



RESPONSE TO COMMENT ON BRAFFETT ET AL.

Association of Insulin Dose, Cardiometabolic Risk Factors, and Cardiovascular Disease in Type 1 Diabetes During 30 Years of Follow-up in the DCCT/EDIC Study. *Diabetes Care* 2019;42:657–664

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Snaith et al. (1) suggest that the relationship between insulin dose and adverse cardiometabolic profile might be mediated by insulin resistance and cite data linking clamp-derived measurement of insulin resistance and coronary artery calcification (2). We do not have any direct assessment of insulin resistance in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study; however, the association among weight gain, insulin resistance, and adverse cardiometabolic risk factors is well known and was discussed in our article (3). Insulin-mediated downregulation (via degradation) of insulin receptors certainly occurs and could be one of numerous receptor and postreceptor mechanisms underlying insulin resistance (4). Snaith et al. further suggest that improving insulin sensitivity in type 1 diabetes could improve cardiovascular risk, in support of which they cited the Reducing with Metformin Vascular Adverse Lesions

(REMOVAL) study (5) on the effect of metformin on carotid intima-media thickness (cIMT). Notably, the REMOVAL study did not find a significant effect of metformin on the primary outcome of progression of cIMT, thus the significance of the finding regarding maximal cIMT (a tertiary end point) is unclear.

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*A complete list of participants in the DCCT/EDIC Research Group is presented in the Supplementary Material published online for the article in *N Engl J Med* 2017;376:1507–1516.

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