

Editorial

The conundrum of exercise dose: when the unknown gets knowable

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The motto “Exercise is a medicine” has reached plethoric tone and the beneficial effects of exercise are nowadays blatant. In the clinical arena, the recommendations of regular physical activity (PA) and exercise are well documented and represent an essential component of primary and secondary prevention strategies [1,2]. However, when it comes to prescription and adherence to exercise training and programs, these behavioural interventions have showed limited efficacy [3]. As a result, physical inactivity remains largely prevalent among general and unhealthy populations. In addition, for people with several chronic diseases, physical inactivity is an increasingly worsening factor. The concept of optimal dose of exercise is still a matter of debate. This is the key for designing individually tailored programs so to yield health benefits, at the minimally conceived level.

In a pandemic context of environmental syndromic factors, dose-response studies are urgently advocated to determine the clear-cut therapeutic effects and the multiple health-promoting benefits of exercise.

What is meant by *dose*, that is the cocktail of training variables

The concept of “exercise dose” is well established in literature [4]: as quantification of exercise exposure, at the simplest level, doses are intended as the product of three discrete variables: (1) duration; (2) frequency; (3) intensity. Whereas the volume can be seen as the product of the duration by the intensity of a training session.

Given that one size does not fit all, these variables ought to be wisely orchestrated in the individuals’ schedules to favourably maximize the pleiotropic effect of exercise.

An in-depth understanding of several scientific endeavours may shed light on the underlying mechanisms behind the positive effects of exercise, and therefore being harnessed at the wider community level [5,6].

The relationship between habitual PA or structured exercise (a sub-category of PA) and health benefits is curvilinear [7]. That means that amounts of PA are associated with cardiovascular and metabolic health outcomes, with greatest benefits at the lower end of the dose-response curve [8]. In fact, at the upper end of this dose-response curve, there is insufficient evidence to identify the exact level at which PA stops providing benefits in terms of reduced risks of mortal-

ity with no increased risks of harms. However, there is high certainty evidence about the inverse relationship between PA and all-cause mortality, cardiovascular disease mortality, incident type 2 diabetes [9], and incident site-specific cancers in adults. Still, studies on total energy expenditure showed that these models are not a simple linear function of PA, rather increased PA is associated with reduced energy spent [10]. In other words, total energy expenditure is maintained within a narrow range in a constrained model, and not in an additive one.

Furthermore, diverse types of exercise (aerobic, strength or combined) and different domains of PA (occupational, leisure, transport) may vary the extent of the health outcomes. Current evidence indicates that a combined training results as optimal [11].

Exercise prescriptions according to international agencies

The World Health Organization (WHO) has released recommendations [7] according to the different stages of life and the presence of chronic conditions (Table 1, Ref. [7]). In healthy adults, the practice of moderate- to vigorous-intensity aerobic PA is advised, ideally divided in 5 sessions/week [12]. To gain additional health benefits, individuals are also encouraged to gradually increase the weekly amount of aerobic PA performed. Along with the aerobic training, a muscle-strengthening activity involving the major muscle groups, is highly recommended.

Biological and psychological factors could influence health response to PA in men and women [13]. For instance, men seem to obtain more health gains from performing vigorous exercise, while women are more suited to moderate-intensity long-duration sport activities [13,14]. Although intriguing, this does not always apply since the response to different PA doses varies upon a multitude of factors, including the targeted clinical outcome. Also, the paucity of evidence as well as the presence of confounders such as the gender-specific effects on mental health and the different background level of training in men and women, render difficult the translation of these preliminary insights into practice. Further research should assess whether the gender-specific response to PA is enough impactful to worth the attention of the major organs of health surveillance.



Table 1. Minimum dose of PA recommended according to age and clinical conditions [7].

Class of individuals (y-old)	Type	Duration/frequency	Intensity
Children and adolescents (5–17)	Mostly aerobic PA	60 min/day	Moderate-to-vigorous
	Aerobic activities	3 days/week	Vigorous
	Strength exercise	3 days/week	Vigorous
Adults (18–65)	Aerobic PA	150–300 min/week (>300 min/week desirable) or 75–150 min/week (>150 min/week desirable)	Moderate Vigorous
	Strength exercise	2 days/week	
Elderlies (>65) and patients with chronic conditions*	Same as for adults	=	=
	Multicomponent PA for functional balance and strength	3 days/week (>3 days/week desirable)	Moderate-to-vigorous

*Hypertension, type 2 diabetes, HIV, and cancer survivors.

Being engaged in constant PA is of critical importance for maintaining a proper cardio-metabolic fitness and helps preventing chronic cardiovascular conditions, which represent the first cause of hospitalization and death worldwide. Indeed, the WHO guidelines have been endorsed by both the American Diabetes Association and the American Heart Association [15], and most of other international medical agencies. Altogether, these organizations strongly advise the adherence to such exercise plans for the preservation of a proper cardio-metabolic health.

Closing remarks: the need for technology and a multifaceted teamwork

PA, such as other medications, should be best prescribed individually, with consideration of the dose. In this regard, a tighter interplay between clinicians and physical trainers is highly warranted. Cutting-edge devices will help trainers and physicians to translate novel scientific insights into clinical practice. For instance, technological gears can facilitate the measurements of patients' PA. Novel tools may also support the development of tailored PA protocols based on the individual-specific response to different types of exercise. Future research challenges are open to unexplored avenues of investigation.

Author contributions

RC designed the work. RC and LDG performed the literature search and wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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Conflict of interest

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