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Letter to the editor: Authors' Reply: Healthy Controls in Non-Alcoholic Fatty Liver Disease Management: a Biomedical Research Perspective

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To the Editor

We thank Dr. Pandey(1) for her interest in our recent study(2). We completely agree with Dr. Pandey that matching in case-control studies increases study power and allows one to control for important confounders such as age and ethnicity. However, there are several limitations to that approach.

First, the use of matching must be applicable to the study design. Our study was a cross-sectional study to identify rates of presumed NAFLD in a given population, not a case-control study. The case-control analysis was only performed to show that the presumed NAFLD subjects indeed “fit the mold” for what is known about the disease. In that context, it is important to report what the rates of presumed NAFLD (27.9%) and truly normal subjects (29.4%) are. Insisting on maintaining identical numbers of subjects in both groups would have defeated that purpose.

Second, matching should be based on some knowledge and should be limited to covariates that can be confounders. Although age and race are important confounders, in our analysis they are actually informative dependent variables. For example, by addressing them as such, our study informs clinical investigators that research participants with NAFLD tend to be older, and thus can allow them to better stratify their subjects. To explore Dr. Pandey's suggestion of age-matching we did reexamined our data. As shown in the Table below, at each stratified age-cohort, the presumed NAFLD subjects had significantly greater evidence of metabolic derangements in the young and middle aged volunteers. As the number of

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Study concept and design: Rotman, Takyar

Acquisition of data: n/a

Analysis and interpretation of data: Takyar

Drafting of the manuscript: Takyar

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Statistical Analysis: Takyar

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volunteers aged > 50 was low, differences did not reach statistical significance although the trend for worse metabolic parameters persisted.

Finally, one must recognize that, at some point, pragmatism may supersede stringent matching criteria to allow for efficient subject recruitment and to control the cost of research.

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Abbreviations

NAFLD	non-alcoholic fatty liver disease
ALT	alanine aminotransferase
AST	aspartate aminotransferase
MR	magnetic resonance

References

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Hepatic and Metabolic Parameters in Healthy Controls and Presumed NAFLD stratified by Age Cohorts

Table

Parameter (mean/SD)	Age Cohort (years)					
	18–35		>35–50		>50	
	Healthy Control (N=752)	Presumed NAFLD (N=441)	Healthy Control (N=138)	Presumed NAFLD (N=305)	Healthy Control (N=39)	Presumed NAFLD (N=135)
BMI (kg/m ²)	22.3 (1.8)	31.0 (5.9) [#]	22.6 (1.7)	31.3 (5.4) [#]	22.6 (1.8)	31.5 (5.3) [#]
ALT (U/L)	18 (6)	41 (21) [#]	19 (7)	41 (20) [#]	17 (5)	37 (15) [#]
AST (U/L)	18 (6)	26 (15) [#]	19 (16)	26 (17) [#]	18 (4)	24 (8) [#]
Total Cholesterol (mg/dL)	163 (30)	173 (37) [#]	179 (34)	189 (40) [#]	190 (37)	197 (39)
HDL-C (mg/dL)	63 (17)	52 (16) [#]	67 (19)	50 (16) [*]	60 (13)	55 (17)
LDL-C (mg/dL)	85 (24)	101 (34) [#]	98 (30)	115 (34) [#]	110 (28)	114 (32)
Triglycerides (mg/dL)	78 (40)	103 (61) [#]	76 (30)	121 (79) [#]	92 (37)	140 (99) [#]
Hemoglobin A1c (%)	5.2 (0.4)	5.4 (1.0) [*]	5.2 (0.3)	5.6 (0.9) [#]	5.5 (0.6)	5.8 (0.6)
Serum Glucose (mg/dL)	89 (13)	92 (23) [*]	91 (13)	93 (17)	98 (16)	100 (24)
NAFLD Fibrosis Score	-3.5 (0.8)	-3.0 (1.0) [#]	-2.7 (1.2)	-2.4 (1.0) [*]	-2.1 (1.0)	-1.6 (0.9) [*]

^{*} p<0.01,

[#] p<0.0001 for the comparison with Healthy Controls in the same age cohort