On the Adjustment for Covariates in Genetic Association Analysis: A Novel, Simple Principle to Infer Direct Causal Effects

Stijn Vansteelandt et al

Genetic Epidemiology 33: 394–405 (2009)

CGene: an R package for implementation of causal genetic analyses

Peter J Lipman and Christoph Lange

European Journal of Human Genetics (2011) 19, 1292–1294

Stijn Vansteelandt (pildil pummeldamas Toomel) tegi GWAS uuringu...

Millised SNP’id mõjutavad FEV1-te (kui palju õhku suudate sekundi jooksul endast välja puhuda?). Üht-teist leiti...

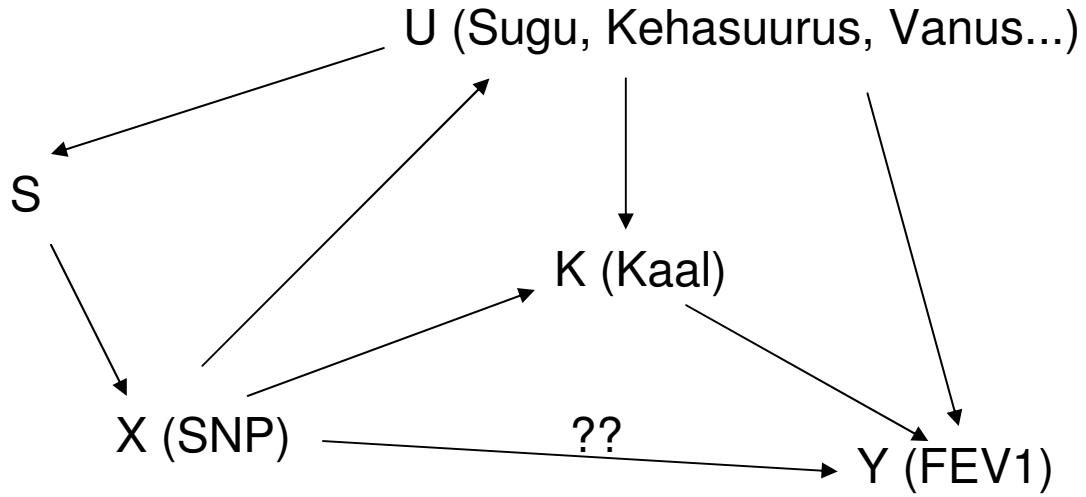
Täpsemalt...

- Hinnati mudel(eid), kus

  FEV1 sõltus SNP'ist, kaalust, vanusest,...

Parim SNP (rs2415815) kahjuks polnud statistiliselt oluline, küll aga osutus oluliseks mudelis, kus uuriti vaid SNP ja FEV1 vahelist sõltuvust...

Mõte...

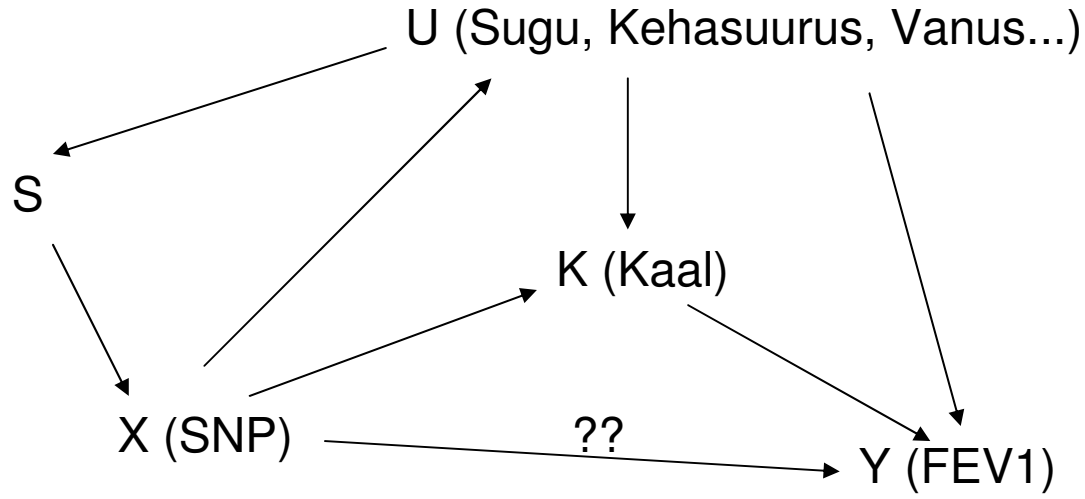


Mõte...

X -> Y -> Z seos X ja Z vahel

X <- Y -> Z seos X ja Z vahel

X -> Y <- Z seost pole

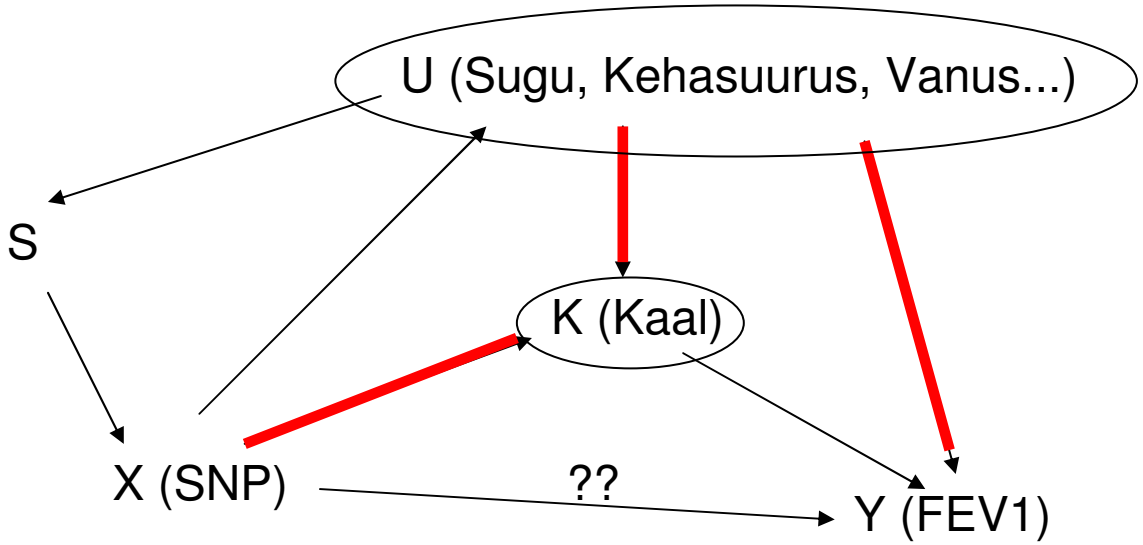


Mõte...

X -> (Y) -> Z seost pole

X <- (Y) -> Z seost pole

X -> (Y) <- Z seos X ja Z vahel

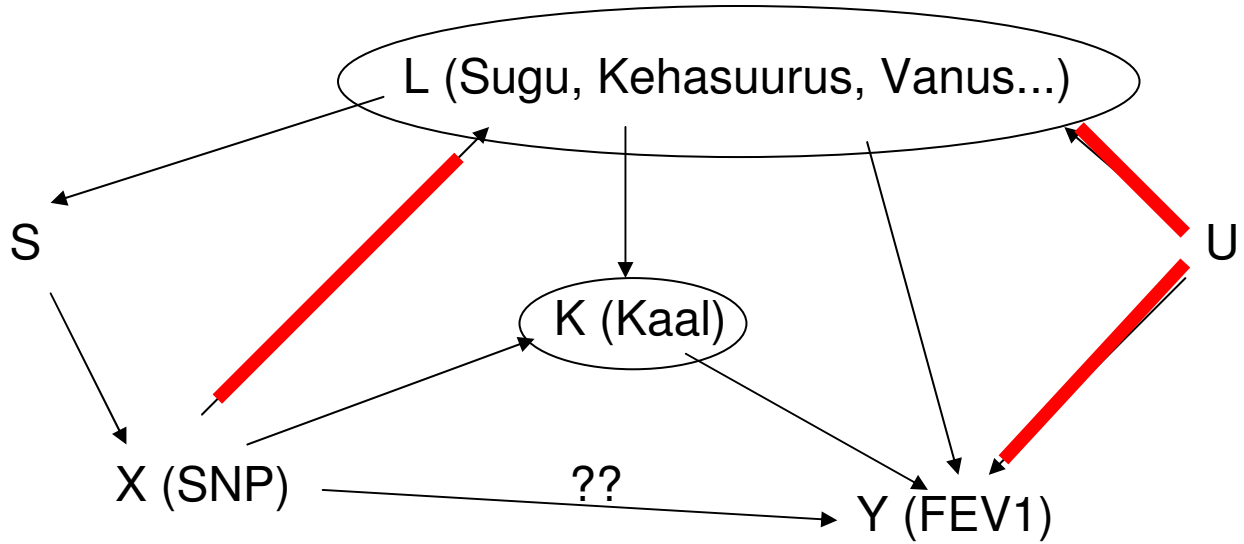


Mõte...

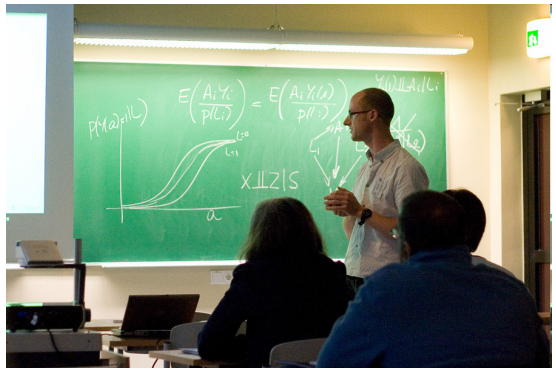
X ->(Y)-> Z seost pole

X <-(Y)-> Z seost pole

X ->(Y)<- Z seos X ja Z vahel



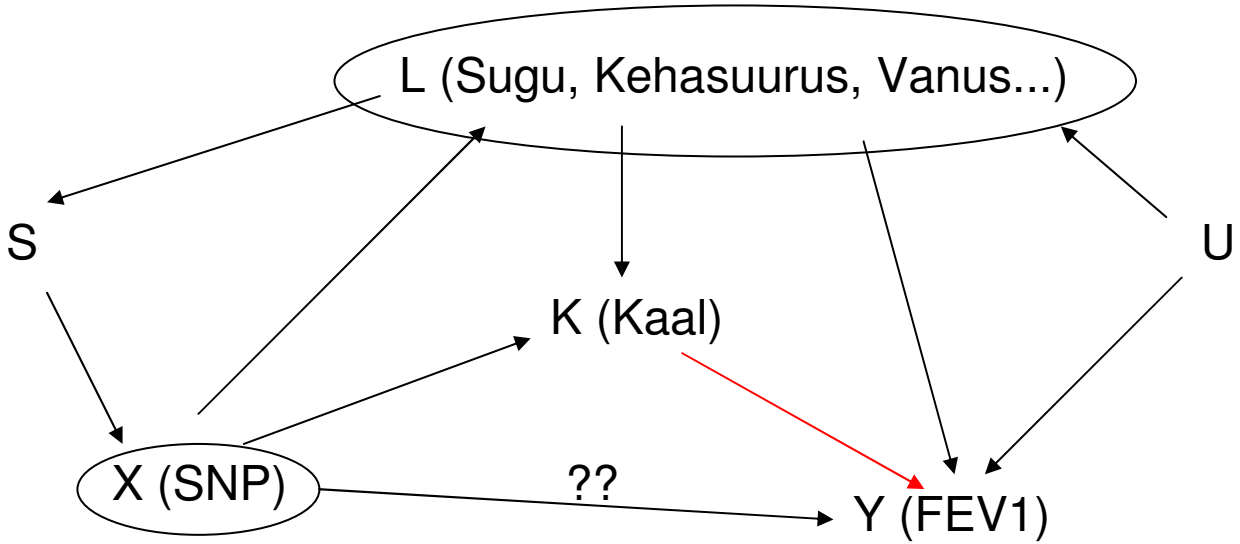
Stijn'i lahendus



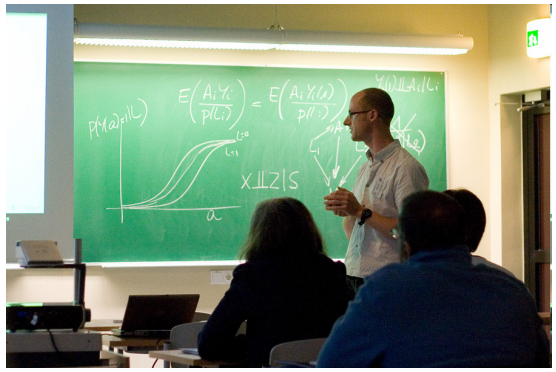
1. K mõju Y-le hinnatav:

Y~X+K+L

$$\tilde{Y}_i = Y_i - \overline{y} - \hat{\gamma}_1(K_i - \overline{k}),$$



Stijn'i lahendus



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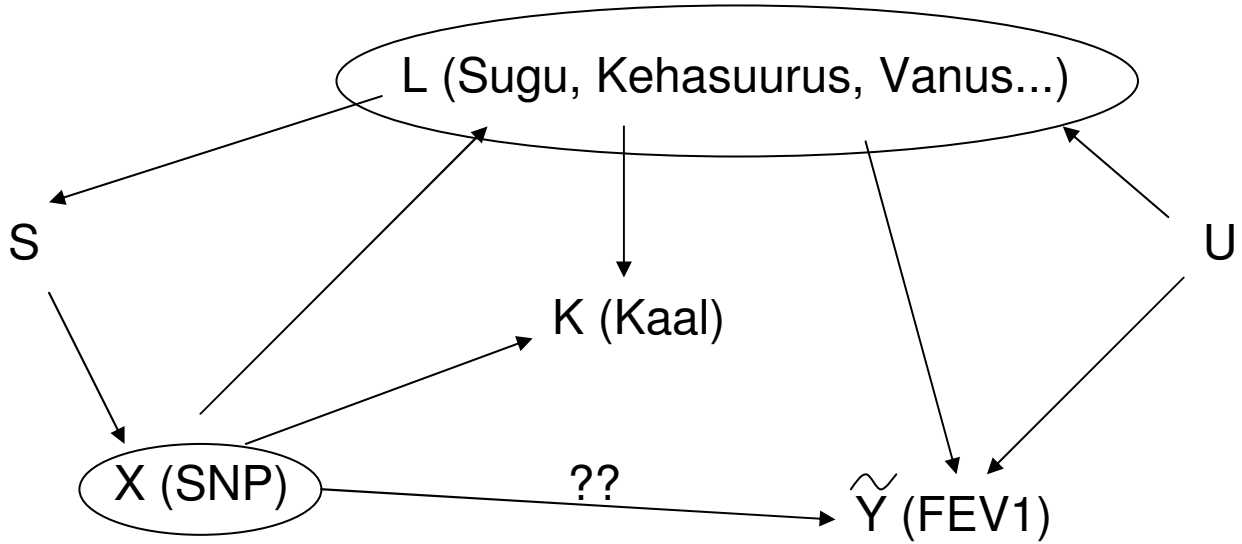
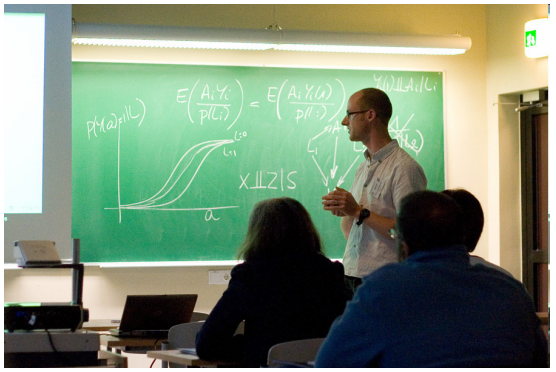


Stijn'i lahendus



1. K mõju Y-le hinnatav:
2. X mõju $\widetilde{Y}$-le hinnatav!

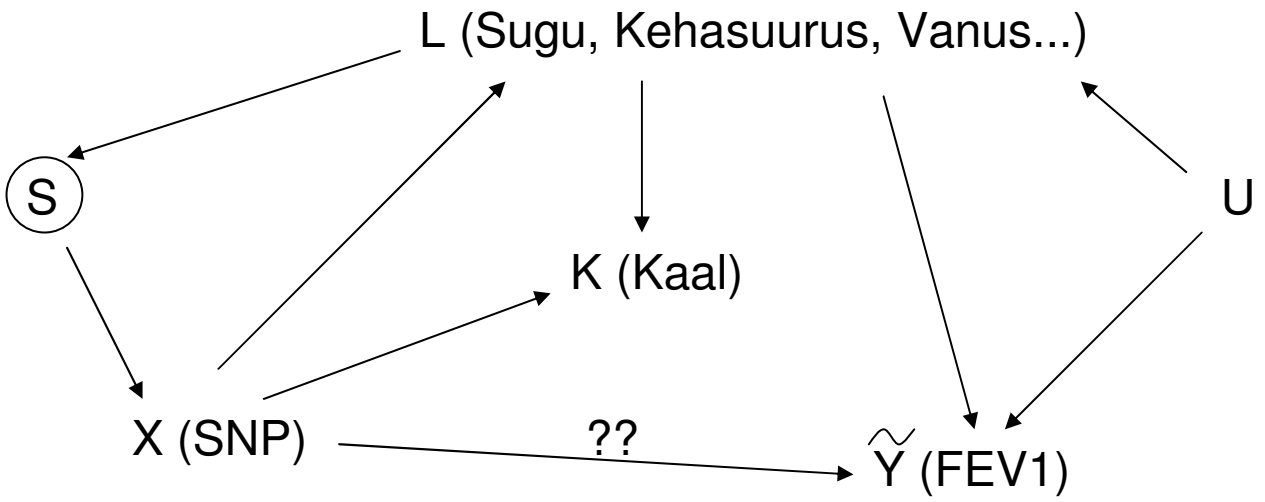


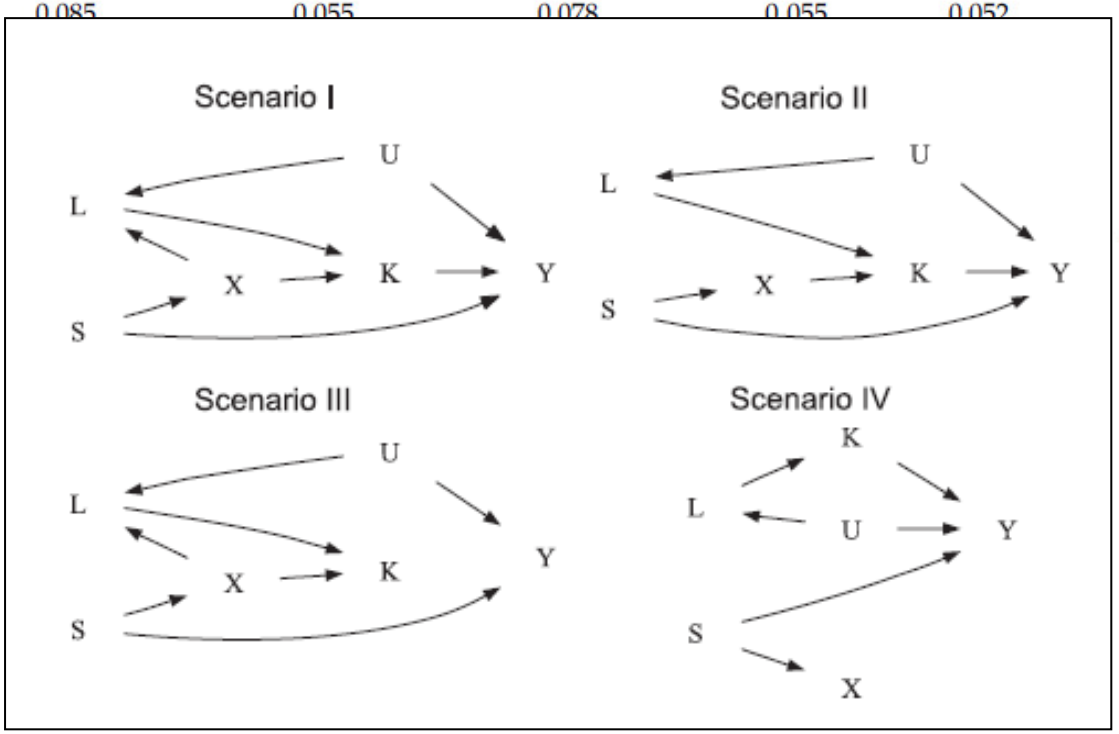
TABLE I. Association with rs2415815 in the Framingham Heart Study (FHS), the CAMP Study and the British Birth Cohort (BBC): overall association (overall), direct association based on standard residuals adjusting for K (direct-standard) and based on proposed residuals (direct-proposal)

			FHS			CAMP			BBC
Target phenotype Y	Intermediate phenotype K	Adjustment	Effect	95% CI	P	Effect	95% CI	P	P
FEV1	Weight	Overall			0.038			0.59	0.44
		Direct-standard	−0.35	−2.38 to 1.68	0.74	1.78	−1.17 to 4.72	0.24	
		Direct-proposal	−1.34	−2.94 to 0.27	0.10	−0.45	−3.57 to 2.77	0.78	
Weight	FEV1	Overall			0.0054			0.00053	0.0445*
		Direct-standard	−1.20	−2.22 to −0.18	0.021	−0.14	−0.26 to −0.0064	0.040	
		Direct-proposal	−1.34	−2.32 to −0.35	0.0087	−0.16	−0.27 to −0.055	0.0033	

*Measured as BMI.

TABLE II. Empirical type-1 errors at 5% significance level of Wald tests for genetic effects, (a) based on residuals adjusted for (S, K, L), (S, K), (b) directly adjusted for (S, K, L), (S, K) and (c) adjusted with the proposed adjustment principle (D, along with bias and standard error of the direct effect size estimate)

		Wald test on residuals adjusted for		Wald test on trait adjusted for		Proposed adjustment principle		
Scenario	Freq	(S,K,L)	(S,K)	(S,K,L)	(S,K)	(D)	Bias $\times 10^3$	SE
I	0.05	0.080	0.150	0.044	0.134	0.051	−2.05	0.43
	0.1	0.085	0.079	0.065	0.075	0.047	3.1	0.30
	0.15	0.092	0.059	0.079	0.057	0.053	−2.3	0.25
	0.2	0.083	0.047	0.075	0.047	0.047	−4.0	0.21
	0.25	0.089	0.057	0.081	0.056	0.056	5.0	0.20
	0.3	0.093	0.058	0.086	0.058	0.057	6.1	0.19
	0.35	0.083	0.051	0.075	0.051	0.047	5.1	0.18
	0.4	0.085	0.055	0.078	0.055	0.052	5.0	0.18
	0.45						1.4	0.17
II	0.05						−1.7	0.40
	0.1						−4.1	0.29
	0.15						−6.9	0.24
	0.2						1.4	0.22
	0.25						−0.023	0.20
	0.3						4.0	0.19
	0.35						−0.97	0.18
	0.4						−1.9	0.17
	0.45						2.9	0.17
III	0.05						1.9	0.43
	0.1						−4.0	0.30
	0.15						1.2	0.24
	0.2						−6.8	0.22
	0.25						0.32	0.20
	0.3						−4.9	0.19
	0.35						−1.6	0.18
	0.4						−2.2	0.17
	0.45						0.23	0.17



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Peter J Lipman*,[1,2] and Christoph Lange[1,2]

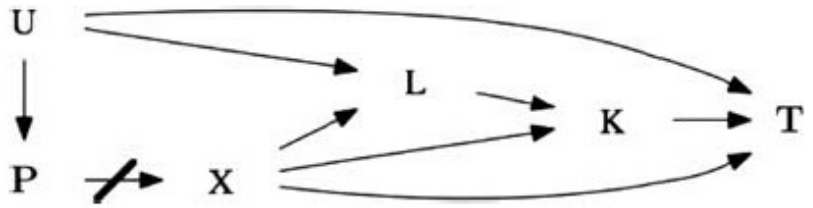

Figure 1 Causal DAG.

Eeldustest