

British Journal of
Sports Medicine

**The Fat but Fit Paradox: What We Know and Don't Know
 About It**

Journal:	<i>British Journal of Sports Medicine</i>
Manuscript ID	bjsports-2016-097400.R4
Article Type:	Editorial
Date Submitted by the Author:	n/a
Complete List of Authors:	Ortega, Francisco; University of Granada and Karolinska Institutet Ruiz, Jonatan; University of Granada, Physical activity and sport Labayen, Idoia Lavie, Carl; The University of Queensland School of Medicine, Cardiovascular Diseases, John Ochsner Heart & Valve Institute, Ochsner Clinical School Blair, Steven; University of South Carolina, Departments of Exercise Science and Epidemiology & Biostatistics
Keywords:	Fitness, Fat, Fat percentage, Aerobic fitness, Cardiovascular

SCHOLARONE™
 Manuscripts

The Fat but Fit Paradox: What We Know and Don't Know About It

Francisco B Ortega, PhD^{1*}; Jonatan R Ruiz, PhD¹; Idoia Labayen², PhD; Carl J Lavie³ MD; Steven N Blair⁴, PED.

¹ PROFITH “PROmoting FITness and Health through physical activity” research group, Department of Physical Education and Sports, Faculty of Sport Sciences, University of Granada, Spain.

² Department of Nutrition and Food Science, University of the Basque Country, UPV/EHU, Vitoria, Spain.

³ Department of Cardiovascular Diseases, John Ochsner Heart and Vascular Institute, Ochsner Clinical School-the University of Queensland School of Medicine, New Orleans, Louisiana, U.S.A.

⁴ Department of Exercise Science and Department of Epidemiology and Biostatistics, University of South Carolina, Columbia, South Carolina, U.S.A.

* Correspondence to:

Francisco B Ortega, Department of Physical Education and Sports, Faculty of Sport Sciences, University of Granada, Carretera de Alfacar s/n, Granada 18071, Spain.

Tel. +34 958 244374. Fax. +34 958244369

E-mail: ortegaf@ugr.es

What We Know About It

In the late 1980s, one of us (SB) published a study that demonstrated that individuals with a low (below 1st quintile=20th percentile) cardiorespiratory fitness level had a higher risk of mortality 8 years later, when compared with those who were at least moderately fit¹. Since then, many longitudinal studies have consistently confirmed this notion in men and women, as well as in healthy and diseased individuals, for all-cause mortality, as well as for cardiovascular disease (CVD) mortality².

Obesity is related to multiple physical and mental comorbidities, and it is an incontrovertible risk factor for all-cause and CVD mortality³. It has been suggested, however, that being fit might attenuate some of the adverse consequences of obesity, independently of some key potential confounders. In this context, in the late 1990s, some studies provided first evidence for what was later known as the Fat but Fit paradox (See review by Ortega et al.³). These studies demonstrated that all-cause and CVD mortality risk in obese individuals, as defined by body mass index (BMI), body fat percentage or waist circumference, who are fit (i.e. cardiorespiratory fitness level above the age- and sex-specific 20th percentile) is not significantly different from their normal-weight and fit counterparts (i.e. the theoretically healthiest group possible) (**Figure 1**).

Being Normal-Weight Might Not Be Enough: Being Fit Plays a Major Role in Health

There is a general belief that being normal-weight is synonymous with being healthy, yet this notion could be wrong. In many cases, normal-weight but unfit individuals have significantly higher risk of all-cause and CVD mortality than normal-weight fit individuals. In addition, some readers will find even more interesting the fact that several studies have reported that normal-weight but unfit individuals could be at a higher risk than obese but fit individuals (**Figure 1**), which might seem paradoxical ³.

Role of Genes and Physical Activity (PA)

As for many other phenotypes, genes and environment jointly influence both adiposity and cardiorespiratory fitness. Heritability of both obesity and cardiorespiratory fitness might be up to 50% (e.g. results from the HERITAGE Family Study led by Prof. Bouchard and colleagues), leaving environmental factors to explain the rest of the variance. Among environmental factors, regular PA and, particularly, that of vigorous intensity has shown to be the most effective in improving cardiorespiratory fitness. For more detailed information about how to improve cardiorespiratory fitness through PA, see Tables 7 and 8 from the recently published Scientific Statement from the American Health Association ².

What We Still Don't Know About It

There is emerging evidence suggesting that a moderately to high cardiorespiratory fitness might counteract the negative consequences of obesity on many other health outcomes, especially in certain population age-groups, such as children and adolescents. Below, we highlight potential research directions for future studies.

The Fat but Fit Paradox in Children and Adolescents

Our recent meta-analysis demonstrated a strong link between cardiorespiratory fitness and cardiometabolic risk factors in children and adolescents, providing cut-points that more accurately delineate CVD risk (derived from ROC -receiver operating characteristic- analyses) ⁴. Worldwide reference values (sex- and age-specific) for cardiorespiratory fitness have also been recently published ⁵. These two meta-analyses have major practical implications as they allow children's cardiorespiratory fitness level to be properly interpreted and ranked. Specific information about the Fat but Fit paradox in young populations is scarce; yet, there is evidence suggesting that having moderate to high levels of cardiorespiratory fitness may attenuate the deleterious metabolic consequences ascribed to an excess total and central adiposity ^{6,7}.

The Fat but Fit Paradox and other Health Outcomes

Fat but Fit individuals have a 50% reduction in the risk of developing depression compared with their Fat and Unfit peers⁸. It is very likely that fitness and fatness counteract in their association with many physical and mental health outcomes, such as psychiatric disorders (e.g. attention deficit hyperactivity disorder, ADHD), self-esteem, cancer, disability pension, heart rate variability, hepatic steatosis (fatty liver), brown adipose tissue volume and activity, cognition, brain structure and function, etc.

The Fat but Fit Paradox in Randomized Controlled Trials (RCTs)

Please note that all evidence available for the Fat but Fit paradox comes from observational studies. Consequently, even if most of the studies are prospective cohorts and their findings provide highly valuable prognostic information, cause-effect relationships cannot be confirmed. Although exercise interventions in obese individuals lowered CVD risk, even without weight loss, literature is limited regarding whether these improvements in health without weight loss are driven by increases in cardiorespiratory fitness. In other words, such studies will be able to test the Fat but Fit paradox using an experimental design. Future exercise-based RCTs conducted in obese population should therefore include an accurate assessment of cardiorespiratory fitness before and after intervention so that formal mediation analyses can be performed.

Take Home Message

Obesity, and especially severe/morbid obesity (BMI >35kg/m²), is a major public health problem. Lifestyle intervention programs for obesity with special focus on exercise and a healthy diet are important public health goals. However, focus should not be placed exclusively on losing weight/fat, but also on increasing cardiorespiratory fitness, since a medium-high cardiorespiratory fitness level may attenuate the adverse consequences of obesity on health. The information summarized in this Editorial support that future public health strategies planned for obese individuals should target, in parallel, both weight/fat reduction and cardiorespiratory fitness improvement, especially if the obese person is classified as unfit, i.e. below the sex- and age-specific 20th percentile.

Table 1 will help sport specialists, physicians, and other healthcare practitioners to classify individuals as unfit vs. fit, which together with the internationally accepted definition of obesity (BMI equal or greater than 30kg/m²), results in the definition of Fat but Fit.

Disclaimer: The views expressed are those of the authors and do not reflect the official policy or position of the Institutions they belong to.

1
2
3 **Contributors:** FBO wrote an initial draft of the article, which was then discussed and refined
4 with the other authors.
5

6 **Competing interests:** None declared.
7

8 **Funding:** Dr. Ortega was supported by the Spanish Ministry of Economy and Competitiveness –
9 MINECO (RYC-2011-09011). Additional support was obtained from the MINECO/FEDER
10 (DEP2013-47540-R and DEP2016-79512-R); the University of Granada, Plan Propio de
11 Investigación 2016, Excellence actions: Units of Excellence, Unit of Excellence on Exercise and
12 Health (UCEES); the European Union’s Horizon 2020 research and innovation programme
13 under grant agreement No 667302; the SAMID III network, RETICS, funded by the PN I+D+I
14 2017-2021 (Spain), ISCIII- Sub-Directorate General for Research Assessment and Promotion,
15 the European Regional Development Fund (ERDF) (Ref. RD16/0022) and the EXERNET
16 Research Network on Exercise and Health in Special Populations (DEP2005-00046/ACTI). Dr.
17 Lavie has served as a consultant and speaker on fitness/obesity for the Coca-Cola Company and
18 has published a book on the *obesity paradox* with potential royalties. Prof. Blair has served as
19 consultants for weight loss and fitness companies and for the Coca-Cola Company, which has
20 also provided them unrestricted research grants.
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

REFERENCES

1. Blair SN, Kohl 3rd HW, Paffenbarger Jr. RS, et al. Physical fitness and all-cause mortality. A prospective study of healthy men and women. *JAMA* 1989;**262**:2395-401.
2. Ross R, Blair SN, Arena R, et al. Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign: A Scientific Statement From the American Heart Association. *Circulation* 2016;**134**(24):e653-e99.
3. Ortega FB, Lavie CJ, Blair SN. Obesity and Cardiovascular Disease. *Circ Res* 2016;**118**(11):1752-70.
4. Ruiz JR, Cavero-Redondo I, Ortega FB, et al. Cardiorespiratory fitness cut points to avoid cardiovascular disease risk in children and adolescents; what level of fitness should raise a red flag? A systematic review and meta-analysis. *Br J Sports Med* 2016. bjsports-2015-095903. doi: 10.1136/bjsports-2015-095903.
5. Tomkinson GR, Lang JJ, Tremblay MS, et al. International normative 20 m shuttle run values from 1 142 026 children and youth representing 50 countries. *Br J Sports Med* 2016. bjsports-2016-095987. doi: 10.1136/bjsports-2016-095987.
6. DuBose KD, Eisenmann JC, Donnelly JE. Aerobic fitness attenuates the metabolic syndrome score in normal-weight, at-risk-for-overweight, and overweight children. *Pediatrics* 2007;**120**(5):e1262-8.
7. Mesa JL, Ruiz JR, Ortega FB, et al. Aerobic physical fitness in relation to blood lipids and fasting glycaemia in adolescents: influence of weight status. *Nutr Metab Cardiovasc Dis* 2006;**16**(4):285-93.
8. Becofsky KM, Sui X, Lee DC, et al. A prospective study of fitness, fatness, and depressive symptoms. *Am J Epidemiol* 2015;**181**(5):311-20.
9. Kaminsky LA, Arena R, Myers J. Reference Standards for Cardiorespiratory Fitness Measured With Cardiopulmonary Exercise Testing: Data From the Fitness Registry and the Importance of Exercise National Database. *Mayo Clin Proc* 2015;**90**(11):1515-23.
10. Kaminsky LA, Imboden MT, Arena R, et al. Reference Standards for Cardiorespiratory Fitness Measured With Cardiopulmonary Exercise Testing Using Cycle Ergometry: Data From the Fitness Registry and the Importance of Exercise National Database (FRIEND) Registry. *Mayo Clin Proc* 2017;**92**(2):228-33.

Table 1. Cardiorespiratory fitness (maximal oxygen consumption, VO_{2max} , ml/kg/min) cut-points to classify individuals as unfit.

An individual will be classified as Unfit if his/her VO_{2max} **
is below these cut-points, and as Fit otherwise

Age group (years)	Treadmill test		Bike test	
	Boys/Men	Girls/Women	Boys/Men	Girls/Women
8-19*	42.0	35.0	42.0	35.0
20-29	38.1	28.6	33.2	21.6
30-39	34.1	24.1	25.4	17.0
40-49	30.5	21.3	22.2	15.8
50-59	26.1	19.1	21.5	14.9
60-69	22.4	16.5	19.0	14.0
70+	19.2	15.1	16.7	12.8

* The cut-points for individuals aged 8 to 19 come from a meta-analysis recently published by Ruiz et al.⁴. In studies in which the 20m shuttle run test was used to assess cardiorespiratory fitness in children or adolescents, an alternative definition of unfit can be done using the percentile 20th (equivalent to the 1st quintile used in adults) of the international reference value derived from the recent meta-analysis published by Tomkinson et al.⁵

The cut-points for adults correspond to the sex- and age-specific first quintile from the data (2014-2015) from 7783 maximal (respiratory exchange ratio ≥ 1.0) treadmill tests from men and women (aged 20-79 years) without cardiovascular disease from the Fitness Registry and the Importance of Exercise: A National Data Base (FRIEND)⁹. Equivalent reference values derived from maximal bike tests, also from FRIEND, are provided (N=4494)¹⁰. To our knowledge, these are the most accurate, largest and more updated fitness reference values covering all the adult age groups to date.

** It is important to note that heavier individuals are penalized when cardiorespiratory fitness is expressed as VO_{2max} , ml/kg/min. In these cases, alternatively, total treadmill time in an incremental maximal exercise test could be used as indicator of fitness level, for which the reference values of the Cooper Institute can be used (Physical Fitness Assessments and Norms for Adults and Law Enforcement; Cooper Institute; 2013).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

FIGURE LEGEND

Figure 1. Illustration of the Fat but Fit paradox in relation with cardiovascular disease mortality and all-cause mortality in men and women. Adapted from Ortega et al.³, with permission of the publisher.

BMI indicates Body mass index.

Confidential: For Review Only

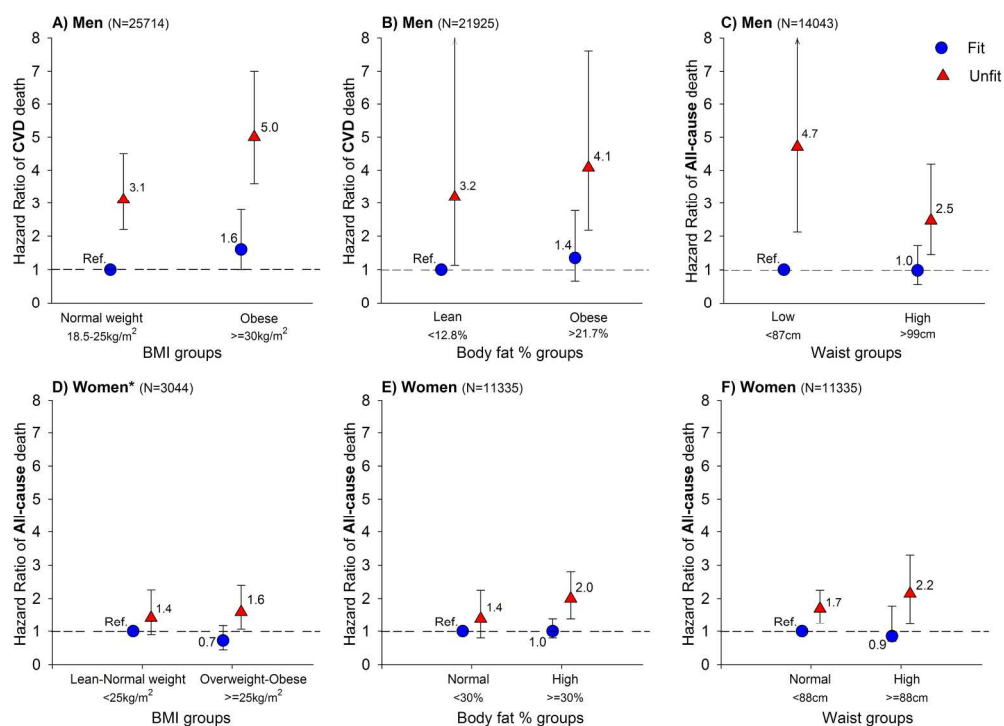


Figure 1. Illustration of the Fat but Fit paradox in relation with cardiovascular disease mortality and all-cause mortality in men and women. Adapted from Ortega et al.³, with permission of the publisher. BMI indicates Body mass index.

201x148mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

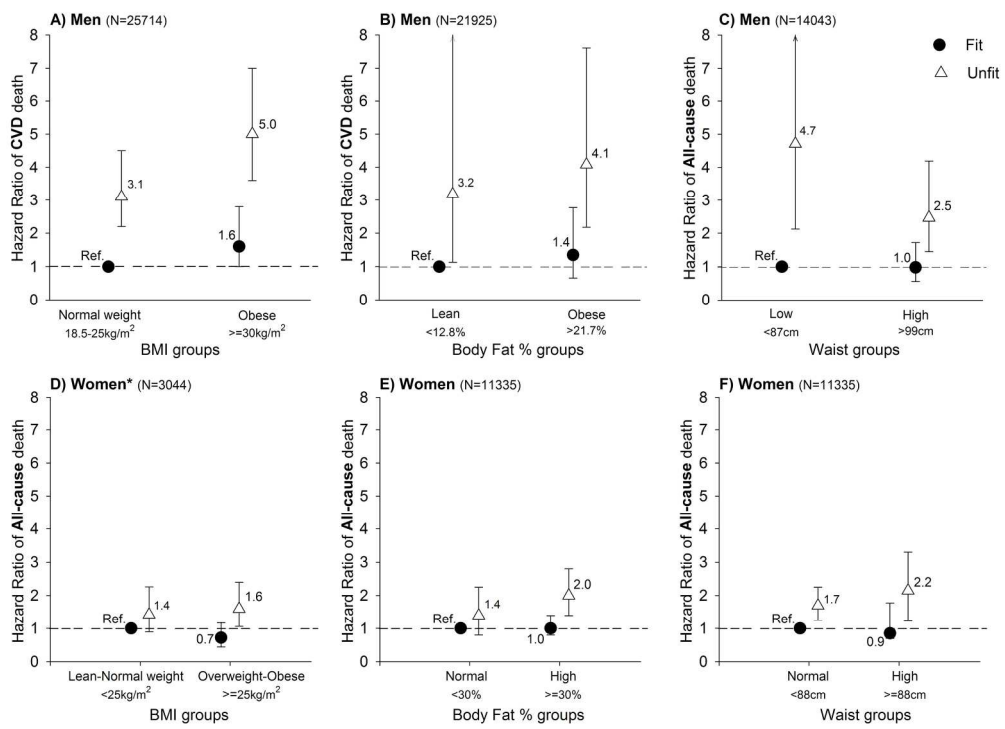


Figure 1. Illustration of the Fat but Fit paradox in relation with cardiovascular disease mortality and all-cause mortality in men and women. Adapted from Ortega et al.3, with permission of the publisher. BMI indicates Body mass index.

201x148mm (300 x 300 DPI)

Review Only