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Christian Funck-Brentano

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Assessment of the Change of a Continuous Variable as a Function of its Initial Value

Letter in Reply to: Association of Baseline Low-Density Lipoprotein Cholesterol and Percentage Low-Density Lipoprotein Cholesterol Reduction With Statins, Ezetimibe, and PCSK9 Inhibition by Daniel P. Marcusa et al. *JAMA Cardiol* doi:10.1001/jamacardio.2020.6184 Published online November 13, 2020.

Christian Funck-Brentano MD, PhD^{1,2}

- ¹ AP-HP Sorbonne Université, Pitié-Salpêtrière University Hospital, Department of Pharmacology and Clinical Investigation Centre, F-75013 Paris, France
- ² INSERM, CIC-1901 and UMR-S 1166, Sorbonne University, Faculty of Medicine, F-75013
 Paris, France

Correspondence to: Professor Christian Funck-Brentano

Clinical Investigation Center, Pitié-Salpêtrière Hospital, 47-83 Boulevard de l'Hôpital, 75013

Paris, France

Email: christian.funck-brentano@aphp.fr

Tel: +33 1 42 16 17 06

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Marcusa et al¹ have examined the influence of baseline Low-Density Lipoprotein Cholesterol (LDL-C) levels on percentage LDL-C reduction with statins, ezetimibe, and PCSK9 Inhibition. Using this mode of calculation, they report a higher percentage reduction in LDL-C with evolocumab in patients with lower baseline LDL-C levels, compared with a less marked percentage LDL-C reduction with simvastatin at lower baseline LDL-C levels, and no significant reduction of LDL-C levels with ezetimibe at lower baseline values. However, the use of percentage changes might be misleading since it is influenced by absolute baseline values, e.g. a 30% reduction from 100 mg/dL converts to 70 mg/dL, a 30 mg/dL absolute reduction, whereas a 30% reduction from 70 mg/dL converts to 49 mg/dL, a 21 mg/dL absolute reduction. More importantly, assessing the change of a parameter as a function of its baseline value is subject to bias because baseline values are used to calculate percentage changes.^{2,3} An analysis of the slope and intercept of the regression lines between LDL-C levels under treatment and baseline LDL-C levels using both linear and log scales, as promoted by MacGregor et al², seems more appropriate and might yield different results. This mode of analysis and of graphical display would allow a better comparison of evolocumab, simvastatin and ezetimibe.

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