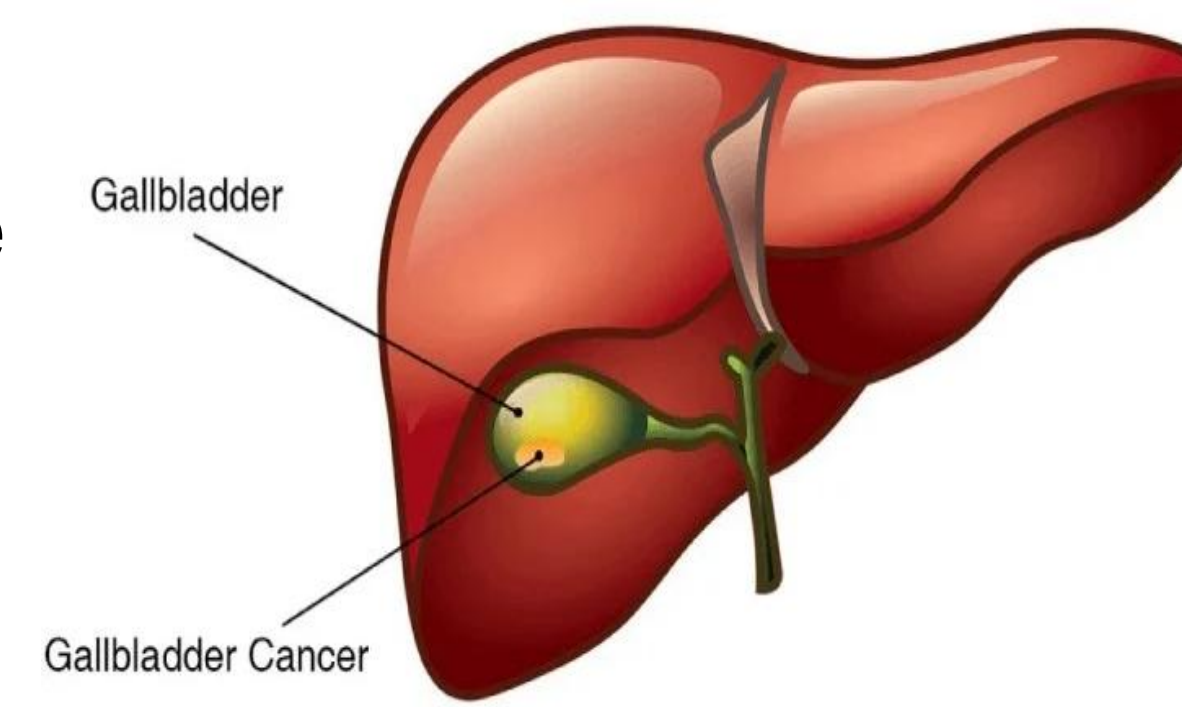


Association Between Diabetes and Gallbladder Cancer Risk Among Chilean Women with Gallstones: Findings from the Chile Biliary Longitudinal Study

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BACKGROUND

- Gallbladder cancer (GBC): a highly lethal malignancy with particularly high incidence in Chile, especially among women.
- Gallstones: known to be a major risk factor.
- However, most individuals with gallstones never develop GBC.
- Diabetes mellitus: risk modifying factor among those with gallstones.



Objective: To examine the association between diabetes and GBC risk among Chilean women with gallstones.

METHODS

- The Chile Biliary Longitudinal Study cohort:
 - N= 4,711 women aged 50-74 years with ultrasound-detected gallstones from south-central Chile (2016-2019).
- Outcomes classified as:
 - GBC or high-grade dysplasia (HGD) (diagnosed at cholecystectomy)
 - Clinical GBC (diagnosed during medical visits).
- Multivariable-adjusted Cox proportional hazard models estimated hazard ratios (aHRs) and 95% confidence intervals (CIs):
 - Overall and stratified by urban/rural residence.

RESULTS

- Over a median of 4.8-year follow-up (range=2.0 to 7.7), 120 women (2.5%) newly diagnosed with GBC.
- Median age at diagnosis: 59 years (Table 1).

RESULTS

Table 1. Descriptive statistics by disease status

	Overall	Cases		Non-cases	
		n (%)			
		120 (2.5)	4588 (97.4)		
Age categories (Tertile)					
Tertile 1: 50-55	1651 (35.1%)	30 (25.0)	1620 (35.3)		
Tertile 2: 56-62	1389 (29.5%)	35 (29.2)	1353 (29.5)		
Tertile 3: 63-74	1671 (35.5%)	55 (45.8)	1615 (35.2)		
Diabetes					
No	3454 (73.2%)	87 (72.5)	3364 (73.3)		
Yes	1186 (25.2%)	33 (27.5)	1153 (25.1)		
Ethnicity					
Mapuche	1182 (25.1%)	41 (34.2)	1140 (24.9)		
Non-Mapuche	3425 (72.7%)	77 (64.2)	3346 (72.9)		
Urban/rural					
Urban	2889 (61.3%)	66 (55.0)	2820 (61.5)		
Rural	1805 (38.3%)	54 (45.0)	1751 (38.2)		
Education level					
0-8 years	2510 (53.3%)	68 (56.7)	2442 (53.2)		
9-12 years	1739 (36.9%)	43 (35.8)	1695 (36.9)		
13+ years	383 (8.1%)	9 (7.5)	372 (8.1)		
BMI					
15-24	424 (9.0%)	15 (12.5)	409 (8.9)		
25-29	1420 (30.1%)	35 (29.2)	1383 (30.1)		
30-34	1500 (31.8%)	34 (28.3)	1466 (32.0)		
35-39	852 (18.1%)	27 (22.5)	824 (18.0)		
40+	459 (9.7%)	9 (7.5)	450 (9.8)		
Parity					
Nulliparous	321 (6.9)	316 (7.0)	5 (4.2)		
1	493 (10.6)	480 (10.6)	12 (10.1)		
2	1153 (24.9)	1127 (25.0)	24 (20.2)		
3+	2671 (57.6)	2593 (57.4)	78 (65.6)		
Family history of GBC					
No	4573 (97.1)	4457 (97.1)	113 (94.2)		
Yes	138 (2.9)	131 (2.8)	7 (5.8)		

- Diabetes and Clinical GBC:
 - Overall: ↑ risk: aHR=3.4; 95%CI: 1.3-9.0
 - Urban women: ↑ risk: aHR=8.1; 95%CI: 2.3-28.3 (Figure 1).

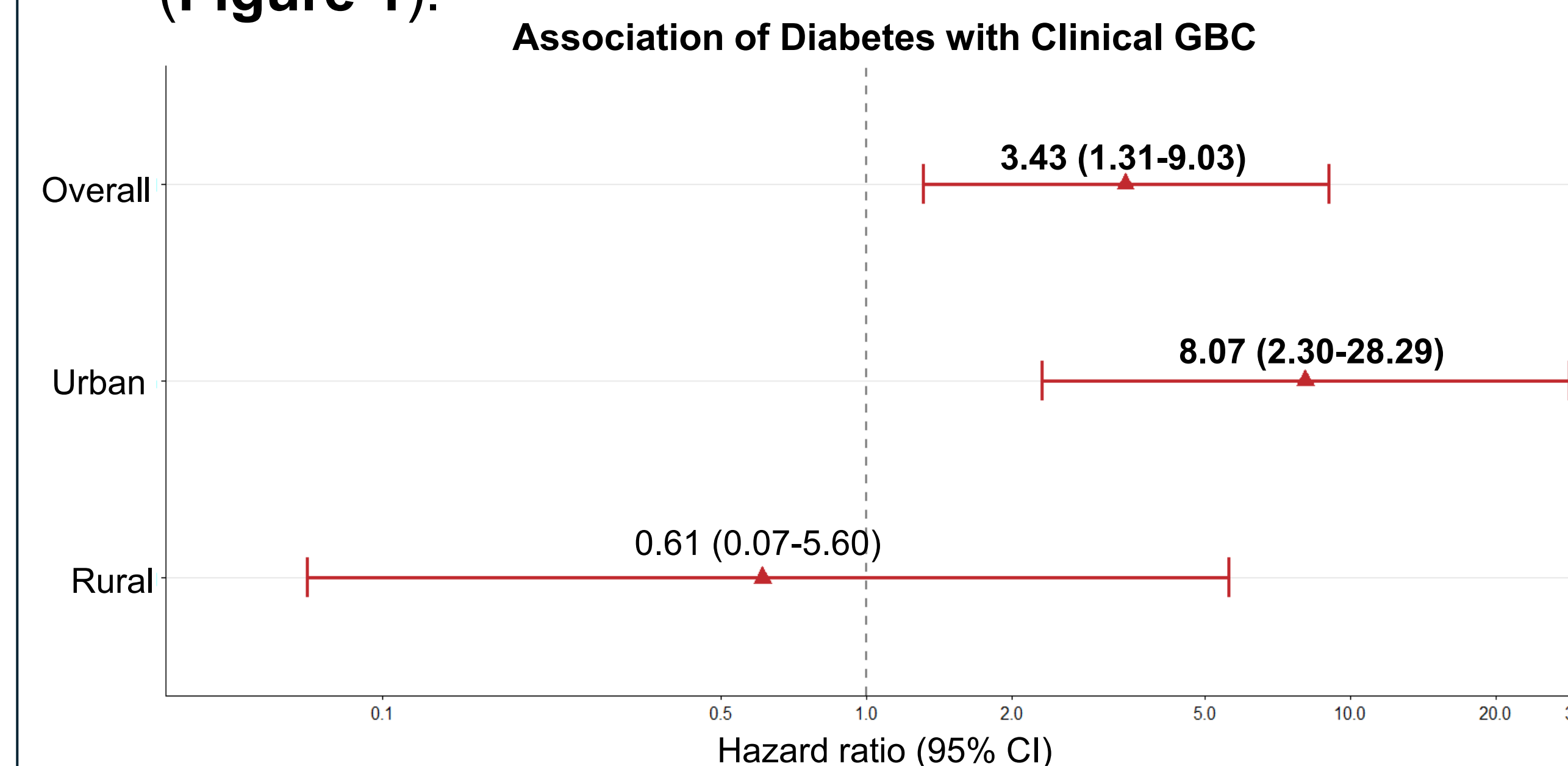


Figure 1. Association of Diabetes with Clinical GBC Risk

RESULTS

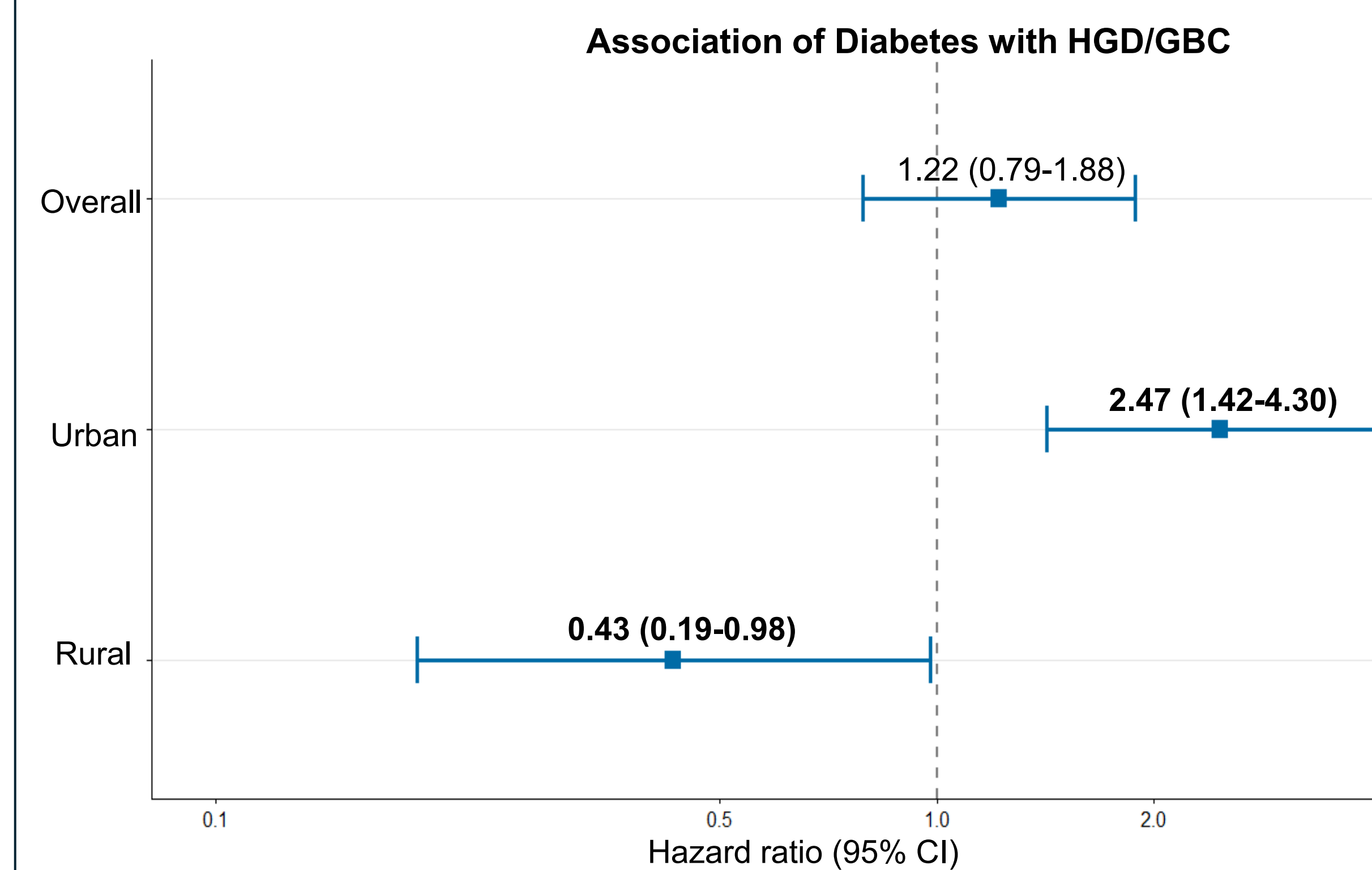


Figure 2. Association of Diabetes with HGD/GBC Risk

- Diabetes and HGD/GBC risk:
 - Overall: aHR=1.2; 95%CI: 0.8-1.9
 - Urban women: ↑ risk: aHR=2.5; 95%CI: 1.4-4.3
 - Rural women: ↓ risk: aHR=0.43; 95%CI: 0.19-0.98 (Figure 2).
- No statistically significant associations were observed for cholecystectomized GBC or HGD either overall or in stratified analyses.

CONCLUSIONS

- Among Chilean women with gallstones, diabetes was associated with increased GBC risk for those residing in urban settings but lower risk in rural areas.
- Reasons underlying this urban-rural disparity remain unclear and warrant further investigation.
 - Potential explanations:
 - Differences in diabetes management
 - Healthcare access or detection bias
 - Lifestyle factors, or environmental exposures between urban and rural populations.
- Diabetic women with gallstones in urban areas: A high-risk population that could benefit from enhanced surveillance; pending confirmation in additional studies.

What's the disease?

Gallbladder cancer is a deadly cancer that's especially common in Chile, particularly among women. It's hard to catch early and difficult to treat.

What did we want to know?

Gallstones (hard deposits in the gallbladder) increase the risk of this cancer. Diabetes might play a role. So, we wanted to understand: among women who already have gallstones, does having diabetes make gallbladder cancer more or less likely?

Who did we study?

Nearly 4700 Chilean women (ages 50-74) who had gallstones detected by ultrasound. They were followed for about 5 years to see who developed gallbladder cancer.

What did we find?

- Overall, diabetes didn't clearly increase or decrease cancer risk among all women with gallstones.
- But location mattered:
 - Women living in cities with diabetes have 2.5 times higher risk of developing gallbladder cancer than those without diabetes.
 - Women living in rural areas with diabetes had lower risk than those without diabetes.
 - For cancers detected during clinical visit, diabetes was linked to much higher risk, especially in cities.

What does this mean?

Women living in cities who have both gallstones and diabetes might be at high risk and could benefit from closer monitoring by their doctors. Unclear reasons why city and rural women showed opposite patterns, it might relate to differences in diabetes care, access to healthcare, lifestyle, or environmental factors.

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