RESPONSE TO COMMENT ON JURASCHEK ET AL.

Cardiorespiratory Fitness and Incident Diabetes: The FIT (Henry Ford ExercIse Testing) Project. Diabetes Care 2015;38:1075–1081

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We thank Krachler and Lindahl for their letter (1), which highlights the complex relationship between fitness, obesity, and the pathogenesis of diabetes.

Along with obesity, fitness is a strong risk factor for diabetes in multiple cohort studies (2–4). However, the extent to which obesity serves as a confounder of this relationship is unclear. Our study shows that fitness is associated with incident diabetes independent of an incomplete measure of obesity, ascertained via self-report and medical records (5). However, even after accounting for BMI, available in medical records of 11,750 patients, the relationship between fitness and incident diabetes remained strong. While obesity may to some extent confound the relationship between fitness and incident diabetes (see Supplementary Table 3 in ref. 5), it does not fully account for this association, an important conclusion of our article.

One of the concerns raised by Krachler and Lindahl (1) pertains to the mischaracterization of fitness in obese patients, which could alter the magnitude of the associations reported in our study as well as affect our conclusion that there was no effect modification by obesity. To address this concern, we have included with this letter an additional stratified analysis by BMI <30 vs. ≥ 30 kg/m^2 (Table 1). Ultimately, having a BMI ≥ 30 kg/m^2 did seem to modify the association between fitness and incident diabetes among patients achieving a MET value ≥ 12 (hazard ratio of 0.56 among obese vs. 0.73 among nonobese). However, after accounting for all MET values (as performed in our original article [5], Fig. 2), the difference was not significant (*P* interaction $= 0.06$).

Another concern raised by Krachler and Lindahl (1) and highlighted in our original article (5) is selection bias. In clinical practice, physicians take into account participants' ability to achieve a maximal heart rate when referring them for treadmill testing. As a result, our study does not reflect the general population. Indeed only 20% of our patients had a history of obesity. It is possible that the obese patients included in the study were more fit than those excluded, resulting in the underrepresentation of obese patients with low fitness. As less fit participants served as the reference group and obesity is a risk factor for diabetes, exclusion of unfit obese patients could attenuate our results. This is speculative, however, and perhaps less concerning than the overall generalizability of our findings to a healthier population—patients referred for treadmill testing are likely at greater risk for diabetes. Nonetheless, our results are extremely pertinent to those patients with clinical concern for underlying coronary disease, who are at high risk of developing diabetes and likely to benefit from greater fitness.

Despite some limitations, we believe our data are convincing with regard to an independent relationship between fitness and diabetes. In the next phase of studies in The FIT Project, we are abstracting additional BMI measures in all FIT patients. We hope to comprehensively examine the complex relationship between BMI, fitness, and diabetes in future studies using these newly obtained BMI data.

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Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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Table 1—Association between METs achieved and incident diabetes among participants without diabetes at baseline according to strata of BMI <30 or ≥30 kg/m²

	Model 1	Model 2	Model 3
BMI <30 kg/m² (*N* = 7,574)			
Categories of fitness			
<6	1.0 (reference)	1.0 (reference)	1.0 (reference)
6–9	1.07 (0.90, 1.26)	1.09 (0.92, 1.29)	1.09 (0.92, 1.29)
10–11	0.88 (0.74, 1.04)	0.93 (0.78, 1.11)	0.94 (0.78, 1.12)
≥12	0.65 (0.53, 0.80)	0.72 (0.58, 0.89)	0.73 (0.59, 0.91)
P trend across categories as ordinal variable	<0.001	<0.001	0.001
METs per 1 unit	0.95 (0.93, 0.97)	0.96 (0.94, 0.98)	0.96 (0.94, 0.98)
P value	<0.001	<0.001	<0.001
BMI ≥30 kg/m² (*N* = 4,176)			
Categories of fitness			
<6	1.0 (reference)	1.0 (reference)	1.0 (reference)
6–9	0.83 (0.71, 0.97)	0.83 (0.71, 0.97)	0.88 (0.75, 1.03)
10–11	0.75 (0.63, 0.89)	0.76 (0.64, 0.91)	0.84 (0.70, 1.01)
≥12	0.46 (0.35, 0.59)	0.49 (0.38, 0.64)	0.56 (0.42, 0.73)
P trend across categories as ordinal variable	<0.001	<0.001	<0.001
METs per 1 unit	0.94 (0.92, 0.96)	0.94 (0.92, 0.97)	0.96 (0.93, 0.98)
P value	<0.001	<0.001	0.001

Data are hazard ratio (95% CI). *P* value for the interaction comparing the association of METs achieved (METs per 1 unit) with incident diabetes (model 3) across strata of BMI (<30 vs. ≥30 kg/m²) was 0.06. Model 1: adjusted for age, sex, race. Model 2: model 1 plus history of hypertension, hypertension medication use, ACE inhibitor use, angiotensin II receptor blocker use, β-blocker use, diuretic use, history of hyperlipidemia, lipid-lowering medication use, statin use, history of obesity, family history of coronary heart disease, current smoking status, sedentary lifestyle, treated pulmonary disease, depression medication use, and indication for stress testing. Model 3: model 2 plus BMI.