstract]	722	756
#16	Cardiorespiratory Fitness [Title/Abstract]	4.654	5.092
	Physical Endurance [Title/Abstract]		
#17	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR	458	468
#18	#7 OR #8	5.772	5.894
	#9 OR #10 OR #11 OR #12 OR# 13 OR #14		
#19	OR #15 OR #16 OR #17	24.736	27.892
	#18 AND #19		
#20		33	42

### Table 2

Keywords in Web of Science

	Keywords	Hits in November	Hits on March
		2019	30 <sup>th</sup> , 2020
#1	TOPIC: (Blood Flow Restriction)	3.796	3.900
#2	TOPIC: (Blood Flow Moderation)	14	16
#3	TOPIC: (BFR)	1.717	1.767
#4	TOPIC: (BFRT)	40	43
#5	TOPIC: (Occlusion Training)	3.801	3.968
#6	TOPIC: (Ischemic Training)	2.553	2.619
#7	TOPIC: (KAATSU)	174	182
#8	TOPIC: (Vascular Occlusion)	23.314	23.664
#9	TOPIC: (VO2max)	5.563	5.731
#10	TOPIC: (VO2peak)	1.957	2.034
#11	TOPIC: (Maximal Oxygen Uptake)	8.856	9.007
#12	TOPIC: (Maximal Oxygen Consumption)	6.478	6.599
#13	TOPIC: (Aerobic Capacity)	15.857	16.270
#14	TOPIC: (Aerobic Fitness)	11.608	12.007
#15	TOPIC: (Aerobic Performance)	19.288	19.998
#16	TOPIC: (Cardiorespiratory Fitness)	9.378	9.770
#17	TOPIC: (Physical Endurance)	11.982	12.365
#18	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR	33.611	34.281
	#7 OR #8		
#19	#9 OR #10 OR #11 OR #12 OR# 13 OR #14	63.349	65.211
	OR #15 OR #16 OR #17		
#20	#18 AND #19	403	416

# Table 3Keywords in Scopus

	Keywords	Hits in November	Hits on March
		2019	30 <sup>th</sup> , 2020
#1	TITLE-ABS-KEY: (Blood Flow Restriction)	6.082	6.210
#2	TITLE-ABS-KEY: (Blood Flow Moderation)	36	36
#3	TITLE-ABS-KEY: (BFR)	2.163	2.235
#4	TITLE-ABS-KEY: (BFRT)	44	49
#5	TITLE-ABS-KEY: (Occlusion Training)	3.969	4.194
#6	TITLE-ABS-KEY: (Ischemic Training)	3.837	3.946
#7	TITLE-ABS-KEY: (KAATSU)	163	171
#8	TITLE-ABS-KEY: (Vascular Occlusion)	69.111	70.090
#9	TITLE-ABS-KEY: (VO2max)	9.337	9.690
#10	TITLE-ABS-KEY: (VO2peak)	3.046	3.240
#11	TITLE-ABS-KEY: (Maximal Oxygen Uptake)	10.422	10.605
#12	TITLE-ABS-KEY: (Maximal Oxygen	19.157	19.424
	Consumption)		
#13	TITLE-ABS-KEY: (Aerobic Capacity)	21.916	22.416
#14	TITLE-ABS-KEY: (Aerobic Fitness)	11.440	11.771
#15	TITLE-ABS-KEY: (Aerobic Performance)	18.741	19.402
#16	TITLE-ABS-KEY: (Cardiorespiratory	7.545	8.002
	Fitness)		
#17	TITLE-ABS-KEY: (Physical Endurance)	31.044	31.711
#18	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR	83.571	85.008
	#7 OR #8		
#19	#9 OR #10 OR #11 OR #12 OR# 13 OR #14	89.266	91.582
	OR #15 OR #16 OR #17		
#20	#18 AND #19	898	925

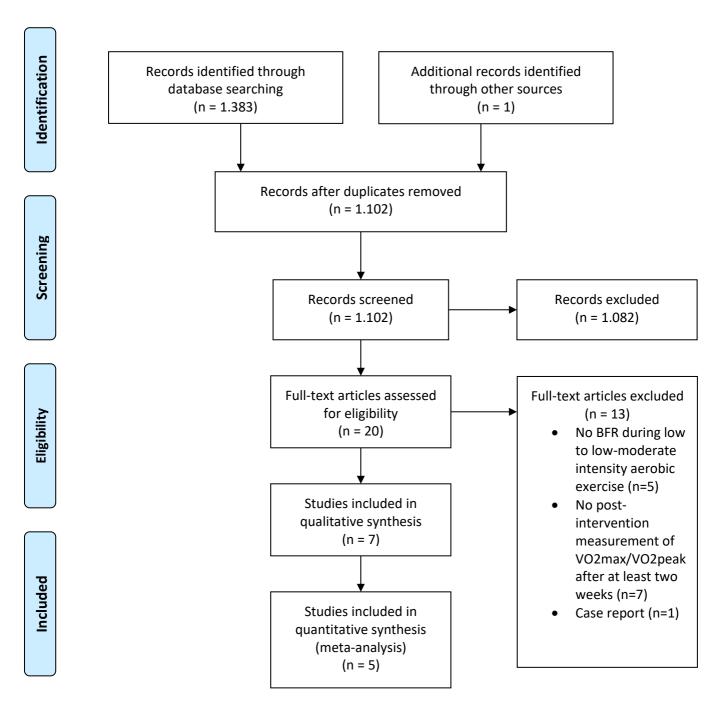


Figure 1. PRISMA flow diagram of the literature search.

Reason of exclusion	Number of studies (N= 195)	References
Based on abstract	182	
Population	2	Naderi-Boldaji, Joukar, Noorafshan, and Bahreinipour (2019); Naderi-boldaji, Joukar, Noorafshan, Raji-amirhasani, Naderi-boldaji, and Bejeshk (2018).
Inter- vention	146	Alqahtani, Alajam, Eickmeyer, Vardey, and Liu (2019); Amani, Sadeghi, and Afsharnezhad (2018); Belardinelli, Georgiou, Cianci, and Purcaro (1999); Bernardi (2001); Brechue, Ameredes, Barclay, and Stainsby (1995); Bruce et al. (1977); Burtscher, Gatterer, Szubski, Pierantozzi, and Faulhaber (2010); Cardozo, Oliveira, and Farinatti (2015); Chrif, Chaouach and Ahmaidi (2017); Chomiuk, Folga, and Mamcara (2013); Clevidence, Mowery, and Kushnick (2012); Cruz, De Aguiar, Turnes, Pereira, and Caputo (2015); Currie, Thomas, and Goodman (2009); Da Mota, Willis, Sobral, Borrani, Billaut, and Millet (2019); Dankel et al. (2019); De Groot, Thijsen, Sanchez, Ellenkamp, and Hopman (2010); Dressendorfer (1979); Dressendorfer, Smith, Amsterdam, and Mason (1982); Dushanin, Kuprienko, and Beregovoï (1987); Farhani and Riyahi (2019); Fatone et al. (2016); Ferguson, Wylde, Benson, Cannon, and Rossiter (2016). T. Ferreira et al. (2016); Foster et al. (1999); Galetta et al. (2012); Gardner, Montgomery, Flinn, and Katzel (2005); Gloc and Nowak (2016); Grace, Herbert, Elliott, Richards, Beaumont, and Sculthorpe (2018); Haykowsky, Brubaker, Stewart, Morgan, Eggebeen, and Kitzman (2012); Helal, do Nascimento Salvador, De Luca: and Guglielmo (2019); Hepple, Babits, Plyley, and Goodman (1999); Hernandez and Frank (2005); Hittinger et al. (2015); Ho et al. (2019); Hopker, O'Grady, and Pageaux (2017); Iten et al. (2011); Jeffries, Evans, Waldron, Coussens, and Patterson (2019); Jeffries, Waldron, Pattison, and Patterson (2018); Kacin and Strazar (2011); Kemmler, Engelke, Lauber, Weineck, Hensen, and Kalender (2002); Karamidas, Kounalakis, and Geladas (2012); Keslacy et al. (2005); Kiding, Sequeira, and Wood (2013); C. Kim, Choi, and Lim (2016); Klecha et al. (2007); Korshøj et al. (2015); Kraemer, Kubo, Rector, Brunsvold, and Bahk, (1993); Lavie et al. (2015); Liu-Ambrose et al. (2016); Matilla-Morron et al. (2018); Marocolo, da Mota, Londe, Patterson, Neto, and Marocolo (2017); Muta, Murias, and Paterson (2017); Malor

## Table 4 Summary of excluded studies and reason of exclusion

		Spalding, Lyon, Steel, and Hatfield (2004); Ståhle, Nordlander, and Bergfeldt (1999); Stewart (1989); Sumide, Sakuraba, Sawaki, Ohmura, and Tamura (2009); Sunami et al. (1999); Suter, Mart Tschopp, Wanner, Wenk, and Gutzwiller (1990); Svacinová et al. (2008); Syrkin, Glazachev Kopylov, Dudnik, Zagaynaya, and Tuter (2017); Takada et al. (2012); Takano et al (2005);
		Takarada, Sato, and Ishii (2002); H. Tanaka (2009); Taylor, Ingham, and Ferguson (2016); Thijssen, De Groot, Smits, and Hopman (2007); Thompson, Whinton, Ferth, Spriet, and Burr (2018); Tocco et al. (2015); Toledano-Zarhi, Tanne, Carmeli, and Katz-Leurer (2011); Tucker (2014); Van Thienen and Hespel (2016); Vasconcellos et al. (2016); Vasiliauskas et al. (2007); Vigorito, Incalzi, Acanfora, Marchionni, and Fattirolli (2003); Villelabeitia Jaureguizar et al. (2016); Villelabeitia Jaureguizar et al. (2019); Villelabeitia Jaureguizar et al. (2017); Wang et al. (2014); Welsch et al. (2008); Wernbom, Augustsson, and Thomeé (2006); Wernbom, Järrebring, Andreasson, and Augustsson (2009); Wientzek et al. (2014) Willenheimer, Erhardt, Cline, Rydberg, and Israelsson (1998); Wojcik, Knapp, and Gorski (2018); Wosornu, Bedford, and Ballantyne (1996); Xing, Yang, Dong, Wang, Feng, and Zhang (2018); Yasuda, Ogasawara, Sakamaki, Ozaki, Sato, and Abe (2011); Yokokawa, Hongo, Urayama, Nishimura, and Kai (2008); Yuza, Ishida, and Miyamura (2000); Zhao, Li, Ren, Meng, and Ji (2018); Zheng, Zheng, Li, Duan, Tao, and Chen (2019).
Outcome	22	Barili et al. (2018); Bunevicius et al. (2019); da Silva et al. (2019); A. Ferreira et al. (2019); M. Ferreira et al. (2017); Fortin and Billaut (2019); Ilett, Rantalainen, Keske, May, and Warmington, (2019); Loenneke, Kearney, Thrower, Collins, and Pujol (2010); Mahoney, Dicks, Lyman, Christensen, and Hackney (2019); McLay, Gilbertson, Pogliaghi, Paterson, and Murias (2016); Mendonca, Vaz, Teixeira, Grácio, and Pezarat-Correia (2014); Nakajim et al. (2012); Ozaki et al. (2010); Peyrard, Willis, Place, Millet, Borrani, and Rupp (2019); Sabino-Carvalho et al. (2019); Sakamaki-Sunaga, Loenneke, Thiebaud, and Abe (2012); Silva et al. (2019); Sundberg, Eiken, Nygren, and Kaijser (1993); Sundblad, Kölegård, Rullman, and Gustafsson (2018); Timmons et al. (1998); Willis, Alvarez, Borrani, and Miller (2018); Yasuda, Fukumura, Sato, Yamasoba, and Nakajima (2014).
Design	12	Behringer and Willberg (2019); Cardoso (2019); A. Ferreira Jr, de Araujo, Chimin, and Okuno (2019); Hackney, Brown, Stone, and Tennent (2018); Heitkamp (2015); D. kim et al (2012); Kuepper, Morrison, Gieseler, and Schoeffl (2009); Oliveira et al. (2019); Segal (2014); Swain and Franklin (2006); H. Tanaka and Shindo (1992); Valenzuela et al. (2018).
Based on full text evaluation	13	
Inter- vention	5	Abe et al. (2010a); Amani-Shalamzari et al. (2019); Ozaki et al. (2011); Tanaka and Takarada (2018); Wiggins, Constantini, Paris, Mickleborough, and Chapman (2019).
Outcome	7	Brurok, Tørhaug, Leivseth, Karlsen, Helgerud, and Hoff (2012); Corvino, Oliveira, Denadai, Rossiter, and Caputo (2019); Corvino, Rossiter, Loch, Martins, and Caputo (2017); D. Kim, Loenneke, Thiebaud, Abe, and Bemben (2015); Kumagai et al. (2012); Smiles et al. (2017) Thomas, Scott, and Peiffer (2018).

#### 4.2. Results quality assessment

Seven studies, consisting of five randomized controlled trials, one controlled trial and one study without a control group were assessed on quality using the "Revised Cochrane risk-of-bias tool for randomized trials (RoB2)" (Higgins et al., 2019).

In all included studies the allocation was randomly performed, except for the study of De Oliveira, Caputo, Corvino and Denadai (2016). None of the studies reported information on concealment. There were no differences in baseline characteristics between intervention groups. Due to lacking information on allocation concealment, all studies were judged to raise 'some concerns' for the first domain, i.e. the randomization process.

The second domain, i.e. the intervention procedure, was judged to be at 'low risk of bias' for all studies. Due to the explicit method of the intervention, i.e. BFR, blinding of the participants and researchers was impossible. However, deviations because of non-blinding were not to be expected. Only in the study of Held et al. (2020), non-protocol interventions were balanced between groups. In all other studies, this was not applicable. Adequate intervention implementation and adherence in all studies were probable.

In six out of seven studies, data of all participants were available. In the study of Ursprung (2016), two of the ten participants did not complete the study because they were sent on deployment in the U.S. Air Force. There was probably no bias on the missing data. The third domain, i.e. missing outcome data, was judged to be at 'low risk of bias' for all studies.

Measurement methods were appropriate and were the same for all participants within individual studies. Although assessors were not blinded, their knowledge of the assigned intervention was not expected to influence the results. Therefore, the fourth domain, i.e. the outcome measurement, was judged to be at 'low risk of bias' for all studies.

The fifth domain, i.e. selection of the reported result, was judged to be at 'low risk of bias' for all studies, since the data was analysed in accordance with a pre-specified analysis plan. Furthermore, the numerical result of the outcome measure was not selected on the basis of the results from multiple eligible outcome measurements or multiple eligible analyses of the data.

All studies were judged to raise "some concerns" for final overall risk of bias. Therefore, no study was excluded due to a high risk of bias. Details can be found in table 5.

Items	Abe et al. (2010b)	Conceição et al. (2019)	De Oliveira, Caputo, Corvino and Denadai (2016)	Held, Behringer and Donath (2020)	Kim et al. (2016)	Park, Kim, Choi, Kim, Beekley and Nho (2010)	Ursprung (2016)
Randomization process							
Allocation random?	Υ	Y	NI	Υ	Υ	Y	NA
Allocation concealed?	NI	NI	NI	NI	NI	NI	NA
Baseline differences?	Ν	Ν	Ν	Ν	Ν	Ν	NA
Assignment to intervention	n						
Participant blinded?	N	Ν	Ν	Ν	Ν	Ν	Ν
Researchers blinded?	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Deviations from intended	PN	PN	PN	PN	PN	PN	PN
intervention?							
Deviations affect	PN	PN	PN	PN	PN	PN	PN
outcome?							
Deviations balanced?	NI	NI	NI	NI	NI	NI	NI
Appropriate analysis for	PY	РҮ	РҮ	PY	ΡΥ	РҮ	ΡΥ
effect of assignment?							
Inappropriate analysis	NA	NA	NA	NA	NA	NA	NA
affect outcome?							
Adherence to intervention							
Participants blinded?	N	Ν	Ν	Ν	Ν	Ν	Ν
Researchers blinded?	N	Ν	Ν	N	N	Ν	Ν
Non-protocol	NA	NA	NA	γ	NA	NA	NA
interventions balanced?							
Failures in intervention	PN	PN	PN	PN	PN	PN	PN
implementation?							

### Table 5

Non-adherence?	N	Ν	Ν	Ν	Ν	Ν	Ν
Appropriate analysis for	NI						
effect of adherence							
Missing outcome data							
Data for all participants available?	Υ	Y	Y	Y	Υ	Y	Ν
Bias by missing data?	N	N	N	N	N	N	PN
Missingness depend on true value?	NA						
Measurement of outcome							
Measurement methods appropriate?	Y	Y	Υ	Y	Y	Y	Y
Measurement differed	N	Ν	Ν	Ν	N	Ν	Ν
between groups?							
Assessors blinded?	Ν	Ν	Ν	Ν	N	Ν	Ν
Influenced by knowledge?	PN						
Selection of the reported re	esult						
Data analyzed in accordance with pre- specified analysis plan?	Y	Y	Y	Y	Y	Y	Y
Result selected on basis of results from multiple outcome measurements?	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Result selected on basis of results from multiple analyses of the data?	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Overall risk-of-bias	Some						
judgement	Concerns						

Note. Y, yes; PY, probably yes; N, no; PN, probably not; NI, no information; NA, not applicable

#### 4.3. Results data-extraction

Tables 6 and 7 describe data-extraction for methodology and results respectively. Data is provided from 168 participants in total.

#### 4.3.1. Elite athletes

Held et al. (2020) and Park, Kim, Choi, Kim, Beekley and Nho (2010) respectively included 31 healthy elite rowers (mean age: 21.8±3.2-3.7 and BMI: 22.6 kg/m<sup>2</sup>) and 12 healthy male elite basketball players (mean age: 20±4.5 and BMI: 24.2 kg/m<sup>2</sup>) in their studies. Both studies found a significant improvement in VO2max in the intervention groups. In both studies, there was no control of dietary patterns, nor adjustment of training intensity performed after a few weeks.

Held et al. (2020) found a mean difference of 6.7 ml/kg/min which is a significant improvement of 9.1  $\pm$  6.2% (P < 0.001) in VO2max in the intervention group only. The control group obtained a mean difference of 1.7 ml/kg/min which is a non-significant change of 2.5  $\pm$  6.1% (P > 0.05). The researchers assessed the effects of a 5-week continuous intervention. The participants of both groups performed their usual exercise routine consisting of rowing at a low, moderate and high intensity, cross training (running and cycling) and strength training for three days per week to the same extent. The intervention group performed the boat and indoor rowing training with a practical BFR elastic wrap pulled to 75% of maximal length on thighs, exclusively applied during a low intensity session, i.e. below an individual HR corresponding to a blood lactate level below 2 mmol/L. The extent of restriction was validated using ultrasound, whereby only venous pooling without arterial occlusion arose. These training sessions took two times ten minutes continuous rowing interspersed by a ten-minute break. The control group performed an identical training without pBFR.

Similarly, Park et al. (2010) found a mean difference of 5.6 ml/kg/min which is a significant improvement of 11.6% (P = 0.005) in VO2max in the intervention group and a mean difference of 0.6 ml/kg/min which is a non-significant change in the control group of -1% (P > 0.05).

The participants performed a two-week interval intervention of six days per week, every day consisting of a morning and an afternoon session. They walked on a treadmill for five sets of three minutes, interspersed by one-minute rest, at 4-6 km/h and 5% grade which was equivalent to an intensity of 40% of VO2max. The intervention group wore a pressure belt that was strapped around the thighs at a pressure of 160 mmHg to eventually 220 mmHg.

Restriction of leg muscle blood flow was applied throughout the entire session, including rest periods. They did not perform an assessment of LOP or AOP. The control group performed the same training protocol without occlusion.

#### 4.3.2. Healthy elderly

The study of Abe et al. (2010b) revealed a mean difference of -0.6 ml/kg/min which is a nonsignificant change of -2.2% (P > 0.05) in estimated VO2peak in the intervention group and a mean difference of 0.5 ml/kg/min which is a non-significant change of -1.5% (P > 0.05) in the control group.

A group of 19 healthy, physically active elderly, i.e. people aged older than 60 years, as population sample (BMI: 23.4 kg/m<sup>2</sup>) was included in the study. By simultaneously increasing the grade of the treadmill and maintaining a constant speed, the participants reached 80% of their age-predicted maximum HR (220-age). Peak oxygen consumption was estimated with further calculations.

Abe et al. (2010b) conducted a trial of six weeks continuous treadmill walking for 20 minutes at a speed of 67 m/min equivalent to an intensity of 45% of HRR for five days per week. No adjustment of training intensity was performed after a few weeks. The treadmill speed was similar to their usual walking speed and ensured that exercise intensity did not exceed the habitual walk exercise performed by the control group, as mentioned in Abe et al. (2010b). This program was performed by the intervention group, who wore a pressure belt on both thighs at a pressure of 160 to eventually 200 mmHg while the control group did not receive any intervention and just continued their daily walking. Abe et al. (2010b) did not perform a control of dietary patterns, nor an assessment of LOP or AOP.

#### 4.3.3. Healthy adults

The remaining studies included a population of healthy young adults aged between 20 and 42 years.

A mean difference of 2.6 ml/kg/min which is a significant improvement of 5.6  $\pm$  4.2% (P = 0.006) in VO2max was found in the intervention group of De Oliveira et al. (2016). The HIT control group and the combined control group also revealed a significant improvement of 9.2  $\pm$  6.5% (P = 0.002) with a mean difference of 4.1 ml/kg/min and of 6.5  $\pm$  5.5% (P = 0.03) with a mean difference of 2.9 ml/kg/min. There were no significant differences observed between

the three groups. A mean difference of 0.2 ml/kg/min was found in the low intensity interval cycling control group which is a non-significant change  $0.4 \pm 4.7\%$  (P = 0.75).

The study of De Oliveira et al. (2016) is the only one to include both males and females leading to a total sample of 37 recreationally active participants (BMI: 22.7 kg/m<sup>2</sup>). They evaluated a low intensity short-term interval training program with a duration of four weeks, performed on a cycle ergometer at 30% of Pmax. The program consisted of three sessions per week comprising of two sets of five repetitions of two minutes cycling for the first week to eventually two sets of eight repetitions of cycling by adding one repetition each week. Each repetition was interspersed by one-minute passive rest. The rest interval between sets was five minutes, comprising of three minutes active recovery at 30% Pmax with deflated cuffs, followed by two minutes passive rest.

The intervention group wore pressure belts on the thighs at a pressure of 140 to eventually 200 mmHg intermittently, i.e. only inflated during active cycling repetitions. The same exercise protocol was used for the low intensity interval cycling control group and high intensity interval training (HIT) control group at 110% Pmax with 5% decrease every 30sec. Both control groups exercised without pressure cuff belts. The same exercise protocol was also used for the combined HIT and BFRT control group performing one set HIT modality and the other set BFRT modality in a random order.

Ursprung (2016) demonstrated a mean difference of 1.5 ml/kg/min which is a significant change of 3.5% (p= 0.034) in VO2max in a sample of eight well trained men with a mean age of 34.3 ± 7.07 (BMI: 26.7). They completed a three-week program for five sessions per week of continuous treadmill walking for 20 minutes at 45% VO2reserve. Every session was divided into five stages of four minutes. Each stage 1% grade was added while adjusting the walking speed to maintain the intensity. Inflatable cuffs on both thighs were used to perform BFR. Ursprung (2016) reported a beefy red coloration of the limbs with the strongest pulsation sensible and capillary refill time of three seconds as the optimal pressure. The intervention was not compared with a control group.

In the study of Conceição et al. (2019) a mean difference of 3.9 ml/kg/min which is a significant improvement in VO2max of 11% (P = 0.012) in the intervention group and a mean difference of 6.3 ml/kg/min which is a significant improvement of 21% (P < 0.001) in the endurance training control group were reported. The resistance training control group showed a mean

difference of 0.9 ml/kg/min which is not an important change in VO2max (2.9%, P = 0.541). Conceição et al. (2019) reported no significant differences between groups.

A sample of 30 sedentary young males with a mean age of  $22.7 \pm 2.7$  was equally divided and they were assigned to one of the following groups. The intervention group performed an eight-week program of four sessions per week of continuous cycling. Each session consisted of 30 minutes cycling at 40% of VO2reserve with strapped inflatable cuffs on the thighs. The mean pressure of 95 ± 4.2 mmHg was equivalent to 80% of LOP. The endurance training control group performed the same intervention but without the cuffs and at an intensity of 70% of VO2reserve. The resistance training control group performed leg presses for four sets of ten repetitions at 70% of 1RM with 60 seconds rest. No information to calculate the BMI was available.

Conversely, the study of Kim et al. (2016) found no significant improvement in VO2peak in any group. The reported mean differences and percentual changes were the following: 0.8 ml/kg/min and 1.96% (P > 0.05) in the intervention group, 2.2 ml/kg/min and 5.25% (P > 0.05) in the vigorous intensity control group and -0.5 ml/kg/min and -1.17% (P > 0.05) in the 'no exercise' control group. Kim et al. (2016) included 31 physically active young males with a mean age of 22.4  $\pm$  3.0 (BMI: 24.8 kg/m<sup>2</sup>). The intervention group performed a six-week program for three sessions per week of continuous cycling. Each session consisted of 20 minutes cycling at 30% of HRR with inflatable elastic cuffs on the thighs at a pressure of 160 to eventually 180 mmHg after three weeks. The vigorous intensity control group cycled for 20 minutes at 60-70% of HRR while the other control group received no specific exercise intervention.

Finally, no control of dietary patterns was performed. No adjustment of training intensity was performed in abovementioned studies except in the study of Conceição et al. (2019) after four weeks. Only in Conceição et al. (2019), they used a doppler to assess 80% of LOP.

Items	Abe et al. (2010b)	Conceição et al. (2019)	De Oliveira, Caputo, Corvino and Denadai (2016)	Held, Behringer and Donath (2020)	Kim et al. (2016)	Park, Kim, Choi, Kim, Beekley and Nho (2010)	Ursprung (2016)
Study characte	eristics						
Intervention duration (weeks)	6	8	4	5	6	2	3
Sessions per week	5	4	3	3	3	6 (2 per day)	5
Adjustment training intensity	No	After 4 weeks	No	Νο	No	No	No
Participant cha	aracteristics						
Population	Healthy, physically active older adults	Healthy, sedentary young males	Healthy, recreationally active young adults	Healthy elite rowers	Healthy, physically active young males	Healthy elite male basketball players	Healthy well trained males
Mean age in years ± SD	60-78	22.7 ± 2.7	23.8 ± 4	21.8 ± 3.2-3.7	22.4 ± 3.0	20 ± 4.5	34.3 ± 7.07
Sample size	19	30	37	31	31	12	10****

Gender distribution intervention group (F:M)	9:2	0:10	2:8	4:12	0:11	0:7	0:10****
Gender distribution control groups (F:M)	6:2	RT 0:10 CC 0:10	LI-IC 3:4 HIIT 3:7 HIIT + BFR 7:3	4:11	VIC 0:10 NO 0:10	0:5	No control group
BMI (kg/m²) intervention group pre-test	23.4	NI	22.7	22.6	24.8	24.2	26.7
Intervention gr	oup						
Exercise type	Treadmill walking	Cycling	Cycling	Boat and indoor rowing*	Cycling	Treadmill walking	Treadmill walking
Exercise modality	Continuous	Continuous	Interval	Continuous	Continuous	Interval	Continuous
Exercise duration	20 min	30 min	2 sets of 5-8 reps of 2 min + 1 min passive rest. Between sets rest: 3 min active at 30% Pmax + 2 min passive rest	2 sets 10 min with 10 min rest	20 min	2 sessions per day: 5 sets of 3 min walk, 1 min rest	20 min in 5 stages (+1% grade every stage with adjusting walking speed to maintain intensity)

Exercise intensity	45% of HRR 67 m/min	40% VO2reserve	30% Pmax	Below individual HR corresponding to blood lactate of <2mmol/L	30% HRR	4 to 6 km/h, 5% grade = 40% VO2max	45% VO2reserve
BFR modality	Pressure belt on both thighs: 160 to 200 mmHg	Strapped 18 cm wide inflatable cuff on thighs: 80% occlusion. Pressure mean of 95 ± 4.2 mmHg	18 cm wide pressure cuff belts on thighs: 140 to 200 mmHg Intermittent use, inflation only during exercise bout	Practical BFR: 13 cm wide customized elastic wraps on thighs **	5 cm wide inflatable elastic cuff on thighs: 160 to 180 mmHg	11 cm wide pressure belt on thighs: 140 to 220 mmHg	Inflatable cuff on thighs: optimal pressure is beefy red coloration of limbs, strongest pulsation and capillary refill time of 3 sec
Assessment of LOP or AOP?	No	Doppler used to assess 80% LOP	No	Extent of restriction was validated using ultrasound**	No	No	No
Control groups							
Exercise type and modality	No exercise, continued daily walking	Resistance training: leg press 4 sets, 10 reps, 60 sec rest	Interval cycling without BFR	Identical training without pBFR	Vigorous intensity cycling	Interval treadmill walking without BFR	NA

Exercise duration	NA	NI	Same training protocol	Identical without pBFR	20 min	Same training protocol	NA
Exercise intensity	NA	70% 1RM	Low intensity	Identical without pBFR	60-70% HRR	Same intensity	NA
Exercise type and modality	NA	Continuous cycling	High-intensity interval cycling	NA	No exercise	NA	NA
Exercise duration	NA	30 min	Same training protocol	NA	NA	NA	NA
Exercise intensity	NA	70% VO2reserve	110% Pmax with 5% decrease every 30 sec.	NA	NA	NA	NA
Exercise type and modality	NA	NA	Combined HIIT (50% BFR and 50% HIIT)	NA	NA	NA	NA
Exercise duration	NA	NA	Same protocol	NA	NA	NA	NA
Exercise intensity	NA	NA	Same intensity	NA	NA	NA	NA
Outcome chara	cteristics						
Measurement instrument	Automated breath-by- breath mass spectrometry system	Automated breath-by- breath metabolic system	Breath-by- breath gas analyzer	Breath-by- breath system	Indirect spirometry (metabolic measurement system)	Breath-by- breath ergo- spirometry	Integrated metabolic system on treadmill

Primary	Estimated	VO2max	VO2max	VO2max	VO2peak	VO2max	VO2max
outcome	VO2peak						
measure							

*Note.* NA, not applicable; NI, no information; LOP, limb occlusion pressure; AOP, arterial occlusion pressure; pBFR, practical BFR; RT, resistance training; CC, continuous cycling; LI-IC, low intensity interval cycling; HIIT, high intensity interval training; VIC, vigorous intensity cycling; NO, no exercise

\*Rowing (low, moderate and high intensity), cross (running and cycling) and strength training in both groups to same extent but none with BFR. \*\*pBFR: only venous pooling, no arterial occlusion; pulled to 75% of maximal length.

\*\*\*Only eight subjects completed the study because two were sent on deployment during the course of the study.

	Abe et al.	Conceição et	De Oliveira,	Held,	Kim et al.	Park, Kim,	Ursprung
	(2010b)	al. (2019)	Caputo, Corvino and Denadai (2016)	Behringer and Donath (2020)	(2016)	Choi, Kim, Beekley and Nho (2010)	(2016)
Intervention gr	oup with BFR						
	Continuous treadmill walking:	Continuous cycling:	Interval cycling:	Continuous boat and indoor rowing:	Continuous cycling:	Interval treadmill walking:	Continuous treadmill walking:
Pre-test <sup>1</sup> (mean ± SD)	31.8 ± 6.3	34.5 ± 9.4	47.6 ± 7.8	63.0 ± 7.0	40.5 ± 7.0	48.9 ± 4.8	44.2 ± 7.3
Post-test <sup>1</sup> (mean ± SD)	31.2 ± 6.2	38.4 ± 6.8	50.2 ± 7.7	69.7 ± 9.4	41.3 ± 6.7	54.5 ± 4.2	45.7 ± 6.4
Change (%, ± SD)	-2.2	11	5.6 ± 4.2	9.1 ± 6.2	1.96	11.6	3.5
Significance	P > 0.05	P = 0.012	P = 0.006	P < 0.001	P > 0.05	P = 0.005	P = 0.034
F-value	/	/	/	F = 35.481	/	/	/
Control group							
	No exercise:	Resistance training:	Interval cycling:	Identical without BFR:	Vigorous intensity cycling:	Interval treadmill walking:	NA
Pre-test <sup>1</sup> (mean ± SD)	33.3 ± 5.4	34.6 ± 4.3	44.6 ± 4.0	63.2 ± 8.5	41.9 ± 5.9	47.4 ± 4.5	NA
Post-test <sup>1</sup> (mean ± SD)	32.8 ± 5.3	35.5 ± 3	44.8 ± 4.7	64.9 ± 8.6	44.1 ± 5.6	46.8 ± 2.4	NA

Change (%, ± SD)	-1.5	2.9	0.4 ± 4.7	2.5 ± 6.1	5.25	-1	NA
Significance	P > 0.05	P = 0.541	P = 0.75	P > 0.05	P > 0.05	P > 0.05	NA
	NA	Continuous cycling:	HIIT:	NA	No exercise:	NA	NA
Pre-test <sup>1</sup> (mean ± SD)	NA	33.7 ± 6.7	45.1 ± 4.2	NA	42.8 ± 5.8	NA	NA
Post-test <sup>1</sup> (mean ± SD)	NA	40 ± 5.9	49.2 ± 4.9	NA	42.3 ± 6.7	NA	NA
Change (%, ± SD)	NA	21	9.2 ± 6.5	NA	-1.17	NA	NA
Significance	NA	P < 0.001	P = 0.002	NA	P > 0.05	NA	NA
	NA	NA	HIIT + BFR:	NA	NA	NA	NA
Pre-test <sup>1</sup> (mean ± SD)	NA	NA	44.3 ± 8.3	NA	NA	NA	NA
Post-test <sup>1</sup> (mean ± SD)	NA	NA	47.2 ± 9.0	NA	NA	NA	NA
Change (%, ± SD)	NA	NA	6.5 ± 5.5	NA	NA	NA	NA
Significance	NA	NA	P = 0.03	NA	NA	NA	NA

Note. <sup>1</sup>, values of VO2max or VO2peak (ml/kg/min); NA, not applicable; HIIT, high intensity interval training

#### 4.4. Results statistical analyses

Five studies were included in the meta-analysis. The studies of Abe et al. (2010b) and Kim et al. (2016) were not included because necessary data for the meta-analysis were not available and the authors could not be contacted for data requests. In the five studies retained, data sets are provided from 73 participants in intervention groups.

The overall effect of low- to low-moderate intensity aerobic exercise with BFR on VO2max is found to be statistically significant (Z = 7.22; p < 0.00001) with a mean difference of 3.16 ml/kg/min [95% CI = 2.30, 4.01] pre-BFRT versus post-BFRT. A test for heterogeneity showed a significant Chi<sup>2</sup>-test of 18.92 (p = 0.0008), which indicates that a between-study variance exists in the effects of VO2max.

A first sub-analysis was conducted on population. Both the elite athletes and healthy adults subgroups showed a significant improvement in VO2max of respectively 6.31 ml/kg/min [95% CI = 4.54, 8.08] (Z = 6.99; p < 0.00001) and of 2.19 ml/kg/min [95% CI = 1.21, 3.17] (Z = 4.38; p < 0.0001). While there was a significant difference between both subgroups (Chi<sup>2</sup> = 15.94; p < 0.0001), there were no significant differences within the subgroups. Details can be found in Figure 2.

A second sub-analysis was conducted on exercise type. All types revealed a significant improvement in VO2max. The cycling subgroup showed a mean difference of 2.92 ml/kg/min [95% CI = 1.52, 4.33] (Z = 4.07; p < 0.0001), the treadmill walking subgroup of 2.22 ml/kg/min [95% CI = 0.98, 3.46] (Z = 3.51; p = 0.0004) and the rowing subgroup of 6.70 ml/kg/min [95% CI = 4.50, 8.90] (Z = 5.96; p < 0.00001). There was a significant difference between subgroups (Chi<sup>2</sup> = 12.23; p = 0.002) and within the treadmill walking subgroup (Chi<sup>2</sup> = 6.08; p = 0.01). This difference was not observed within the cycling subgroup (Chi<sup>2</sup> = 0.61; p=0.43). Details can be found in Figure 3.

A last sub-analysis was conducted on exercise modality. Both modalities showed a significant effect. The continuous aerobic exercise modality yielded a mean difference of 3.08 ml/kg/min [95% CI = 2.01, 4.15] (Z = 5.62; p < 0.00001) and the interval aerobic exercise modality yielded a mean difference of 3.29 ml/kg/min [95% CI = 1.87, 4.72] (Z = 4.53; p < 0.00001). No significant difference was observed between subgroups, nor within the interval aerobic exercise subgroup. On the contrary, a significant difference was observed within the continuous aerobic exercise group (Chi<sup>2</sup> = 15.83; p = 0.0004). Details can be found in Figure 4.

				Mean Difference	Mean Difference
Study or Subgroup M	ean Difference	SE	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
2.1.1 Elite Athletes					
Held, Behringer and Donath (2020)	6.7	1.125	15.1%	6.70 [4.50, 8.90]	<b>_</b>
Park, Kim, Choi, Kim, Beekley and Nho (2010) Subtotal (95% CI)	5.6	1.51		5.60 [2.64, 8.56] <b>6.31 [4.54, 8.08]</b>	
Heterogeneity: $Chi^2 = 0.34$ , $df = 1$ (P = 0.56); $I^2 = 0\%$ Test for overall effect: Z = 6.99 (P < 0.00001)					
2.1.2 Healthy Adults					
Conceiçao et al. (2019)	3.9	1.439	9.2%	3.90 [1.08, 6.72]	
De Oliveira, Caputo, Corvino and Denadai (2016)	2.6	0.829	27.8%	2.60 [0.98, 4.22]	<b></b>
Ursprung (2016)	1.5	0.696	39.5%	1.50 [0.14, 2.86]	<b></b>
Subtotal (95% CI)			76.5%	2.19 [1.21, 3.17]	•
Heterogeneity: $Chi^2 = 2.64$ , $df = 2$ (P = 0.27); $I^2 = 242$ Test for overall effect: Z = 4.38 (P < 0.0001)	%				
Total (95% CI)			100.0%	3.16 [2.30, 4.01]	•
Heterogeneity: $Chi^2 = 18.92$ , $df = 4$ (P = 0.0008); $I^2 = Test$ for overall effect: Z = 7.22 (P < 0.00001)	79%				-4 -2 0 2 4
Test for subgroup differences: $Chi^2 = 15.94$ , df = 1 (F	<sup>2</sup> < 0.0001), l <sup>2</sup> =	93.7%			Favours [Pre-BFRT] Favours [Post-BFRT]

## *Figure 2.* Forest plot displaying the effect size of BFRT on VO2max according to population.

Study or Subgroup Mea	n Difference	SE	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% Cl
1.1.1 Cycling					
Conceiçao et al. (2019)	3.9	1.439	9.2%	3.90 [1.08, 6.72]	
De Oliveira, Caputo, Corvino and Denadai (2016) Subtotal (95% CI)	2.6	0.829		2.60 [0.98, 4.22] <b>2.92 [1.52, 4.33]</b>	
Heterogeneity: $Chi^2 = 0.61$ , $df = 1$ (P = 0.43); $I^2 = 0\%$					
Test for overall effect: $Z = 4.07 (P < 0.0001)$					
1.1.2 Treadmill walking					
Park, Kim, Choi, Kim, Beekley and Nho (2010)	5.6	1.51	8.4%	5.60 [2.64, 8.56]	
Ursprung (2016) Subtotal (95% CI)	1.5	0.696		1.50 [0.14, 2.86] <b>2.22 [0.98, 3.46]</b>	
Heterogeneity: $Chi^2 = 6.08$ , $df = 1$ (P = 0.01); $I^2 = 84\%$					-
Test for overall effect: $Z = 3.51 (P = 0.0004)$					
1.1.3 Rowing					
Held, Behringer and Donath (2020) Subtotal (95% CI)	6.7	1.125		6.70 [4.50, 8.90] <b>6.70 [4.50, 8.90]</b>	
Heterogeneity: Not applicable					
Test for overall effect: $Z = 5.96 (P < 0.00001)$					
Total (95% CI)			100.0%	3.16 [2.30, 4.01]	•
Heterogeneity: $Chi^2 = 18.92$ , $df = 4$ (P = 0.0008); $I^2 = 7$	9%				
Test for overall effect: $Z = 7.22$ (P < 0.00001)					–4 –2 0 2 4 Favours [Pre-BFRT] Favours [Post-BFRT]
Test for subgroup differences: $Chi^2 = 12.23$ , $df = 2$ (P =	0.002), $I^2 = 8$	33.6%			ravouis (rie-bixi) Favouis (Post-BFRI)

## *Figure 3.* Forest plot displaying the effect size of BFRT on VO2max according to exercise type.

Study or Subgroup M	ean Difference	SE	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% Cl
3.1.1 Continuous aerobic exercise			-		
Conceiçao et al. (2019)	3.9	1.439	9.2%	3.90 [1.08, 6.72]	
Held, Behringer and Donath (2020)	6.7	1.125	15.1%	6.70 [4.50, 8.90]	
Ursprung (2016) Subtotal (95% Cl)	1.5	0.696		1.50 [0.14, 2.86] 3.08 [2.01, 4.15]	
Heterogeneity: $Chi^2 = 15.83$ , $df = 2$ (P = 0.0004); $I^2 =$ Test for overall effect: Z = 5.62 (P < 0.00001)	87%				
3.1.2 Interval aerobic exercise					
De Oliveira, Caputo, Corvino and Denadai (2016)	2.6	0.829	27.8%	2.60 [0.98, 4.22]	
Park, Kim, Choi, Kim, Beekley and Nho (2010) Subtotal (95% CI)	5.6	1.51		5.60 [2.64, 8.56] <b>3.29 [1.87, 4.72]</b>	•
Heterogeneity: $Chi^2 = 3.03$ , $df = 1$ (P = 0.08); $I^2 = 679$ Test for overall effect: Z = 4.53 (P < 0.00001)	6				
Total (95% CI)			100.0%	3.16 [2.30, 4.01]	•
Heterogeneity: $Chi^2 = 18.92$ , $df = 4$ (P = 0.0008); $I^2 =$ Test for overall effect: Z = 7.22 (P < 0.00001) Test for subgroup differences: $Chi^2 = 0.06$ , $df = 1$ (P =				—	-4 -2 0 2 4 Favours [Pre-BFRT] Favours [Post-BFRT]

Figure 4. Forest plot displaying the effect size of BFRT on VO2max according to exercise

modality.

## 5. Discussion

The main objective of this systematic review and meta-analysis was to investigate the effects of low- to low-moderate intensity aerobic exercise with blood flow restriction on cardiorespiratory fitness in healthy people. Additional analyses were performed to compare different healthy populations and types and modalities of exercise.

#### 5.1. Reflection on quality of studies

Five randomized controlled trials, one controlled trial and one study without a control group were included in this systematic review. All studies were judged to raise "some concerns" for final overall risk of bias. Sample sizes in all studies ranged from 10 to 37 participants, which could be considered as small sample sizes.

In none of the studies information was provided on allocation concealment. Therefore, an allocation bias could be possible if the randomization procedures were not correctly conducted from a methodical perspective. A possible performance bias may be present since participants as well as researchers were not blinded for the intervention. However, as performance bias implies that the intervention group would have received more attention than the control group, this bias would not have influenced the result of our meta-analysis since our design is a pre-test versus post-test effect size calculation of the intervention group only. On the other hand, this may have overestimated the results within an individual study and consequently overestimated the effect size. Assessors of outcome data were not blinded in any study which could imply a detection bias. Data for all participants were available and were assessed, except for the study of Ursprung (2016) as two participants were sent on deployments during the course of the study. However, an attrition bias is not suspected since the drop-out was not the result of musculoskeletal injuries, cardiac problems or other side effects caused by the intervention with BFR. This finding is in line with the statements on safety applications of BFR during aerobic exercise in Silva et al. (2019).

## 5.2. Reflection on findings in function of the research question

#### 5.2.1. Overall effect on VO2max

The present meta-analysis showed a significant overall effect of 3.16ml/kg/min on VO2max. This improvement can be considered small in relation to observed effects as high as 5.5 ml/kg/min and 5.45 ml/kg/min in two recent meta-analyses conducted by Milanovic, Sporis

and Weston (2015) and Wen et al. (2019) respectively, who evaluated the effects of high intensity interval training (without BFR) in healthy adults on VO2max. However, compared to the observed effects of 6.3 ml/kg/min, 4.1 ml/kg/min and 2.2 ml/kg/min in the high intensity exercise control groups in the studies of Conceição et al. (2019), De Oliveira et al. (2016) and Kim et al. (2016) respectively, our overall effect is within those boundaries.

Compared to the non-significant improvements observed in the low intensity control groups of 0.2 ml/kg/min, 1.7 ml/kg/min and 1.4 ml/kg/min in the studies of De Oliveira et al. (2016), Held et al. (2020) and Park et al. (2010) respectively, our overall effect is relatively large. These groups underwent the same training protocol and intensity as the intervention groups, without the application of BFR. Therefore, those results seem to support the recommendation of Scribbans et al. (2016), that an exercise intensity of approximately 60% of VO2max is needed to improve cardiorespiratory fitness.

Furthermore, a very recent systematic review with meta-analysis was performed by Formiga et al. (2020). In a subgroup analysis according to exercise intensity, they compared the effects of low-to-moderate aerobic exercise with BFR with the effects of low-to-moderate aerobic exercise without BFR. Therefore, the following result could not be compared with our overall effect. They revealed a significant standardized mean difference of 0.57 in favour of the BFR group. Two, i.e. De Oliveira et al. (2016) and Park et al. (2010), out of five studies were also included in our meta-analysis, since they met our inclusion criterium on intensity.

In summary, our meta-analysis showed that low- to low-moderate intensity aerobic exercise with BFR is an appropriate solution for providing a low mechanical stimulus and still obtaining a small but significant improvement in VO2max.

A large heterogeneity (Chi<sup>2</sup> = 18.92) was shown over all studies, probably due to the outlying results of Held et al. (2020) and Park et al. (2010). This between-study variance in the overall effect of VO2max may be explained by the heterogeneity in study and participant characteristics, exercise types, exercise modalities, BFR modalities (i.e. cuff pressure, cuff width and material) and objective assessment of LOP or AOP. To further explore to which extent those factors contribute to the overall effect is beyond the scope of this study. However, based on the results of this systematic review and meta-analysis, the most determining factors to the researcher's (L.T. and M.T.) opinion are described.

First, a higher overall and within-study effect could have been observed when training was performed at 40% to 80% of AOP, as recommended by the Position Stand paper of Patterson et al. (2019), instead of at a fixed cuff pressure for all participants within a study. Except for Conceição et al. (2019), the included studies did not report an assessment of LOP or AOP, causing a non-objective and non-standardized (i.e. not the same percentage of LOP for all participants within studies due to different amounts of lean- and fat mass on the thighs and blood pressures) application of BFR which may have affected the results. Furthermore, Ursprung (2016) used a merely subjective blood flow restriction method. The cuffs were inflated until a beefy red coloration of the limbs with the strongest pulsation sensible and capillary refill time of three seconds was seen and therefore only venous return was restricted. Secondly, only the study of Conceição et al. (2019) adjusted the training intensity after four weeks by performing a mid-point VO2max-test. Therefore, maintenance of a preset intensity could be guaranteed. The remaining studies may not have obtained optimal improvements due to a decreasing relative training intensity along the study duration. Besides that, longer interventions will also lead to greater improvements.

Lastly, dietary patterns could have been a possible variable which may have affected the results in both ways. When eating too little and not reaching the daily intake recommendations, an optimal recovery could have been inhibited and could have led to sub-optimal improvements. Otherwise, when taking supplements, additional improvements could have been obtained. Despite the advice to maintain normal dietary patterns to participants in the studies of Conceição et al. (2019), De Oliveira et al. (2016), Kim et al. (2016) and Ursprung (2016), there was no adequate control performed.

#### 5.2.2. Effect on VO2max according to population

The study of Abe et al. (2010b) showed a non-significant decline in VO2max of 0.6 ml/kg/min in the elderly population. This was remarkable as this elderly had the lowest pre-test VO2max values of all studies. In spite of a relatively high exercise volume (6 weeks, 5 session/week, 20 minutes treadmill walking/session), no adjustment of training intensity nor an assessment of LOP or AOP was performed, which could imply methodological limitations. Therefore, the intervention may not be a stimulus sufficient enough for this population to increase cardiorespiratory fitness. Furthermore, a mere estimation of the VO2max was performed. Note that the first author was not contactable for a request of necessary data and therefore the result of this study could not be included in the meta-analysis leading to a possible overestimation of our overall and subgroup effect.

A recent systematic review investigated the acute and chronic effects of aerobic exercise combined with BFR on neuromuscular, metabolic and hemodynamic variables (Silva et al., 2019). In total, 35 studies were included of which seven evaluated the chronic effects on cardiorespiratory fitness. They found an improvement in VO2max in both younger and older individuals. This improvement in elderly can be explained by the inclusion of the study of Tanaka and Takarada (2018). They used an exercise intensity up to 70% of VO2max, which is not 'low intense', in elderly men with heart failure. Therefore, a valid comparison between our and their findings could not be made.

Based on the results of the sub-analysis for population, both elite athletes and healthy adults showed a significant improvement in VO2max, with a significant difference between subgroups. The elite athletes in the studies of Park et al. (2010) and Held et al. (2020) showed a greater mean difference than healthy adults in the studies of Conceição et al. (2019), De Oliveira (2016) and Ursprung (2016). This is remarkable when assuming that, in contrast to healthy adults, elite athletes already have a high cardiorespiratory fitness which is more difficult to further increase. Conversely, one may assume that highly trained athletes are likely to have a greater recovery capacity than others. It could be that the participants in the subgroup of healthy adults were not fully recovered when the next BFR session was applied. In other words, an exercise stimulus was provided too early, which could have impeded an optimal improvement of VO2max.

Another possible explanation for this significant difference may be due to the higher total training volume the elite athletes of both Held et al. (2020) and Park et al. (2010) underwent. Despite the higher training volume performed by the elite rowers in Held et al. (2020), the control group showed no significant effect following the identical training without pBFR. This reveals that pBFR, exclusively applied during a low intensity session, could be the determining factor for the outlying result in the intervention group. On the other hand, a possible interaction effect between the higher training volume and pBFR could be the reason for this result. This same reasoning can apply to Park et al. (2010) where no significant improvement was found in the control group, who performed exactly the same protocol without BFR.

A significant weighted mean difference in VO2max was observed in the subgroup of healthy adults.

The study of Conceição et al. (2019) showed a significant improvement, which was clearly higher than all other studies in the subgroup 'healthy adults'. This could be explained by the adjustment in training intensity after four weeks to maintain training at 40% of VO2reserve. Furthermore, the standardized training at 80% of LOP could contribute to this superior improvement. A third explanation could be the relatively long duration of eight weeks. A last explanation could be that Conceição et al. (2019) used a population of sedentary young males with a pre-test VO2max which was clearly lower than that of the physically active young adults in De Oliveira et al. (2016) and the well-trained males in Ursprung (2016). Sedentary young males are expected to obtain greater improvements in cardiorespiratory fitness when exposed to training in comparison with more physically active individuals.

Ursprung obtained the smallest significant improvement of 1.5 ml/kg/min in VO2max. This could be due to the abovementioned methodological limitation of subjective BFR application. However, it has the smallest confidence interval and therefore the largest weight is assigned to this study, as depicted by the thinnest horizontal line and the greatest size of the block in the forest plot. Therefore, it dominates in the calculation of the summary result.

The study of Kim et al. (2016) was not included in this meta-analysis because the first author was not contactable for a request of necessary data, leading to a possible overestimation of our overall and subgroup effect. It showed a non-significant improvement of 0.8 ml/kg/min in VO2peak. As mentioned by the authors of Kim et al. (2016), this could be due to the exercise intensity of 30% HRR. Lida et al. (2007) stated that using heart rate reserve as determination for exercise intensity might not be appropriate during a BFR training since an increase in HR is due to the decrease in venous return to the heart and not by the exercise effort, in order to maintain a stable cardiac output. Therefore, the intensity of 30% HRR could have been too low to obtain improvements in VO2max since 30% HRR could have been reached too early. As this study was not included in the meta-analysis, the weighted mean difference of this subgroup may be overestimated.

#### 5.2.3. Effect on VO2max according to exercise type

All exercise types could be used to improve VO2max, since they all obtained significant effects. However, this subgroup-analysis shows that rowing obtains a result that is twofold the result observed in the cycling and in the treadmill walking group. A conclusion on the superiority of rowing with respect to the other exercise types is misleading as its result is based on only one study, i.e. Held et al. (2020). Therefore, differences are most likely explained by factors other than exercise type. The effects of cycling and treadmill walking are shown to be similar.

## 5.2.4. Effect on VO2max according to exercise modality

Both the continuous and interval aerobic exercise modalities could improve VO2max to the same extent, since there were significant effects in both subgroups with no differences between them. Further interpretation of these results is not appropriate since they can be confounded by other variables (e.g. the underlying population).

## 5.3. Reflection on strengths and weaknesses of the literature study

A first limitation of the present systematic review and meta-analysis is the small amount of individual studies included due to the scarcely available literature on this topic. Therefore, the power of the meta-analysis is low and conclusions should be made with caution.

Secondly, the small amount of studies included did not allow for further exploration of heterogeneity among individual studies and among subgroups by means of formal tests. Neither a stratified analysis nor a meta-regression was executed. These methods are generally not considered when fewer than ten studies are included in the meta-analysis. Rather, informal comparisons of the magnitude of the effects have been done observationally. (Deeks, Altman & Bradburn, n.d.; Deeks, Higgins & Altman, 2019).

Thirdly, the meta-analysis does not involve the comparison of the intervention group, i.e. BFRT, with a fixed control group due to the heterogeneity of control group methodologies over all studies. Instead, a pre-test versus post-test analysis within the intervention group was performed. Furthermore, not all articles in the systematic review could be included in the meta-analysis because necessary data were not provided in the study, nor could the authors be contacted. The presence of highly influential studies, which might bias the analyses, was not identified since no sensitivity analysis was carried out.

A relative strength of this systematic review is that this was the first investigation of the effect of low- to low-moderate intensity aerobic exercise with BFR on VO2max. Additionally, subgroup analyses to compare different healthy populations and types and modalities of exercise were performed. Another strength is that the two investigators performed the selection process, quality assessment and data-extraction independently. Further, in order to compensate for the relative novelty of aerobic exercise with BFR, no filter on date was set and all available studies were included. Furthermore, no eligibility criteria were established regarding age, gender distribution, physical level, BFR modality, exercise type and exercise modality to increase the amount of information.

Lastly, there is no reporting bias since the authors performed a critical systematic review with meta-analysis and since they reported both positive and negative results.

## 5.4. Practical implications

Based on this systematic review with meta-analysis, low- to low-moderate intensity aerobic exercise with the application of BFR could be used in clinical practice or performance settings to improve cardiorespiratory fitness in healthy adults and elite athletes. It can be assumed that all exercise types and modalities can be used.

Individuals suffering from musculoskeletal injuries or recovering from surgery, for whom high mechanical load is not appropriate, may also benefit from low- to low-moderate intensity aerobic exercise with BFR to increase or maintain their cardiorespiratory fitness. Additionally, cycling can be performed when even walking with BFR leads to a too high mechanical stress.

Low- to low-moderate intensity aerobic exercise with BFR could be an alternative for elite athletes to decrease their training intensity during a macrocycle while improving their VO2max, as mentioned in Held et al. (2020) for elite rowers.

Furthermore, it could be used by elderly and obese people to limit the decline in VO2max or to improve VO2max if unable to perform high intense training (Conceição et al., 2019).

Despite the improvements in the study of Held et al. (2020), the authors of the present study do not recommend using pBFR with elastic knee wraps for individuals who do not have a handheld Doppler or Doppler ultrasound to measure LOP or AOP. Since LOP or AOP was not assessed in Held et al. (2020) and only venous pooling occurs, individuals cannot replicate this on their own.

It is appropriate to assess the LOP or AOP of individuals at least once a week since hypertrophy can occur due to aerobic exercise with BFR and therefore a higher pressure is needed to achieve the desired amount of occlusion (Slysz et al., 2016; Centner et al., 2019). Furthermore, it is also appropriate to adjust training intensity after four weeks.

Based on our systematic review a frequency of three to four times a week of low- to lowmoderate intensity aerobic exercise with BFR for healthy adults and elite athletes is recommended to improve VO2max. This is in contrast with the recommendations of two to three times a week, provided in the Position Stand paper of Patterson et al. (2019). Another contrast in recommendation is that the authors (L.T. & M.T.) recommend an intervention duration of at least four weeks for healthy adults and more than three weeks for well-trained adults or elite athletes with possible higher improvements when more than four weeks are performed. Patterson et al. recommended at least three weeks of intervention. Lastly, a restriction time of 20-30 minutes is recommended for low- to low-moderate intensity aerobic exercise with BFR, instead of 5-20 minutes recommended in Patterson et al. (2019). For further recommendations on BFR application during aerobic exercise (i.e. pressures to achieve 40% to 80% AOP and cuff widths), the authors (L.T. & M.T.) refer to Patterson et al. (2019).

## 5.5. Recommendations for further research

Further research should be performed on comparisons between low- to low-moderate intensity aerobic exercise with BFR and high intensity aerobic exercise. High quality randomized controlled trials (RCT's) with longer durations of at least six to eight weeks, a midpoint measurement of VO2max to adjust for training intensity and control of dietary patterns are needed. The authors (L.T. & M.T.) also recommend the use of an inflatable cuff and Doppler ultrasound or a handheld Doppler instead of a fixed cuff pressure to assess the LOP or AOP of individuals at least once a week. Both determined a similar arterial occlusion pressure level in the study of Laurentino et al. (2018), providing evidence for the validity of a handheld Doppler. Both the use of an inflatable cuff and handheld Doppler contributes to a more objective application of BFR.

Populations in further research should moreover include elite athletes and healthy adults with contraindications for high intensity aerobic exercise such as musculoskeletal injuries or post-operative recovery. There is also a need of high quality RCT's to investigate the effect of low-

to low-moderate intensity aerobic exercise on cardiorespiratory fitness in the older population.

Furthermore, individual RCT's should investigate the comparison between different populations, between exercise types (i.e. walking, cycling and rowing) and between exercise modalities (i.e. continuous and interval) performed with identical control groups without the application of BFR.

Lastly, despite the fact that blinding participants is not feasible in BFR interventions, different training locations could reduce a performance bias in future investigations (Centner et al., 2019).

## 6. Conclusion

In the present study, low- to low-moderate intensity aerobic exercise with Blood Flow Restriction significantly improved cardiorespiratory fitness in elite athletes and healthy adults and therefore may offer an appropriate alternative for high intensity aerobic exercise to improve or maintain cardiorespiratory fitness. However, no effect was observed in healthy elderly. Exercise type and modality does not seem to highly affect training results. However, these results must be interpreted with caution due to methodological variations in included studies.

#### 7. Reference list

#### 7.1 References of included studies, introduction, methods, results and discussion

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## BIJLAGEN

## COVID-19 Addendum - Masterproef 2

Gelieve dit document in te laten vullen door de promotor en ingevuld toe te voegen aan je masterproef.

Naam promotor(en) Anouk Agten (promotor), Frank Vandenabeele (copromotor)

Naam studenten Mathias Thoelen en Liam Thijs

1) Duid aan welk type scenario is gekozen voor deze masterproef:

Scenario 1: masterproef bestaat uit een meta-analyse - masterproef liep door zoals voorzien

 $\Box$  scenario 2: masterproef bestaat uit een experiment - masterproef liep door zoals voorzien

 $\Box$  scenario 3: masterproef bestaat uit een experiment - maar een deel van de voorziene data is verzameld

 $\hfill\square$  3A: er is voldoende data, maar met aangepaste statische procedures verder gewerkt

 $\hfill\square$  3B: er is onvoldoende data, dus gewerkt met een descriptieve analyse van de aanwezige data

 $\Box$  scenario 4: masterproef bestaat uit een experiment - maar er kon geen data verzameld worden

 $\Box$  4A: er is gewerkt met reeds beschikbare data

 $\Box$  4B: er is gewerkt met fictieve data

2) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:

- NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.

- 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.

- 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.

- 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering

- 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.

- 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag						$\boxtimes$
Methodologische uitwerking						$\boxtimes$
Data acquisitie						$\boxtimes$
Data management						$\boxtimes$
Dataverwerking/Statistiek						$\boxtimes$
Rapportage						$\boxtimes$

Datum

22/05/2020

#### Gunstig advies dr. Anouk Agten:



#### Anouk AGTEN

aan Vicky, mij, Liam, Frank, Sjoerd ▼ Beste Mathias en Liam,

cc: Vicky

Bij deze gaan wij akkoord met de ingevulde formulieren in bijlage van jullie mail (incl. het inventarisatieformulier). Wij geven jullie dan ook GUNSTIG advies voor indiening eerste zittijd.

De documenten (bijlagen) mogen als dusdanig ingediend bij het studentensecretariaat. Wij hebben mevr. Vanhille reeds in cc gezet.

Met vriendelijke groeten, dr. Anouk Agten (promotor) Prof. dr. Frank Vandenabeele (copromotor) drs. Sjoerd Stevens (Begeleider)

dr. Anouk Agten Doctor-Assistent - Post-doctoral researcher

REVAL- Rehabilitation Research Center BIOMED - Biomedical Research Center Faculteit Geneeskunde & Levenswetenschappen Faculty of Medicine & Life sciences

e-mail anouk.agten@uhasselt.be T +32(0)11 26 92 03

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		Student(e):



# AFSPRAKENNOTA

## 1. Organisatie

Naam	Universiteit Hasselt/transnationale Universiteit Limburg (Hierna: UHasselt/tUL)
Adres	Martelarenlaan 42 3500 Hasselt
Sociale doelstelling	De UHasselt/tUL is een dynamisch kenniscentrum van onderwijs, onderzoek en dienstverlening.
	Faculteiten
	De UHasselt telt zes faculteiten die het onderwijs en onderzoek aansturen:
Werking van de organisatie	<ul> <li><u>faculteit Architectuur en kunst</u></li> <li><u>faculteit Bedrijfseconomische wetenschappen</u></li> <li><u>faculteit Geneeskunde en levenswetenschappen</u></li> <li><u>faculteit Industriële ingenieurswetenschappen</u></li> <li><u>faculteit Rechten</u></li> <li><u>faculteit Wetenschappen</u></li> </ul>
	Elke faculteit stelt per opleiding een <u>onderwijsmanagementteam</u> (OMT) en een <u>examencommissie</u> samen.
	Vakgroepen
	Binnen de faculteiten opereren diverse <u>vakgroepen</u> . Zij groeperen alle personeelsleden die onderzoek en onderwijs verrichten binnen eenzelfde discipline. Elke vakgroep bestaat vervolgens uit een of meerdere <u>onderzoeksgroepen</u> . Zij staan in voor de organisatie van het gespecialiseerd onderzoek.
	Deze klassieke boomstructuur van faculteiten, onderzoeksgroepen en vakgroepen wordt doorkruist door de <u>onderzoeksinstituten</u> . De instituten groeperen onderzoekers uit verschillende onderzoeksgroepen die in bepaalde speerpuntdomeinen onderzoek uitvoeren. Daarbij wordt het volledige onderzoekspectrum afgedekt, van fundamenteel over toegepast onderzoek tot concrete valorisatietoepassingen.
Juridisch statuut	Autonome openbare instelling

Verantwoordelijke van de organisatie, die moet verwittigd worden bij ongevallen.

Naam	Dr. Anouk Agten
Functie	Post-doctoral researcher
Tel GSM	011269203

## 2. De vrijwilliger: student-onderzoeker

Naam	Thoelen Mathias
Corresponden tieadres	mathias.thoelen@gmail.com
Tel GSM	0479108487

## 3. Verzekeringen

Waarborgen	De burgerlijke aansprakelijkheid van de organisatie.
Maatschappij	Ethias
Polisnummer	45009018

Waarborgen	Lichamelijke schade die geleden is door vrijwilligers bij ongevallen tijdens de uitvoering van het vrijwilligerswerk of op weg naar- en van de activiteiten.
Maatschappij	Ethias
Polisnummer	45055074

## 4. Vergoedingen

De organisatie betaalt geen vergoeding aan de vrijwilliger.

## 5. Aansprakelijkheid

# De organisatie is burgerrechtelijk aansprakelijk voor de schade die de vrijwilliger aan derden veroorzaakt bij het verrichten van vrijwilligerswerk.

Ingeval de vrijwilliger bij het verrichten van het vrijwilligerswerk de organisatie of derden schade berokkent, is hij enkel aansprakelijk voor zijn bedrog en zijn zware schuld. Voor lichte schuld is hij enkel aansprakelijk als die bij hem eerder gewoonlijk dan toevallig voorkomt.

**Opgelet:** voor het materiaal dat de vrijwilliger zelf meebrengt, is hij/zij zelf verantwoordelijk.

## 6. Geheimhoudingsplicht – verwerking persoonsgegevens

De vrijwilliger verleent de UHasselt toestemming om de gegevens die in het kader van zijn/haar inschrijving aan UHasselt werden verzameld, ook te gebruiken voor de uitvoering van deze afsprakennota (de evaluatie van de vrijwilliger alsook het aanmaken van een certificaat). UHasselt zal deze informatie vertrouwelijk behandelen en zal deze vertrouwelijkheid ook bewaken na de beëindiging van het statuut student-onderzoeker. De UHasselt neemt hiertoe alle passende maatregelen en waarborgen om de persoonsgegevens van de vrijwilliger conform de Algemene Verordening Gegevensbescherming (EU 2016/679) te verwerken.

De vrijwilliger verbindt zich ertoe om alle gegevens, documenten, kennis en materiaal, zowel schriftelijk als mondeling ontvangen in de hoedanigheid van student-onderzoeker aan de UHasselt als strikt vertrouwelijk te behandelen, ook indien deze niet als strikt vertrouwelijk werd geïdentificeerd. Indien de vertrouwelijke gegevens van de UHasselt ook persoonsgegevens bevatten dient de stagiair hiertoe steeds de Algemene Verordening Gegevensbescherming (EU 2016/679) na te leven en bij elke verwerking het advies van het intern privacycollege van de UHasselt in te winnen. Hij/zij verbindt zich ertoe om in geen geval deze vertrouwelijke informatie mee te delen aan derden of anderszins openbaar te maken, ook niet na de beëindiging van het statuut student-onderzoeker.

## 7. Concrete afspraken

# Functie van de vrijwilliger

De vrijwilliger zal volgende taak vervullen: Literatuuronderzoek Deze taak omvat volgende activiteiten: Systematic Review + Meta-Analysis De vrijwilliger voert zijn taak uit onder verantwoordelijkheid van de faculteit Revalidatiewetenschappen

De vrijwilliger wordt binnen de faculteit begeleid door dr. Anouk Agten Zijn vaste werkplek voor het uitvoeren van de taak is off-campus

De vrijwilliger zal deze taak op volgende tijdstippen uitvoeren:

- op de volgende dag(en):
  - <mark>0 maandag</mark>
  - <mark>O dinsdag</mark>
  - <mark>0 woensdag</mark>
  - <mark>0 donderdag</mark>
  - <mark>0 vrijdag</mark>
  - <mark>0 zaterdag</mark>
  - o zondag
- het engagement wordt aangegaan voor de periode van 1-1-2019 tot 1-1-2020 (deze periode kan maximaal 1 kalenderjaar zijn en moet liggen tussen 1 januari en 31 december).

# Begeleiding

De organisatie engageert zich ertoe de vrijwilliger tijdens deze proefperiode degelijk te begeleiden en te ondersteunen en hem/haar van alle informatie te voorzien opdat de activiteit naar best vermogen kan worden uitgevoerd.

De vrijwilliger voert de taken en activiteiten uit volgens de voorschriften vastgelegd door de faculteit. Hij/zij neemt voldoende voorzorgsmaatregelen in acht, en kan voor bijkomende informatie over de uit te voeren activiteit steeds terecht bij volgende contactpersoon: dr. Anouk Agten

De vrijwilliger krijgt waar nodig vooraf een vorming. Het volgen van de vorming indien aangeboden door de organisatie, is verplicht voor de vrijwilliger.

De vrijwilliger heeft kennis genomen van het 'reglement statuut student-onderzoeker' dat als bijlage aan deze afsprakennota wordt toegevoegd en integraal van toepassing is op de vrijwilliger.

## Certificaat

Indien de vrijwilliger zijn opdracht succesvol afrondt, ontvangt hij/zij een certificaat van de UHasselt ondertekend door de decaan van de faculteit waaraan de vrijwilliger zijn opdracht voltooide.

## 8. Einde van het vrijwilligerswerk.

Zowel de organisatie als de vrijwilliger kunnen afzien van een verdere samenwerking. Dat kan gebeuren:

- bij onderlinge overeenstemming;
- op vraag van de vrijwilliger zelf;
- op verzoek van de organisatie.

Indien de samenwerking op initiatief van de vrijwilliger of de organisatie wordt beëindigd, gebeurt dit bij voorkeur minstens 2 weken op voorhand. Bij ernstige tekortkomingen kan de samenwerking, door de organisatie, onmiddellijk worden beëindigd.

Datum: 28/05/2020

Naam en Handtekening decaan vrijwilliger

Naam en

Handtekening

melen

Thoelen Mathias

Opgemaakt in 2 exemplaren waarvan 1 voor de faculteit en 1 voor de vrijwilliger.

Bijlage 1

## Reglement betreffende het statuut van student-onderzoeker<sup>1</sup>

## Artikel 1. Definities

Voor de toepassing van dit reglement wordt verstaan onder:

student-onderzoeker: een regelmatig ingeschreven bachelor- of masterstudent van de UHasselt/tUL die als vrijwilliger wordt ingeschakeld in onderzoeksprojecten. De opdrachten uitgevoerd als studentonderzoeker kunnen op geen enkele wijze deel uitmaken van het studietraject van de student. De opdrachten kunnen geen ECTS-credits opleveren en zij kunnen geen deel uitmaken van een evaluatie van de student in ket kader van een opleidingsonderdeel. De onderzoeksopdrachten kunnen wel in het verlengde liggen van een opleidingsonderdeel, de bachelor- of masterproef.

## Artikel 2. Toepassingsgebied

Enkel bachelor- en masterstudenten van de UHasselt/tUL die voor minstens 90 studiepunten credits hebben behaald in een academische bacheloropleiding komen in aanmerking voor het statuut van student-onderzoeker.

## Artikel 3. Selectie en administratieve opvolging

§1 De faculteiten staan in voor de selectie van de student-onderzoekers en schrijven hiervoor een transparante selectieprocedure uit die vooraf aan de studenten kenbaar wordt gemaakt.
§2 De administratieve opvolging van de dossiers gebeurt door de faculteiten.

## Artikel 4. Preventieve maatregelen en verzekeringen

§1 De faculteiten voorzien waar nodig in de noodzakelijke voorafgaande vorming van studentonderzoekers. De student is verplicht deze vorming te volgen vooraleer hij/zij kan starten als student-onderzoeker.

§2 Er moet voor de betrokken opdrachten een risicopostenanalyse opgemaakt worden door de faculteiten, analoog aan de risicopostenanalyse voor een stagiair van de UHasselt/tUL. De faculteiten zien er op toe dat de nodige veiligheidsmaatregelen getroffen worden voor aanvang van de opdracht. §3 De student-onderzoekers worden door de UHasselt verzekerd tegen:

Pargerlijke aansprakelijkheid

🛛 Lichamelijke ongevallen

en dit ongeacht de plaats waar zij hun opdrachten in het kader van het statuut uitoefenen.

## Artikel 5. Vergoeding van geleverde prestaties

§1 De student-onderzoeker kan maximaal 40 kalenderdagen, gerekend binnen één kalenderjaar, worden ingeschakeld binnen dit statuut. De dagen waarop de student-onderzoeker een vorming moet volgen, worden niet meegerekend als gepresteerde dagen.

§2 De student-onderzoeker ontvangt geen vrijwilligersvergoeding voor zijn prestaties. De student kan wel een vergoeding krijgen van de faculteit voor bewezen onkosten. De faculteit en de student maken hier aangaande schriftelijke afspraken.

## Artikel 6. Dienstverplaatsingen

De student-onderzoeker mag dienstverplaatsingen maken. De faculteit en de student maken schriftelijke afspraken over deal dan niet vergoeding voor dienstverplaatsingen. De student wordt tijdens de dienstverplaatsingen en op weg van en naar de stageplaats uitsluitend verzekerd door de UHasselt voor lichamelijke ongevallen.

<sup>&</sup>lt;sup>1</sup> Zoals goedgekeurd door de Raad van Bestuur van de Universiteit Hasselt op 15 juni 2017.

## Artikel 7. Afsprakennota

§1 Er wordt een afsprakennota opgesteld die vooraf wordt ondertekend door de decaan en de student-onderzoeker. Hierin worden de taken van de student-onderzoeker alsook de momenten waarop hij/zij de taken moet uitvoeren zo nauwkeurig mogelijk omschreven.

§2 Aan de afsprakennota wordt een kopie van dit reglement toegevoegd als bijlage.

## Artikel 8. Certificaat

Na succesvolle beëindiging van de opdracht van de student-onderzoeker, te beoordelen door de decaan, ontvangt hij een certificaat van de studentenadministratie. De faculteit bezorgt de nodige gegevens aan de studentenadministratie. Het certificaat wordt ondertekend door de decaan van de faculteit waaraan de student-onderzoeker zijn opdracht voltooide.

## Artikel 9. Geheimhoudingsplicht

De student-onderzoeker verbindt zich ertoe om alle gegevens, documenten, kennis en materiaal, zowel schriftelijk (inbegrepen elektronisch) als mondeling ontvangen in de hoedanigheid van studentonderzoeker aan de UHasselt, als strikt vertrouwelijk te behandelen, ook indien deze niet als strikt vertrouwelijk werd geïdentificeerd. Hij/zij verbindt zich ertoe om in geen geval deze vertrouwelijke informatie mee te delen aan derden of anderszins openbaar te maken, ook niet na de beëindiging van zijn/haar opdracht binnen dit statuut.

## Artikel 10. Intellectuele eigendomsrechten

Indien de student-onderzoeker tijdens de uitvoering van zijn/haar opdrachten creaties tot stand brengt die (kunnen) worden beschermd door intellectuele rechten, deelt hij/zij dit onmiddellijk mee aan de faculteit. Deze intellectuele rechten, met uitzondering van auteursrechten, komen steeds toe aan de UHasselt.

## Artikel 11. Geschillenregeling

Indien zich een geschil voordoet tussen de faculteit en de student-onderzoeker met betrekking tot de interpretatie van dit reglement of de uitoefening van de taken, dan kan de ombudspersoon van de opleiding waarbinnen de student-onderzoeker zijn taken uitoefent, bemiddelen. Indien noodzakelijk, beslecht de vicerector Onderwijs het geschil.

## Artikel 12. Inwerkingtreding

Dit reglement treedt in werking met ingang van het academiejaar 2017-2018.



# AFSPRAKENNOTA

## 1. Organisatie

Naam	Universiteit Hasselt/transnationale Universiteit Limburg (Hierna: UHasselt/tUL)
Adres	Martelareniaan 42 3500 Hasselt
Sociale doelstelling	De UHasselt/tUL is een dynamisch kenniscentrum van onderwijs, onderzoek er dienstverlening.
	Faculteiten De UHasselt telt zes faculteiten die het onderwijs en onderzoek aansturen:
	<ul> <li>faculteit Architectuur en kunst</li> <li>faculteit Bedrijfseconomische wetenschappen</li> <li>faculteit Geneeskunde en levenswetenschappen</li> <li>faculteit Industriëte ingenieurswetenschappen</li> <li>faculteit Rechten</li> <li>faculteit Wetenschappen</li> </ul>
Werking van de organisatie	Elke faculteit stelt per opleiding een <u>onderwijsmanagementteam</u> (OMT) en eer sxamencommissie samen. Vakgroepen
	Binnen de faculteiten opereren diverse <u>vakgroepen</u> . Zij groeperen alle personeelsleden die onderzoek en onderwijs verrichten binnen eenzelfde discipline. Elke vakgroep bestaat vervolgens uit een of meerdere <u>onderzoeksgroepen</u> . Zij staan in voor de organisatie van het gespecialiseerd onderzoek.
	Deze klassieke boomstructuur van faculteiten, onderzoeksgroepen en vakgroepen wordt doorkruist door de <u>onderzoeksinstituten</u> . De instituten groeperen onderzoekers uit verschillende onderzoeksgroepen die in bepaalde speerpuntdomeinen onderzoek uitvoeren. Daarbij wordt het volledige onderzoekspectrum afgedekt, van fundamenteel over toegepast onderzoek tot concrete valorisatietoepassingen.
Juridisch statuut	Autonome openbare instelling

Verantwoordelijke van de organisatie, die moet verwittigd worden bij ongevallen.

Naam	Dr. Anouk Agten
Functie	Post-doctoral researcher
Tel GSM	011269203

## 2. De vrijwilliger: student-onderzoeker

Naam	Thijs Liam
Correspond entieadres	Liam.ţi.thijs@gmail.com
Tel GSM	0477390292

## 3. Verzekeringen

Waarborgen	De burgerlijke aansprakelijkheid van de organisatie.
Maatschappij	Ethias
Polisnummer	45009018

Waarborgen	Lichamelijke schade die geleden is door vrijwilligers bij ongevallen tijdens de uitvoering van het vrijwilligerswerk of op weg naar- en van de activiteiten.
Maatschappij	Ethias
Polisnummer	45055074

## 4. Vergoedingen

De organisatie betaalt geen vergoeding aan de vrijwilliger.

## 5. Aansprakelijkheid

De organisatie is burgerrechtelijk aansprakelijk voor de schade die de vrijwilliger aan derden veroorzaakt bij het verrichten van vrijwilligerswerk.

Ingevel de vrijwilliger bij het verrichten van het vrijwilligerswerk de organisatie of derden schade berokkent, is hij enkel aansprakelijk voor zijn bedrog en zijn zware schuld. Voor lichte schuld is hij enkel aansprakelijk als die bij hem eerder gewoonlijk dan toevallig voorkomt.

Opgelet: voor het materiaal dat de vrijwilliger zelf meebrengt, is hij/zij zelf verantwoordelijk.

## 6. Geheimhoudingsplicht – verwerking persoonsgegevens

De vrijwilliger verleent de UHasselt toestemming om de gegevens die in het kader van zijn/haar inschrijving aan UHasselt werden verzameld, ook te gebruiken voor de uitvoering van deze afsprakennota (de evaluatie van de vrijwilliger alsook het aanmaken van een certificaat). UHasselt zal deze informatie vertrouwelijk behandelen en zal deze vertrouwelijkheid ook bewaken na de beëindiging van het statuut studentonderzoeker. De UHasselt neemt hiertoe alle passende maatregelen en waarborgen om de persoonsgegevens van de vrijwilliger conform de Algemene Verordening Gegevensbescherming (EU 2016/679) te verwerken.

De vrijwilliger verbindt zich ertoe om alle gegevens, documenten, kennis en materiaal, zowel schriftelijk als mondeling ontvangen in de hoedanigheid van student-onderzoeker aan de UHasselt als strikt vertrouwelijk te behandelen, ook indien deze niet als strikt vertrouwelijk werd geïdentificeerd. Indien de vertrouwelijke gegevens van de UHasselt ook persoonsgegevens bevatten dient de stagiair hiertoe steeds de Algemene Verordening Gegevensbescherming (EU 2016/679) na te leven en bij elke verwerking het advies van het intern privacycollege van de UHasselt in te winnen. Hij/zij verbindt zich ertoe om in geen geval deze vertrouwelijke informatie mee te delen aan derden of anderszins openbaar te maken, ook niet na de beëindiging van het statuut student-onderzoeker.

#### 7. Concrete afspraken

#### Functle van de vrijwilliger

De vrijwilliger zal volgende taak vervullen: masterthesis schrijven

Deze taak omvat volgende activiteiten: literatuurstudie met data-anlyses

De vrijwilliger voert zijn taak uit onder verantwoordelijkheid van de faculteit geneeskunde en levenswetenschappen

De vrijwilliger wordt binnen de faculteit begeleid door Dr. Anouk Agten

Zijn vaste werkplek voor het uitvoeren van de taak is thuis en op de universiteit Hasselt

De vrijwilliger zal deze taak op volgende tijdstippen uitvoeren:

- op de volgende dag(en):
  - e maandag
  - e dinsdag
  - e woensdag
  - donderdag
  - e vrijdag
  - e zaterdag
  - o zondag
- het engagement wordt aangegaan voor de periode van 30-9-2019 tot 30-5-2020 (deze periode kan maximaal 1 kalenderjaar zijn en moet liggen tussen 1 januari en 31 december).

#### Begeleiding

De organisatie engageert zich ertoe de vrijwilliger tijdens deze proefperiode degelijk te begeleiden en te ondersteunen en hem/haar van alle informatie te voorzien opdat de activiteit naar best vermogen kan worden uitgevoerd.

De vrijwilliger voert de taken en activiteiten uit volgens de voorschriften vastgelegd door de faculteit. Hij/zij neemt voldoende voorzorgsmaatregelen in acht, en kan voor bijkomende informatie over de uit te voeren activiteit steeds terecht bij volgende contactpersoon: Dr Anouk Agten

De vrijwilliger krijgt waar nodig vooraf een vorming. Het volgen van de vorming indien aangeboden door de organisatie, is verplicht voor de vrijwilliger. De vrijwilliger heeft kennis genomen van het 'reglement statuut student-onderzoeker' dat als bijtage aan deze afsprakennota wordt toegevoegd en integraal van toepassing is op de vrijwilliger.

#### Certificaat

Indien de vrijwilliger zijn opdracht succesvol afrondt, ontvangt hij/zij een certificaat van de UHasselt ondertekend door de decaan van de faculteit waaraan de vrijwilliger zijn opdracht voltooide.

## 8. Einde van het vrijwilligerswerk.

Zowel de organisatie als de vrijwilliger kunnen afzien van een verdere samenwerking. Dat kan gebeuren:

- bij onderfinge overeenstemming;
- op vraag van de vrijwilliger zelf;
- op verzoek van de organisatie.

Indien de samenwerking op initiatief van de vrijwilliger of de organisatie wordt beëindigd, gebeurt dit bij voorkeur minstens 2 weken op voorhand. Bij ernstige tekortkomingen kan de samenwerking, door de organisatie, onmiddellijk worden beëindigd.

Datum: 28-5-2020

Naam en Handtekening decaan

Naam en Handtekening vrijwilliger

Liam Thij

Opgemaakt in 2 exemplaren waarvan 1 voor de faculteit en 1 voor de vrijwilliger.

Bijlage 1

#### Reglement betreffende het statuut van student-onderzoeker<sup>1</sup>

#### Artikel 1. Definities

Voor de toepassing van dit reglement wordt verstaan onder:

student-onderzoeker: een regelmatig ingeschreven bachelor- of masterstudent van de UHasselt/tUL die als vrijwilliger wordt ingeschakeld in onderzoeksprojecten. De opdrachten uitgevoerd als studentonderzoeker kunnen op geen enkele wijze deel uitmaken van het studietraject van de student. De opdrachten kunnen geen ECTS-credits opleveren en zij kunnen geen deel uitmaken van een evaluatie van de student in ket kader van een opleidingsonderdeel. De onderzoeksopdrachten kunnen wel in het verlengde liggen van een opleidingsonderdeel, de bachelor- of masterproef.

#### Artikel 2. Toepassingsgebied

Enkel bachelor- en masterstudenten van de UHasselt/tUL die voor minstens 90 studiepunten credits hebben behaald in een academische bacheloropleiding komen in aanmerking voor het statuut van student-onderzoeker.

#### Artikel 3. Selectie en administratieve opvolging

§1 De faculteiten staan in voor de selectie van de student-onderzoekers en schrijven hiervoor een transparante selectieprocedure uit die vooraf aan de studenten kenbaar wordt gemaakt. §2 De administratieve opvolging van de dossiers gebeurt door de faculteiten.

#### Artikel 4. Preventieve maatregelen en verzekeringen

§1 De faculteiten voorzien waar nodig in de noodzakelijke voorafgaande vorming van studentonderzoekers. De student is verplicht deze vorming te volgen vooraleer hij/zij kan starten als studentonderzoeker.

§2 Er moet voor de betrokken opdrachten een risicopostenanalyse opgemaakt worden door de faculteiten, analoog aan de risicopostenanalyse voor een stagiair van de UHasselt/tUL. De faculteiten zien er op toe dat de nodige veiligheidsmaatregelen getroffen worden voor aanvang van de opdracht. §3 De student-onderzoekers worden door de UHasselt verzekerd tegen:

8 Burgerlijke aansprakelijkheid

Il Lichamelijke ongevallen

en dit ongeacht de plaats waar zij hun opdrachten in het kader van het statuut uitoefenen.

#### Artikel 5. Vergoeding van geleverde prestaties

§1 De student-onderzoeker kan maximaal 40 kalenderdagen, gerekend binnen één kalenderjaar, worden ingeschakeld binnen dit statuut. De dagen waarop de student-onderzoeker een vorming moet volgen, worden niet meegerekend als gepresteerde dagen.

§2 De student-onderzoeker ontvangt geen vrijwilligersvergoeding voor zijn prestaties. De student kan wel een vergoeding krijgen van de faculteit voor bewezen onkosten. De faculteit en de student maken hier aangaande schriftelijke afspraken.

#### Artikel 6. Dienstverplaatsingen

De student-onderzoeker mag dienstverplaatsingen maken. De faculteit en de student maken schriftelijke afspraken over deal dan niet vergoeding voor dienstverplaatsingen. De student wordt tijdens de dienstverplaatsingen en op weg van en naar de stageplaats uitsluitend verzekerd door de UHasselt voor lichamelijke ongevallen.

<sup>&</sup>lt;sup>1</sup> Zoals goedgekeurd door de Raad van Bestuur van de Universiteit Hasselt op 15 juni 2017.

#### Artikel 7. Afsprakennota

§1 Er wordt een afsprakennota opgesteld die vooraf wordt ondertekend door de decaan en de studentonderzoeker. Hierin worden de taken van de student-onderzoeker alsook de momenten waarop hij/zij de taken moet uitvoeren zo nauwkeurig mogelijk omschreven.

§2 Aan de afsprakennota wordt een kopie van dit reglement toegevoegd als bijlage.

#### Artikel 8. Certificaat

Na succesvolle beëindiging van de opdracht van de student-onderzoeker, te beoordelen door de decaan, ontvangt hij een certificaat van de studentenadministratie. De faculteit bezorgt de nodige gegevens aan de studentenadministratie. Het certificaat wordt ondertekend door de decaan van de faculteit waaraan de student-onderzoeker zijn opdracht voltooide.

#### Artikel 9. Geheimhoudingsplicht

De student-onderzoeker verbindt zich ertoe om alle gegevens, documenten, kennis en materiaal, zowel schriftelijk (inbegrepen elektronisch) als mondeling ontvangen in de hoedanigheid van studentonderzoeker aan de UHasselt, als strikt vertrouwelijk te behandelen, ook indien deze niet als strikt vertrouwelijk werd geidentificeerd. Hij/zij verbindt zich ertoe om in geen geval deze vertrouwelijke informatie mee te delen aan derden of anderszins openbaar te maken, ook niet na de beëindiging van zijn/haar opdracht binnen dit statuut.

#### Artikel 10. Intellectuele eigendomsrechten

Indien de student-onderzoeker tijdens de uitvoering van zijn/haar opdrachten creaties tot stand brengt die (kunnen) worden beschermd door intellectuele rechten, deelt hij/zij dit onmiddellijk mee aan de faculteit. Deze intellectuele rechten, met uitzondering van auteursrechten, komen steeds toe aan de UHasselt.

#### Artikel 11. Geschillenregeling

Indien zich een geschil voordoet tussen de faculteit en de student-onderzoeker met betrekking tot de interpretatie van dit reglement of de uitoefening van de taken, dan kan de ombudspersoon van de opleiding waarbinnen de student-onderzoeker zijn taken uitoefent, bemiddelen. Indien noodzakelijk, beslecht de vicerector Onderwijs het geschil.

#### Artikel 12. Inwerkingtreding

Dit reglement treedt in werking met ingang van het academiejaar 2017-2018.

## **VHASSELT**

#### Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit Revalidatiewetenschappen aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

- Ik ben ingeschreven als student aan de UHasselt in de opleiding Revalidatiewetenschappen & Kinesitherapie, waarbij ik de kans krijg om in het kader van mijn opleiding mee te werken aan onderzoek van de faculteit Revalidatiewetenschappen aan de UHasselt. Dit onderzoek wordt beleid door dr. Anouk Agten en kadert binnen het opleidingsonderdeel Wetenschappelijke stage/ masterproef deel 2. Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van de musculoskeletale revalidatie (hierna: "De Onderzoeksresultaten").
- Bij de creatie van De Onderzoeksresultaten doe ik beroep op de achtergrondkennis, vertrouwelijke informatie<sup>1</sup>, universitaire middelen en faciliteiten van UHasselt (hierna: de "Expertise").
- Ik zal de Expertise, met inbegrip van vertrouwelijke informatie, uitsluitend aanwenden voor het uitvoeren van hogergenoemd onderzoek binnen UHasselt. Ik zal hierbij steeds de toepasselijke regelgeving, in het bijzonder de Algemene Verordening Gegevensbescherming (EU 2016-679), in acht nemen.
- 4. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.
- 5. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modellenrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.
- 6. In zoverre De Onderzoeksresultaten auteursrechtelijk beschermd zijn, omvat bovenstaande overdracht onder meer de volgende exploitatiewijzen, en dit steeds voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding:
  - het recht om De Onderzoeksresultaten vast te (laten) leggen door alle technieken en op alle dragers;
  - het recht om De Onderzoeksresultaten geheel of gedeeltelijk te (laten) reproduceren, openbaar te (laten) maken, uit te (laten) geven, te (laten) exploiteren en te (laten) verspreiden in eender welke vorm, in een onbeperkt aantal exemplaren;

<sup>&</sup>lt;sup>3</sup> Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

# ▶ UHASSELT

- het recht om De Onderzoeksresultaten te (laten) verspreiden en mee te (laten) delen aan het publiek door alle technieken met inbegrip van de kabel, de satelliet, het internet en alle vormen van computernetwerken;
- het recht De Onderzoeksresultaten geheel of gedeeltelijk te (laten) bewerken of te (laten) vertalen en het (laten) reproduceren van die bewerkingen of vertalingen;
- het recht De Onderzoeksresultaten te (laten) bewerken of (laten) wijzigen, onder meer door het reproduceren van bepaalde elementen door alle technieken en/of door het wijzigen van bepaalde parameters (zoals de kleuren en de afmetingen).

De overdracht van rechten voor deze exploitatiewijzen heeft ook betrekking op toekomstige onderzoeksresultaten tot stand gekomen tijdens het onderzoek aan UHasselt, eveneens voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding.

Ik behoud daarbij steeds het recht op naamvermelding als (mede)auteur van de betreffende Onderzoeksresultaten.

- Ik zal alle onderzoeksdata, ideeën en uitvoeringen neerschrijven in een "laboratory notebook" en deze gegevens niet vrijgeven, tenzij met uitdrukkelijke toestemming van mijn UHasseltbegeleider dr. Anouk Agten.
- Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

Naam: Thoelen Mathias

Adres: Russeltstraat 117A, 3830 Wellen

Geboortedatum en -plaats : 28-11-1997 te Hasselt

Datum: 20-05-2020

Handtekening:

**VHASSELT** 

#### Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit Revalidatiewetenschappen aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

- Ik ben ingeschreven als student aan de UHasselt in de opleiding Revalidatiewetenschappen & Kinesitherapie, waarbij ik de kans krijg om in het kader van mijn opleiding mee te werken aan onderzoek van de faculteit Revalidatiewetenschappen aan de UHasselt. Dit onderzoek wordt beleid door dr. Anouk Agten en kadert binnen het opleidingsonderdeel Wetenschappelijke stage/ masterproef deel 2. Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van de musculoskeletale revalidatie (hierna: "De Onderzoeksresultaten").
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<sup>&</sup>lt;sup>1</sup> Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo anel mogelijk op de hoogte brengt.

## ▶ UHASSELT

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Gelezen voor akkoord en goedgekeurd,

Naam: Thijs Liam

Adres: Wommelgemsesteenweg 40, 2531 VREMDE

Geboortedatum en -plaats : 12-11-1997 te Hong Kong

Datum: 22-05-2020

Handbekening: