Early-life body mass index has a causal relationship with type 2 diabetes: multivariate and mediated mendelian randomization analysis

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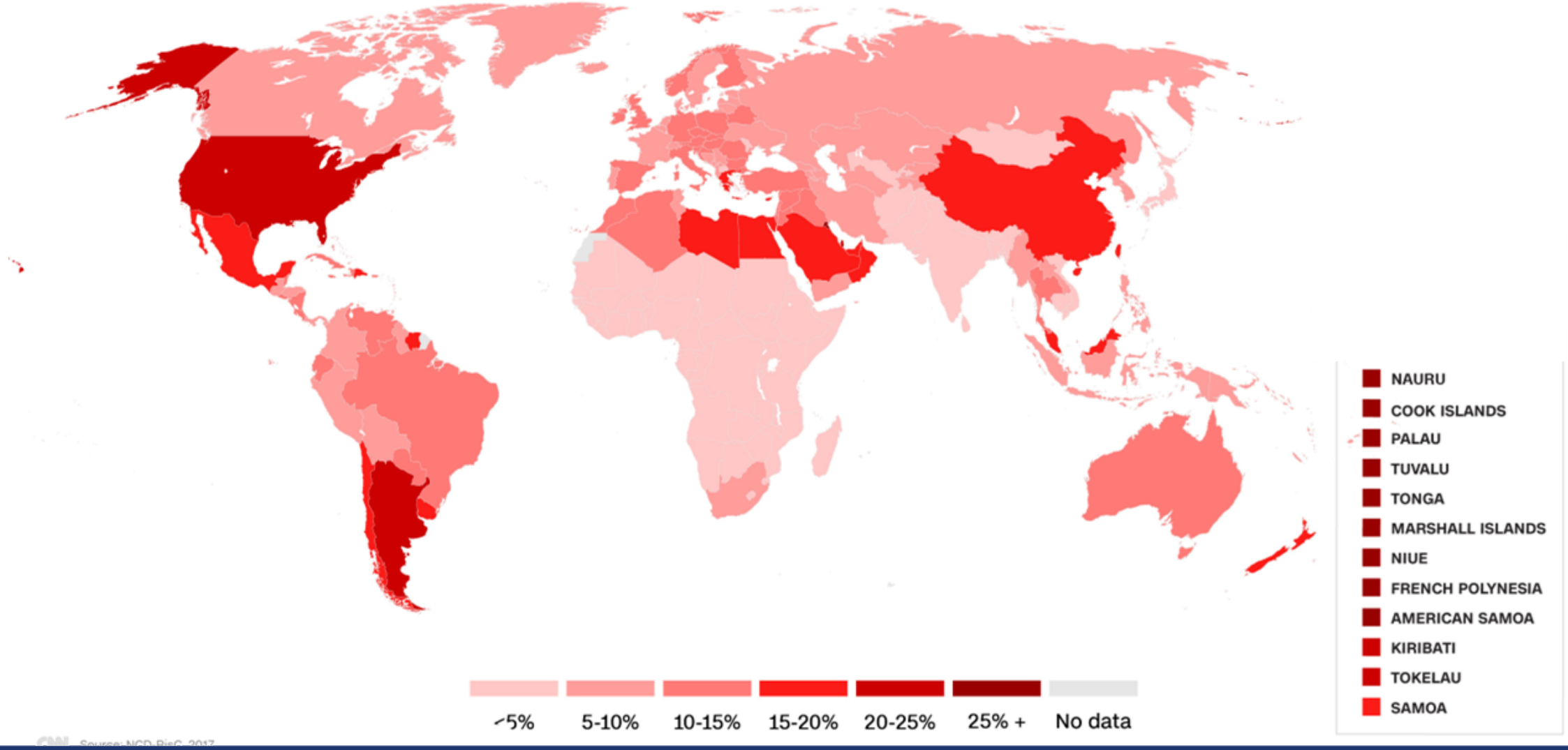
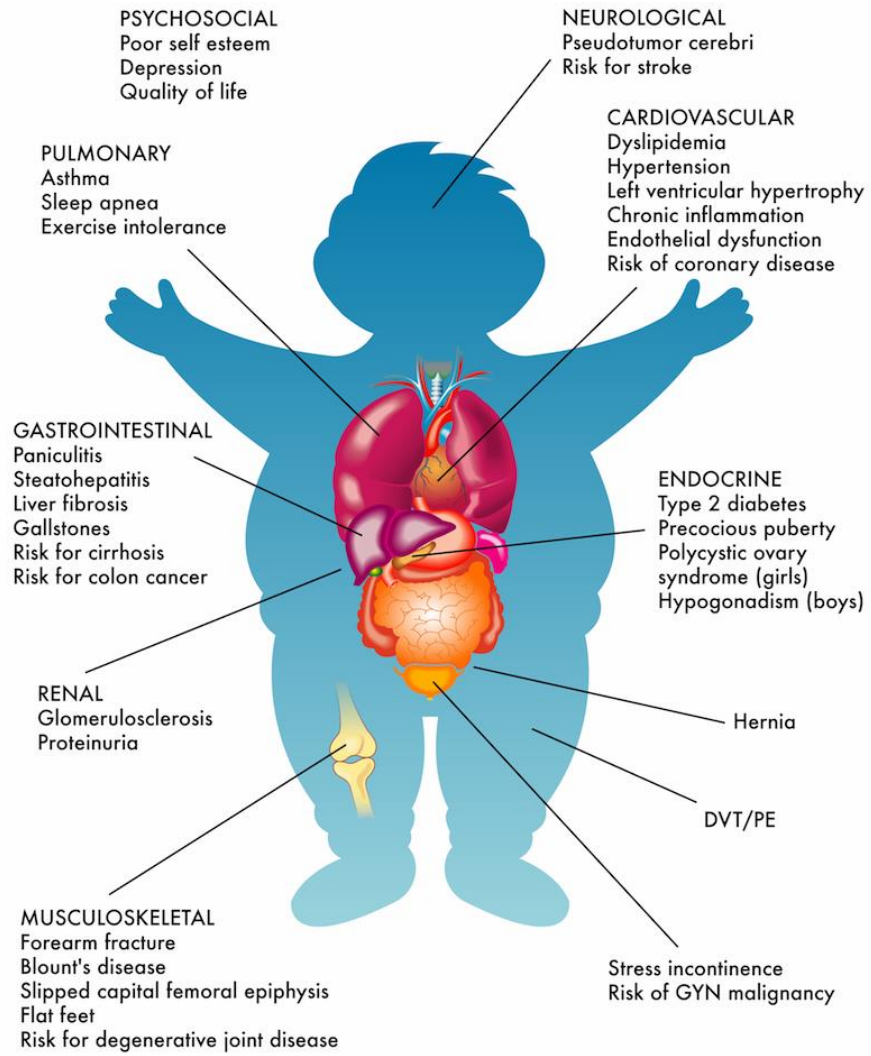


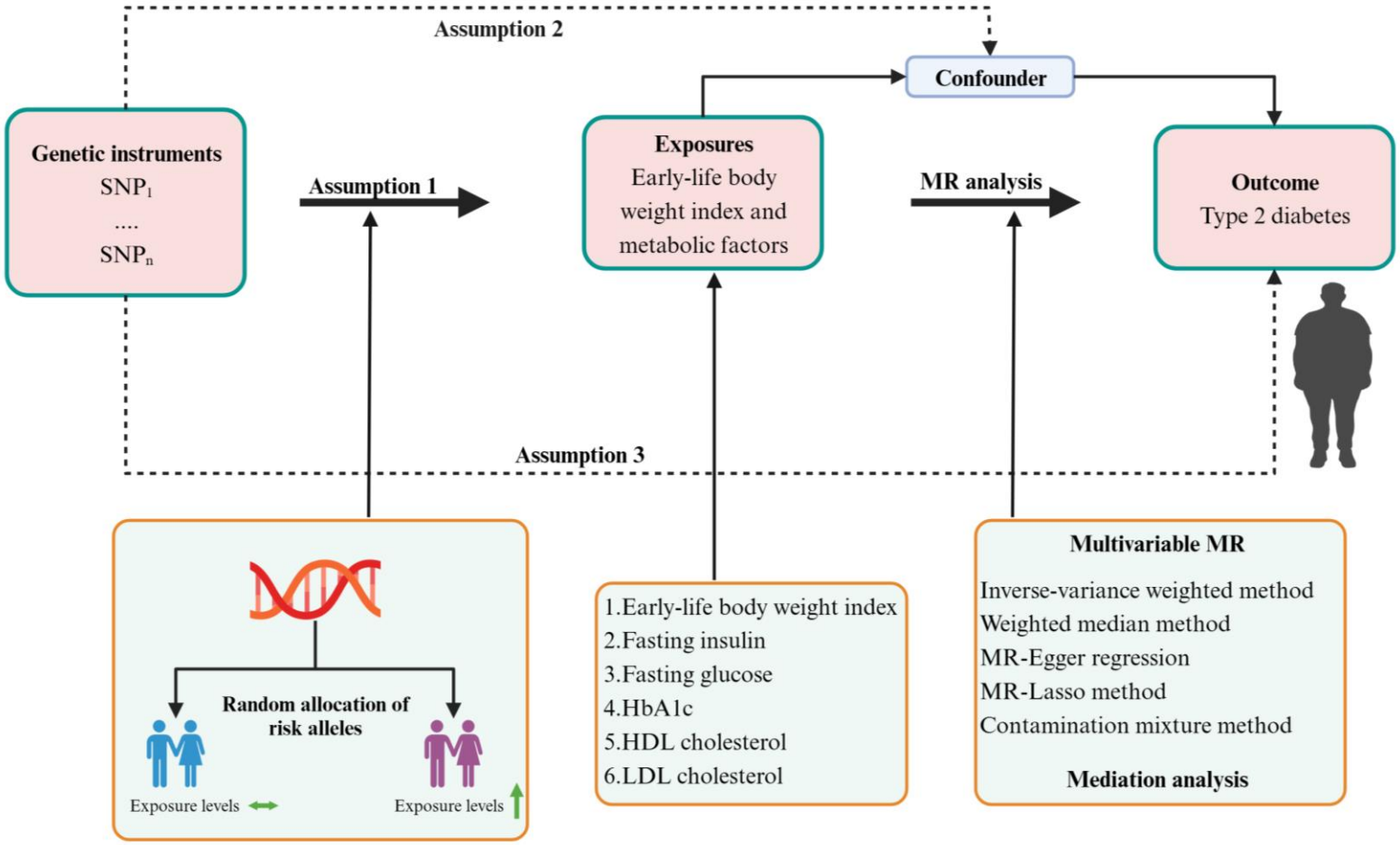
Background

Type 2 diabetes is a global public health issue, and early-life body mass index (BMI) may play a critical role in its development. The increase in BMI during childhood is primarily associated with the increase in subcutaneous and visceral fat, and is less likely to be influenced by confounding factors such as muscle and skeletal tissues.



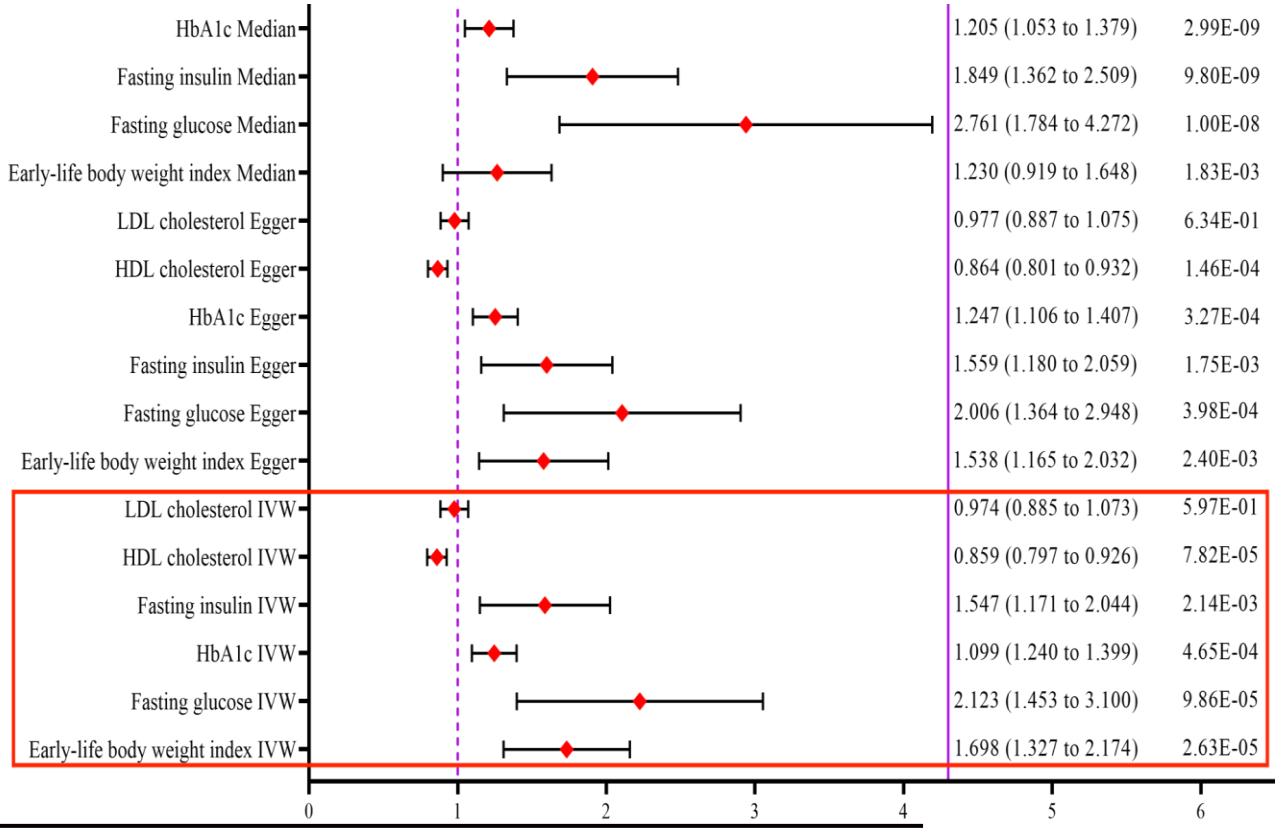
Methods

Research on the connection between early-life exposures and future outcomes has traditionally been conducted through longitudinal observational cohort studies, which require continuous follow-up over several years or even decades to collect data related to exposures and outcomes. Therefore, we have adopted Mendelian randomization analysis, a method that uses genetic variants as instrumental variables to infer causal relationships.



Results

The results indicate a causal relationship between early-life BMI and the risk of type 2 diabetes in adulthood. These risk factors remain significant even after adjusting for metabolic factors. For every one standard deviation increase in early-life BMI, the risk of type 2 diabetes in adulthood increases by **31.2%**. Furthermore, mediation analysis shows that part of the causal effect is due to excessive intake of sugary foods during childhood.



Mediator	Total effect[a]	Direct effect[b]	Direct effect[c]	Mediationeffect[d]	*p*	Mediated Proportion (%) β (95% CI)
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)		
physical activity		0.26（-0.05 to 0.57）	0.61（0.40 to 0.82）	-0.26（-0.50 to -0.02）	0.024	75.50（6.59 to 44.41）
Sedentary behavior	0.35（0.23 to 0.46）	0.01（-0.02 to -0.04）	4.57（0.60 to 8.54）	-4.22（-8.20 to -0.25）	0.037	17.29（62.78 to 71.79）
Eating habits		**0.04 (0.03 to 0.05)**	**4.88 (0.82 to 8.94)**	**-13.06 (-8.59 to -0.47)**	**0.029***	**6.05 (36.27 to 75.84)**

Thanks