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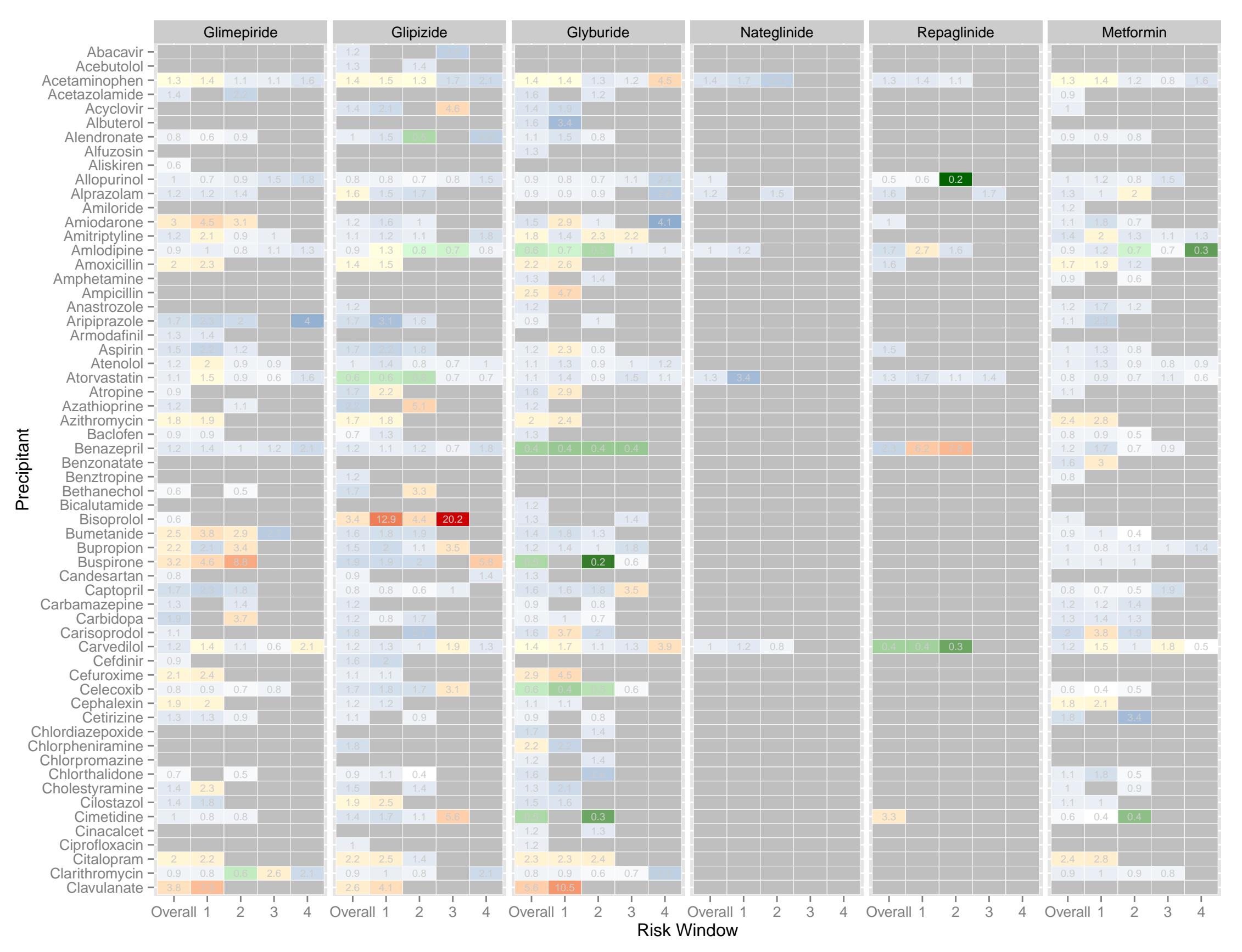
### **Model specification**

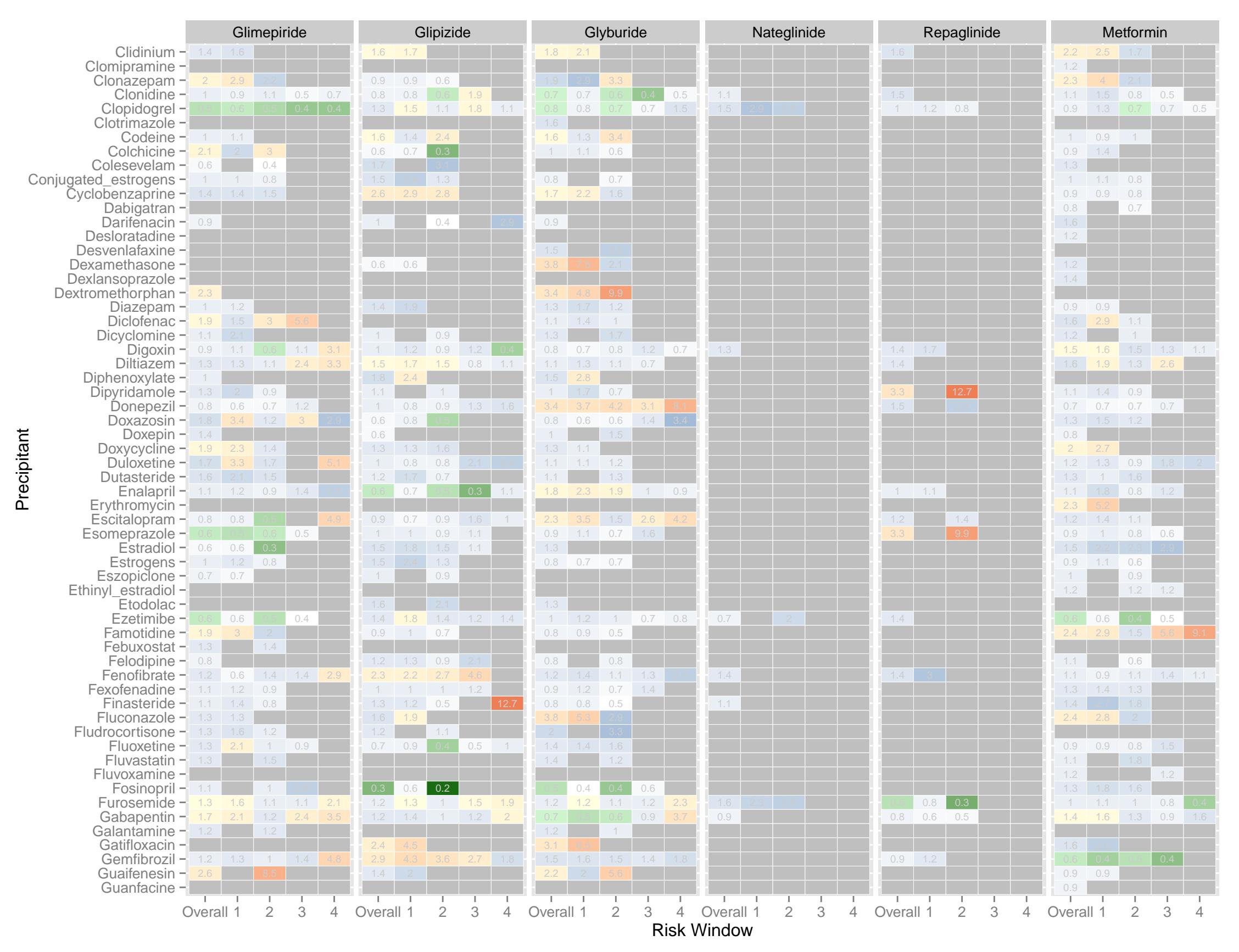
**SAS program code to estimate unadjusted overall rate ratios**

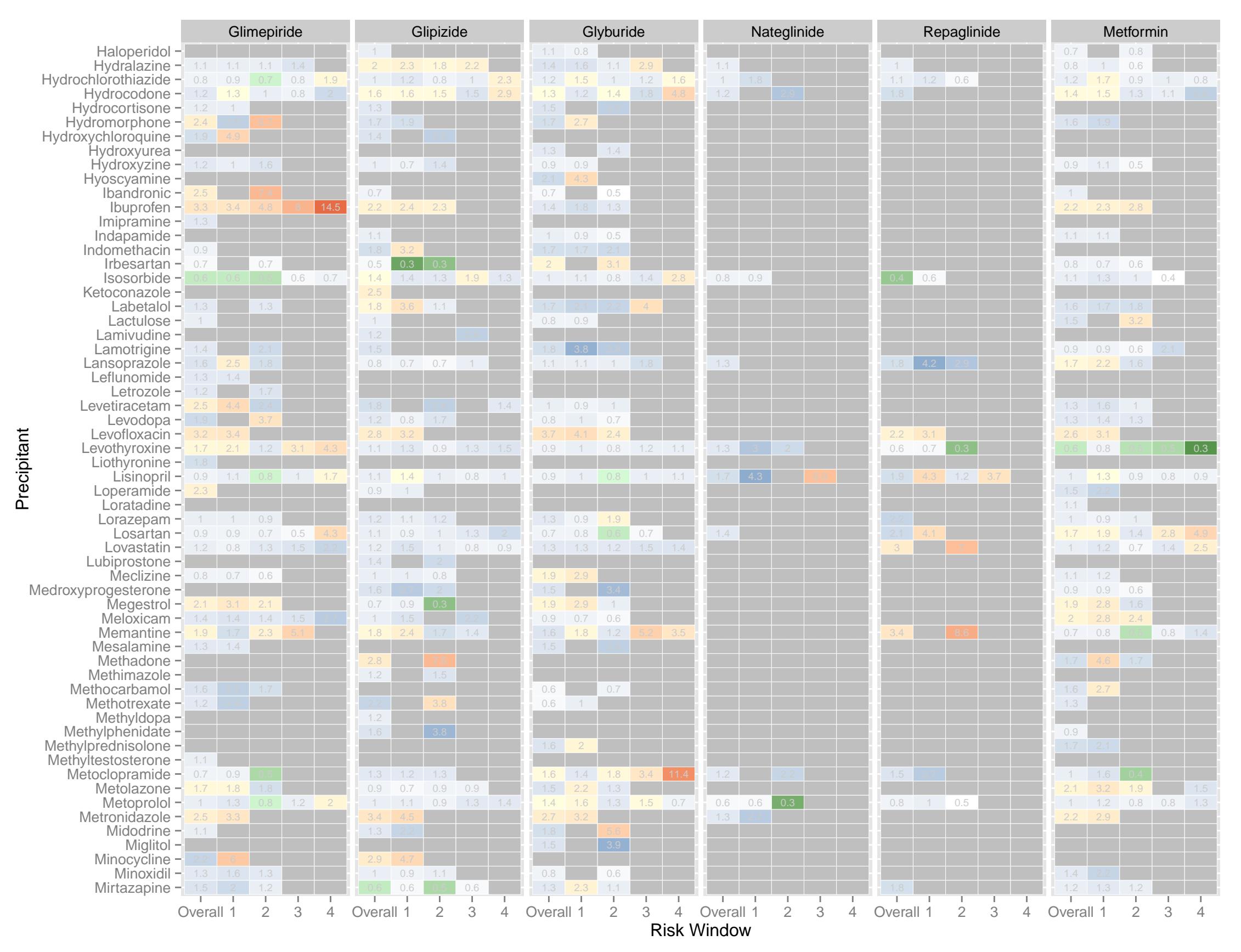
**SAS program code to estimate unadjusted rate ratios for risk periods**

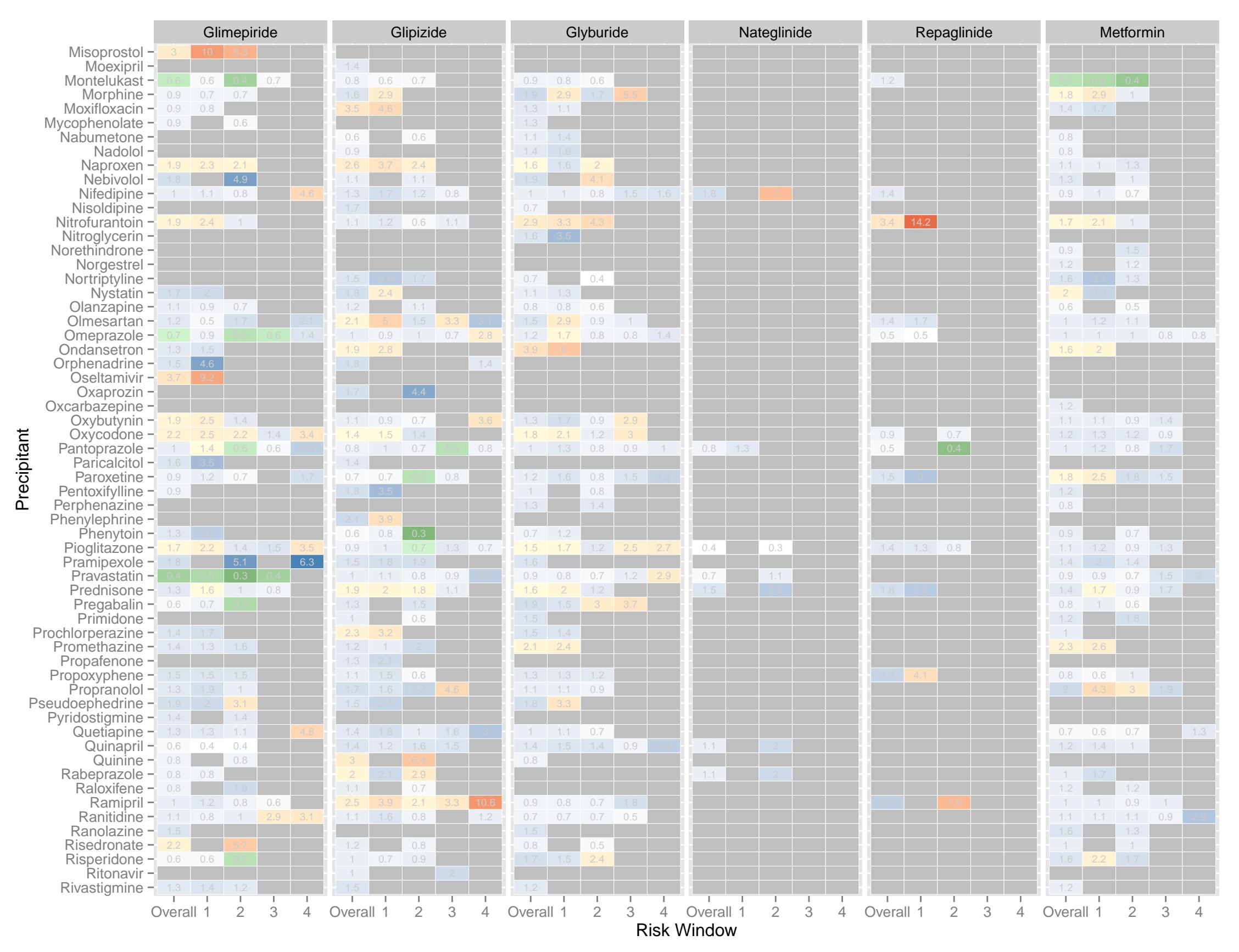
**R program code for semi-Bayes shrinkage**

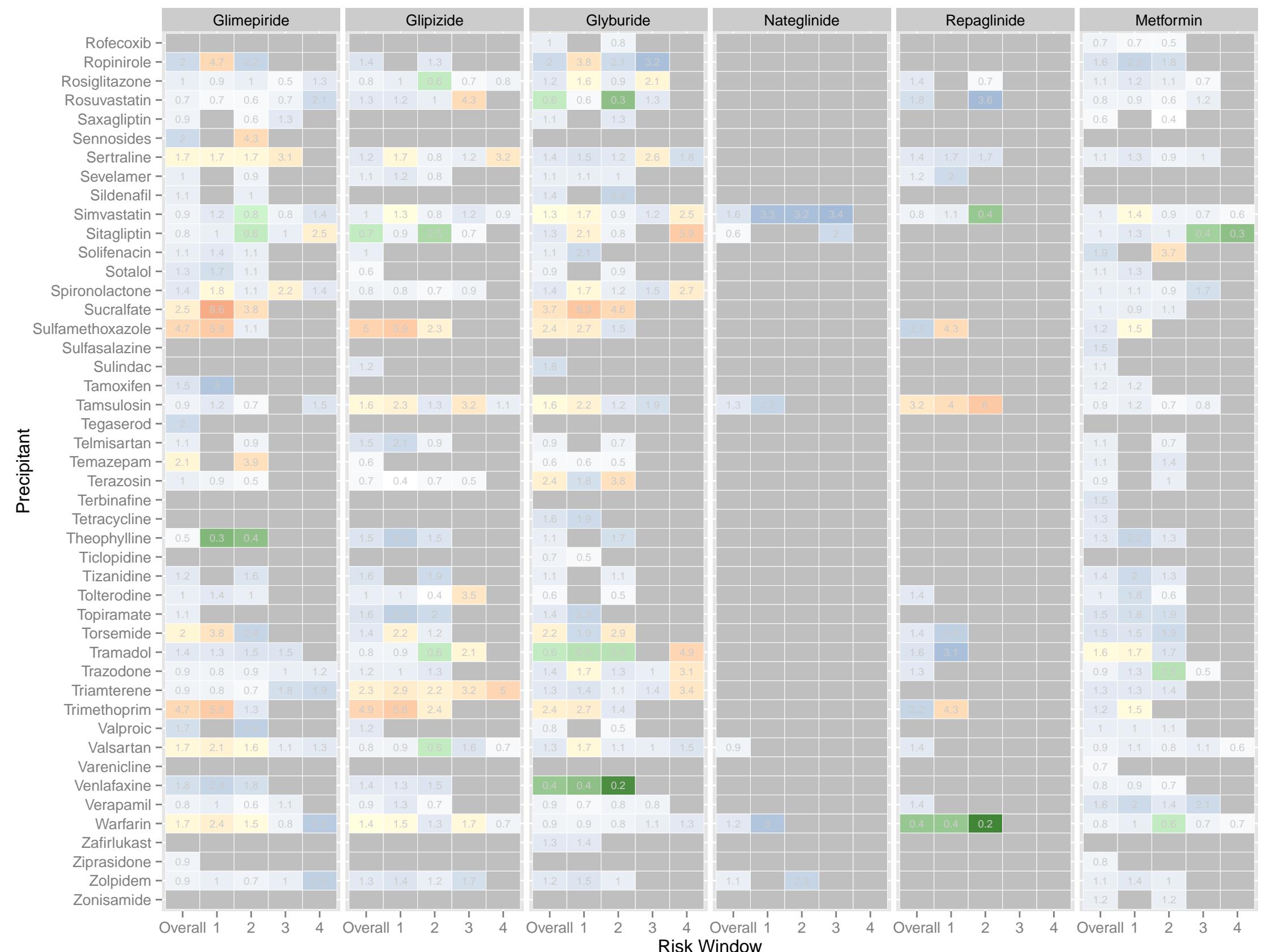
### **Reference**



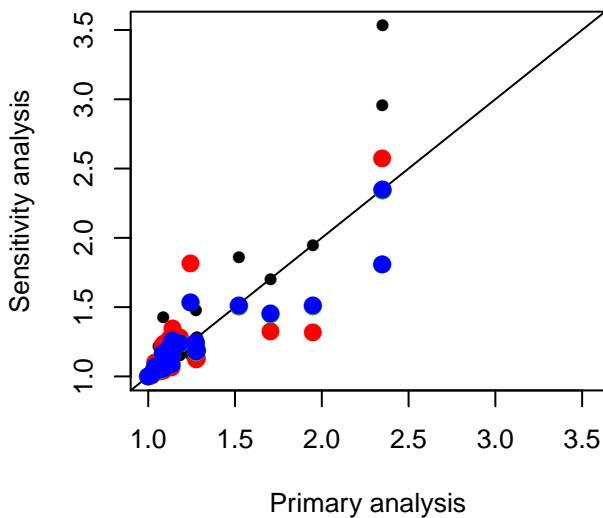




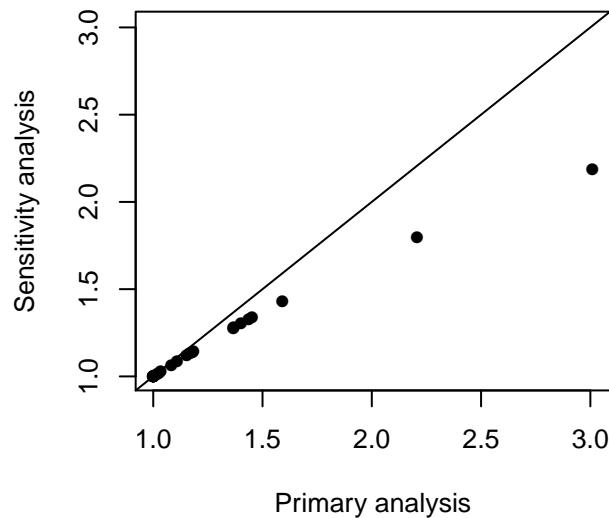




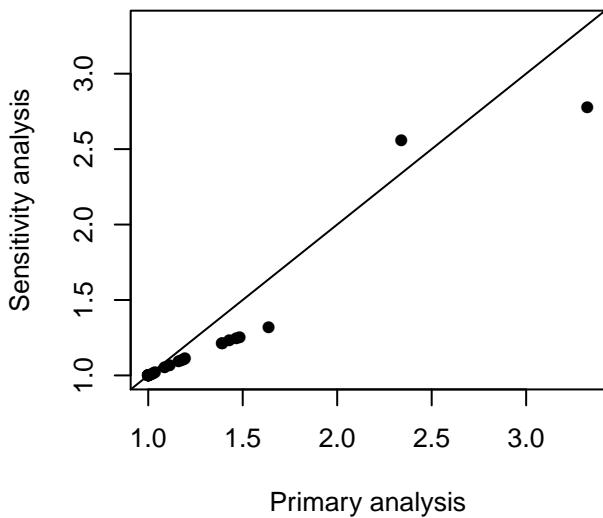
**eFigure 2. (a) Glyburide**



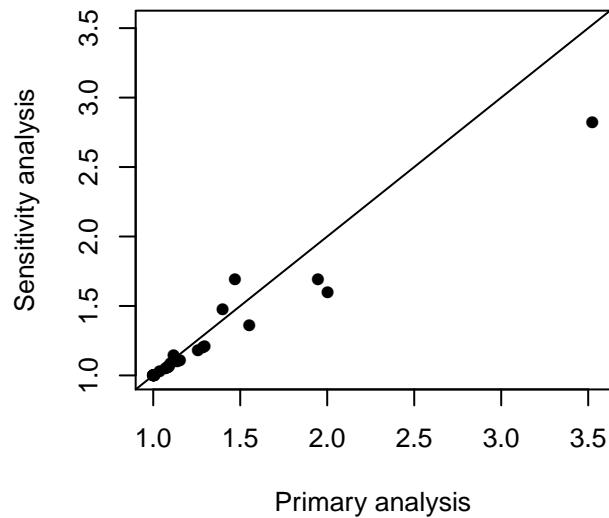
**eFigure 2. (b) Glipizide**



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**eFigure 2. (d) Repaglinide**



**eTable 1.** Exclusionary diagnoses\* suggesting manifestations other than hypoglycemia

<b>ICD-9-CM code(s)<sup>1</sup></b>	<b>Code descriptor</b>	<b>Potential diabetic manifestation</b>
259.8	Other specified endocrine disorders	Secondary diabetic glycogenosis
272.2	Mixed hyperlipidemia	Diabetic lipidosis
681.XX	Cellulitis and abscess of finger and toe	Cellulitis
682.XX	Other cellulitis and abscess	
686.9	Unspecified local infection of skin and subcutaneous tissue	Ulcers of the lower extremity
707.1X	Ulcer of lower limbs, except pressure ulcer	
707.2X	Pressure ulcer stages	
707.8	Chronic ulcer of other specified sites	
707.9	Chronic ulcer of unspecified site	
709.3	Degenerative skin disorders	Necrobiosis lipoidica diabetorum
730.0X	Acute osteomyelitis	Osteomyelitis
730.1X	Chronic osteomyelitis	
730.2X	Unspecified osteomyelitis	
731.8	Other bone involvement in diseases classified elsewhere	

ICD-9 = International Classification of Diseases, 9<sup>th</sup> Revision, Clinical Modification

1. Adapted from Ginde et al. *BMC Endocrine Disorders*. 2008;8:4.

\* considered only for outcomes meeting the operational definition based on ICD-9-CM 250.8X

(diabetes with other specified manifestations)

**eTable 2.** Parameters values of the secretagogues in pharmacokinetic simulation

	Fraction of hepatic metabolism through CYP pathways ( $f_m$ )						Fraction of renal excretion ( $f_e$ )
	CYP2C 8	CYP2C 9	CYP2C1 9	CYP3 A	Unknow n	Reference	
Glipizide	-	<b>1</b>	-	-	-	<sup>1</sup>	0.045
	-	0.81	-	-	0.19	<sup>2</sup>	
Glyburide	-	<b>0.28</b>	<b>0.08</b>	<b>0.5</b>	<b>0.14</b>	<sup>1</sup>	-
	-	0.2	0.3	0.5	-	<sup>3</sup>	
	-	0.64	0.04	0.25	0.07	<sup>4</sup>	
	-	0.5	0.06	0.35	0.1	<sup>5</sup>	
	-	0.5	0.06	0.35	0.1	<sup>6</sup>	
Glimepiride	-	<b>1</b>	-	-	-	<sup>7</sup>	-
	-	0.63	-	-	0.38	<sup>2</sup>	
Repaglinide	<b>0.48</b>	-	-	<b>0.52</b>	-	<sup>8</sup>	0.015
	0.61	-	-	0.39	-	<sup>9</sup>	
Nateglinide	-	<b>0.7</b>	-	<b>0.3</b>	-	<sup>10</sup>	0.13

*F<sub>m</sub>* values in bold were used in the original simulation, and the others were used in sensitivity analysis.

eTable 3. Area under curve ratios (AUCR) and semi-Bayes adjusted rate ratios (RRSB)

Recipient	AUCR	Glipizide			Glibizide			Glyburide			Nateglinide			Repaglinide			Metformin														
		Overall	0-30 Days	31-60 Days	61-120 Days	>120 Days	AUCR	Overall	0-30 Days	31-60 Days	61-120 Days	>120 Days	AUCR	Overall	0-30 Days	31-60 Days	61-120 Days	>120 Days	AUCR	Overall	0-30 Days	31-60 Days	61-120 Days	>120 Days	Overall	0-30 Days	31-60 Days	61-120 Days	>120 Days		
Acarbose																															
Acetabutol	1.3 (1.07, 1.57)	1.42 (1.15, 1.75)	1.1 (0.85, 1.41)	1.07 (0.58, 1.96)	1	1.43 (1.21, 1.69)	1.46 (1.22, 1.76)	1.33 (1.04, 1.69)	1.71 (0.97, 2.98)	2.07 (0.88, 4.89)	1.03 (1.14, 1.61)	1.36 (1.11, 1.67)	1.38 (0.99, 1.63)	1.28 (0.81, 2.27)	1.17 (2.07, 5.95)	4.54 (0.68, 1.07)	1.01 (0.61, 4.93)	1.45 (0.8, 8.16)	1.74 (0.8, 8.16)	2.55 (0.8, 8.16)	1.03 (0.7, 2.5)	1.33 (1.14, 1.66)	1.42 (0.64, 3.13)	1.1 (0.39, 3.09)	1.31 (1.14, 1.66)	1.37 (1.14, 1.66)	1.18 (0.91, 1.52)	0.77 (0.41, 1.49)	1.56 (0.65, 3.78)		
Acetaminophen	1.8 (1.03, 1.18)	1.8 (1.03, 1.18)	1.8 (0.99, 7.9)	2.11 (0.72, 1.18)	1	1.45 (0.79, 1.79)	2.07 (0.94, 4.48)	4.6 (1.17, 18.05)	1.44 (0.74, 1.79)	2.91 (0.88, 4.48)	1.03 (1.14, 1.61)	1.36 (1.11, 1.67)	1.38 (0.99, 1.63)	1.28 (0.81, 2.27)	1.17 (2.07, 5.95)	4.54 (0.68, 1.07)	1.01 (0.61, 4.93)	1.45 (0.8, 8.16)	1.74 (0.8, 8.16)	2.55 (0.8, 8.16)	1.03 (0.7, 2.5)	1.33 (1.14, 1.66)	1.42 (0.64, 3.13)	1.1 (0.39, 3.09)	1.31 (1.14, 1.66)	1.37 (1.14, 1.66)	1.18 (0.91, 1.52)	0.77 (0.41, 1.49)	1.56 (0.65, 3.78)		
Aciclovine																															
Albuterol																															
Alendronate	0.81 (0.54, 1.23)	0.58 (0.3, 1.15)	0.9 (0.56, 1.45)	0.99 (0.64, 1.54)	0.92 (0.5, 2.59)	0.49 (0.26, 0.91)	2.62 (0.78, 8.79)	1	1.37 (0.7, 8.79)	1.37 (0.8, 8.79)	1.03 (0.68, 1.07)	1.45 (0.61, 4.93)	1.45 (0.8, 8.16)	1.44 (0.8, 8.16)	0.53 (0.26, 1.5)	0.63 (0.06, 0.55)	0.18 (0.4, 1.55)	1.05 (0.24, 1.16)	1.17 (0.26, 1.24)	0.79 (0.4, 1.55)	1.53 (0.66, 4.45)	1.05 (0.24, 1.24)	1.17 (0.26, 1.24)	0.79 (0.4, 1.55)	1.53 (0.66, 4.45)						
Alfuzosin																															
Allikem	0.5 (0.2, 1.9)																														
Alispironol	0.97 (0.65, 1.45)	0.75 (0.42, 1.35)	0.95 (0.59, 1.53)	1.5 (0.77, 2.91)	1	0.79 (0.54, 1.17)	0.82 (0.51, 1.25)	0.69 (0.44, 1.08)	0.77 (0.39, 1.51)	1.5 (0.65, 3.46)	0.86 (0.54, 1.44)	0.84 (0.45, 1.38)	0.73 (0.5, 1.23)	1.11 (0.52, 2.37)	2.38 (0.89, 6.4)	1 (0.4, 2.51)	1.03 (0.68, 1.07)	1.45 (0.61, 4.93)	1.74 (0.8, 8.16)	2.55 (0.8, 8.16)	0.53 (0.26, 1.5)	0.63 (0.06, 0.55)	0.18 (0.4, 1.55)	1.05 (0.24, 1.24)	1.17 (0.26, 1.24)	0.79 (0.4, 1.55)	1.53 (0.66, 4.45)	1.05 (0.24, 1.24)	1.17 (0.26, 1.24)	0.79 (0.4, 1.55)	1.53 (0.66, 4.45)
Alprazolam	2.1 (0.71, 2.13)	1.8 (0.67, 2.13)	2.1 (0.81, 2.85)	2.1 (0.71, 1.67)	1	1.44 (0.74, 2.85)	2.07 (0.85, 2.81)	1.5 (0.97, 3.15)	1.44 (0.74, 2.85)	2.07 (0.88, 9.03)	1.03 (0.69, 3.07)	1.45 (0.61, 4.93)	1.44 (0.8, 8.16)																		
Amberlite																															
Amidarone	2.96 (1.8, 4.88)	4.51 (2.49, 8.29)	3.7 (1.3, 5.07)	2.69 (0.92, 7.81)	1	1.18 (0.73, 1.9)	1.64 (0.92, 2.98)	1 (0.55, 1.81)	1.44 (0.71, 1.81)	1 (0.55, 1.81)	1.03 (0.65, 2.97)	1.49 (0.64, 5.66)	2.91 (0.5, 2.02)	1 (1.16, 5.66)	1 (1.16, 5.66)	1.45 (0.68, 1.24)	1 (1.16, 5.66)														
Amiriptiline	1 (0.71, 2.13)	1 (0.78, 4.07)	1 (0.45, 1.75)	1 (0.29, 2.66)	1	1.11 (0.71, 1.81)	1.35 (0.64, 2.32)	1.25 (0.61, 2.89)	1.11 (0.76, 4.49)	1 (1.16, 2.8)	1.11 (0.71, 1.81)	1.35 (0.64, 2.32)	1.25 (0.61, 2.89)	1 (1.16, 4.5)																	
Amiodarone	0.94 (0.51, 1.19)	1.03 (0.59, 1.07)	0.82 (0.38, 1.07)	1.14 (0.79, 1.62)	1	0.94 (0.51, 1.14)	1.27 (0.61, 1.26)	0.69 (0.44, 0.99)	0.69 (0.49, 0.97)	1.5 (0.51, 1.3)	0.62 (0.38, 1.4)	0.7 (0.45, 1.22)	0.48 (0.32, 1.22)	1.44 (0.5, 1.22)	2.38 (0.89, 6.4)	1 (0.4, 2.51)	1 (0.68, 1.07)	1.01 (0.61, 4.93)	1.22 (0.8, 8.16)	1.55 (0.8, 8.16)	1 (0.7, 2.5)	1.11 (0.26, 1.5)	1.17 (0.26, 1.24)	0.89 (0.4, 1.55)	1.53 (0.66, 4.45)	1.05 (0.24, 1.24)	1.17 (0.26, 1.24)	0.89 (0.4, 1.55)	1.53 (0.66, 4.45)		
Amoxillin	2.0 (1.47, 2.85)	2.0 (1.58, 3.22)	2.0 (1.58, 3.22)	2.0 (1.04, 2.15)	1	1.44 (0.99, 1.44)	1.44 (0.98, 2.11)	0.89 (0.55, 1.54)	0.74 (0.45, 1.22)	1.04 (0.55, 1.97)	1.03 (0.68, 1.74)	1.09 (0.64, 2.05)																			
Amoxicillin	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.21 (0.7, 2.87)	1.21 (0.6, 2.98)	1.21 (0.6, 2.98)	1.21 (0.6, 2.98)	1.21 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)				
Amoxaprol	1.01 (0.7, 1.76)	1.01 (0.34, 2.98)	1.01 (0.52, 4.42)	1.01 (0.34, 1.8)	1	1.01 (0.7, 2.87)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.6, 2.98)	1.01 (0.68, 1.24)	1.24 (0.65, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.97)	1 (0.5, 2.9																

Area Under Curve Ratio (AUCR) and semi-logarithmic adjusted rate ratios (RRs) (RRs).



Nebivolol	1.85 (0.75, 4.45)	4.9 (0.91, 26.49)	3.46 (1.77, 6.76)	1.06 (0.52, 2.15)	1.11 (0.36, 3.4)	1.88 (0.83, 4.24)	4.07 (1.06, 15.54)	1	1.29 (0.59, 2.79)	0.98 (0.27, 3.59)
Nicardpine	1.07		1.07		1.03		1.05		1.01	
Nifedipine	1.01 (0.55, 1.86)	1.09 (0.48, 2.45)	0.78 (0.35, 1.72)	1.28 (0.61, 2.05)	1.72 (0.65, 3.1)	1.2	0.84 (0.58, 1.61)	1.46 (0.62, 3.49)	1.65 (0.56, 4.88)	1.4 (0.58, 3.19)
Nozopride	1		1		1		1		1	
Nofluronate	1.92 (1.24, 2.97)	2.45 (1.52, 5.93)	1.05 (0.48, 2.7)	1.05 (0.56, 1.86)	1.25 (0.72, 2.56)	0.59 (0.28, 1.4)	1.08 (0.53, 2.08)	2.05 (0.58, 4.66)	3.54 (1.56, 11.86)	1.55 (1.25, 9.78)
Norgestodrel					0.64 (0.64, 3.89)		1.45 (0.67, 17.76)		1.42 (1.32, 57.31)	
Nostidine	5		1		1		1		1	
Novethidrone	1		1		1		1		1	
Norgestrel									0.9 (0.43, 1.86)	5.51 (0.54, 4.11)
Nortripazine	5		1		1		1		1.7 (0.44, 3.12)	1.17 (0.32, 11.73)
Nystatin	1.73 (0.91, 2.29)	2.04 (0.88, 4.82)		1.55 (0.72, 3.34)	2.84 (0.83, 9.34)	1.7	0.72 (0.31, 1.68)	0.35 (0.08, 1.62)	1	3.05 (0.71, 3.41)
Olanzapine	1.09 (0.51, 2.28)	0.93 (0.25, 2.98)	0.71 (0.24, 1.8)	1.16 (0.58, 3.43)	1.26 (0.65, 9.35)	1.11	0.8 (0.34, 1.22)	0.56 (0.21, 1.24)	1	2.5 (0.62, 3.96)
Olmesartan	1.29 (0.77, 1.97)	1.57 (0.21, 1.3)	1.73 (1.12, 2.67)	2.15 (1.14, 3.89)	5.01 (2.26, 11.1)	1.31 (0.66, 3.47)	3.31 (0.75, 1.52)	3.08 (0.59, 9.54)	2.76 (0.36, 2.52)	1.4 (0.52, 3.72)
Omeprazole	1.08 (0.55, 0.94)	0.96 (0.48, 1.28)	0.6 (0.41, 0.76)	0.84 (0.78, 1.29)	1.02 (0.63, 1.22)	0.75 (0.46, 1.22)	0.75 (0.56, 4.88)	1.45 (0.85, 2.48)	0.95 (0.43, 1.79)	0.48 (0.21, 1.11)
Ondansetron	1.32 (0.77, 1.72)	1.46 (0.27, 1.79)		1.95 (1.04, 3.65)	2.76 (1.27, 5.98)		1.95 (0.86, 1.84)	1.79 (0.53, 1.12)	1.76 (0.45, 1.29)	1.36 (0.73, 2.54)
Orphenadrine	0.76 (0.6, 1.75)	0.73 (0.6, 2.37)		1.15 (0.72, 4.32)	1.15 (0.48, 13.71)		1.37 (2.1, 7.07)	2.05 (2.87, 12.47)		1.54 (1.04, 2.37)
Oxaprozin			1.73 (0.72, 4.17)		4.39 (0.92, 21.64)					
Oxcarbazepine									1.17 (0.44, 3.12)	
Oxybutynin	1.88 (1.01, 3.49)	2.54 (1.11, 5.78)	1.4 (0.62, 3.15)	0.71 (0.31, 1.61)	1.13 (0.72, 8.82)	0.68 (0.42, 1.93)	3.65 (1.56, 8.55)	1.26 (0.73, 2.18)	1.71 (0.63, 4.44)	0.86 (0.41, 1.75)
Oxycodone	2.2 (0.85, 1.28)	2.45 (0.84, 3.37)	2.1 (0.64, 3.31)	1.41 (0.74, 2.43)	1.5 (0.74, 2.43)	1.41 (0.74, 2.43)	1.27 (0.58, 1.43)	1.17 (0.58, 1.43)	2.98 (0.58, 1.54)	1.24 (0.41, 0.55)
Pantoprazole	1.02 (0.73, 1.28)	0.97 (0.44, 1.97)	1.43 (0.45, 0.9)	1.02 (0.64, 1.12)	0.72 (0.73, 1.44)	0.53 (0.28, 1)	0.76 (0.46, 1.24)	0.78 (0.46, 1.24)	1.02 (0.71, 2.12)	1.02 (0.71, 2.12)
Paracetamol	0.69 (0.69, 1.7)	0.73 (0.69, 1.72)		1.05 (0.72, 2.42)	1.05 (0.72, 2.42)		1.05 (0.72, 2.42)	1.05 (0.72, 2.42)	1.05 (0.72, 2.42)	1.05 (0.72, 2.42)
Paracetamol	0.95 (0.52, 2.22)	1.16 (0.52, 2.24)	0.7 (0.32, 2.24)	1	0.85 (0.42, 1.94)	0.66 (0.21, 2.44)	0.85 (0.42, 1.94)	1.54 (0.72, 2.89)	1.56 (0.72, 2.81)	1.56 (0.72, 2.81)
Pentazocine	1		1		1		1		1	
Pentoxifylline	0.94 (0.41, 2.13)			1.81 (0.77, 4.25)	3.5 (0.88, 14.31)		0.95 (0.45, 2.15)	0.84 (0.21, 3.46)		1.23 (0.53, 0.8)
Perphenazine	1		1		1		1		0.81 (0.33, 1.96)	
Phenobarbital	1		1		1.09 (0.53, 1.09)		1		1	
Phenylephrine			2.05 (0.9, 4.73)		3.94 (1.25, 14.76)				0.95 (0.44, 2.06)	0.92 (0.32, 2.08)
Phenytoin	1.64 (0.58, 3)	1.32 (0.72, 9.66)	1.4 (1.0, 1.5)	1.5 (1.59, 1.2)	1.72 (1.34, 1.73)	1.5 (1.11, 0.78)	1.14 (0.56, 1.29)	1.15 (0.56, 2.87)	1.31 (0.56, 2.87)	1.31 (0.56, 2.87)
Phlegmatizol	1	1.72 (1.28, 3.32)	2.25 (1.58, 3.2)	1.4 (0.99, 1.99)	1.5 (0.85, 2.64)	1.08 (0.66, 1.1)	0.85 (0.72, 1.37)	1.08 (0.66, 2.02)	1.26 (0.66, 1.16)	1.35 (0.66, 1.15)
Picrasic acid	1.01		1		1		1		1	
Pimavasertide	1.84 (0.74, 4.58)	5.06 (0.91, 26.16)	3.06 (0.89, 17.58)	1.55 (0.78, 3.07)	5.12 (0.84, 5.21)	1.82 (0.78, 4.8)	1.57 (0.65, 3.78)	1.59 (0.65, 2.86)	1.57 (0.65, 2.86)	1.38 (0.65, 2.86)
Pravastatin	0.42 (0.38, 1.23)	0.48 (0.38, 1.27)	0.33 (0.38, 0.57)	0.43 (0.38, 0.57)	1.12 (0.65, 1.56)	0.79 (0.65, 1.56)	0.93 (0.53, 1.57)	2.56 (0.65, 2.87)	1.26 (0.65, 2.87)	0.71 (0.31, 1.51)
Prednisone	1.28 (0.57, 1.69)	1.59 (0.71, 2.15)	0.79 (0.41, 1.95)	1.41 (1.24, 2.75)	1.82 (1.72, 2.75)	1.42 (1.24, 2.64)	1.06 (0.53, 1.42)	1.2 (0.53, 1.42)	2.63 (0.68, 10.17)	1.75 (0.81, 1.79)
Pregabalin	0.36 (0.36, 1.08)	0.38 (0.36, 1.48)	0.25 (0.25, 0.92)	0.38 (0.36, 1.2)	0.28 (0.25, 0.92)	0.27 (0.25, 0.92)	0.27 (0.25, 0.92)	1.45 (0.94, 3.81)	1.45 (0.94, 3.81)	1.45 (0.94, 3.81)
Prisondine	1.01		1		1		1		1.01	
Prochlorperazine	1.45 (0.76, 7.6)	1.74 (0.74, 4.09)		2.05 (0.74, 2.27)	3.94 (0.74, 2.27)		1.47 (0.74, 2.27)	1.43 (0.74, 2.27)	1.47 (0.74, 2.27)	1.38 (0.74, 2.27)
Propethazine	1.46 (0.84, 2.26)	1.51 (0.84, 2.54)	1.52 (0.55, 3.67)	1.36 (0.74, 2.27)	1.55 (0.74, 2.27)	1.41 (0.74, 2.27)	1.27 (0.58, 1.41)	1.34 (0.58, 1.41)	1.24 (0.58, 1.41)	1.04 (0.58, 1.41)
Propoxyphene	1.46 (0.84, 2.26)	1.51 (0.84, 2.54)	1.52 (0.55, 3.67)	1.36 (0.74, 2.27)	1.55 (0.74, 2.27)	1.41 (0.74, 2.27)	1.27 (0.58, 1.41)	1.34 (0.58, 1.41)	1.24 (0.58, 1.41)	1.04 (0.58, 1.41)
Propranolol	1.26 (0.6, 2.97)	1.35 (0.55, 6.51)	1.35 (0.29, 3.35)	1.26 (0.74, 3.78)	1.35 (0.74, 3.78)	1.26 (0.74, 3.78)	1.26 (0.74, 3.78)	1.26 (0.74, 3.78)	1.26 (0.74, 3.78)	1.26 (0.74, 3.78)
Pseudoevodimine	1.86 (0.55, 1.33)	2 (0.55, 1.33)	1.42 (0.57, 3.09)	1.33 (0.57, 3.09)	1.42 (0.57, 3.09)	1.33 (0.57, 3.09)	1.42 (0.57, 3.09)	1.42 (0.57, 3.09)	1.42 (0.57, 3.09)	1.42 (0.57, 3.09)
Pseudogymnophyllum	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)	1.35 (0.55, 1.33)
Quazepam	1.27 (0.74, 2.4)	1.31 (0.56, 3.07)	1.28 (0.51, 2.29)	1.27 (0.74, 2.27)	1.37 (0.81, 3.63)	1.02 (0.51, 2.06)	1.08 (0.54, 2.45)	1.07 (0.97, 9.04)	1.01 (0.58, 1.65)	1.01 (0.49, 1.42)
Quinapril	0.55 (0.55, 1.4)	0.59 (0.55, 1.4)	0.44 (0.54, 1.08)	0.55 (0.55, 1.04)	1.41 (0.85, 2.4)	0.55 (0.55, 2.4)	1.54 (0.85, 2.37)	1.41 (0.85, 2.37)	1.54 (0.85, 2.37)	1.41 (0.85, 2.37)
Ranitidine	1.11 (0.58, 1.87)	0.84 (0.58, 1.87)		2.97 (1.07, 3.66)	3.57 (0.83, 5.45)	6.41 (1.31, 6.77)	0.81 (0.58, 1.87)	1.11 (0.58, 2.17)	1.11 (0.58, 2.17)	1.4 (0.58, 2.17)
Reboxetine	1.06 (0.58, 1.44)	0.78 (0.58, 1.44)	1.21 (0.76, 1.44)	1.06 (0.58, 1.44)	1.21 (0.76, 1.44)	1.06 (0.58, 1.44)	0.91 (0.58, 1.44)	0.91 (0.58, 1.44)	1.02 (0.58, 1.44)	1.02 (0.58, 1.44)
Reserpine	2.21 (1.01, 5.95)	5.72 (1.76, 14.44)	4.25 (2.36, 7.85)	1.98 (0.58, 1.82)	2.12 (0.58, 1.82)	1.98 (0.58, 1.82)	0.81 (0.58, 1.82)	0.81 (0.58, 1.82)	0.81 (0.58, 1.82)	1.01 (0.58, 1.82)
Risendrone	0.6 (0.37, 1.02)	0.6 (0.37, 1.02)	0.65 (0.37, 1.02)	0.55 (0.37, 0.95)	1.01 (0.56, 1.82)	0.95 (0.56, 1.82)	1.01 (0.56, 1.82)	1.01 (0.56, 1.82)	1.01 (0.56, 1.82)	1.01 (0.56, 1.82)
Ritavirine	1.09		1.08 (0.44, 2.43)		1.08 (0.44, 2.43)		1.07 (0.44, 2.43)		1.34 (0.76, 1.95)	
Roxat皆素	1.28 (0.61, 2.68)	1.44 (0.61, 4.47)	1.23 (0.41, 3.66)	1.25 (0.61, 2.68)	1.25 (0.61, 2.68)	1.25 (0.61, 2.68)	1.25 (0.61, 2.68)	1.25 (0.61, 2.68)	1.25 (0.61, 2.68)	1.25 (0.61, 2.68)
Rofecoxib	1		1		1		1		1	
Rosemarine	2.02 (0.58, 4.74)	4.68 (0.58, 4.74)	2.24 (0.58, 4.74)	2.22 (0.58, 4.74)	1.43 (0.76, 3.73)	1.25 (0.76, 3.73)	1.25 (0.76, 3.73)	0.96 (0.58, 2.02)	0.96 (0.58, 2.02)	0.96 (0.58, 2.02)
Rosiglitazone	1.09 (0.54, 1.44)	1.41 (0.54, 1.44)	0.78 (0.41, 1.41)	0.54 (0.41, 1.41)	1.75 (0.79, 1.82)	1.02 (1.03, 2.8)	0.84 (0.55, 1.39)	1.27 (0.65, 2.58)	1.19 (0.65, 2.58)	1.05 (0.54, 1.39)
Rouxavatol	0.7 (0.47, 1.18)	0.65 (0.47, 1.18)	0.65 (0.47, 1.18)	0.75 (0.47, 1.18)	1.16 (0.74, 2.13)	1.21 (0.57, 2.72)	0.95 (0.45, 1.43)	4.33 (0.58, 1.96)	1.23 (0.58, 1.96)	1.11 (0.58, 1.96)
Ruxolitinib	1.01 (0.54, 2.21)	1.04 (0.54, 2.21)		1	1.41 (0.76, 1.82)	1.02 (0.55, 1.65)	1.19 (0.65, 1.82)	1.26 (0.65, 1.82)	1.26 (0.65, 1.82)	1.26 (0.65, 1.82)
Saxagliptin	0.44 (0.44, 1.8)	0.55 (0.44, 1.8)	0.55 (0.44, 1.8)	0.55 (0.44, 1.8)	1.01 (0.83, 1.24)	0.82 (1.01, 1.65)	1.23 (0.65, 1.65)	0.93 (0.62, 1.43)	1.23 (0.62, 1.43)	1.23 (0.62, 1.43)
Selagine	1		1		1		1		1	
Semidesmolidine	2.04 (0.58, 4.74)	3.49 (0.58, 4.74)	3.46 (0.58, 4.74)	1	1.28 (0.58, 2.15)	1.11 (0.58, 3.4)	1.28 (0.58, 2.15)	1.05	1.05	1.05
Serrataline	1.09 (1.51, 2.68)	2.65 (1.51, 2.68)	3.06 (1.48, 6.33)	1	1.2 (0.79, 1.82)	1.72 (1.03, 2.8)	0.84 (0.55, 1.39)	1.38 (0.55, 2.58)	1.18 (1.01, 2.8)	1.05 (0.58, 1.39)
Sevelamer	1.09 (0.54, 2.11)	1.09 (0.54, 2.11)	1.09 (0.54, 2.11)	1.06 (0.54, 2.11)	1.25 (0.86, 1.89)	0.82 (0.55, 1.83)	1.04 (0.64, 1.83)	1.04 (0.64, 1.83)	1.04 (0.64, 1.83)	1.04 (0.64, 1.83)
Sildenafil	1		1		1		1		1	
Simeprevir	1.02 (0.75, 1.6)	1.29 (0.75, 1.6)	0.84 (0.57, 1.23)	1	1.01 (0.83, 1.24)	1.29 (1.01, 1.65)	0.82 (0.55, 1.66)	1.23 (0.62, 1.66)	1.23 (0.62, 1.66)	1.23 (0.62, 1.66)
Sirulimus	1		1		1		1		1	
Slatiglip	0.83 (0.61, 1.15)	0.59 (0.48, 0.86)	0.98 (0.51, 1.58)	0.65 (0.45, 0.94)	0.86 (0.56, 1.34)	0.46 (0.38, 1.2)	0.68 (0.34, 1.2)	1.28 (0.58, 1.55)	0.77 (0.44, 1.37)	0.64 (0.29, 1.77)
Sofenamic acid	1.19 (0.56, 2.33)	1.39 (0.47, 4.31)	1.21 (0.47, 4.31)	1.03 (0.47, 2.33)	1.25 (0.58, 2.0)	1.02 (0.47, 2.0)	0.83 (0.47, 2.0)	1.25 (0.58, 2.0)	1.25 (0.58, 2.0)	1.25 (0.58, 2.0)
Sortadol	1		1		1		1		1	
Sotagliflozin	1.05 (0.56, 1.55)	1.54 (0.56, 1.55)	1.06 (0.56, 1.55)	1.05 (0.56, 1.55)	1.28 (0.57, 2.71)	0.95 (0.55, 1.83)	1.28 (0.57, 2.71)	1.28 (0.57, 2.71)	1.28 (0.57, 2.71)	1.28 (0.57, 2.71)
Spiromalconate	1.35 (0.58, 1.6)	1.81 (0.58, 1.6)	1.06 (0.58, 1.6)	2.15 (0.58, 1.6)	0.76 (0.58, 1.6)	0.68 (0.58, 1.6)	0.94 (0.58, 1.6)	1.39 (0.58, 1		

Table 3. Area under curve ratios (AUCR) and semi-Bayes adjusted rate ratios (BBSR).xlsx

Succinate	2.52 (1.09, 5.81)	8.63 (2.4, 31.04)	3.8 (1, 14.38)	3.3 (1.33, 8.21)		3.69 (2.05, 4.63)	6.3 (3.02, 13)	4.63 (2.13, 10.20)			2.15 (0.94, 4.95)	4.29 (1.36, 11.59)	1.05 (0.56, 1.92)	0.95 (0.39, 2.32)	1.07 (0.45, 2.54)			
Sulfamethoxazole	4.43 (1.40, 6.44)	1.37 (4.1, 9.9)	1.25 (0.42, 2.64)		5.03 (3.87, 6.53)	5.92 (4.54, 7.71)	2.28 (1.15, 4.51)			3.3 (1.21, 3.13)	3.3 (2.02, 3.6)	1.46 (0.74, 2.78)		1.1 (0.86, 1.77)	1.1 (1.02, 2.18)			
Sulfafazaine													0.63 (0.63, 3.50)	1.14 (0.46, 2.91)				
Sulfadiazine																		
Tacrolimus	1				1				1			1						
Tadalafil	1				1				1			1						
Tamoxifen	1 (0.61, 3.91)	1.54 (0.51, 17.7)	0.9 (0.26, 1.98)	0.67 (0.41, 1.06)	1	1.64 (1.08, 2.5)	2.33 (1.41, 3.88)	1.25 (0.76, 2.06)	3.19 (1.69, 6.01)	1.05 (0.39, 2.88)	1.59 (1.06, 2.39)	2.21 (1.38, 3.53)	1.2 (0.74, 1.95)	1.87 (0.82, 4.27)	1 (0.51, 3.21)	1.28 (1.53, 6.73)	2.17 (1.52, 10.77)	6.04 (2.48, 14.72)
Tasignap	1 (0.89, 4.41)				1	1.47 (0.73, 3.2)	2.06 (0.67, 6.33)	0.88 (0.26, 2.95)		1 (0.41, 1.86)	0.84 (0.61, 1.55)	0.72 (0.58, 0.54)		1 (0.34, 1.09)	1.28 (0.62, 1.31)	1.17 (0.41, 3.12)	1.17 (0.12, 1.71)	
Telmisartan	1 (0.64, 2.43)	1.03 (0.41, 5.13)	2.09 (1.17, 9.83)	1.39 (0.28, 1.23)	1	0.59 (0.28, 1.23)				1 (0.34, 1.09)			1 (0.26, 1.12)		1 (0.56, 1.45)	1.13 (0.63, 2.12)	0.9 (0.39, 1.26)	0.8 (0.33, 1.97)
Temazepam	1 (1.08, 4.06)				1					1 (0.34, 1.09)			1 (0.26, 1.12)					
Tenofovir	1				1					1			1					
Terazosin	0.96 (0.43, 2.15)	0.85 (0.21, 3.28)	0.54 (0.15, 2.01)		0.71 (0.4, 1.25)	0.44 (0.17, 1.13)	0.59 (0.34, 1.41)	0.54 (0.22, 1.33)		2.39 (1.18, 4.60)	1.76 (1.04, 5.74)	3.81 (1.42, 10.12)			0.89 (0.41, 1.83)	1.01 (0.34, 2.06)		
Terbutamine	1				1				1			1				1.54 (0.65, 3.42)		
Terazine	1				1				1			1				1.26 (0.56, 2.69)		
Theophylline	1 (0.27, 1.09)	0.55 (0.11, 0.87)	0.36 (0.14, 0.85)		1 (0.87, 3.88)	2.42 (0.66, 8.70)	1.53 (0.41, 5.68)		1.09 (0.57, 2.3)	1.15 (0.54, 4.44)	1.93 (1.15, 7.72)	1.04 (0.54, 4.44)	1.72 (1.15, 5.56)	1.07 (0.57, 2.3)	1.04 (0.55, 3.87)	1.09 (0.35, 2.1)	1.09 (0.35, 2.1)	2.19 (0.34, 5.55)
Thiothixene					1				1			1						
Ticlopidine	1				1				1			1						
Tizanidine	1.23 (0.55, 2.73)	1.41 (0.49, 5.33)	1.53 (0.49, 4.74)		1.58 (0.73, 3.41)	1.50 (0.6, 6.17)			1 (0.5, 2.46)	1.1 (0.31, 4.28)	1.55 (0.61, 5.1)				1.39 (0.65, 2.99)	1.9 (0.62, 6.1)	1.25 (0.41, 4.43)	
Toherodine	0.97 (0.51, 1.37)	1.37 (0.21, 1.02)	1.02 (0.49, 1.39)		1.03 (0.48, 2.13)	1 (0.31, 4.23)	0.42 (0.19, 1.4)	1.47 (0.64, 3.44)	0.64 (0.21, 2.46)	0.52 (0.19, 1.4)				1.4 (0.52, 5.72)	1.05 (0.35, 3.02)	1.06 (0.42, 3.44)		
Topiramate	1.13 (0.49, 2.62)				1 (0.75, 3.45)	2.44 (0.74, 8.09)	1.37 (0.65, 5.96)		1.61 (0.58, 3.32)	1.9 (0.61, 10.61)	2.29 (0.73, 5.03)				1.51 (0.74, 2.93)	1.78 (0.61, 5.18)	1.9 (0.75, 5.01)	
Torsemide	2.21 (1.03, 4.01)	3.77 (1.55, 9.14)	2.36 (0.98, 5.71)	2.53 (0.89, 7.21)	2.76 (0.78, 2.47)	2.41 (1.04, 4.81)	2.53 (0.55, 2.51)		2.33 (1.15, 4.14)	2.32 (0.73, 5.03)	2.32 (1.24, 6.86)				1.42 (0.62, 3.25)	2.54 (0.76, 8.54)	1.23 (0.77, 4.79)	
Torvastatin	1.98 (0.86, 2.86)	1.31 (0.48, 2.47)	1.52 (0.49, 3.49)	1.55 (0.49, 3.49)	1 (0.8, 1.41)	0.87 (0.49, 2.09)	0.81 (0.4, 2.09)	2.1 (0.63, 4.28)	0.62 (0.32, 2.05)	0.54 (0.29, 1.96)	0.75 (0.38, 20.45)	1 (0.28, 2.05)	0.64 (0.28, 20.45)	1 (0.54, 2.95)	1.6 (0.54, 8.85)	3.12 (0.72, 22.12)	1.6 (0.54, 8.74)	
Triazadone	0.92 (0.61, 1.35)	0.8 (0.47, 1.34)	0.94 (0.51, 1.46)	0.95 (0.45, 2.02)	1 (0.72, 1.85)	1.15 (0.51, 1.89)	0.99 (0.71, 2.21)	1.25 (0.71, 2.25)	1.02 (0.35, 2.12)	1.42 (1.01, 2.75)	1.67 (0.78, 2.04)	1.26 (0.46, 2.32)	1.04 (1.34, 7.25)	3.12 (0.57, 2.05)	1.04 (0.57, 2.05)	1.04 (0.57, 2.05)	1.26 (0.54, 2.05)	
Trimethoprim	1 (1.45, 6.37)	1.49 (4.28, 7.93)	1.32 (0.58, 3)		1 (3.82, 6.64)	4.94 (4.47, 7.58)	5.82 (1.24, 4.57)	2.38 (1.24, 4.57)	1 (1.79, 3.1)	2.36 (2.01, 3.57)	2.68 (0.74, 2.7)	1.41 (0.74, 2.7)		1 (0.54, 4.95)	2.15 (1.36, 13.59)	4.29 (1.06, 2.18)		
Tropism	1				1				1			1						
Valdecoxib	1				1				1			1						
Valproic	1.69 (0.78, 3.68)	2.43 (0.71, 8.3)	1.32 (0.49, 4.64)	2.54 (1, 6.46)	1.23 (0.75, 2.75)	1.50 (0.74, 3.49)	0.81 (0.34, 1.93)	0.5 (0.12, 2.05)	1.74 (0.73, 2.69)	1.70 (0.69, 1.61)	0.5 (0.54, 1.94)	1.03 (0.71, 3.4)	1.55 (0.69, 1.61)	0.93 (0.38, 2.3)	1 (0.6, 3.28)	1.02 (0.51, 1.39)	1.01 (0.66, 1.77)	1.11 (0.54, 2.19)
Varcarizine	1 (1.11, 2.47)	2.15 (1.34, 3.43)	1.1 (0.22, 2.55)	1.05 (0.54, 2.05)	1 (0.58, 1.08)	0.81 (0.41, 1.34)	0.57 (0.39, 0.83)	1.63 (0.58, 2.72)	0.66 (0.31, 1.48)	1 (0.9, 1.86)	1.29 (1.13, 2.69)	1.74 (0.69, 1.61)	1.03 (0.54, 1.94)	1.55 (0.71, 3.4)	1 (0.51, 1.49)	1.02 (0.48, 1.4)	1.01 (0.49, 1.4)	1.11 (0.51, 2.16)
Verapamil	1 (0.47, 3.77)	1.79 (0.71, 7.59)	1.8 (0.58, 5.59)		1 (0.72, 2.46)	1.59 (0.54, 2.86)	1.59 (0.51, 3.21)	1 (0.22, 2.71)	0.83 (0.11, 0.83)	0.53 (0.11, 0.49)				1 (0.54, 1.49)	0.83 (0.48, 1.49)	0.9 (0.46, 1.29)	1.11 (0.51, 2.16)	
Verapamil	0.83 (0.48, 1.42)	0.99 (0.48, 2.02)	0.59 (0.31, 1.16)	1.11 (0.43, 3.03)	1 (0.55, 1.48)	1.33 (0.72, 2.46)	0.67 (0.36, 1.26)	1 (0.51, 1.54)	0.88 (0.26, 1.47)	0.65 (0.21, 1.67)	0.85 (0.33, 1.95)	1 (0.51, 1.54)	0.81 (0.21, 1.67)		1.01 (0.52, 2.72)	1.4 (0.87, 2.92)	2.08 (0.91, 4.49)	
Warfarin	1 (1.3, 3.4)	1.8 (1.7, 3.39)	1.8 (1.06, 2.06)	1.89 (0.36, 1.89)	1 (0.25, 1.81)	1.29 (0.72, 2.12)	1.77 (0.96, 1.77)	1.68 (1.08, 2.62)	0.74 (0.36, 1.56)	1 (0.69, 1.12)	1.26 (0.63, 1.17)	1.68 (0.68, 1.84)	1.26 (0.59, 2.7)	1 (0.49, 1.02)	1.21 (0.19, 5.76)	2.29 (0.57, 15.6)	1 (0.54, 1.26)	
Zafirlukast	1				1				1 (0.48, 3.38)	1.27 (0.14, 13.96)	1				1 (0.54, 1.02)	1.01 (0.19, 5.76)		
Ziprasidone	1 (0.38, 2.02)	0.87 (0.38, 2.02)			1				1			1				0.85 (0.36, 2.02)		
Zoledronic	1 (0.32, 1.27)	0.98 (0.61, 1.52)	0.96 (0.46, 1.13)	1.03 (0.43, 2.44)	1 (0.92, 1.79)	1.38 (0.54, 2.21)	1.44 (0.78, 1.72)	1.16 (0.79, 3.86)	1 (0.8, 1.8)	1.21 (0.53, 2.45)	1.51 (0.62, 1.69)	1.03 (0.49, 2.61)	1.13 (0.55, 9.48)	2.29 (1.04, 2.61)	1 (0.79, 1.67)	1.37 (0.88, 2.16)	0.99 (0.63, 1.55)	
Zonisamide	1				1				1.04			1.02				1.04 (0.44, 3.12)		1.17 (0.12, 11.71)

**eTable 4. Semi-Bayes and metformin adjusted rate ratios (RRSBM)**

Precipitant	Glimipizide				Glipizide				Glyburide				Nateglinide				Repaglinide					
	Overall	0-30 Day	31-60 Day	61-120 Day	≥ 121 Day	Overall	0-30 Day	31-60 Day	61-120 Day	≥ 121 Day	Overall	0-30 Day	31-60 Day	61-120 Day	≥ 121 Day	Overall	0-30 Day	31-60 Day	61-120 Day	≥ 121 Day		
Acetaminophen	0.99 (0.76, 1.29)	1.03 (0.78, 1.37)	0.93 (0.65, 1.35)	1.38 (0.56, 3.38)	0.99 (0.27, 3.72)	1.09 (0.85, 1.39)	1.07 (0.82, 1.39)	1.13 (0.79, 1.6)	2.21 (0.93, 2.5)	1.31 (0.38, 4.5)	1.04 (0.81, 1.33)	1.01 (0.77, 1.32)	1.08 (0.76, 1.54)	1.52 (0.6, 3.86)	2.88 (0.88, 9.4)	1.29 (0.52, 3.19)	1.27 (0.44, 3.65)	2.17 (0.66, 7.13)	1.01 (0.48, 2.16)	1.03 (0.46, 2.33)	0.94 (0.32, 2.71)	
Acetazolamide	1.99 (0.43, 9.29)									2.77 (0.56, 13.72)												
Acyclovir						1.83 (0.48, 7.02)				1.82 (0.47, 7.06)												
Aldendronate	0.87 (0.42, 1.78)	0.64 (0.25, 1.64)	1.09 (0.48, 2.45)			1.07 (0.51, 2.25)	1.67 (0.72, 3.91)	0.59 (0.24, 1.45)		1.25 (0.57, 2.76)	1.68 (0.68, 4.17)	1.01 (0.4, 2.55)						0.36 (0.13, 0.99)	0.54 (0.18, 1.59)	0.28 (0.07, 0.82)		
Allopurinol	0.92 (0.45, 1.89)	0.63 (0.27, 1.51)	1.2 (0.52, 2.74)	0.99 (0.34, 2.86)		0.74 (0.36, 1.5)	0.7 (0.31, 1.58)	0.81 (0.39, 1.96)	0.51 (0.18, 1.48)	0.8 (0.38, 1.65)	0.72 (0.31, 1.66)	0.93 (0.2, 2.1)	0.73 (0.24, 2.25)		0.9 (0.21, 3.86)				1.42 (0.41, 1.94)			
Alprazolam	0.95 (0.46, 1.93)	1.25 (0.52, 3.02)	0.68 (0.29, 1.61)			1.3 (0.63, 2.71)	1.61 (0.66, 3.93)	0.86 (0.35, 2.11)		0.68 (0.33, 1.42)	0.96 (0.39, 2.35)	0.42 (0.17, 1.02)		1.1 (0.27, 4.48)	0.74 (0.11, 5)				0.67 (0.19, 2.36)			
Amiodarone	3.07 (1.34, 7.03)	2.44 (0.98, 6.1)	4.26 (1.63, 11.13)			1.03 (0.45, 2.32)	0.88 (0.36, 2.19)	1.37 (0.52, 3.6)		1.37 (0.57, 3.28)	1.57 (0.64, 4.11)	1.38 (0.49, 3.87)										
Amitriptyline	0.84 (0.38, 1.85)	0 (0.42, 2.5)	0.92 (0.28, 1.7)	0.26 (0.26, 3.3)		0.74 (0.36, 1.55)	0.6 (0.21, 1.44)	0.84 (0.37, 1.9)	1.42 (0.36, 5.56)	1.28 (0.29, 2.59)	0.69 (0.23, 1.61)	1.09 (0.81, 3.86)	1.09 (0.65, 6.03)									
Amlodipine	1.11 (0.78, 1.58)	0.85 (0.56, 1.27)	1.2 (0.81, 1.76)	1.59 (0.97, 2.94)	5.03 (2.01, 12.59)	1.11 (0.84, 1.54)	1.04 (0.72, 1.51)	1.15 (0.8, 1.66)	1.03 (0.6, 1.77)	3.16 (1.27, 7.86)	0.73 (0.51, 1.03)	1.42 (0.38, 0.86)	3.77 (0.47, 1.02)	1.16 (0.82, 2.45)	1 (1.47, 9.66)				2.12 (1.11, 4.06)	2.23 (1.05, 4.76)	2.32 (1.14, 4.73)	
Amoxicillin	1.23 (0.76, 1.99)	1.21 (0.73, 1.99)				0.83 (0.52, 1.33)	0.82 (0.5, 1.34)			1.35 (0.49, 2.18)	1.37 (0.83, 2.25)					1.01 (0.36, 2.83)						
Amphetamine										1.79 (0.24, 13.6)	2.12 (0.14, 32.8)											
Anastrozole						0.97 (0.19, 4.82)				1.02 (0.2, 5.15)												
Aripiprazole	1.78 (0.44, 7.09)	0.98 (0.10, 5.11)				1.8 (0.43, 7.47)	1.69 (0.27, 6.01)	2.13 (0.75, 4.15)		1.19 (0.49, 2.86)	1.8 (0.65, 5)	0.96 (0.35, 2.66)						1.71 (0.46, 6.33)				
Aspirin	1.58 (0.53, 4.73)	1.57 (0.45, 6.14)	1.42 (0.38, 5.33)			1.91 (0.75, 4.87)	1.69 (0.55, 5.2)	2.13 (0.74, 4.15)		1.05 (0.49, 2.86)	1.05 (0.65, 5)	1.05 (0.35, 2.66)										
Atenolol	1.12 (0.62, 2.04)	1.52 (0.79, 2.93)	0.97 (0.51, 1.87)	1.17 (0.47, 2.94)		0.96 (0.58, 1.59)	1.07 (0.6, 1.89)	0.9 (0.52, 1.56)	0.97 (0.45, 2.11)	1.2 (0.43, 2.39)	1.05 (0.62, 1.8)	1.05 (0.53, 1.77)	1.05 (0.59, 1.89)	1.35 (0.61, 2.98)	1.4 (0.48, 4.03)							
Atorvastatin	1.3 (0.89, 1.92)	1.55 (0.99, 2.44)	1.24 (0.81, 1.9)	0.56 (0.28, 1.1)	2.64 (0.98, 7.1)	0.73 (0.5, 1.05)	0.66 (0.42, 1.04)	0.76 (0.5, 1.13)	0.64 (0.35, 1.16)	1.22 (0.48, 3.12)	1.3 (0.87, 1.93)	1.43 (0.9, 2.27)	1.15 (0.75, 1.79)	1.34 (0.72, 2.49)	1.78 (0.63, 5.04)	2.04 (0.49, 8.53)	3.56 (0.63, 20.09)		1.52 (0.66, 3.53)	1.76 (0.65, 4.79)	1.42 (0.55, 3.72)	1.24 (0.36, 4.23)
Atropine	0.71 (0.23, 2.19)					1.62 (0.57, 4.61)				1.45 (0.56, 3.79)												
Azithromycin	0.7 (0.36, 1.35)	0.69 (0.35, 1.35)				0.65 (0.35, 1.22)	0.64 (0.34, 1.21)			0.82 (0.43, 1.53)	0.86 (0.45, 1.62)											
Baclofen	1.17 (0.32, 4.25)	0.95 (0.2, 4.48)				0.79 (0.23, 2.72)	1.35 (0.32, 5.73)			1.93 (0.46, 8)												
Benazepril	1.02 (0.5, 2.12)	0.81 (0.36, 1.83)	1.58 (0.67, 3.7)	1.32 (0.4, 4.31)		1.01 (0.48, 2.14)	0.67 (0.29, 1.57)	1.88 (0.8, 4.42)	0.8 (0.23, 2.72)	0.32 (0.15, 0.67)	0.23 (0.1, 0.56)	0.58 (0.25, 1.36)	0.43 (0.19, 1.39)					3.69 (0.84, 16.27)	3.66 (0.63, 21.45)	11.78 (1.99, 69.6)		
Benztropine						2.06 (0.42, 9.82)				1.28 (0.19, 8.67)												
Bisoprolol	0.44 (0.12, 1.65)					6.75 (1.59, 28.67)				1.81 (0.19, 8.67)	1.74 (0.54, 5.62)	3 (0.89, 10.03)										
Bumetanide	3.64 (1.32, 10.04)	3.8 (1.14, 12.63)	6.54 (1.94, 22.05)			2.15 (0.75, 6.17)	1.78 (0.52, 6.14)	4.28 (1.21, 15.11)		1.81 (0.57, 4.87)	1.74 (0.54, 5.62)	3 (0.89, 10.03)										
Bupropion	2.63 (1.07, 6.47)	2.62 (0.8, 8.59)	3.18 (1.17, 8.64)			1.67 (0.67, 4.14)	2.5 (0.82, 7.64)	1.01 (0.35, 2.89)	3.53 (0.97, 12.79)	1.22 (0.47, 3.18)	1.72 (0.52, 5.69)	0.96 (0.32, 2.88)	1.84 (0.45, 7.52)									
Buspirone	5.53 (1.75, 17.42)	4.73 (1.18, 19)	8.69 (2.41, 31.21)			2.48 (0.8, 7.73)	1.98 (0.45, 8.7)	1.93 (0.5, 7.44)		0.34 (0.12, 1)	0.21 (0.06, 0.77)	0.21 (0.66, 8.41)	0.56 (0.17, 11.92)	1.85 (0.42, 8.13)								
Captopril	2.81 (0.9, 8.77)	3.34 (0.05, 13.17)	3.65 (0.94, 14.17)			0.98 (0.37, 2.64)	1.18 (0.32, 4.4)	1.2 (0.37, 3.93)	0.51 (0.12, 2.09)	2.55 (0.93, 6.98)	2.36 (0.66, 8.41)	1.85 (0.17, 11.92)										
Carbamazepine	0.99 (0.15, 6.49)	0.89 (0.07, 11.74)				0.9 (0.19, 4.17)				1.56 (0.12, 2.35)		0.56 (0.09, 3.35)										
Carbidopa	1.9 (0.52, 6.93)	2.77 (0.63, 12.21)				0.93 (0.28, 3.04)	0.57 (0.13, 2.55)	1.25 (0.32, 4.92)		0.57 (0.2, 1.64)	0.71 (0.2, 2.53)	0.53 (0.15, 1.82)										
Carisoprodol	0.35 (0.09, 1.45)					0.73 (0.21, 2.49)	1.39 (0.33, 1)	1.39 (0.28, 4.98)		0.34 (0.17, 2.71)	0.68 (0.2, 4.73)	0.21 (0.18, 5.61)										
Carvedilol	0.96 (0.61, 1.51)	0.92 (0.56, 1.53)	1.11 (0.68, 1.81)	0.35 (0.17, 0.75)	4.46 (1.53, 13.01)	0.94 (0.61, 1.45)	0.83 (0.51, 1.35)	1.05 (0.65, 1.7)	1.08 (0.55, 2.12)	2.71 (0.89, 8.26)	1.11 (0.69, 1.78)	1.08 (0.64, 1.82)	0.76 (0.68, 1.92)	8.35 (0.37, 1.55)	0.77 (0.26, 2.22)	0.78 (0.23, 2.6)	0.86 (0.24, 3.15)	0.27 (0.14, 0.55)	0.27 (0.12, 0.62)	0.3 (0.14, 0.65)		
Celecoxib	1.41 (0.54, 3.66)	2.12 (0.63, 7.11)	1.21 (0.41, 3.59)			3.37 (1.33, 8.57)	4.13 (1.24, 13.79)	3.15 (1.06, 9.31)		0.95 (0.39, 2.3)	0.95 (0.27, 3.32)	0.95 (0.35, 2.58)										
Cephalexin	1.06 (0.62, 2.18)	0.96 (0.55, 1.65)				0.62 (0.36, 1.05)	0.58 (0.33, 1)	0.58 (0.28, 0.9)		0.56 (0.32, 0.99)	0.5 (0.28, 0.9)	0.5 (0.28, 0.9)										
Cetirizine	0.5 (0.12, 2.2)	0.25 (0.04, 1.48)				0.43 (0.11, 1.67)	0.26 (0.05, 1.38)			0.3 (0.08, 1.18)	0.22 (0.04, 1.12)											
Chlorthalidone	0.52 (0.17, 1.58)					0.68 (0.18, 2.6)				1.97 (0.44, 8.79)												
Cholestyramine	1.51 (0.44, 5.11)					1.62 (0.44, 6.04)				1.39 (0.31, 6.16)												
Cilostazol	2.03 (0.71, 5.79)	1.88 (0.44, 7.95)	2.07 (0.61, 7.05)			3.52 (1.16, 10.75)	4.04 (0.94, 17.43)	2.92 (0.8, 10.76)		0.76 (0.26, 2.25)	0.75 (0.2, 2.77)							15.62 (3.91, 62.31)				
Ciprofloxacin	0.83 (0.55, 1.26)	0.8 (0.36, 1.32)				0.93 (0.39, 1.17)	0.87 (0.39, 1.22)	0.81 (0.29, 1.11)		0.93 (0.44, 1.5)	0.83 (0.44, 1.57)							0.76 (0.26, 2.18)				
Citalopram	0.88 (0.48, 1.63)	0.81 (0.38, 1.75)	0.67 (0.33, 1.35)	3.07 (1.16, 8.09)		0.95 (0.5, 1.81)	1 (0.46, 2.17)	0.88 (0.43, 1.82)		0.77 (0.41, 1.44)	0.87 (0.39, 1.85)	0.77 (0.35, 1.41)		0.77 (0.27, 2.2)								
Clavulanate	0.59 (0.32, 1.11)	0.62 (0.32, 1.22)				0.68 (0.39, 1.17)	0.69 (0.39, 1.22)	0.69 (0.29, 1.11)		0.81 (0.44, 1.5)	0.83 (0.44, 1.57)											
Clindamycin	1.39 (0.46, 4.42)	1.74 (0.52, 5.78)				1.99 (0.75, 5.3)	2.48 (0.87, 7.07)	1.24 (0.32, 4.93)		1.47 (0.54, 3.95)	1.62 (0.55, 4.74)											
Clonazepam	0.82 (0.29, 2.32)	0.72 (0.23, 2.28)	1.05 (0.31, 3.63)			0.28 (0.09, 0.83)	0.23 (0.07, 0.78)	0.27 (0.07, 1.02)		0.83 (0.25, 2.77)	1											

eTable 4. Semi-Bayes and metformin adjusted rate ratios (RRSBM).xlsx

eTable 4. Semi-Bayes and metformin adjusted rate ratios (RRSBM).xlsx

Oxycodone	1.84 (1.17, 2.89)	1.9 (1.16, 5.11)	1.74 (0.97, 7.13)	1.6 (0.47, 5.47)	1.15 (0.73, 1.82)	1.16 (0.7, 1.93)	1.15 (0.63, 2.08)	1.47 (0.96, 2.24)	1.61 (1.03, 2.53)	0.94 (0.5, 1.76)	3.38 (1, 11.38)		0.55 (0.19, 1.56)	0.59 (0.14, 2.59)				
Pantoprazole	0.94 (0.61, 1.47)	1.18 (0.72, 2.94)	0.82 (0.49, 1.38)	0.36 (0.13, 1.01)	0.82 (0.53, 1.27)	0.85 (0.51, 1.41)	0.92 (0.55, 1.54)	0.31 (0.12, 0.76)	0.94 (0.59, 1.49)	1.05 (0.62, 1.79)	1 (0.59, 1.69)	0.5 (0.2, 1.24)	0.7 (0.25, 1.96)	0.36 (0.11, 1.18)				
Paroxetine	0.45 (0.19, 1.03)	0.47 (0.18, 1.2)	0.39 (0.15, 0.98)		0.31 (0.14, 0.67)	0.27 (0.11, 0.68)	0.3 (0.13, 0.71)	0.57 (0.17, 1.89)	0.59 (0.26, 1.31)	0.63 (0.26, 1.56)	0.42 (0.17, 1.03)	1.01 (0.3, 3.4)	0.7 (0.25, 1.96)	0.46 (0.16, 0.82)				
Pentoxifylline	0.57 (0.1, 3.07)				1.88 (0.33, 10.69)			0.59 (0.11, 3.15)		2.34 (0.33, 16.6)			0.89 (0.2, 3.91)	1.21 (0.19, 7.77)				
Perphenazine																		
Phenytoin	1.63 (0.37, 7.06)				0.61 (0.18, 2.06)		0.44 (0.08, 2.34)	0.67 (0.19, 2.37)										
Ploglitzazone	1.67 (1.05, 2.65)	1.8 (1.06, 3.06)	1.54 (0.92, 2.58)	1.12 (0.5, 2.5)	0.8 (0.52, 1.23)	0.8 (0.48, 1.33)	0.75 (0.46, 1.21)	1 (0.5, 2.03)	1.41 (0.89, 2.23)	1.35 (0.79, 2.3)	1.31 (0.79, 2.18)	1.85 (0.89, 3.86)	0.28 (0.1, 0.76)	0.38 (0.11, 1.34)				
Pramipexole	1.78 (0.32, 9.81)		3.48 (0.41, 29.37)		1.09 (0.28, 4.19)	0.88 (0.17, 4.56)	1.36 (0.28, 6.55)		1.23 (0.24, 6.32)					1.32 (0.53, 3.29)	1.08 (0.35, 3.35)			
Pravastatin	0.43 (0.24, 0.76)	0.53 (0.26, 6.09)	0.49 (0.25, 5.94)	0.28 (0.12, 0.66)	1.08 (0.57, 2.06)	1.24 (0.56, 2.42)	1.17 (0.22, 1.7)	1.26 (0.35, 4.57)	0.95 (0.49, 1.84)	0.91 (0.4, 2.06)	1.03 (0.49, 2.19)	0.75 (0.29, 1.99)	1.41 (0.39, 5.07)	0.58 (0.19, 1.72)	1.58 (0.42, 5.93)			
Prednisone	0.93 (0.59, 1.48)	0.93 (0.57, 1.52)	1.02 (0.56, 1.86)	0.48 (0.15, 1.56)	1.38 (0.87, 2.21)	1.18 (0.72, 1.93)	1.95 (1.06, 3.59)	0.63 (0.21, 1.89)	1.19 (0.74, 1.9)	1.15 (0.71, 1.88)	1.29 (0.69, 2.39)		1.47 (0.43, 5.03)	2.83 (0.67, 11.9)	1.51 (0.54, 4.26)			
Pregabalin	0.72 (0.32, 1.6)	0.75 (0.3, 1.89)	0.8 (0.33, 1.97)		1.71 (0.79, 3.7)		2.51 (1.06, 5.99)		3.06 (1.14, 8.22)	1.57 (0.45, 5.47)	5.04 (1.62, 15.61)				1.62 (0.52, 5.06)			
Primidone					0.55 (0.09, 3.41)		0.31 (0.03, 3.61)		1.23 (0.18, 8.32)									
Prochlorperazine	1.62 (0.51, 5.08)		2.94 (1, 8.6)					1.66 (0.5, 5.56)										
Promethazine	0.55 (0.28, 1.05)	0.49 (0.24, 2.1)			0.48 (0.26, 1.92)	0.39 (0.19, 0.79)		0.88 (0.48, 1.61)	0.91 (0.49, 1.7)									
Propoxyphene	2.03 (0.5, 4.44)	1.45 (0.94, 6.31)			1.58 (0.71, 3.49)	2.37 (0.35, 5.9)	0.54 (0.16, 1.84)		1.77 (0.8, 3.91)	2.17 (0.95, 5.46)	1.18 (0.37, 7.76)				4.43 (1.27, 15.5)	6.64 (1.6, 27.54)		
Propranolol	0.54 (0.14, 2.07)	0.43 (0.09, 2.04)	0.32 (0.01, 1.5)		0.8 (0.21, 2.99)	0.37 (0.08, 1.79)	0.76 (0.17, 3.25)	2.32 (0.41, 13.15)	0.36 (0.1, 1.35)	0.25 (0.05, 1.15)	0.29 (0.05, 1.27)							
Quetiapine	2 (0.88, 4.51)	2.06 (0.7, 6.04)	1.57 (0.61, 4.04)		3.64 (0.62, 21.5)	2.16 (0.99, 4.7)	2.81 (1.06, 7.41)	1.48 (0.6, 3.68)	2.26 (0.66, 3.11)	1.43 (0.69, 4.6)	1.02 (0.41, 2.59)		0.97 (0.17, 5.48)	1.99 (0.18, 22.37)				
Quinapril	0.34 (0.13, 0.9)	0.28 (0.08, 0.98)	0.43 (0.14, 1.35)		1.2 (0.51, 2.85)	0.87 (0.3, 2.49)	1.62 (0.62, 4.26)		1.14 (0.48, 2.73)	1.11 (0.4, 3.1)	1.43 (0.54, 3.78)							
Rabeprazole	0.67 (0.17, 2.7)	0.44 (0.08, 2.51)			2.46 (0.68, 8.91)	1.19 (0.23, 6.1)					1.28 (0.19, 8.86)							
Raloxifene	0.47 (0.07, 3.24)		1.59 (0.21, 26.26)		0.84 (0.12, 5.65)		0.59 (0.04, 8.66)											
Ramipril	0.96 (0.43, 2.16)	1.16 (0.45, 1.96)	0.85 (0.35, 2.08)	0.53 (0.13, 2.08)	1.29 (1.7, 6.59)	3.73 (14.1, 9.86)	2.17 (8.6, 5.47)	3.14 (5.01, 10.81)	0.81 (0.35, 1.88)	0.76 (0.28, 2.1)	0.76 (0.31, 1.93)	1.71 (0.43, 6.88)		4.49 (1.11, 18.11)	7.91 (1.32, 47.35)			
Ranitidine	0.94 (0.51, 1.78)	0.73 (0.31, 1.75)	0.87 (0.42, 1.81)	1.38 (1.05, 10.96)	1.07 (0.24, 4.8)	1.01 (0.52, 1.95)	1.48 (0.69, 3.2)	0.71 (0.33, 1.53)	0.39 (0.08, 1.83)	0.63 (0.36, 1.1)	0.7 (0.34, 1.43)	0.64 (0.34, 1.2)	0.57 (0.18, 1.86)					
Ranolazine	0.88 (0.19, 4.17)							0.91 (0.16, 5.07)										
Risedronate	3.42 (0.95, 12.24)	5.55 (1.1, 27.99)			1.29 (0.23, 4.95)		0.78 (0.15, 4.14)		0.65 (0.17, 2.47)		0.51 (0.12, 1.54)				4.49 (1.11, 18.11)	7.91 (1.32, 47.35)		
Risperidone	0.32 (0.13, 0.75)	0.27 (0.1, 0.74)	0.3 (0.11, 0.79)		0.55 (0.22, 1.43)	0.31 (0.1, 1.04)	0.56 (0.19, 1.63)		1.14 (0.41, 3.17)	0.67 (0.19, 2.41)	1.41 (0.45, 4.48)							
Rivastigmine	1.11 (0.18, 7.05)				1.53 (0.19, 12.56)				1.02 (0.14, 7.52)									
Rofecoxib								1.46 (0.48, 4.49)	1.67 (0.41, 6.72)									
Ropinirole	1.54 (0.41, 5.83)	1.94 (0.42, 9.08)	1.19 (0.25, 5.6)		0.84 (0.25, 2.83)		0.66 (0.15, 3.01)		1.4 (0.4, 4.86)	1.58 (0.38, 6.63)	1 (0.26, 4.69)				1.32 (0.36, 4.76)	0.64 (0.12, 3.28)		
Rosiglitazone	0.84 (0.45, 1.57)		0.74 (0.34, 1.58)		0.76 (0.46, 1.77)	0.67 (0.38, 1.21)	0.57 (0.39, 1.54)	0.97 (0.31, 2.99)	1.13 (0.62, 2.04)	1.32 (0.67, 2.59)	0.86 (0.45, 1.65)	2.99 (0.99, 9.09)				3.18 (0.84, 12.07)	5.68 (0.97, 33.29)	
Rosuvastatin	0.91 (0.43, 1.94)	0.75 (0.29, 1.97)	0.97 (0.42, 2.24)	0.64 (0.2, 2.02)	1.66 (0.73, 3.76)	1.4 (0.68, 3.87)	1.51 (0.59, 3.84)	3.7 (1.17, 11.68)	0.68 (0.3, 1.5)	0.55 (0.25, 1.81)	1.13 (0.23, 1.36)	0.57 (0.37, 3.46)						
Saxagliptin	1.63 (0.47, 5.67)		1.35 (0.29, 6.33)					2.02 (0.47, 8.74)		2.95 (0.51, 17.07)								
Sertraline	1.64 (0.03, 2.97)	1.3 (0.64, 6.64)	1.88 (0.98, 3.61)	2.95 (1.03, 8.44)	1.12 (0.6, 2.09)	1.34 (0.65, 2.75)	0.91 (0.45, 1.83)	1.12 (0.37, 3.37)	1.34 (0.72, 2.48)	1.22 (0.59, 2.5)	1.29 (0.64, 2.58)	2.47 (0.87, 7.04)		1.43 (0.27, 7.58)	1.31 (0.17, 18.88)			
Simvastatin	0.9 (0.66, 1.22)	0.83 (0.58, 2.18)	0.88 (0.63, 3.24)	1.16 (0.69, 1.97)	2.22 (1.1, 4.48)	0.98 (0.68, 1.32)	0.94 (0.68, 1.3)	1.71 (0.68, 1.27)	1.44 (0.73, 2.73)	1.22 (0.73, 2.86)	1.06 (0.82, 1.65)	2.99 (0.98, 2.81)	2.11 (1.91, 8.01)	2.33 (0.61, 7.35)	3.68 (0.55, 9.93)	4.67 (0.87, 15.65)	1.79 (0.62, 22.5)	
Sitagliptin	0.8 (0.47, 1.35)	0.74 (0.4, 1.37)	0.62 (0.34, 1.11)	2.29 (0.84, 6.24)	7.08 (1.97, 25.37)	0.61 (0.35, 1.06)	0.64 (0.34, 1.21)	0.48 (0.26, 0.9)	1.59 (0.55, 4.63)	1.28 (0.78, 3.18)	0.8 (0.39, 1.65)	2.95 (4.2, 66.72)	0.44 (0.13, 1.48)	4.68 (0.41, 52.86)				
Solifenacin	0.46 (0.14, 1.52)		0.3 (0.07, 1.25)		0.35 (0.09, 1.31)			0.42 (0.09, 1.92)										
Sotalol	1.24 (0.29, 5.31)		1.25 (0.22, 7.13)			0.33 (0.07, 1.64)			0.72 (0.18, 2.94)									
Spironolactone	1.36 (0.81, 2.3)				0.73 (0.42, 1.26)				1.41 (0.79, 2.5)									
Sucralfate	4.27 (1.15, 15.89)	8.83 (1.85, 42.13)	3.43 (0.7, 16.7)					4.95 (1.89, 13.02)	6.6 (2.08, 20.89)	4.28 (1.35, 13.63)					2.42 (0.8, 7.36)			
Sulfamethoxazole	4.14 (2.54, 6.75)				4.3 (2.71, 6.81)				1.98 (1.24, 3.16)									
Sulindac					1.03 (0.18, 6.03)				2.21 (0.32, 15.14)									
Tamoxifen	1.66 (0.2, 14.04)	2.49 (0.14, 45.25)							1.31 (0.37, 4.6)									
Tamsulosin	1.01 (0.52, 1.96)	1.06 (0.49, 2.29)	0.95 (0.45, 5.02)		1.98 (1, 3.91)	2.01 (0.91, 4.42)	1.77 (0.82, 3.84)	3.96 (1.32, 11.85)	1.91 (0.97, 3.74)	1.9 (0.89, 4.09)	1.71 (0.83, 3.65)	2.31 (0.68, 7.81)		1.8 (0.45, 7.28)	1.88 (0.34, 10.25)		5.34 (2.06, 13.86)	3.5 (1.1, 11.06)
Telmisartan	0.79 (0.14, 4.52)		1.14 (0.12, 11.31)			1.44 (0.32, 6.5)		1.2 (0.18, 7.95)		0.64 (0.14, 2.89)	0.98 (0.14, 6.69)				0.36 (0.16, 8.02)	0.46 (0.17, 12.29)		
Temazepam	2.23 (0.71, 6.97)		2.8 (0.74, 10.49)			0.34 (0.1, 1.15)			0.44 (0.15, 1.26)		0.39 (0.12, 1.3)							
Terazosin	1.01 (0.26, 4.01)	0.52 (0.09, 2.89)			0.78 (0.26, 2.33)		0.68 (0.18, 2.54)		4.15 (1.21, 14.24)		3.74 (0.85, 16.52)							
Tetracycline									1.31 (0.37, 4.6)									
Theophylline	0.27 (0.07, 1.07)	0.14 (0.03, 0.78)	0.26 (0.05, 1.43)		1.17 (0.25, 5.52)	1.07 (0.16, 7.09)	1.11 (0.17, 7.48)		0.76 (0.19, 3.11)		1.27 (0.23, 6.97)							

eTable 4. Semi-Bayes and metformin adjusted rate ratios (RRSBM).xlsx



**eTable 5.** Correlation between area under concentration-time curve ratios (AUCRs) and semi-Bayes adjusted rate ratios (RR<sub>SB</sub>): Pearson's correlation coefficients and the number of precipitants for which both AUCR and RR<sub>SB</sub> were estimated

Risk Period	Glipizide	Glimepiride	Glyburide	Nateglinide	Repaglinide
Overall	0.08 n=96	-0.02 n=94	0.29 n=100	0.17 n=24	-0.14 n=38
0 - 10 Days	0.1 n=80	-0.01 n=76	0.28 n=76	0.1 n=11	-0.14 n=22
11 - 60 Days	0.12 n=75	-0.05 n=73	0.3 n=79	0.21 n=13	-0.19 n=16
61 - 120 Days	0.15 n=43	-0.01 n=39	-0.02 n=40	- 0	- 0
>120 Days	-0.01 n=31	0.12 n=33	-0.08 n=27	- 0	- 0

**eTable 6.** Correlation between area under concentration-time curve ratio (AUCRs) and semi-Bayes and metformin adjusted rate ratios (RR<sub>SBM</sub>): Pearson's correlation coefficients and the number of precipitants for which both AUCR and RR<sub>SB</sub> were estimated

Risk Period	Glimepiride	Glipizide	Glyburide	Nateglinide	Repaglinide
Overall	-0.05 n=86	0.08 n=86	0.02 n=88	-0.06 n=24	0.01 n=38
0 - 10 Days	-0.04 n=72	0.21 n=73	0.07 n=67	-0.18 n=11	0.09 n=22
11 - 60 Days	0.02 n=67	0.3 n=67	0.01 n=68	0.08 n=12	-0.11 n=16
61 - 120 Days	0.34 n=31	0.7 n=31	-0.07 n=32	- 0	- 0
>120 Days	-0.19 n=17	0.07 n=18	0 n=14	- 0	- 0

## Model Specification

### The analysis of the SCCS design

Cases for a given object drug were identified as described in the main text. The observation time for a case consisted of days during which the case had an active prescription for the object drug. For each precipitant, the observation time was categorized as exposed or unexposed with regard to the exposure to the precipitant. The same model, as detailed below, was fit separately for each of the 400 precipitants.

To set up notation, let  $i$  ( $i = 1, \dots, N$ ) index eligible cases for a given object drug. Let  $\tau_i$  denote the total number of days during person  $i$ 's observation time, with  $(i, d)$  being the  $d$ th day of observation. When there were multiple claims for serious hypoglycemia for the same person on the same day, we considered the claims as one event. Let  $y_{id}$  indicate occurrence of the event, where  $y_{id} = 1$  if person  $i$  had an event on day  $(i, d)$ , and 0 otherwise. Let  $x_{id}$  indicate the exposure to a given precipitant, where  $x_{id} = 1$  if person  $i$  had an active prescription for the precipitant on  $(i, d)$ , and 0 otherwise.

In the primary analysis, we estimated the overall rate ratios (RRs) during the entire exposed vs. unexposed observation time. Under the SCCS model, serious hypoglycemia events arise within individuals as a non-homogeneous Poisson process. We assumed that the underlying incidence rate is modulated by the exposure to the precipitant. The event rate for person  $i$  on day  $d$  is

$$\lambda_{id} = e^{\phi_i + \beta x_{id}}$$

Where  $e^{\phi_i}$  represents person  $i$ 's baseline event rate and is constant during the observation time, and  $e^{\beta x_{id}}$  represents the multiplicative effect of the precipitant exposure on the baseline incidence rate. The likelihood for person  $i$  is the joint probability of the observed sequence of events conditional on the observed exposures during the observation time.

$$L_i = P(y_{i1}, \dots, y_{i\tau_i} | x_{i1}, \dots, x_{i\tau_i}) = P(\mathbf{y}_i | \mathbf{X}_i) = \prod_{d=1}^{\tau_i} P(y_{id} | x_{id}) = \prod_{d=1}^{\tau_i} \frac{e^{-\lambda_{id}} \lambda_{id}^{y_{id}}}{y_{id}!}$$

Let  $n_i$  denote the total number of events that person  $i$  had over the entire observation time, then  $n_i = \sum_{d=1}^{\tau_i} y_{id}$ .  $n_i$  is distributed as a Poisson variable with incidence rate equal to the cumulative incidence over the observation time.

$$n_i | \mathbf{X}_i \sim \text{Poisson} \left( \sum_{d=1}^{\tau_i} \lambda_{id} = e^{\phi_i} \sum_{d=1}^{\tau_i} e^{\beta x_{id}} \right)$$

Under the SCCS model, the contribution of person  $i$  to the full likelihood is the joint probability conditional on  $n_i$ . Assuming that persons are independent, the full likelihood has the following form.

$$L = \prod_{i=1}^N \frac{P(\mathbf{y}_i | \mathbf{X}_i)}{P(n_i | \mathbf{X}_i)} \propto \prod_{i=1}^N \prod_{d=1}^{\tau_i} \left( \frac{e^{\beta x_{id}}}{\sum_d e^{\beta x_{id}}} \right)^{y_{id}}$$

This model was fit using Poisson regression with a log link function to estimate the parameter  $\beta$ .

In the secondary analysis, we categorized exposed observation time into four risk periods and examined the RR for serious hypoglycemia during each risk period. Let  $t_i$  ( $1 \leq t_i \leq \tau_i$ ) denote the number of days during a prescription episode for the precipitant. Note that there may be multiple such prescription

episodes during the exposed observation time. Let  $j$  ( $j = 1, \dots, 4$ ) index the four risk period, where  $j = 1$  when  $0 < t_i \leq 30$ ,  $j = 2$  when  $30 < t_i \leq 60$ ,  $j = 3$  when  $60 < t_i \leq 120$ , and  $j = 4$  when  $t_i > 120$ . Let  $x_{ijd}$  indicate the exposure to the precipitant during the  $j$ th risk period on day  $d$ , where  $x_{ijd} = 1$  if person  $i$  is exposed and 0 otherwise. Slightly different from that in the primary analysis, the event rate for person  $i$  during risk period  $j$  on day  $d$  is

$$\lambda_{ijd} = e^{\phi_i + \beta_j x_{ijd}}$$

where  $\beta_j$  is the effect of precipitant exposure on the event rate during the  $j$ th risk period. The distribution of  $n_i$  and the full conditional likelihood are as follows.

$$n_i | \mathbf{X}_i' \sim \text{Poisson} \left( \sum_{j=1}^4 \sum_{d=1}^{\tau_i} \lambda_{id} = e^{\phi_i} \sum_{j=1}^4 \sum_{d=1}^{\tau_i} e^{\beta_j x_{ijd}} \right)$$

$$L = \prod_{i=1}^N \frac{P(\mathbf{y}_i | \mathbf{X}_i')}{P(n_i | \mathbf{X}_i')} \propto \prod_{i=1}^N \prod_{j=1}^4 \prod_{d=1}^{\tau_i} \left( \frac{e^{\beta_j x_{ijd}}}{\sum_j \sum_d e^{\beta_j x_{ijd}}} \right)^{y_{ijd}}$$

where  $\mathbf{X}_i'$  is a  $\tau_i \times 4$  matrix indicating the observed precipitant exposure for person  $i$  with each column representing the exposure during a risk period. The parameter vector  $\boldsymbol{\beta}' = (\beta_1, \beta_2, \beta_3, \beta_4)$  was estimated using Poisson regression similarly.

### Semi-Bayes adjustment

In the primary analysis, a second-stage linear model was fit for each object drug to adjust for multiple estimation. Let  $\hat{\boldsymbol{\beta}}$  be a vector of  $\hat{\beta}$  estimates for the 400 precipitants from Poisson regression described above. The following model was used for linear regression.

$$\hat{\boldsymbol{\beta}} = \boldsymbol{\pi} + \boldsymbol{\varepsilon}$$

$$\boldsymbol{\varepsilon} \sim N(\mathbf{0}, \tau^2 \mathbf{T})$$

Where  $\boldsymbol{\pi}$  is a 400-element vector of coefficients representing the true effects of precipitants on the event rate, and  $\boldsymbol{\varepsilon}$  is a 400-element vector of error terms.  $\tau^2 \mathbf{T}$  is a  $400 \times 400$  covariance matrix. We assumed that the precipitants are independent, thus  $\mathbf{T}$  is a diagonal matrix.  $\tau$  is a parameter used to control the strength of the shrinkage. We set  $\tau$  to 0.67, corresponding to the assumption that at least 95% of  $\boldsymbol{\pi}$  elements would lie within a 25-fold range of each other (e.g. 0.2 - 5). The elements of  $\boldsymbol{\pi}$  estimate were then exponentiated to obtain the overall RRs.

In the secondary analysis, the same second-stage model was run for each object drug for semi-Bayes adjustment.  $\hat{\boldsymbol{\beta}}$  is now a  $400 \times 4$  matrix of parameter estimates from Poisson regression, with each row representing a precipitant and each column representing a risk period. The dimensions of  $\boldsymbol{\pi}$ ,  $\boldsymbol{\varepsilon}$  and  $\mathbf{T}$  change accordingly. We set  $\tau$  to 1.38, assuming that at least 95% of  $\boldsymbol{\pi}$  elements would fall within a 100-fold range of each other (e.g. 0.1 - 10). A larger variation was assumed for true RRs of the risk periods because a) the rate of hypoglycemia following a DDI would change over time; and b) there was less observation time during the risk periods. The elements of  $\boldsymbol{\pi}$  estimate were then exponentiated to obtain the RRs for the risk periods.

# Programming code

## SAS programming code to estimate unadjusted overall rate ratios

```
%include '/project/shennessy/DDID/programs/lib_name.sas';
%include '/project/shennessy/DDID/programs/SCCS programs/element.sas';
%include '/project/shennessy/DDID/programs/SCCS_programs/sccts.sas';
%include '/project/shennessy/DDID/programs/SCCS_programs/poisreg.sas';
options ps=48 ls=122 nosyntaxcheck;

proc format;
  value yn 0='n'
        1='Y';
run;

data cohort_day_by_day;
  set analysis.glipizide day by day;
  format dr_: hypoglycemia_event yn.;

  by patid num_episode date;
  if first.num_episode then patient_episode+1;

  int=1;
run;

data code;
  set code.Precipitant(keep=order drug_name);
  drugname=scan(drug_name,1,' ');

  ** Make acetaminophen come first so that we are assured
     of a 2x2 table;
  if drugname='acetaminophen' then order=-9;
run;
proc sort data=code nodupkey;
  by order drug_name;
run;
data _null_;
  set code end = last;
  call symput(trim(left('drug_name'))||trim(left(_n_)),trim(left(drugname))) ;
  if last then call symput ('last',_n_);
run;

%macro relrisk;
%DO I=1 %TO &last;

  proc freq data=cohort day by day order=formatted;
    ods output CrossTabFreqs=CrossTabFreqs(where=(_TYPE_='11') keep=_TYPE_ dr_:
hypoglycemia_event Frequency)
      RelativeRisks=RelativeRisks(where=(Statistic='Relative Risk (Column 1)')
keep=Statistic Value LowerCL UpperCL);
    tables dr_&&drug_name&i * hypoglycemia_event / relrisk;
  run;

  data results(drop=_TYPE_ Statistic hypoglycemia_event dr_&&drug_name&i runit);
    length Precipitant $32;
    merge CrossTabFreqs(where=(dr_&&drug_name&i=0 and hypoglycemia_event=0)
rename=(Frequency=Unexposed_NoHypo))
      CrossTabFreqs(where=(dr_&&drug_name&i=0 and hypoglycemia_event=1)
rename=(Frequency=Unexposed_Hypo))
      CrossTabFreqs(where=(dr_&&drug_name&i=1 and hypoglycemia_event=0)
rename=(Frequency=Exposed_NoHypo))
      CrossTabFreqs(where=(dr_&&drug_name&i=1 and hypoglycemia_event=1)
rename=(Frequency=Exposed_Hypo))
      RelativeRisks(rename=(Value=RR LowerCL=Lower_RR UpperCL=Upper_RR));
    Precipitant="dr_&&drug_name&i";
  if Exposed_NoHypo=. and Exposed_Hypo=. then do;
```

```

      RR=.;
      Lower_RR=.;
      Upper_RR=.;
end;

runit=0;
if Unexposed_NoHypo ge 5 and Unexposed_Hypo ge 5 and Exposed_NoHypo ge 5 and Exposed_Hypo
ge 5 then runit=1;
call symput('runmodel', runit);
Beta=.;
StdErr=.;

run;

%if &runmodel=1 %then %do;
%poisreg(data=cohort day by day,
y=hypoglycemia_event,
covar=int dr_&&drug_name&i,
class=,
offset=,
elim=patient_episode,
prntyn=Y,
outdata=SCCSresults,
title="Glipizide: dr_&&drug_name&i");
data SCCSresults;
set SCCSresults(keep=params Estimate StErr);
where lowercase(params)="dr_&&drug_name&i";
rename Estimate=Beta;
rename StErr=StdErr;
run;

data results;
merge results SCCSresults(drop=params);
run;
%end;

proc append base=allresults data=results;
run;
%END;
%mend relrisk;

%relrisk;

*** Output to Excel;
proc sort data=allresults;
by Precipitant;
run;
data outresults;
set allresults(drop=Lower_RR Upper_RR);
Var = StdErr*StdErr;
run;
proc export data=outresults

outfile="/project/shennessy/DDID/output/analysis/glipizide/Glipizide_unadjRR_SCCS.csv"
dbms=dlm replace;
delimiter=",";
run;
proc export data=outresults(keep=Precipitant Beta Var where=(Beta ne .))

outfile="/project/shennessy/DDID/output/analysis/glipizide/Glipizide_BetaVar_SCCS.csv"
dbms=dlm replace;
delimiter=" ";
run;

proc print data=allresults;
run;

```

## SAS programming code to estimate unadjusted rate ratios for risk periods

```
%include '/project/shennessy/DDID/programs/lib_name.sas';
%include '/project/shennessy/DDID/programs/SCCS_programs/element.sas';
%include '/project/shennessy/DDID/programs/SCCS_programs/sccts.sas';
%include '/project/shennessy/DDID/programs/SCCS_programs/poisreg.sas';
options ps=48 ls=122 nosyntaxcheck;

proc format;
  value yn 0='n'
    1='Y';
  value riskper 0='0=unexposed'
    1='1= 0-10 dys'
    2='2= 11-60 dys'
    3='3= 61-120 dys'
    4='4= 121+ dys';
run;

data cohort_day_by_day;
  set analysis.glipizide_day_by_day;
  format dr_: hypoglycemia_event yn.;

  by patid num_episode date;
  if first.num_episode then patient_episode+1;

  int=1;
run;

data code;
  set code.Precipitant(keep=order drug_name);
  drugname=scan(drug_name,1,' ');

  ** Make acetaminophen come first so that we are assured
     of a 2x2 table;
  if drugname='acetaminophen' then order=-9;
run;
proc sort data=code nodupkey;
  by order drug_name;
run;
data _null_;
  set code end = last;
  call symput(trim(left('drug_name'))||trim(left(_n_)),trim(left(drugname))) ;
  if last then call symput ('last',_n_);
run;

%macro concomitant;
data cohort_day_by_day;
  set cohort_day_by_day;
  by patid num_episode date;

%do j=1 %to &last;
  if first.num_episode then condys_&&drug_name&j = dr_&&drug_name&j;
  else do;
    if dr_&&drug_name&j=1 then condys_&&drug_name&j+1;
    else if dr_&&drug_name&j=0 then condys_&&drug_name&j=0;
  end;

  dys0to10_&&drug_name&j=0;
  dys11to60_&&drug_name&j=0;
  dys61to120_&&drug_name&j=0;
  dys121plus_&&drug_name&j=0;
  riskperiod_&&drug_name&j=dr_&&drug_name&j;
  if dr_&&drug_name&j=1 then do;
    if 1 le condys_&&drug_name&j lt 11 then do;
      riskperiod_&&drug_name&j=1;
      dys0to10_&&drug_name&j=1;
    end;
    else if 11 le condys_&&drug_name&j lt 61 then do;
```

```

riskperiod_&&drug_name&j=2;
dys11to60_&&drug_name&j=1;
end;
else if 61 le condys_&&drug_name&j lt 121 then do;
riskperiod_&&drug_name&j=3;
dys61to120_&&drug_name&j=1;
end;
else if 121 le condys_&&drug_name&j then do;
riskperiod_&&drug_name&j=4;
dys121plus_&&drug_name&j=1;
end;
end;
format riskperiod_&&drug_name&j riskper.;

%end;
run;
%mend concomitant;

%concomitant;

%macro relrisk;
%DO I=1 %TO &last;

proc freq data=cohort_day_by_day order=formatted;
ods output CrossTabFreqs=CrossTabFreqs(where=(_TYPE_='11') keep=_TYPE_ riskperiod_:
hypoglycemia_event Frequency);
tables riskperiod_&&drug_name&i * hypoglycemia_event / relrisk;
run;

data results(drop=_TYPE_ hypoglycemia_event riskperiod_&&drug_name&i runit);
length Precipitant $32;
merge CrossTabFreqs(where=(riskperiod_&&drug_name&i=0 and hypoglycemia_event=0)
rename=(Frequency=Unexposed NoHypo)
CrossTabFreqs(where=(riskperiod_&&drug_name&i=0 and hypoglycemia_event=1)
rename=(Frequency=Unexposed_Hypo))
CrossTabFreqs(where=(riskperiod_&&drug_name&i=1 and hypoglycemia_event=0)
rename=(Frequency=Dys0to10_NoHypo))
CrossTabFreqs(where=(riskperiod_&&drug_name&i=1 and hypoglycemia_event=1)
rename=(Frequency=Dys0to10_Hypo))
CrossTabFreqs(where=(riskperiod_&&drug_name&i=2 and hypoglycemia_event=0)
rename=(Frequency=Dys11to60_NoHypo))
CrossTabFreqs(where=(riskperiod_&&drug_name&i=2 and hypoglycemia_event=1)
rename=(Frequency=Dys11to60_Hypo))
CrossTabFreqs(where=(riskperiod_&&drug_name&i=3 and hypoglycemia_event=0)
rename=(Frequency=Dys61to120_NoHypo))
CrossTabFreqs(where=(riskperiod_&&drug_name&i=3 and hypoglycemia_event=1)
rename=(Frequency=Dys61to120_Hypo))
CrossTabFreqs(where=(riskperiod_&&drug_name&i=4 and hypoglycemia_event=0)
rename=(Frequency=Dys121plus_NoHypo))
CrossTabFreqs(where=(riskperiod_&&drug_name&i=4 and hypoglycemia_event=1)
rename=(Frequency=Dys121plus_Hypo));
Precipitant="dr_&&drug_name&i";

dys0to10=0;
dys11to60=0;
dys61to120=0;
dys121plus=0;
if Dys0to10_NoHypo ge 5 and Dys0to10_Hypo ge 5 then dys0to10=1;
if Dys11to60_NoHypo ge 5 and Dys11to60_Hypo ge 5 then dys11to60=1;
if Dys61to120_NoHypo ge 5 and Dys61to120_Hypo ge 5 then dys61to120=1;
if Dys121plus_NoHypo ge 5 and Dys121plus_Hypo ge 5 then dys121plus=1;
call symput('dys0to10', dys0to10);
call symput('dys11to60', dys11to60);
call symput('dys61to120', dys61to120);
call symput('dys121plus', dys121plus);

runit=0;
if dys0to10=1 or dys11to60=1 or dys61to120=1 or dys121plus=1 then runit=1;
call symput('runmodel', runit);
run;

*** Delete the records from the data set in the risk periods having cell counts < 5 (if any);

```

```

data use;
  set cohort_day_by_day;
  %if &dys0to10=0 %then %do;
    if riskperiod_&&drug_name&i=1 then delete;
  %end;
  %if &dys11to60=0 %then %do;
    if riskperiod_&&drug_name&i=2 then delete;
  %end;
  %if &dys61to120=0 %then %do;
    if riskperiod_&&drug_name&i=3 then delete;
  %end;
  %if &dys121plus=0 %then %do;
    if riskperiod_&&drug_name&i=4 then delete;
  %end;
run;

%if &runmodel=1 %then %do;
  %poisreg(data=use,
            y=hypoglycemia_event,
            covar=int
            %if &dys0to10=1 %then %do;
              dys0to10_&&drug_name&i
            %end;
            %if &dys11to60=1 %then %do;
              dys11to60_&&drug_name&i
            %end;
            %if &dys61to120=1 %then %do;
              dys61to120_&&drug_name&i
            %end;
            %if &dys121plus=1 %then %do;
              dys121plus_&&drug_name&i
            %end;;
            class=,
            offset=,
            elim=patient_episode,
            prntyn=Y,
            outdata=SCCSresults,
            title="Glipizide: riskperiod_&&drug_name&i");
data SCCSresults;
  merge SCCSresults(keep=params expest expl1 expul Estimate StErr
                     where=(substr(params,1,8)='DYS0TO10')
                     rename=(expest=Dys0to10_RR expl1=Dys0to10_RR_lower
                           expul=Dys0to10_RR_upper
                           Estimate=Dys0to10_Beta StErr=Dys0to10_StdErr))
                    SCCSresults(keep=params expest expl1 expul Estimate StErr
                               where=(substr(params,1,9)='DYS11TO60')
                               rename=(expest=Dys11to60_RR expl1=Dys11to60_RR_lower
                                       expul=Dys11to60_RR_upper
                                       Estimate=Dys11to60_Beta StErr=Dys11to60_StdErr))
                    SCCSresults(keep=params expest expl1 expul Estimate StErr
                               where=(substr(params,1,10)='DYS61TO120')
                               rename=(expest=Dys61to120_RR expl1=Dys61to120_RR_lower
                                       expul=Dys61to120_RR_upper
                                       Estimate=Dys61to120_Beta StErr=Dys61to120_StdErr))
                    SCCSresults(keep=params expest expl1 expul Estimate StErr
                               where=(substr(params,1,10)='DYS121PLUS')
                               rename=(expest=Dys121plus_RR expl1=Dys121plus_RR_lower
                                       expul=Dys121plus_RR_upper
                                       Estimate=Dys121plus_Beta StErr=Dys121plus_StdErr));
run;

data results;
  merge results SCCSresults(drop=params);
run;
%end;

proc append base=allresults data=results;
run;
%END;
%mend relrisk;

```

```

%relrisk;

*** Output to Excel;
proc sort data=allresults;
  by Precipitant;
run;

proc export data=allresults
  outfile="/project/shennessy/DDID/output/analysis/glipizide/Glipizide_riskperiods.csv"
  dbms=dlm replace;
  delimiter=",";
run;

*** Transpose the Beta and Variance estimates for calculating the Semi-Bayes shrinkage;
data SB;
  length Precipitant $32 RiskPeriod $10;
  set allresults(keep=Precipitant Dys0to10_Beta Dys0to10_StdErr in=in0to10
                 rename=(Dys0to10_Beta=Beta Dys0to10_StdErr=StdErr))
      allresults(keep=Precipitant Dys11to60_Beta Dys11to60_StdErr in=in11to60
                 rename=(Dys11to60_Beta=Beta Dys11to60_StdErr=StdErr))
      allresults(keep=Precipitant Dys61to120_Beta Dys61to120_StdErr in=in61to120
                 rename=(Dys61to120_Beta=Beta Dys61to120_StdErr=StdErr))
      allresults(keep=Precipitant Dys121plus_Beta Dys121plus_StdErr in=in121plus
                 rename=(Dys121plus_Beta=Beta Dys121plus_StdErr=StdErr));
  if in0to10 then do;
    window=1;
    RiskPeriod='0 to 10';
  end;
  else if in11to60 then do;
    window=2;
    RiskPeriod='11 to 60';
  end;
  else if in61to120 then do;
    window=3;
    RiskPeriod='61 to 120';
  end;
  else if in121plus then do;
    window=4;
    RiskPeriod='121+';
  end;
  Var = StdErr*StdErr;
run;
proc sort data=SB;
  by Precipitant window;
run;
proc export data=SB(keep=Precipitant RiskPeriod Beta Var where=(Beta ne .))
  outfile="/project/shennessy/DDID/output/analysis/glipizide/Glipizide_BetaVar_riskperiods.csv"
  dbms=dlm replace;
  delimiter=" ";
run;

proc print data=allresults;
run;

```

## R programming code for semi-Bayes shrinkage (Provided by Marine Corbin<sup>11</sup>)

#This function runs Semi-Bayes adjustment towards the global mean for groups of estimates. An “input” folder must be created under the working directory (here E:/Documents ) and for each group of estimates within which Semi-Bayes

#adjustment needs to be perform, a .txt file must be created under the “input” folder containing 3 columns: The first one with variable names (e.g. job or industries codes), the second one with ML beta estimates and the third one

#with the variances of the ML estimates.

```
SemiBayes <- function(directory,vart){
```

```
    setwd(directory)
```

#returns the names of all the files of the "input" directory. These files contains 3 columns: The first one with variable names (here jobcodes), the second one with

# ML beta estimates and the third one with the variances of the ML estimates. There must be one file for each group within which SB adjustment is performed.

```
    file<-c(list.files("input"))
```

```
    file<-as.character(file)
```

#creates the names of the output files

```
    outputsb<-paste("SB_",file,sep="")
```

```
    for (i in 1:length(file)){
```

```
        Data<-
```

```
        read.table(paste("input/",file[i],sep=""),header=TRUE,sep="\t",dec=". ",colClasses=c("character","numeric","numeric"),strip.white=FALSE)
```

```
        Data <- na.omit(Data)
```

```
        bhat<-as.numeric(c(Data[[2]]))
```

```
        vhat<-as.numeric(c(Data[[3]]))
```

```
        name<-as.character(Data[[1]])
```

```
        newbeta<-vector(length=length(bhat))
```

```
        newvar<-vector(length=length(bhat))
```

```
        SB_OR<-vector(length=length(bhat))
```

```
        SB_OR_LL<-vector(length=length(bhat))
```

```
        SB_OR_UL<-vector(length=length(bhat))
```

```
        n <- length(bhat)
```

```

w <- 1/(vhat + vart)
pi <- sum(w*bhat)/sum(w)
D <- bhat - pi
varo <- sum(w*D*D)/sum(w)
varm <- sum(w*vhat)/sum(w)
newbeta<- w*((vart*bhat)+(vhat*pi))
E <- w* vhat*D*sqrt(varm/vhat)
newvar <- vhat * (1-vhat*w) + (2*E*t(E))/n
SB_OR<-c(exp(newbeta))
SB_OR_LL<-c(exp(newbeta-1.96*sqrt(newvar)))
SB_OR_UL<-c(exp(newbeta+1.96*sqrt(newvar)))
newstd<-t(sqrt(newvar))
out<-cbind(name,newbeta,newstd,SB_OR,SB_OR_LL,SB_OR_UL)
b<-as.data.frame(out)
names(b)[c(1)] <- c("Var")
names(b)[c(2)] <- c("SBbeta")
names(b)[c(3)] <- c("SBstd")
names(b)[c(4)] <- c("SBOR")
names(b)[c(5)] <- c("SBlower")
names(b)[c(6)] <- c("SBupper")

write.table(b, paste(""",outputsb[i],sep=""""), sep="\t", col.names=TRUE, row.names=FALSE, quote=F,
na="NA")
}

}

#Runs the function SemiBayes
SemiBayes("E:/Documents",0.25)

```

## Reference

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