

SUPPLEMENTAL MATERIALS FOR:

Real-world effects of second-generation versus earlier intermediate/basal insulin analogues on rates of hypoglycemia in adults with type 1 and 2 diabetes (iNPHORM, US)

AUTHORS

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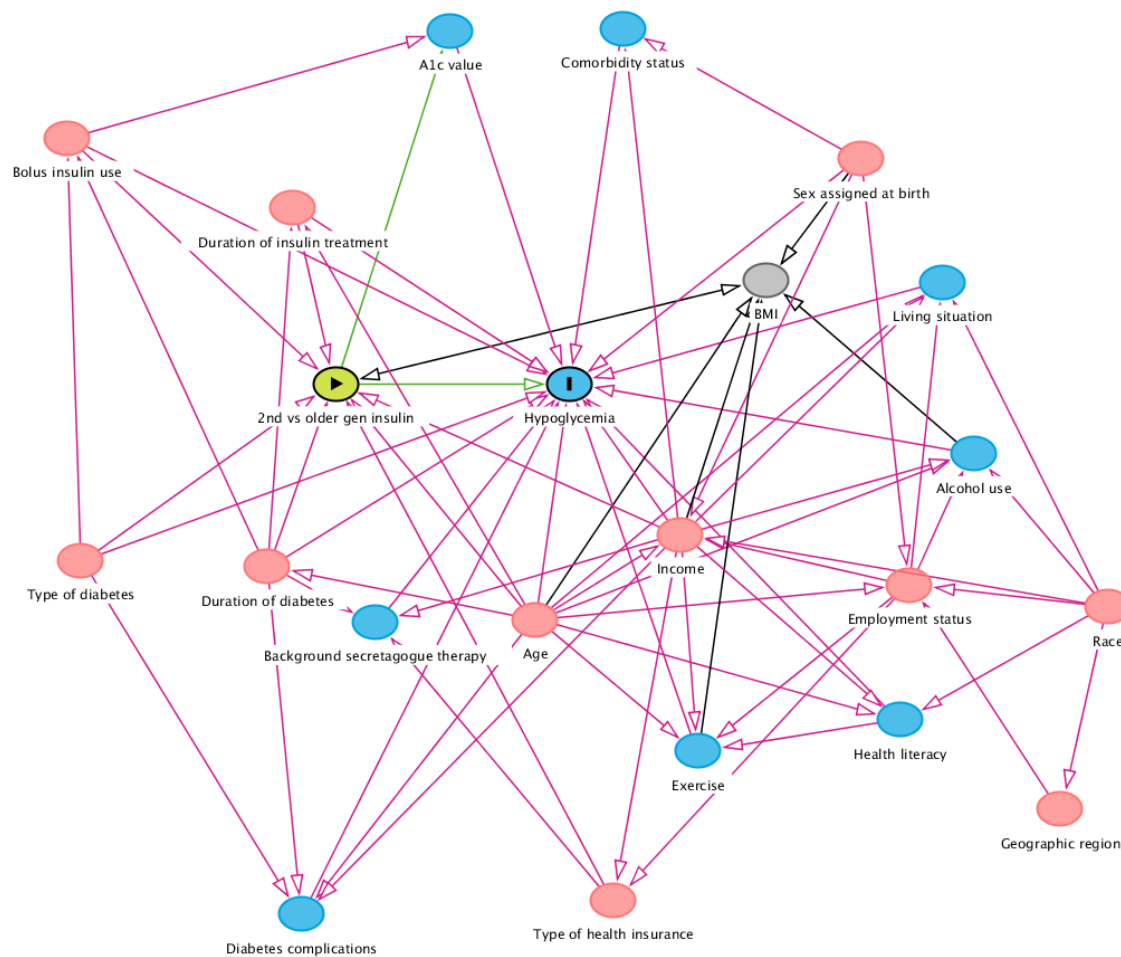
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Supplementary Figure 1: Directed acyclic graph (DAG)* for the relationship between second-generation compared to earlier intermediate/basal insulin analogue use and hypoglycemia



*DAG produced using dagitty plotting tool.

Part-time	1.95 (1.38 to 2.77)	2.24 (1.57 to 3.21)	1.66 (1.08 to 2.55)	0.47 (0.27 to 0.83)	0.49 (0.26 to 0.95)	0.39 (0.18 to 0.85)
Unemployed, student, or retired	1.65 (1.31 to 2.08)	1.79 (1.41 to 2.29)	1.47 (1.1 to 1.97)	0.75 (0.54 to 1.03)	1.02 (0.72 to 1.46)	0.39 (0.25 to 0.62)
Household income (per \$15,000 increase)	1.04 (1.01 to 1.08)	1.05 (1.02 to 1.09)	1.02 (0.98 to 1.07)	0.85 (0.8 to 0.91)	0.86 (0.8 to 0.92)	0.8 (0.73 to 0.88)
Bolus insulin use	1.43 (1.25 to 1.63)	1.33 (1.16 to 1.54)	1.72 (1.42 to 2.08)	1.97 (1.5 to 2.59)	1.97 (1.44 to 2.68)	2.32 (1.55 to 3.47)

Adjusted rate ratios were determined by exponentiating beta coefficients estimated by negative binomial regression using generalized estimating equations.

CI: confidence interval.

Supplementary Table 2: Adjusted hypoglycemia rate ratios comparing second-generation to earlier intermediate/basal insulin analogue use among participants who did not change intermediate/basal insulin analogue type during follow-up, by event severity and timing

Type of hypoglycemia	Adjusted rate ratio (95% CI)	
	All participants (n=413)	Participants who did not change intermediate/basal insulin analogue type (n=385)
Non-severe		
Overall	0.81 (0.68 to 0.97)*	0.80 (0.64 to 1.01)
Daytime	0.91 (0.76 to 1.10)	0.90 (0.71 to 1.14)
Nocturnal	0.57 (0.44 to 0.74)*	0.58 (0.43 to 0.80)*
Severe		
Overall	0.87 (0.65 to 1.16)	0.80 (0.57 to 1.13)
Daytime	0.98 (0.71 to 1.36)	0.90 (0.62 to 1.28)
Nocturnal	0.56 (0.35 to 0.90)*	0.53 (0.30 to 0.93)*

*Statistically significant based on an $\alpha=0.05$ significance level.

Population-average adjusted rate ratios were determined by exponentiating beta coefficients estimated by negative binomial regression using generalized estimating equations, adjusted for age, employment status, household income, diabetes type, diabetes duration, insulin treatment duration, insulin therapy duration, bolus insulin use, and background secretagogue therapy.

CI: confidence interval.