Title: Small steps in fitness, major leaps in health for adults with intellectual disabilities

Short title: Better fitness matters in the unfit

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Abstract page

Abstract:

Physical fitness is positively related to health outcomes like morbidity and all-cause mortality, with minimally-required cut-off values to generate those health benefits. Individuals with intellectual disabilities exhibit very low fitness levels well below those cut-off values. Our novel hypothesis is that even among very unfit, older adults with intellectual disabilities, small changes in fitness translate to major changes in health.

Summary:

Improving physical fitness will likely improve outcomes in extremely unfit populations scoring well under cut-off values for the general population.

Key words:

Physical fitness, morbidity, mortality, intellectual disabilities, aging

Key points (15- words in 3-5 bullet points):

- Previous research has identified cut-off values for the minimum physical fitness levels to gain health benefits with regards to future morbidity and mortality.

- Extremely unfit populations may not be able to reach those cut-off values, and it is unknown how improvements in fitness impacts health in these populations.

- Aging individuals with intellectual disabilities are extremely unfit and will likely not reach those cut-off values identified for the general population.

- Our data support that even small differences at the lower end of the physical fitness spectrum are associated with health benefits, which supports a stronger focus on improving fitness amongst individuals with intellectual disabilities.

INTRODUCTION

Individuals with intellectual disabilities exhibit very low physical activity levels throughout their lives [1]. This is related to population-specific factors including lack of support to become active, accessibility of facilities, and motivational issues [2]. Their lifelong low physical activity levels and associated low fitness levels transition into an extremely sedentary aging population with very poor fitness levels, expressed by cardiorespiratory fitness, strength, balance, and other health-related fitness components [3, 4]. For example, VO_{2max}, the gold standard measurement for cardiorespiratory fitness ranges between 30-40 mL/kg/min for young adults with intellectual disabilities (22-30 mL/kg/min for young adults with Down syndrome) [5], whereas 20-29 years old in the general population average around 45-50 mL/kg/min [6]. Grip strength in 50-year olds with intellectual disabilities was almost half of that of the general population. Grip strength was 29.4 kg in 50-60 years old men with intellectual disabilities versus 50.6 kg in 50-60 years old men in the general population, and in women with intellectual disabilities, grip strength was 21.4 kg in 50-60 years old with ID compared to 30.9 kg in 50-60 years old in the general population [4]. Gait speed, as a measure of dynamic balance, was also lower in 50-years old with intellectual disabilities than in the general population (1.02 m/s for 50-60 years old women versus 1.31 m/s for 50-60 years old women in the general population) [4].

The poor fitness is compounded by other population-specific factors influencing health and daily functioning throughout their lives, such as cognitive limitations, and physical and psychiatric comorbidities, as well as other specific comorbidities related to specific genetic syndromes (i.e. Down syndrome) [7]. As a result, their aging process is neither optimal nor healthy, with high rates of morbidity including cardiovascular disease (CVD) and diminished skills for daily living [8, 9]. This further increases the need for support and care throughout their senior life [10]. As both the identification and treatment of several health conditions in individuals with intellectual disabilities have improved over time, the life expectancy of the majority of this population is currently close to the life expectancy of the general population [11]. This further aggravates the impact of the increased care and support needs [12], both on an individual level as on population level, with health care costs substantially increasing in the last decades of life. As the disability-associated health-care expenditures of individuals with disabilities currently comprise around 25% of the total US annual health care spending[13], any means of reducing these costs would be of major interest to both the individuals involved as to policy makers.

Remarkably, as individuals with intellectual disabilities seem to experience every disadvantage when it comes to a healthy aging process, fitness may still be a potent target to improve health. For the general population, research has defined what minimum amounts of physical activity or physical fitness level (i.e. cut-off values) are required to lower the risk of future negative health outcomes like CVD and all-cause mortality. In populations with activity and fitness levels well below those cut-off values, one might not expect that variance within these lower regions would still result in better future health outcomes. However, strong associations do exist between fitness and health outcomes in this unfit population of individuals with intellectual disabilities. Baseline fitness levels, although very low, of a large group of older adults with intellectual disabilities were still predictive of daily functioning and mobility three years after baseline, and of all-cause mortality five years after baseline [14-16], potentially even more so than obesity (Oppewal and Hilgenkamp, submitted). Our novel hypothesis is that among very unfit, older adults with intellectual disabilities, small changes in fitness translate to major changes in health (Figure 1).

Even small changes within those lowest fitness categories, below any cut-off values, seem to be associated with better future health outcomes, making physical fitness a key target for healthy ageing in individuals with intellectual disabilities. This could have major implications for other sedentary and unfit (patient) populations.

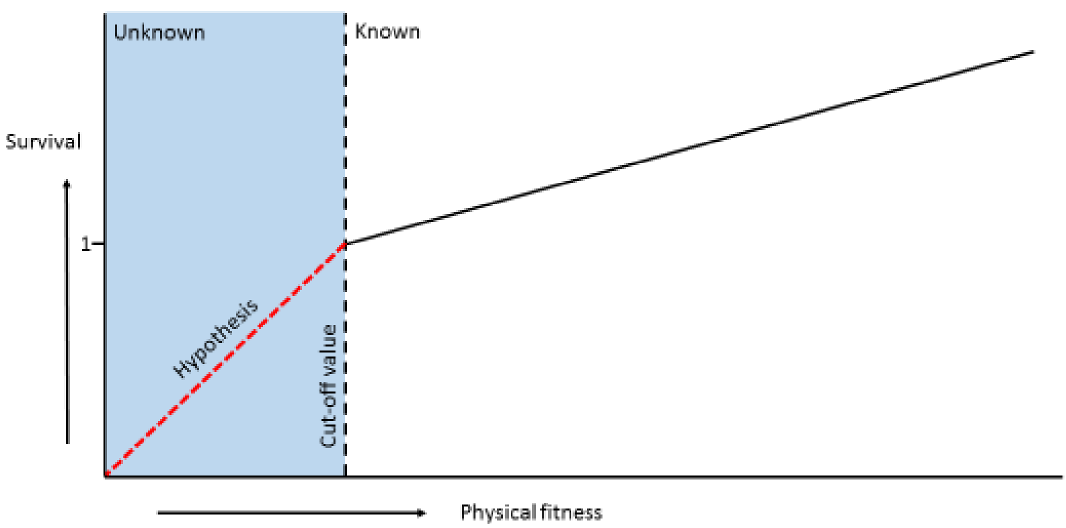

Figure 1: Hypothesis of large health benefits with small changes in fitness at the very low end of the fitness spectrum

FITNESS PREDICTS MORBIDITY AND MORTALITY IN THE GENERAL POPULATION

Physical fitness, in particular health-related physical fitness, predicts morbidity and mortality in the general population. As CVD is the leading cause for mortality in the general population [17], and CVD risk factors are highly prevalent in individuals with intellectual disabilities [18], we will specifically focus on CVD morbidity and on all-cause mortality. Several physical fitness components strongly predict CVD morbidity and mortality in the general population, with the strongest evidence for cardiorespiratory fitness [19, 20], gait speed [21, 22] and grip strength [23].

Meta-analyses of studies in the general population demonstrate that CVD morbidity and all-cause mortality risk is related to baseline fitness levels. In healthy adults (mean age ranging from 37 to 57 years), 1 metabolic equivalent (MET) higher level of cardiorespiratory fitness corresponded with a 13% (RR = 0.87, 95% CI = 0.84 – 0.90) lower risk of all-cause mortality, and a 15% (RR = 0.85, 95% CI = 0.82 – 0.88) lower risk of CVD morbidity [19]. Improvements in cardiorespiratory fitness over time were associated with a reduction in mortality risk, independent of baseline cardiorespiratory fitness [24]. In older adults (65 years and older), a 0.1 m/s faster baseline gait speed resulted in a 12% (HR = 0.88, 95% CI = 0.87 – 0.90) lower risk of all-cause mortality [22]. For grip strength, a 1 kg higher baseline grip strength corresponded with a 4% (HR = 0.96, 95% CI = 0.93 – 0.98) lower risk of all-cause mortality in older adults (60 years and older) [25]. In another study in adults in the general population (35 – 70 years), 5 kg lower grip strength at baseline resulted in a 16% higher all-cause mortality risk (HR = 1.16, 95% CI = 1.13 – 1.20), 17% higher cardiovascular mortality risk (HR = 1.17, 95% CI = 1.11 – 1.24), and 7% higher risk for myocardial infarction (HR = 1.07, 95% CI = 1.02 – 1.11), and 9% higher risk for stroke (HR = 1.09, 95% CI = 1.05 – 1.15) [26]. The abovementioned studies suggest a linear relationship per unit of increase/decrease in physical fitness; however some studies suggest the greatest risk reductions happen when progressing from the least fit and the next least fit groups [20].

The abovementioned studies might seem to be informative across the entire spectrum of physical fitness levels. However, two limitations to generalizing those results to unfit populations need to be addressed. Most of those studies include populations with a wide range of physical fitness levels, which makes it easier to statistically detect an overall correlation which not necessarily applies to the entire range in the same magnitude [19, 22, 26]. Some other studies focused on populations with better overall fitness than our target population [25, 26], thus lacking information on the impact of improvements specifically on the lower end of the physical fitness spectrum.

NORMS AND REFERENCE VALUES IN THE GENERAL POPULATION

In addition to the relative data about the relationships between fitness and health outcomes, the following paragraphs shows that absolute cut-off values exist for physical fitness components that indicate the minimum amount that is required to lower the risk of future CVD morbidity and mortality.

Cardiorespiratory fitness is the most-often studied physical fitness component with regard to CVD morbidity and all-cause mortality. The ACSM reports norms by sex and age for cardiorespiratory fitness [6]. Low cardiorespiratory fitness, often defined as the lowest quartile or quintile for each sex/age category, is associated with a higher risk of CVD morbidity, CVD mortality and all-cause mortality [6]. In a meta-analysis in healthy adults, the minimum cardiorespiratory fitness level to be associated with lower CVD and mortality risk in men was at 9 METs at 40 years, 8 METs at 50 years, and 7 METs at 60 years. In women, this was slightly lower with 7 METs at 40 years, 6 METs at 50 years, and 5 METs at 60 years[19]. In various patient populations including those with cardiovascular disease, epidemiological studies found cardiorespiratory fitness levels above 8 to 10 METs to be associated with survival, and a cardiorespiratory fitness level under 5 METs to be associated high mortality risk [19, 20].

The normal range for comfortable gait speed is 1.2-1.4 m/s, with an increase from childhood up to early adulthood where there is a period of maintenance after which gait speed decreases during or following mid adulthood (30-40 years of age) [27]. In older adults, a comfortable gait speed below 1.0 m/s and below 0.8 m/s is often used as a cut-off for an increased all-cause mortality risk [22, 27-29]. Cut-off values between 0.8 – 1.3 m/s were identified for CVD morbidity risk in older adults (60 years and over) [21]. This range in cut-off values suggest that there may be an 'area of risk' instead of a single cut-off value, with a gait speed of 0.8 m/s seen as the lower end.

Grip strength increases up to early adulthood followed by a period of maintenance, after which it generally declines after mid adulthood. The peak in grip strength for men is between 29 to 39 years of age (51 kg) and between 26 to 42 years of age for women (31 kg) [30]. The ACSM reports norms by sex and age categorized from poor to excellent [6], and numerous studies have reported norm scores, mostly focused on older adults [30-32]. Although no absolute cut-off values have been defined, low grip strength is an important predictor for CVD morbidity and mortality and all-cause mortality [33]. Relative cut-off values are most often based on tertiles for men and women separately. The grip strength values of the consecutive tertiles for women were 17.2 kg, 24.6 kg, 32.4 kg, and for men 27.5 kg, 38.7 kg, 49.9 kg, with a median age of 50 years [IQR = 42 – 58] for the total study sample [26]. For grip strength, quartiles for women were <14 kg, 14.01 – 18.2 kg, 18.21 – 22.5 kg, and ≥22.51 kg, and for men <22 kg, 22.01 – 30 kg, 30.01 – 35kg, and ≥ 35.01 kg with a mean age of 72.8 years of the total study sample [25, 34].

As shown, these cut-offs seem to indicate that only when you are crossing a certain threshold of physical fitness, the risk of CVD morbidity and mortality decreases considerably. Furthermore, this concept could imply that small improvements below those cut-off values would not really reduce the risk of CVD morbidity and mortality. With little to no supporting evidence for a focus on improving physical fitness in populations that are extremely low fit, this may result in a passive approach towards the unfit individuals that may need it most.

LOW FITNESS IN ADULTS WITH INTELLECTUAL DISABILITIES

Individuals with intellectual disabilities have consistently demonstrated low physical fitness levels [4, 5, 35]. A recent review summarized the results of 13 studies on cardiorespiratory fitness in individuals with intellectual disabilities across different countries, settings and the lifespan [5]. That review showed that cardiorespiratory fitness is lower in individuals with intellectual disabilities, and even lower in individuals with Down syndrome[36]. The single largest dataset of VO_{2max} results of individuals with intellectual disabilities with and without Down syndrome showed a lower VO_{2max} for individuals with Down syndrome, however no difference between individuals with intellectual disabilities and a control group [37]. Upon closer examination, this was caused by a different ratio of men and women in each group (much higher number of men in the group with intellectual disabilities compared to a majority of women in the control group), After controlling for sex a significant difference in VO_{2max} between individuals with intellectual disabilities and the control group was confirmed in this dataset as well [38].

In the Healthy Ageing and Intellectual Disabilities (HA-ID) study, the physical fitness of older adults with intellectual disabilities (defined as 50 years and older) has been studied on a wide range of physical fitness components, among which cardiorespiratory fitness, gait speed and grip strength [39]. Cardiorespiratory fitness was evaluated with the 10-m incremental shuttle walking test, and the test score was the distance covered by the participant during the test. This distance was used to calculate VO_{2max} x [40]. Comfortable gait speed was evaluated by measuring the time it took to cover 5 meters, and maximal grip strength was measured with a hand dynamometer. A more detailed description of the tests and the execution can be found elsewhere [4]. In figures 2-4 the cardiorespiratory fitness, gait speed and grip strength levels of older adults with ID are plotted against the norm values of the general population [4]. It can be seen that the largest part of the population scores below the lower limits of the average ranges in the general population. For gait speed, 43% of the men and 54% of the women with intellectual disabilities scored below the reference values (representing the average range, defined as the 95% confidence interval) in the general population, whereas this was (by design) only 2.5% for the general population [4]. For grip strength, the difference was even larger, with 77% of the men and 67% of the women with intellectual disabilities scoring below the reference values (defined as the 95% confidence interval) compared to 2.5% in the general population [4]. For cardiorespiratory fitness, 100% of the individuals with intellectual disabilities scored below what was considered the average reference range (based on the lowest quintile as the lower limit), whereas 20% of the general population was expected to score below that reference range [4].

When using the available cut-off values to determine CVD morbidity and mortality developed for the general population, older adults with intellectual disabilities clearly land in the bottom categories, or even below the lowest categories. For example, with regard to cardiorespiratory fitness, in figure 2 it can be seen that older adults with intellectual disabilities score below 5 METs (VO_2 max of 17.5 ml/kg/min), the minimum cardiorespiratory fitness level associated with risk reductions [4, 19]. For gait speed, older adults with intellectual disabilities score around or below the 1.0 m/s cut-off point, often used as a cut-off point for increased mortality risk [22, 28]. For grip strength no clear cut-off values are available, but 67-77% of older adults with intellectual disabilities scored below the lower limits of the norm values of the general population.

Based on these cut-off values, individuals with intellectual disabilities do not meet the minimum levels in fitness to expect any health benefits in terms of reducing risks of future morbidity or mortality. Moreover, they are categorized as being at a high/the highest risk of developing CVD morbidity and of mortality, even the relatively more fit individuals within this population. This might suggest that differences in physical fitness within this lower end of the spectrum, and consequently improvements still below these cut-off values, are not worthwhile to focus on/are not relevant in terms of lowering the risk of CVD morbidity and mortality.

Figure 2: (a and b) Mean (with standard deviation) VO_{2max} in the general population and HA-ID (Reprinted with permission from Hilgenkamp et al. 2012, Research in Intellectual Disabilities, 33, 1048-1058)

Figure 3: (a and b) Mean (with standard deviation) comfortable gait speed in the general population and HA-ID (Reprinted with permission from Hilgenkamp et al. 2012, Research in Intellectual Disabilities, 33, 1048-1058)

Figure 4: (a and b) Mean (with standard deviation) grip strength in the general population and HA-ID (Reprinted with permission from Hilgenkamp et al. 2012, Research in Intellectual Disabilities, 33, 1048-1058)

SMALL DIFFERENCES BETWEEN UNFIT INDIVIDUALS: DOES IT MATTER?

The HA-ID study was the first to provide data on the actual impact of these very poor physical fitness levels on mortality risk in this population with extremely low fitness levels (3 and 5 years post baseline).

Even in this extremely unfit population, better baseline cardiorespiratory fitness, comfortable gait speed, and grip strength were independently associated with a lower mortality risk [16]. Each additional meter walked on the 10-m incremental shuttle walking test resulted in a 0.3% lower mortality risk (HR = 0.997, 95% CI = 0.995 – 0.999) [16]. Higher gait speed, in increments of 1 km/h, resulted in a 35% lower mortality risk (HR = 0.65, 95% CI = 0.54 – 0.78) [16]. Expressed as m/s, a 1 m/s increment resulted in a 78.7% lower mortality risk (HR = 0.213, 95% CI = 0.11 – 0.41). Comparing this to the 12% lower mortality risk seen in the general older population with an increment of 0.1 m/s, this is somewhat lower (78.7% /10 = 7.8%) but still a significant reduction of mortality risk [22]. An increase in grip strength of 1 kg resulted in a 3% lower mortality risk (HR = 0.97, 95% CI = 0.94 – 0.99) [16]. This is comparable to the 4% reduction seen in the general older population [25]. These risk reductions in older adults with intellectual disabilities occurred at much lower fitness levels than in the general population, and in a younger population (50 years and older instead of 60/65 years and older).

This data supports for the first time the hypothesis that even at the very low end of the physical fitness spectrum, small improvements do make a difference in mortality risk. This finding is extremely relevant for our understanding of the needs of the population of individuals with intellectual disabilities across the lifespan, but may also translate to other very unfit populations without intellectual disabilities. Although we recognize that individuals with intellectual disabilities may differ from other populations with regard to both their specific physical and physiological characteristics and their risk of developing CVD morbidity and mortality, our hypothesis is that small differences in physical fitness will still have a big impact on future outcomes in any very unfit population.

SMALL IMPROVEMENTS WITHIN AN UNFIT INDIVIDUAL: WILL IT MATTER?

Having established the importance of the small differences within the lower end of the physical fitness spectrum, the remaining question is whether this translates to individual risk reductions when someone is actively improving their physical fitness levels, without switching reference categories or surpassing cut-off values. This would support a causal relationship between fitness and future health outcomes, beyond the current evidence of a correlation, which could also be indicative of a healthy survivor bias.

Intervention studies have demonstrated the effects of physical fitness programs in individuals with intellectual disabilities. Heller et al. reviewed 11 studies with a physical activity/exercise program in individuals with intellectual disabilities and reported improvements in balance, strength and cardiorespiratory capacity [2]. Another review by Bartlo et al. included 11 intervention studies with different physical activity/ exercise programs, but with overall moderate to strong evidence for improvements in balance, muscle strength and quality of life [41]. As this very unfit population is able to improve fitness levels, future research needs to include health outcomes related to morbidity and mortality, preferably following participants over a longer period of time, to answer the question whether better fitness significantly improves future health outcomes.

Our hypothesis is also in line with the research on physical activity benefits, summarized in the new 2018 Physical Activity Guidelines for Americans [42] which report improvements in health with small increases in physical activity within the lower end of the physical activity spectrum.

For the first time the Key Guidelines for Adults state that ‘Some physical activity is better than none’[42]. The Guidelines even include a graph summarizing the dose-response relationship between physical activity and mortality, in which the risk of mortality decreases exponentially with more physical activity, with a very steep decrease on the lower end of the physical activity spectrum (from inactive to a little bit of physical activity) (2018 PA Guidelines for Americans Fig6.2 Relationships of Moderate-to-Vigorous Physical Activity to All-Cause Mortality). A comparable exponential decrease in mortality risk may be seen for physical fitness as well, but this will require more dose-response research across the entire spectrum of physical fitness.

For individuals with intellectual disabilities however, the Physical Activity Guidelines define important gaps of knowledge that need to be addressed. One of the major issues is the generalizability of the physical activity research to the population of individuals with intellectual disabilities. Although the Guidelines for the first time devote an entire chapter to individuals with intellectual disabilities, this chapter highlights the lack of evidence for the effects of physical activity on comorbidity, physical functioning and health-related quality of life in this specific population [42]. A recent review on the effectiveness of physical activity interventions for individuals with intellectual disabilities showed that programs are able to increase physical activity in this population, but also supported the need for methodologically strong research designs in future research [43].

Future research needs to address how to effectively improve fitness in those very unfit populations with methodologically strong intervention studies that adapt their exercise programs to the lower starting level and expected incremental steps in work load. Furthermore, there is a need for longitudinal studies that include physical fitness as a baseline measure, but preferably monitor physical fitness levels at the same time points as the morbidity and mortality outcome measures, to investigate how differences in physical fitness over time impact the risk of morbidity and mortality.

CONCLUSION

Our novel hypothesis is that small changes in fitness translate to major changes in health among very unfit older adults with intellectual disabilities.

Whereas the lowest levels of fitness usually predict poor health outcomes, even small changes in those lower regions seem to be associated with big leaps in health, making physical fitness a key aspect for healthy ageing in individuals with intellectual disabilities.

Supporting author publications (list 2-3)**:**

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3. Oppewal A., Hilgenkamp T. *Physical fitness is predictive for survival over a 5-year follow-up period in older adults with intellectual disabilities – results of the HA-ID study* April 2019 Journal of Applied Research in Intellectual Disabilities

Submitted:

1. Oppewal A, Hilgenkamp TIM *Is fatness or fitness key for survival in older adults with intellectual disabilities?*

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