

Physical exercise and HIV:

From a medical/scientific and patient perspective

Axel VANDERPERRE – UTOPIA_BXL

Exercise Is Medicine

1. HIV: More than anti-retroviral therapy

2. Health aging

- Aging is more that biology
- WHO Model of healthy aging
- 3. Non_aids defining comorbidities
- 4. Exercise physical activities
 - sustains the hallmarks of age
 - Training and its he effects of exercise training
- 5. My summary and my view





Conflicts of interest

- Educational grants and support
- Consultancy
- ➢ by Gilead, ViiV, MSD

1. HIV: More than anti-retroviral therapy

People living with HIV are getting much older:

- High prevalence of cardiovascular risk factors and comorbidities
- Low physical fitness
- o Sarcopenia "epidemic"
- Accelerated aging and frailty with HIV (chronic inflammation, immune senescence)

9 Years Less Life Expectancy - 77 for PLWH vs 86

mean age 41 (10.8), 87% male; 25.1%) were non-Hispanic black and 87 191 (24.3%) were Hispanic; HIV+ more poor; drug use disorders, ever smoked, lower rate of obesity or overweight, 70% MSM



Julia Marcus et al. JAMA Network Open 2020





1. HIV: More than anti-retroviral therapy Mechanisms? Factors Associated with Co-morbidities in PLWH



2. Healthy aging WHO Model of healthy aging

A process of developing and maintaining functional abilities that enables well-being in older age

Intrinsic capacities

(Composite of all physical and mental capacities)

- Cognition
- Locomotion
- Psychological
- Vitality
- Sensory







3. Non_AIDS defining comorbidities



FIG. 1. Potential benefits of physical activity on chronic HIV infection. HIV-positive patients present a low level of chronic immune activation and inflammation associated with an increased incidence of non-AIDS-defining illnesses and accelerated aging. Even antiretroviral therapy can contribute to accelerated aging and to the occurrence of adverse effects, despite the undeniable benefits that it is able to give. The introduction of regular physical exercise in HIV treatment may have a significant therapeutic effect: it could reduce the impact of immune activation and non-AIDS-defining illness linked to chronic inflammation. Moreover, physical activity could generate improvements in neuropsychological function and metabolic assessment.

healthhiv.be

Taming HIV-Related Inflammation with Physical Activity. Gabriella d'Ettorre et al. AIDS RESEARCH AND HUMAN RETROVIRUSES Volume 30, Number 10, 2014



3. Non_AIDS defining comorbidities The cardiovascular risk in people living with HIV is higher than explainable by traditional risk factors





Grinspoon S. CROI 2015. Seattle, WA. Oral #O134



3. Non_AIDS defining comorbidities



Association of Cardiorespiratory Fitness With Long-term Mortality Among Adults Undergoing Exercise Treadmill Testing

Kyle Mandsager, MD; Serge Harb, MD; Paul Cremer, MD; Dermot Phelan, MD, PhD; Steven E. Nissen, MD; Wael Jaber, MD



C Comorbidities and performance groups

ESRD, end-stage renal disease

f

Variable	HR (95% CI)	P Value	
Comorbidity			
Smoking	1.41 (1.36-1.46)	<.001	
CAD	1.29 (1.24-1.35)	<.001	
Diabetes	1.40 (1.34-1.46)	<.001	
Hypertension	1.21 (1.16-1.25)	<.001	
ESRD	2.78 (2.53-3.05)	<.001	
Group comparison			
Low vs Elite	5.04 (4.10-6.20)	<.001	(
Low vs High	3.90 (3.67-4.14)	<.001	
Low vs Above Average	2.75 (2.61-2.89)	<.001	
Low vs Below Average	1.95 (1.86-2.04)	<.001	
Below Average vs Elite	2.59 (2.10-3.19)	<.001	
Below Average vs High	2.00 (1.88-2.14)	<.001	+
Below Average vs Above Average	1.41 (1.34-1.49)	<.001	
Above Average vs Elite	1.84 (1.49-2.26)	<.001	
Above Average vs High	1.42 (1.33-1.52)	<.001	
High vs Elite	1.29 (1.05-1.60)	.02 —	
		1	

n=122.007

Follow up: 8.4 J.

Adjusted HR

1/1



JAMA Network Open. 2018;1(6):e183605. doi:10.1001/jamanetworkopen.2018.3605



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3. Non_AIDS defining comorbidities Incidence of frailty in people living with HIV – and exercise program

CLINICAL SCIENCE

Frequency, Risk Factors, and Mediators of Frailty Transitions During Long-Term Follow-Up Among People With HIV and HIV-Negative AGE_bIV Cohort Participants

Eveline Verheij, MD,^{ab} Ferdinand W. Wit, MD, PhD,^{abc} Sebastiaan O. Verboeket, MD,^{ab} Maarten F. Schim van der Loeff, MD, PhD,^{d.e} Jeannine F. Nellen, MD, PhD,^a Peter Reiss, MD, PhD, a.b.c and Gregory D. Kirk, MD, PhD

Background: We previously demonstrated a higher prevalence of frailty among AGE, IV-cohort participants with HIV (PWH) than

OPEN

Received for publication June 29, 2020; accepted September 7, 2020. From the "Department of Global Health and Division of Infectious Diseases me Department of Global Heath and Division of Intectous Diseases, mesterdam Infection and Immunity Institute and Amsterdam Public Health esearch Institute, Amsterdam University Medical Centers, University of

- Amsterdam, Amsterdam, the Netherlands; ⁵Amsterdam Institute for Global Health and Development, Amsterdam, the Netherlands; ⁵HIV Monitoring Healih and Development, Amsterdam, the Netherlands, "HIV Monitorng Foundation, Amsterdam, the Netherlands, "Engemment of Infectious Disanses, Public Health Service of Amsterdam, Amsterdam, the Nether-lands,"Amsterdam University Medical Center, Amsterdam Infection and Immunity Institute and Amsterdam, Public Health Research Institute, University of Amsterdam, Amsterdam, the Netherlands, and Departments Unversity of Amsterdam, Amsterdam, the Netherlands, and Departments of Epidemiology and Medicine, Schools of Public Heath and Medicine, Johns Hopkins University, Baltimore, MD. Supported by The Netherlands Organization for Health Research and Development (ZonMW) (Grant number 300020007) and AIDS Fonds
- Development (2010499) (Grant number 30002007) and ADS Fords (Grant number 200963). Additional unreader and the second second second from Gikad Sciences; Vii V Healthcare; Janssen Pharmaceuticals NV; and Merck & Co. Nene of these finding bodies had a role in the design or conduct of the study, the analysis and interpretation of the results, the writing of the report, or the decision to publish. Presented in part at AIDS2018 (abstract number: THAB0105); July 23-27, 2018; Amsterdam, The Netherlands.

P.R. through his institution has received independent scientific grant suppor from Gilead Sciences, Janssen Pharmaceuticals Inc, Merck & Co and trom Gielad Sciences, Jansen Pfarmacutecak inc, Merck & Co and Vil Healthcar, and has served on scientific advisory boards for Gikad Sciences, Vil Y Healthcare, Merck & Co, Teva pharmaceutical industries, for which honornia were all path to his institution. O.D.K. was supported by a Fubright Gikela Scholar award (US Department of State) and by for Mational Institute of Allergy and Infectious Disease (Grant number K24-se). National instance of Netrogy and Infectious Decases (on an Indine R 24 A1118591), F. W.W. has served on scientific advisory boards for ViiV and Gilead sciences. M.F.S.V.D.L. has received independent scientific grant support from Sanofi Pasteur, MSD Janssen Infectious Diseases and Vaccines and Merck, he has served on the advisory board of GSK and has

Vacciese and Merck, he has served on the arhivery band of OSE and has nearing an employed in a sport of most highing praching to define out, and service and service of the service of the service of the service segmental digital content is not able for this article. Direct URL, cattrons are the service of this article on the journal r. Web wite (over ables, com), we are the service of the Amsterdam hasting of Lindle and Development, Amsterdam University Medical Certers, University of Amsterdam (sensit: C4, Panakowstow 52, 1105 DF Amsterdam, The Netherland (sensit: e.verheii@am

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among age- and lifestyle-comparable HIV-negative participants Furthermore, frailty was associated with the development of comorbidities and mortality. As frailty may be a dynamic state, we evaluated the frequency of transitions between frailty states, and explored which factors were associated with transition toward frailty in this cohort.

Methods: The study enrolled 598 PWH and 550 HIV-negativ participants aged ≥45 years. Of those, 497 and 479 participants, respectively, participated in ≥2 consecutive biennial study-visits between October 2010 and October 2016, contributing 918 and 915 visit-pairs, respectively. We describe the frequency, direction, and risk factors of frailty transitions. Logistic regression models with generalized estimating equations were used to evaluate determinants for transition to frailty, including HIV-status, socio-demographic, behavioral, HIV-related factors, and various inflammatory and related biomarkers.

Results: Transitioning between frailty states in any direction occurred in 36% of a total of 1833 visit-pairs. The odds of nonfrail participants transitioning toward frailty were significantly higher for PWH, occurring in 35 PWH (7.3%) and 25 (5.2%) HIV-negative nonfrail participant respectively (odd ratio_{HTV} 2.19, 95% confidence interval 1.28 to 3.75). The increased risk among PWH was attenuated when sequentially adjusting for waist-hip ratio, number of pre-existent comorbidities, and the presence of depressive symptoms

Conclusion: PWH are at increased risk of transitioning to frailty, and thereby at increased risk of adverse health outcomes. Whether optimizing the management of obesity, comorbidity, or depressive symptoms may modify the risk of becoming frail requires further investigation

Key Words: frailty, HIV, transitions, comorbidities, depression (J Acquir Immune Defic Syndr 2021;86:110-118)

INTRODUCTION

For people living with HIV (PWH) with access to combination antiretroviral therapy (cART), HIV-infection has become a chronic condition, and as they continue to age, comorbidities have become the primary causes of morbidity and mortality in this population. Frailty is conceptualized as a state of decreased physical resilience because of deficits across multiple organ systems,

J Acquir Immune Defic Syndr • Volume 86, Number 1, January 1, 2021

A 12-week multicomponent exercise MEP program enhances frailty by increasing robustness, improves physical performance, and preserves muscle mass in older adults with HIV: MOVINNG study -

Public Health, 17 April 2024 Sec. Aging and Public Health Volume 12 - 2024 | https://doi.org/10.3389/fpubh.2024.1373910 Fátima Brañas – Geriatrics Department, Hospital Universitario Infanta Leonor, Madrid, Spain et al.

A 12-week MEP enhances frailty by increasing robustness in OAWH, and improves physical performance, and preserves muscle mass in older adults with good adherence to the MEP independently of HIV status. In addition, they found significant improvements in anxiety and depression symptoms after the 12-week

598 PLHIV and 550 HIV-negative participants ≥45 years (AGE_hIV)

Risk for frailty in HIV: 2.19-fold \uparrow (95% CI 1.28 to 3.75)

positive healthhiv.be

Verheij E et al. J AIDS 2021 & Public Health, Sec. Aging and Public Health Volume 12 - 2024



4. Exercise – physical activities Exercise sustains the hallmarks of health.



style is associated with a significantly lower risk of total mor-

tality and a longer life expectancy.5 Together with a healthy

and adequate dietary pattern, exercise represents a promising

strategy for reducing the risk of chronic metabolic and



https://doi.org/10.1016/j.ishs.2022.10.00 Cite this article: Qiu Y, Fernández-García B, Lehmann HI, et al. Exercise sustains the hallmarks of health. J Sport Health Sci 2023;12:8-35

Peer review under responsibility of Shanghai University of Sport

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Abstract

SIRT-1: Sirtuin-1, GDF15: Growth differentiation factor 15, FGF21: Fibroblast Growth Factor 21

Qiu Y et al. J Sport Health Sci 2023



PLOS ONE

combined aerobic and resistance exercise (CARE)

		CAR	E	No	Exerci	se		Std. Mean Difference	Std. Mean Difference
Study or Subg	roup Me	an S	D Tot	al Mear	SD SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.3.1 Health st	atus								
Fillipas et al, 2	006	14 17	4 1	7 -6.8	37.5	18	7.0%	0.69 [0.00, 1.37]	
Ogalha et al, 2	011 20	0.8 17	8 3	5 11.9	18.3	28	7.4%	0.49 [-0.02, 0.99]	
Rojas et al, 20	03	9 15	7 1	9 -1.6	21.1	14	7.0%	0.57 [-0.14, 1.28]	
Subtotal (95%	CI)		27211	1	222	60	21.4%	0.56 [0.21, 0.91]	
Heterogeneity:	Tau* = 0.00;	Chi*=	0.21, d	= 2 (P =	0.90);1	*= 0%			
Test for overall	effect: $Z = 3$.	12 (P=	0.002)						
1.3.2 Energy/V	itality								
Fillipas et al. 2	006	6 2	24 1	7 1.5	18.3	18	7.1%	0.21 [-0.46, 0.87]	
Ogalha et al. 2	011 17	7.1 14	1 3	5 7	13	28	7.4%	0.73 (0.22, 1.25)	
Rojas et al, 20	03 6	8.8 12	1 1	9 0.2	16.7	14	7.0%	0.59 [-0.12, 1.30]	
Subtotal (95%	CI)		17	1		60	21.4%	0.55 [0.20, 0.90]	•
Heterogeneity: Test for overall	Tau* = 0.00; effect: Z = 3.	Chi* = 05 (P =	1.52, d 0.002)	= 2 (P =	0.47);1	*= 0%			
1.3.3 Social fu	nction								
Fillipas et al, 2	006	-1 87	.2 1	7 10	38.7	18	7.1%	-0.16 [-0.83, 0.50]	
Mutimura et al,	2008 0	0.6 0	2 4	9 (0.01	49	6.9%	4.20 [3.48, 4.92]	
Ogalha et al, 2	011 11	1.5 17	6 3	5 12.3	10.9	28	7.4%	-0.05 [-0.55, 0.44]	
Rojas et al, 20 Subtotal (95%	03 (CI)	3.9 11	.5 1	9 0.8 0	22.9	14	7.0%	0.46 [-0.24, 1.16] 1.10 [-0.79, 3.00]	
Heterogeneity. Test for overall	Tau ² = 3.62; effect: Z = 1.	Chi ² = 14 (P =	106.22	df = 3 (F	< 0.00	001); P	= 97%		
1.3.4 Physical	function								
Fillipas et al, 2	006 16	6.7 29	7 1	7 1.3	21	18	7.0%	0.59 [-0.09, 1.27]	
Mutimura et al,	2008 0	0.2 0	1 4	9 0	0.1	49	7.4%	1.98 [1.50, 2.47]	
Ogalha et al, 2	011 19	3.2 17	2 3	5 13.1	23.8	28	7.4%	0.30 [-0.20, 0.80]	
Rojas et al, 20	03 9	9.8 13	5 1	9 -1.5	23.7	14	7.0%	0.60 [-0.11, 1.30]	
Subtotal (95%	CI)		12	0		109	28.8%	0.88 [0.02, 1.73]	
Heterogeneity Test for overall	Tau ² = 0.67; effect: Z = 2.	Chi [#] = 02 (P =	25.95, 0.04)	if=3 (P	< 0.000	01); P=	: 88%		
Total (95% CI)			38	2		338	100.0%	0.79 [0.27, 1.32]	•
Heterogeneity:	Tau ² = 0.92;	Chi ^z =	138.76	df = 13 (P = 0.0	0001);	P= 91%		1 5 6 5
Test for overall	effect: Z = 2.	94 (P=	0.003)						Favours (No Exercise) Favours (C)
Test for subarr	up difference	es: Chi	^a = 0.80	. df = 3 (P = 0.85	5), P = 0	196		fire mererel fer

The Impact of Moderate or High-Intensity Combined Exercise on Systemic Inflammation Among Older Persons With and Without HIV - Kristine M. Erlandson et al. Exercise and Inflammation in HIV • The Journal of Infectious Diseases 2021:223 (1 April) •

People with HIV have Similar or Greater Improvements in Function with Exercise

- Exercise for Healthy Aging (NIA K23, 2014-2019) 70 people with and without HIV, aged ≥50 years
 - 12 weeks moderate intensity exercise
 - Randomized to 12 additional weeks of moderate or high exercise intensity
- 10-45% improvement in both groups
 - People with HIV experienced <u>greater</u> gains in 400-m walk time, stair climb, VO2 max

Physical Function Findings:

Percent Improvement in Functional Measures with 12 and 24 Weeks of Cardiovascular and Resistance Exercise (Moderate/High Intensity Combined)



Percent improvement between 0-12 weeks (darker bar) and 13-24 weeks (lighter bar)



Differing Exercise Response at the Tissue Level in Some (not all) Markers



Does this impact fatigue and can it impact longer-term adherence?





Do These Findings Change Our Recommendations for Exercise in Older PWH?



- Older adults with HIV have similar if not greater improvements in physical function with exercise
- Higher-intensity exercise may result in further improvements in measures of strength
- Based on poor uptake of physical activity, blunted improvements in IL-10 & mitochondrial protein content, stable epigenetic age, and lack of long-term adherence, adjuvant therapies may be needed

22 - 26 July - Munich, Germany and virtual

aids2024.org



Kristine Erlandson





Effectiveness of aerobic exercise for adults living with HIV: systematic review and meta-analysis using the Cochrane Collaboration protocol

Kelly K. O'Brien et al <u>BMC Infectious Diseases</u> volume 16, Article number: 182 (2016)

Research Question



What is the effectiveness of aerobic (AER) and/or progressive resistive exercise (PRE) on...

- Immunological and virological
- Cardiopulmonary
- Weight and body composition
- Strength and

oositive

healthhiv.be

Psychological outcomes

.. in adults living with HIV?

Characteristics	Aerobic Exercise Review	Resistive Exercise (PRE) Review				
# studies met inclusion criteria	24 studies	20 studies				
14 studies overlap (PRE+AER; or PRE versus AER versus no exercise)						
# participants @ baseline	1242 participants	959 participants				
Mean age range (years)	30-49 years	32-49 years				
% women @ completion	22%	23%				
Withdrawal rate	~24% (0-76%)	~20% (0-38%)				
% studies published ≥1996	20 (83%)	17 (85%)				
Length of intervention	5 to 52 weeks	6 to 52 weeks				
Supervised exercise	18 (75%)	17 (85%)				
# mate encluses performed	59	34				

Physical Therapy UNIVERSITY OF TORONTO

BOUNDLESS



https://doi.org/10.1186/s12879-016-1478-2

Effectiveness of aerobic exercise for adults living with HIV: systematic review and meta-analysis using the Cochrane Collaboration protocol

Kelly K. O'Brien et al <u>BMC Infectious Diseases</u> volume 16, Article number: 182 (2016)

Quality of life: SF36 questionnaire (AER)

Aerobic (or AER+PRE) versus No Exercise

Domain	Weighted Mean Diffe	rence (WMD) (95% CI)
General Health	4.73 (3.13, 9.75)	
Mental Health	11.58 (1.35, 21.81)	
Role Physical	6.56 (3.17, 9.96)	
Role Emotional	10.95 (8.19, 13.71)	Clinically Important Improvement
Pain	-6.59 (-9.83, -3.36)	
Physical Function	16.30 (6.89, 25.72)	
Energy / Vitality	5.03 (1.33, 8.72)	
Social Function	2.73 (-4.84, 10.30)	

Statistically significant improvement on 6 out of 8 SF36 domain **QOL sub**scales for exercisers compared with non-exercisers (n=59; 2 studies).



BOUNDLESS

Health-related quality of life

Meta-analyses were performed for the eight sub-scales of the SF-36 questionnaire . Results demonstrated statistically significant and clinically important improvements (>10 point change) on

 mental health, role emotional and physical functioning, role physical, general health, and energy/vitality sub-scale scores
 for participants in the aerobic or combined aerobic and PRE group compared with participants in the non-exercising control group.



ttps://doi.org/10.1186/s12879-016-1478-2



7. My summary and my view







Webinars Well-being and Physical activity:

NEEDS ASSESSMENT : Principal health challenges, barriers to physical activity and links to HIV+ status



Poster BREACH 2024

RESULTS

- The health status of PLHIV is generally average to poor, particularly in terms of relational and sexual health.
 The primary obstacles to engaging in regular physical activity according to the respondents are a lack of motivation (50%) and a lack of energy (43%).
- PLHIV predominantly attribute the obstacles that they face in obtaining regular and satisfactory physical activity to their serological status.
- In a similar fashion, PLHIV primarily associate their various health issues with their serological status.
- Despite a relatively high level of education, the respondents primarily cite financial and community

Supported by Gilead and ViiV





NEEDS ASSESSMENT: Principal health challenges, barriers to physical activity and links to HIV+ status



WEBINARS "Physical Activity, Respiration & Visualisation"

Webinaires : octobre, novembre, décembre 2024	- PROGRAMME
D'EXERCICES	

1. ÉTIREMENTS / F	ORCE : En	tre		
3-5x/semaine				
Étirements 15 seco	ondes			
chaque.				
			Pas besoin	de repos entre les
Tête (étirements)	6	15 secondes	étirements	-
Épaule		15 répétitions vers l'	avant Selon le	
S	2	et vers l'arrière	besoin	
(mobilisations)				
Bras			30-60	Flexion et extension du
(renforcement)	6	3x10	secondes	3 x 10 répétitions
debout ou assise				
			30-60	-
Tronc	1	3x10	secondes	9
(Couché sur le				NE N
ventre)				
			30-60	
Tronc	2	3x10	secondes	
(quatre pattes)				
			30-60	
Tronc	1	3x10	secondes	
(couché sur le dos)				
(couche sur le dos)			30-60	
Tronc	1	3v10	secondes	Constant of the local division of the
(dobout	L _	5710	secondes	
	1			

 Webinaires : octobre, novembre, décembre 2024

 PROGRAMME D'EXERCICES

 3.Exercices de

 respiration :

 J1 : prise de conscience de votre respiration (2 ou 3 minutes) + respiration abdominale, costale et pectorale (3 minutes par étage).

J2 : prise de conscience de votre respiration (2 ou 3 minutes).

J3 : prise de conscience de votre respiration (2 ou 3 minutes) + Respiration abdominale, costale et pectorale + Test BOLT (3 minutes).

4. Pour la visualisation:

J1: Sophronisation <u>https://youtu.be/-</u> de base (SB). Audio <u>kULMIXmaQo</u> J3: Sophronisation <u>https://youtu.be/-</u> de base (SB): Audio <u>kULMIXmaQo</u> et Évacuation des <u>https://youtu.be/texF8J</u> tensions inutiles: Audio <u>mMcV4</u>



Une initiative d'Utopia_BXL , avec l'aide de l'Observatoire du Sida et des Sexualités avec le support de GILEAD et ViiV

2. Exercises d'aerobies (suggestions) Entre 2-4x/semaine durant 15-25 min



Pilot Programme Webinars "Well-being and physical activity" : questionnaires on vitality, general health and physical activity answered by PLHIV participants

Q4 Over the past 4 weeks, how tired have you felt?



Q5 Over the past few weeks, have you felt constantly stressed?

Q6 In total, how much time have you spent walking in the last 7 days?



Physical Activity General Health Vitalité - VT - SF-36



0 2 4 6 8 10 12 14 16 18 20

WEBINARS oct-nov-dec 2024 "Physical Activity and Well-being"

Strength

- Clear, pedagogical videos focused on demonstration.
- Webinars designed by experts HCPs.
- Potential for individualized coaching



Supported by grant by Gilead and ViiV

Weakness

- Lack of human interaction in webinars.
- Home exercise requires strong discipline.
- Digital barriers for some participants.

Threat

- Reliance on technology excludes some.
- Cultural resistance to adopting routines.
- Difficulty maintaining longterm efforts.





Opportunity

- In-person workshops to enhance interaction.
- Tailored coaching to meet individual needs.
- Addressing effects of HIV
 treat
 treat
 treat





Exercise Is Medicine





