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Athletic ‘oldest-old’: alive and kicking

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On October 13th 2018, an 86-year-old Japanese man, Hiromu Inada, finished the Ironman Triathlon World Championship (Hawaii) in 16 hours and 54 minutes. The Ironman triathlon is the paradigm of grueling endurance races, with its 2.4-mile swim, 112-mile cycle and 26.2-mile Marathon all rolled into one event held under extreme heat, humidity and wind conditions. And yet this is just one of the many feats accomplished worldwide by the so-called ‘oldest-old’ (those aged ≥ 85) in both endurance or more ‘power’-oriented sports (**Figure**).¹ Instead of viewing such performances as biological exceptions, why not consider the medically relevant message they convey, that is humans can retain remarkable functionality until the end of their lifespan...if they train for it.

Some non-modifiable factors (notably, genetics) might contribute to the odds of reaching the status of oldest-old in good health conditions. For instance, the “risk” $\epsilon 4$ -allele of the gene encoding apolipoprotein E (*ApoE*) has been reported to exert a negative influence on healthy exceptional longevity (living 100+ years with no major disease conditions) with the $\epsilon 2$ -allele variant exerting the opposite effect.² Indeed, a recent population-based longitudinal study with 79-year-old individuals found that carriage of the $\epsilon 4$ -allele was associated with a greater decline in muscle strength compared with non-carriers.³ Beyond genetics, there is strong evidence to support an association between regular physical exercise and healthy aging, as confirmed by a recent meta-analysis of longitudinal studies that found a corrected effect size for this association of 1.27 (95% confidence interval, 1.11–1.45) when analyzing data from a total of 174,114 participants (30% men) with age ranges from 20 to 87 years.⁴ There is in fact a strong biological rationale for a link between physical exercise and healthy aging, including also from an evolutionary perspective. Crosstalk between contracting muscles and many tissues and systems (heart, vessels, fat, brain, pancreas, liver) has been shaped over years of evolution (our survival as hunter-gatherers being linked to

daily exercise).⁵ Thus, an active, well-preserved muscle is being increasingly viewed as an endocrine organ able to release molecules, or so-called myokines, with a myriad of multi-organ, ‘anti-aging’ benefits such as decreased inflammation or insulin resistance, or increased muscle growth and neurotrophism.^{5–7}

Also, there is increasing, albeit often ignored, evidence that with proper exercise training *per se* muscle function can be remarkably preserved, if not augmented, as we age. Regular exercise practice during lifetime prevents or at least attenuates the degeneration of muscle mass, cardiorespiratory fitness and skeletal muscle metabolic status at an advanced age (>70 years).^{8–10} Importantly, exercise benefits do not exclude the frail or diseased oldest-old, as corroborated by meta-analytical evidence.^{11,12} Institutionalized nonagenarians increased their leg muscle strength by ~17% solely in response to a leg press training-based 8-week program with no concomitant intervention (drugs, supplements).¹³ Likewise, a recent trial showed that exercise training during acute hospitalization (median of 5 days) reversed hospital-induced functional decline in patients aged 87–88 years.¹⁴ The program, which included individualized supervised progressive resistance, balance, and walking-training exercises, required little investment and proved safe.

Societies are progressively aging, and the oldest-old, which are expected to more than triple by 2050,¹⁵ are the most rapidly expanding population segment. Thus, how we should preserve functional reserve across multiple systems to combat frailty and disability at advanced ages is a major challenge for modern medicine that, at least up until now, cannot be resolved with drugs or drug combinations. For instance, the prevalence of frailty rises exponentially with increasing age, passing from 6.5% to 65% in those aged 60–69 years and ≥90 years, respectively.¹⁶ It seems difficult to understand why physical function assessment in the oldest-old does not receive the same consideration in the clinical setting as other vital signs (body temperature, blood

pressure, pulse or breathing rate). In this respect, an assessment tool easy to implement in the geriatric context is the handgrip test – a surrogate of overall muscle strength and a proven predictor of all-cause mortality in the oldest-old population in a follow-up of 555 participants (65% women) from the Leiden 85-plus study.¹⁶ The short physical performance battery (SPPB) has also been proposed as an effective screening tool, with a recent meta-analysis of 17 studies (n = 16,534 participants with a mean age of 76 ± 3 years) showing that a score lower than 10 is predictive of all-cause mortality in elders.¹⁷ Moreover, physical function impairment during hospitalization – as assessed with aforementioned SPPB or by simply measuring the ability to perform basic activities of daily living such as eating, transferring from bed to chair, walking, using the toilet, bathing, dressing – is associated with a higher risk of re-hospitalization, institutionalization or death after hospital discharge in elderly patients.^{19,20} Thus, daily assessment of physical function might help to identify functional decline at an early stage of hospitalization, before a point of no return is reached. Acute hospitalized older patients, including those who are able to walk independently, spend most of their hospital time in bed.^{21,22} In addition to deteriorating their functional status, bedrest increases the risk for cognitive decline and dementia in the elderly.²³ The epidemic of low mobility during hospitalization reflects the failure to apply efficient models for management of older patients.^{24,25} Despite the traditional hospital design and culture of bedrest, together with the belief that reducing mobility will prevent falls, there is meta-analytic evidence supporting the need for comprehensive geriatric assessment (including evaluation of physical function and implementation of rehabilitation) to increase the odds of survival and living in their own home for up to 12 months in acutely hospitalized elders.²⁶

In summary, we believe that physical exercise should be a cornerstone in the fight against the decline of intrinsic capacity in the oldest-old and particularly in those

institutionalized/hospitalized, for whom physical exercise – or even the so-called ‘exercise mimetics’ such as neuromuscular electrical stimulation when volitional exercise is unfeasible²⁷ – should be a first-line treatment.²⁸ Efforts are needed to implement strategies, such as the growing mHealth approach (*i.e.*, the use of mobile applications for health promotion),²⁹ aiming at facilitating the assessment of physical function and the promotion of physical exercise in this population segment. In the era of immortal cell research, why not also muscle in on aging while alive? It is never too late to do so.

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References

1. Lepers R, Stapley PJ, Cattagni T. Centenarian athletes: Examples of ultimate human performance? *Age Ageing*. 2016;45(5):729-733. doi:10.1093/ageing/afw111
2. Garatachea N, Emanuele E, Calero M, et al. ApoE gene and exceptional longevity: Insights from three independent cohorts. *Exp Gerontol*. 2014;53:16-23. doi:10.1016/j.exger.2014.02.004
3. Skoog I, Hörder H, Frändin K, et al. Association between APOE genotype and change in physical function in a population-based swedish cohort of older individuals followed over four years. *Front Aging Neurosci*. 2016;8(OCT):1-7. doi:10.3389/fnagi.2016.00225

4. Daskalopoulou C, Stubbs B, Kralj C, Koukounari A, Prince M, Prina AM. Physical activity and healthy ageing: A systematic review and meta-analysis of longitudinal cohort studies. *Ageing Res Rev.* 2017;38:6-17. doi:10.1016/j.arr.2017.06.003
5. Fiuza-Luces C, Santos-Lozano A, Joyner M, et al. Exercise benefits in cardiovascular disease: beyond attenuation of traditional risk factors. *Nat Rev Cardiol.* 2018;15:731-743. doi:10.1038/s41569-018-0065-1
6. Valenzuela P, Morales J, Fiuza-Luces C, de la Villa P, Santos-Lozano A, Lucia A. Preventing Alzheimer's Disease: Why Not Targeting the Muscle First? *JAMDA.* 2019;20(1):101-102.
7. Garatachea N, Pareja-Galeano H, Sanchis-Gomar F, et al. Exercise Attenuates the Major Hallmarks of Aging. *Rejuvenation Res.* 2015;18(1):57-89. doi:10.1089/rej.2014.1623
8. Pollock RD, O'Brien KA, Daniels LJ, et al. Properties of the vastus lateralis muscle in relation to age and physiological function in master cyclists aged 55–79 years. *Aging Cell.* 2018;17(2). doi:10.1111/accel.12735
9. Mckendry J, Breen L, Shad BJ, Greig CA. Muscle morphology and performance in master athletes: A systematic review and meta-analyses. *Ageing Res Rev.* 2018;45(January):62-82. doi:10.1016/j.arr.2018.04.007
10. Gries KJ, Raue U, Perkins RK, et al. Cardiovascular and skeletal muscle health with lifelong exercise. *J Appl Physiol.* 2018;125(5):1636-1645. doi:10.1152/jappphysiol.00174.2018
11. Chou CH, Hwang CL, Wu YT. Effect of exercise on physical function, daily living activities, and quality of life in the frail older adults: A meta-analysis. *Arch*

Phys Med Rehabil. 2012;93(2):237-244. doi:10.1016/j.apmr.2011.08.042

12. Giné-Garriga M, Roqué-Fíguls M, Coll-Planas L, Sitjà-Rabert M, Salvà A. Physical exercise interventions for improving performance-based measures of physical function in community-dwelling, frail older adults: A systematic review and meta-analysis. *Arch Phys Med Rehabil.* 2014;95(4). doi:10.1016/j.apmr.2013.11.007
13. Serra-Rexach JA, Bustamante-Ara N, Hierro Villarán M, et al. Short-term, light- to moderate-intensity exercise training improves leg muscle strength in the oldest old: A randomized controlled trial. *J Am Geriatr Soc.* 2011;59(4):594-602. doi:10.1111/j.1532-5415.2011.03356.x
14. Martínez-Velilla N, Casas-Herrero N, Zambon-Ferraresi F, et al. Effect of Exercise Intervention on Functional Decline in Very Elderly Patients During Acute Hospitalization: A Randomized Clinical Trial. *JAMA Intern Med.* 2019;179(1):28-36.
15. He W, Goodkind D, Kowal P. *U.S. Census Bureau, International Population Reports.* Washington, DC: U.S. Government Publishing Office; 2016. doi:10.1007/978-3-642-19335-4_63
16. Gale CR, Cooper C, Sayer AA. Prevalence of frailty and disability: findings from the English Longitudinal Study of Ageing. *Age Ageing.* 2015;44(1):162-165. doi:10.1093/ageing/afu148
17. Ling CHY, Taekema D, De Craen AJM, Gussekloo J, Westendorp RGJ, Maier AB. Handgrip strength and mortality in the oldest old population: The Leiden 85-plus study. *CMAJ.* 2010;182(5):429-435. doi:10.1503/cmaj.091278
18. Pavašini R, Guralnik J, Brown JC, et al. Short Physical Performance Battery

- and all-cause mortality: Systematic review and meta-analysis. *BMC Med.* 2016;14(1):1-9. doi:10.1186/s12916-016-0763-7
19. Volpato S, Cavalieri M, Sioulis F, et al. Predictive value of the Short Physical Performance Battery following hospitalization in older patients. *Journals Gerontol - Ser A Biol Sci Med Sci.* 2011;66 A(1):89-96. doi:10.1093/gerona/glq167
20. Covinsky KE, Pierluissi E, Story THEPS. Hospitalization-Associated Disability “She Was Probably Able to Ambulate, but I’m Not Sure”. *JAMA.* 2011;306(16):1782-1793.
21. Brown CJ, Redden DT, Flood KL, Allman RM. The underrecognized epidemic of low mobility during hospitalization of older adults. *J Am Geriatr Soc.* 2009;57(9):1660-1665. doi:10.1111/j.1532-5415.2009.02393.x
22. Martínez-Velilla N, Urbistondo-Lasa G, Veintemilla-Erice E, Cambra-Contín K. Determining the hours hospitalised patients are bedridden due to their medical condition and functional impairment and secondary mortality. *Rev Esp Geriatr Gerontol.* 2013;48(2):96.
23. Ehlenbach WJ, Crane PK, Haneuse SJPA, Carson SS, Curtis JR, Larson EB. Association Between Acute Care and Critical Illness Hospitalization. *JAMA.* 2010;303(8):763-770.
24. Greysen SR. Activating Hospitalized Older Patients to Confront the Epidemic of Low Mobility. *JAMA Intern Med.* 2016;176(7):928. doi:10.1001/jamainternmed.2016.1874
25. Baztán J, Suárez-García F, López-Arrieta J, Rodríguez-Mañas L, Rodríguez-Artalejo F. Effectiveness of acute geriatric units on functional decline, living at

- home, and case fatality among older patients admitted to hospital for acute medical disorders: meta- analysis. *BMJ*. 2009;338:b50. doi:10.1136/bmj.b50
26. Ellis G, Whitehead MA, O'Neill D, Langhorne P, Robinson D. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database Syst Rev*. 2011;6(7):CD00621.
27. Valenzuela PL, Morales JS, Pareja-Galeano H, et al. Physical strategies to prevent disuse-induced functional decline in the elderly. *Ageing Res Rev*. 2018;47(July):80-88. doi:10.1016/J.ARR.2018.07.003
28. Lazarus NR, Izquierdo M, Higginson IJ, Harridge. SDR. Exercise Deficiency Diseases of Ageing: The Primacy of Exercise and Muscle Strengthening as First Line Therapeutic Agents to Combat Frailty. *J Am Med Dir Assoc*. 2018;In press.
29. Valenzuela P, Morales J, Santos-Lozano A, Serra-Rexach J, Izquierdo M, Lucia A. mHealth and Aging. *JAMDA*. 2018;19(9):810-811.

191 **Figure caption**

192 Representative examples of athletic feats accomplished by 'oldest-old'.

193

Figure

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Athletic 'oldest old': alive and kicking

Exercise training including multi-component (walking-balance and strength/resistance) exercises attenuates age-induced functional decline even at highly advanced ages. Several illustrative cases confirm that the oldest can still show remarkable physical performance.

86 years

Hiromu Inada
IRONMAN finisher
16 hours 53 minutes

100 years

Donald Pellmann
100-metre dash
26.99 seconds

100 years

Mieko Nagaoka
1500-metre freestyle swimming
1 hour 14 minutes

100 years

Fauja Singh
Marathon finisher
8 hours 11 minutes

101 years

Ruth Frith
Javelin throw
6.43 metres

103 years

Robert Marchand
1-hour track cycling
26.925 kilometres

105 years

Stanislaw Kowalski
100-metre dash
34.5 seconds

105 years

Jaring Timmerman
50-metre freestyle swimming
2 minutes 52 seconds