Association of milk intake with hay fever, asthma, and lung function: a Mendelian Randomization analysis

Tea Skaaby[1], Tuomas O. Kilpeläinen[2], Yuvaraj Mahendran[2], Betina H. Thuesen[1], Line Lund Kårhus[1], Katja Biering Leth-Møller[1], Niels Grarup[2], Torben Hansen[2], Oluf Pedersen[2], Stephen Burgess[3,4], Marcus R. Munafò[3,4], Allan Linneberg[1,5]

1) Center for Clinical Research and Prevention, Frederiksberg and Bispebjerg Hospital, Frederiksberg, Denmark.
2) Novo Nordisk Foundation Center for Basic Metabolic Research, Section of Metabolic Genetics, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
3) MRC Biostatistics Unit, University of Cambridge, Cambridge, UK
4) Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK
5) Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Background
Previous observational studies have indicated a protective effect of drinking milk on asthma and allergy. In Mendelian Randomization, one or more genetic variants are used as unbiased markers of exposure to examine causal effects. We examined the causal effect of milk intake on hay fever, asthma, forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) by using the lactase rs4988235 genotype associated with milk intake.

Methods
We included a total of 363961 participants from the UK Biobank. Data were analyzed by traditional observational and Mendelian randomization analyses.

Results
Observational analyses showed that self-reported milk-drinkers vs. non-milk drinkers had an increased risk of hay fever: odds ratio (OR)=1.36 (95% CI: 1.32, 1.40, $p<0.001$), and asthma: OR=1.33 (95% CI: 1.38, 1.29, $p<0.001$), and higher FEV1: $\beta=0.022$ (SE=0.004, $p<0.001$) and higher FVC: $\beta=0.026$ (SE=0.005, $p<0.001$). Genetically determined drinking vs. not drinking milk was associated with lower risk of hay fever: OR=0.791 (95% CI: 0.636, 0.982, $p=0.033$) and asthma: OR=0.587 (95% CI: 0.442, 0.779, $p=0.001$) and lower FEV1: $\beta=-0.154$ (standard error, SE=0.034, $p<0.001$) liter and FVC: $\beta=-0.223$ (SE=0.034, $p<0.001$) liter.

Conclusions
As opposed to our traditional observational results, our genetic results indicate that drinking milk has a protective effect on hay fever and asthma but may also have a negative effect on lung volume.