HSLU Hochschule Luzern

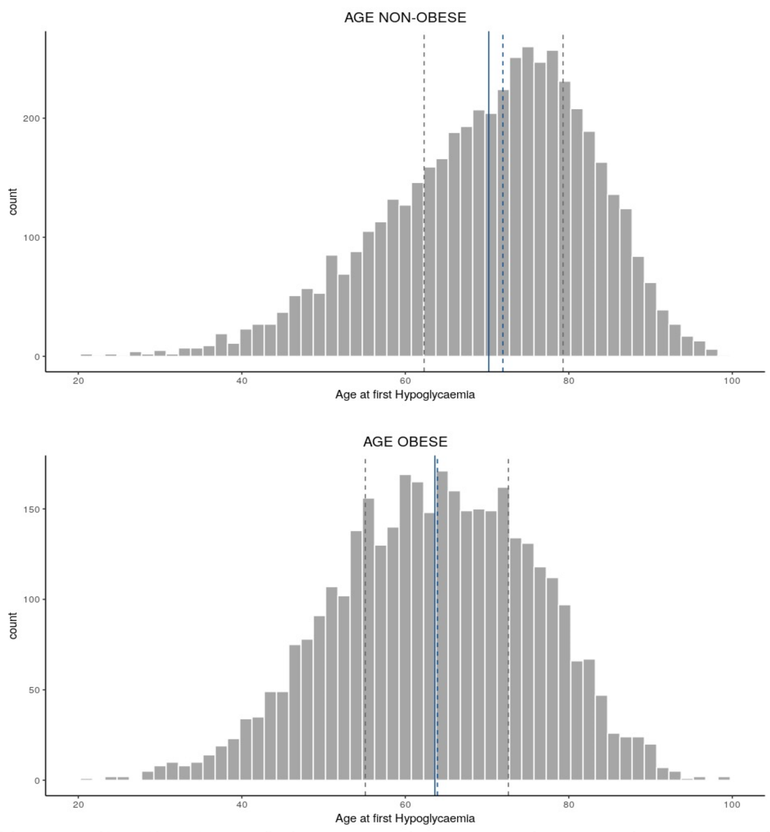
Technik & Architektur
Data Science

MSc Data Science

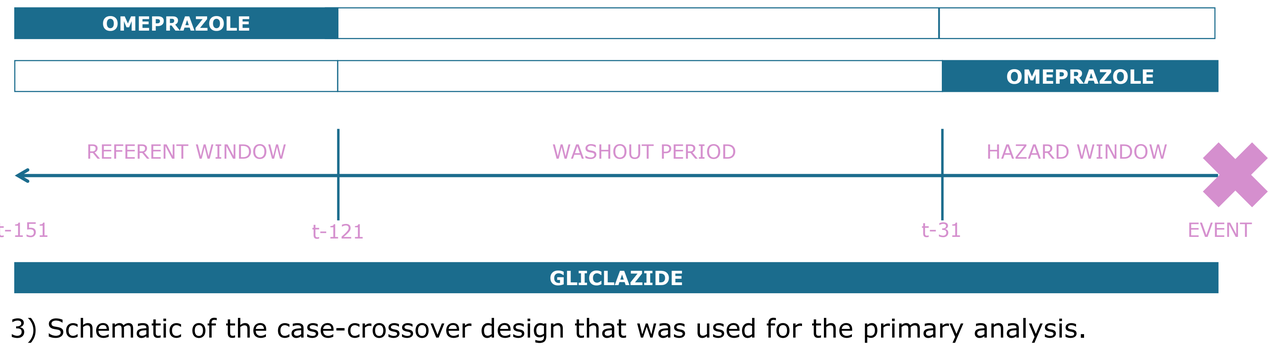
Risk of hypoglycemia due to an interaction between omeprazole and gliclazide and the interplay with obesity

	Overall	Non-Obese BMI < 30	Obese BMI >= 30
N	8532	4872 (57.1%)	3593 (42.1%)
Mean Age (years (SD))	67.50 (12.88)	70.21 (12.49)	63.62 (12.27)
Mean time NIAD to HYPO (years (SD))	5.54 (4.32)	5.60 (4.28)	5.52 (4.37)
Gender (% Male)	4518 (53.0%)	2686 (55.1%)	1806 (50.3%)
Alcohol			
current	5182 (63.9%)	2945 (63.6%)	2222 (64.6%)
former	517 (6.4%)	286 (6.2%)	227 (6.6%)
never	2409 (29.7%)	1399 (30.2%)	992 (28.8%)
missing	424 (5.0%)	242 (5.0%)	151 (4.2%)
Smoking			
current	1279 (15.2%)	749 (15.6%)	522 (14.8%)
former	3173 (37.8%)	1784 (37.1%)	1378 (39.0%)
never	3936 (46.9%)	2272 (47.3%)	1630 (46.2%)
missing	144 (1.7%)	67 (1.4%)	62 (1.7%)
# NIADs			
1	3620 (42.4%)	2186 (44.9%)	1396 (38.9%)
2	3725 (43.7%)	2111 (43.3%)	1589 (44.2%)
3+	1187 (13.9%)	575 (11.8%)	608 (16.9%)
# Medications			
1	60 (0.7%)	34 (0.7%)	26 (0.7%)
2-4	1022 (12.0%)	596 (12.2%)	416 (11.6%)
5-9	3612 (42.3%)	2114 (43.4%)	1471 (40.9%)
10+	3838 (44.9%)	2128 (43.6%)	1680 (46.7%)

1) Table 1 including the patient characteristics



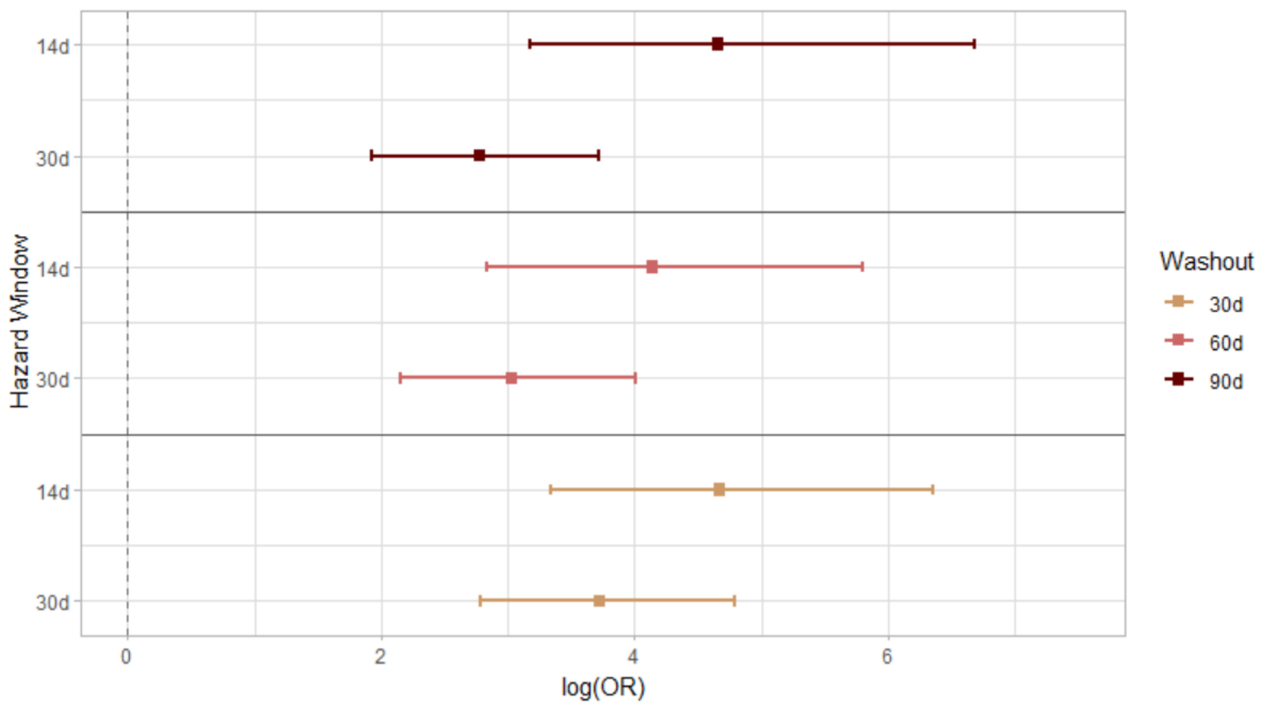
2) Age distribution of the non-obese vs obese sub-cohort showing that obese patients were younger at first hypoglycemic event



3) Schematic of the case-crossover design that was used for the primary analysis.

	gliclazide with omeprazole				omeprazole only				
	Hazard window exposed	Referent window exposed	Odds Ratio (95%CI)	Adj OR (95%CI)	Hazard window exposed	Referent window exposed	Odds Ratio (95%CI)	Adj OR (95%CI)	ORR
All	56	15	13.9 (6.4-32.3)	**16.1** (6.9-41.2)	131	45	8.5 (5.3-13.8)	**8.3** (5.1-13.9)	1.94
Non-obese	33	9	13.4 (5.0-40.4)	15.3 (5.2-52.0)	69	23	9.0 (4.7-17.9)	8.7 (4.4-17.9)	1.76
obese	23	< 7	10.0 (2.9-40.0)	12.7 (3.1-65.8)	38	21	3.3 (1.6-7.1)	3.0 (1.3-7.0)	4.23

4) Results of the primary analysis with the overall odds ratios as well as the stratified results



5) Results of the sensitivity analysis showing odds ratios for all variations of window lengths

Introduction

Type 2 diabetes mellitus (T2DM) is one of the leading diseases worldwide both in numbers and in healthcare costs and is closely linked to the obesity pandemic. T2DM comes with various comorbidities increasing the chance of polypharmacy. This leads to an increased risk for harmful drug-drug interactions. The most common pharmacokinetic drug interactions involve cytochrome P450 enzymes (CYP).
The CYP2C19 isoenzyme is involved in the metabolism of both gliclazide and omeprazole, two of the most prescribed drugs in diabetic patients.

The aim of this study was to investigate the risk of hypoglycemia due to a possible interaction between these two drugs and the influence that obesity might have on this interaction. Further, it was attempted to develop a screening method to identify new drug interactions.

Methods

We conducted a case-crossover designed analysis (3) looking at the additional exposure to omeprazole in continuous gliclazide users and stratified by obesity. Odds ratios (OR) were calculated, using logistic regression, to detect any increased risks and sensitivity analyses with time-varying window lengths were conducted.

Results

The study consisted of 8,532 patients with a mean age of 67.5 years (SD: 12.9 years) (1), (2). The adjusted OR for experiencing hypoglycemia when exposed to gliclazide and omeprazole (56 patients) compared to being exposed to gliclazide alone (15 patients) was 16.1 (95% CI 6.9-41.2) (4). The ratio of odds ratios (ORR) for the combined exposure versus exposure to omeprazole alone was 1.94. Sensitivity analyses supported these findings with ORR being greater than 1.7 for all window variations (5). Further, the obese population showed higher ORR than the non-obese population with 4.23 vs 1.76. The screening method detected novel drug combinations showing elevated risks for hypoglycaemia (gliclazide/beclometazone, gliclazide/trimethoprim).

Conclusion

In conclusion this study provides important new insights about the interaction between gliclazide and omeprazole and its impact on the risk of hypoglycaemia, as well as the modifying effect of obesity on this interaction. The results suggest that the co-administration of gliclazide and omeprazole should be avoided if possible, or closely monitored if it is deemed necessary. However, to clarify the contradicting literature around the influence of obesity on CYP2C19 activity, further research is necessary.

Tom Daniël Christen

Advisors
Prof. Dr. Fabian Ille
Dr. Philipp Stämpfli

Partners
Prof. Dr. Andrea Burden
Franziska Ulrich

ETH zürich
MSE | MASTER OF SCIENCE IN ENGINEERING

FH Zentralschweiz