

Improved prognosis in gastric adenocarcinoma among metformin users

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Study population: Diabetes patients diagnosed with gastric adenocarcinoma between between 1st July 2005 and 31st December 2018
Exposure: Metformin use within two years before the diagnosis of gastric adenocarcinoma
Outcome: mortality due to gastric adenocarcinoma (disease-specific mortality) and all-cause mortality
Data sources: The Prescribed Drug Registry; The Cancer Registry; The Cause of Death Registry; The Patient Registry

Methods:
Cox proportional hazard regression was used to estimate hazard ratios (HRs) with 95% confidence intervals (95% CIs) for mortality outcomes comparing metformin users with non-users.

A multivariable model with adjustment for sex, age at gastric adenocarcinoma diagnosis, calendar year of diagnosis, comorbidity (Charlson Comorbidity Index), use of non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin (yes or no), and use of statins (yes or no).

A competing-risks model accounting for death due to other causes was used for calculate sub-HR and depict mortality curves.

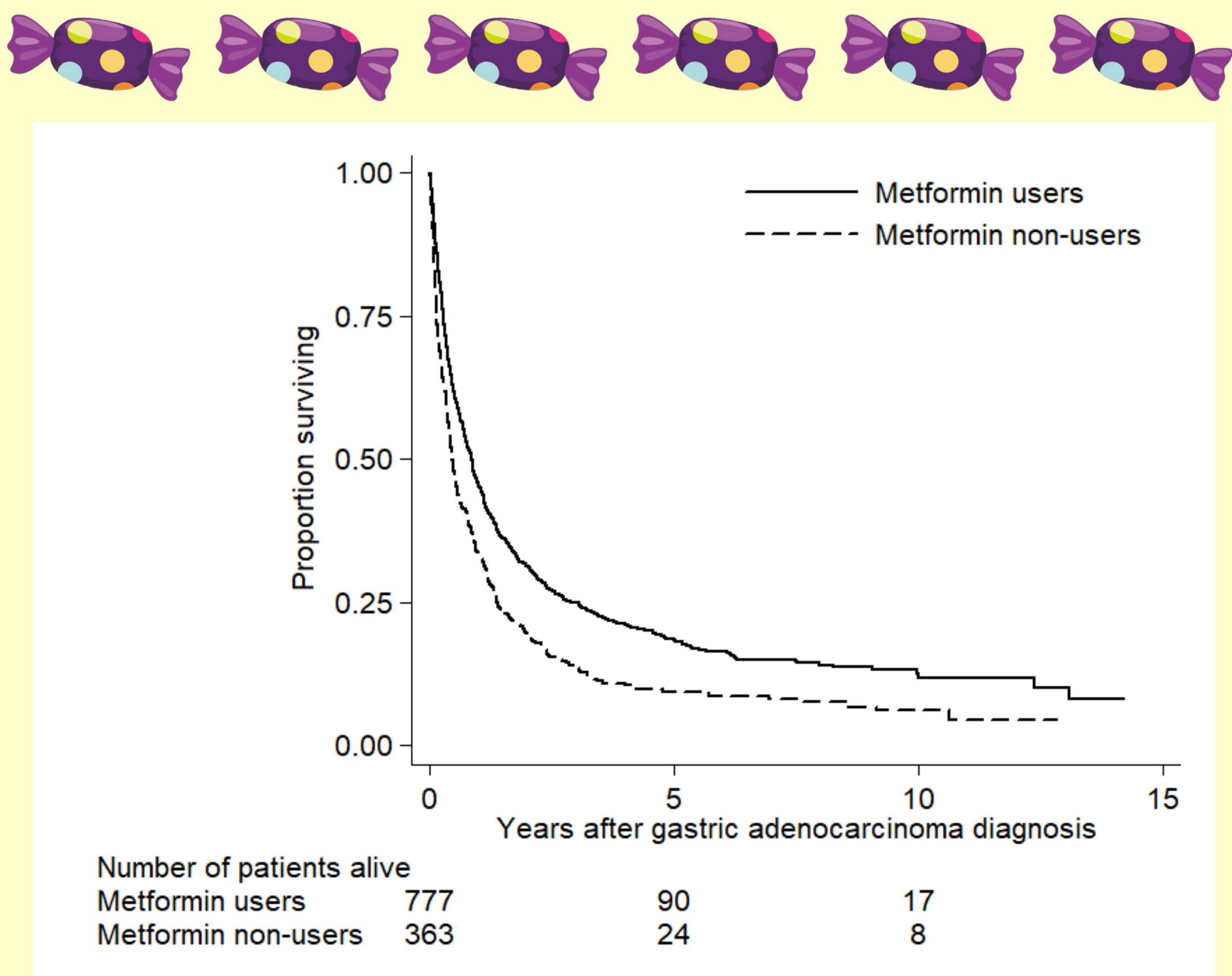
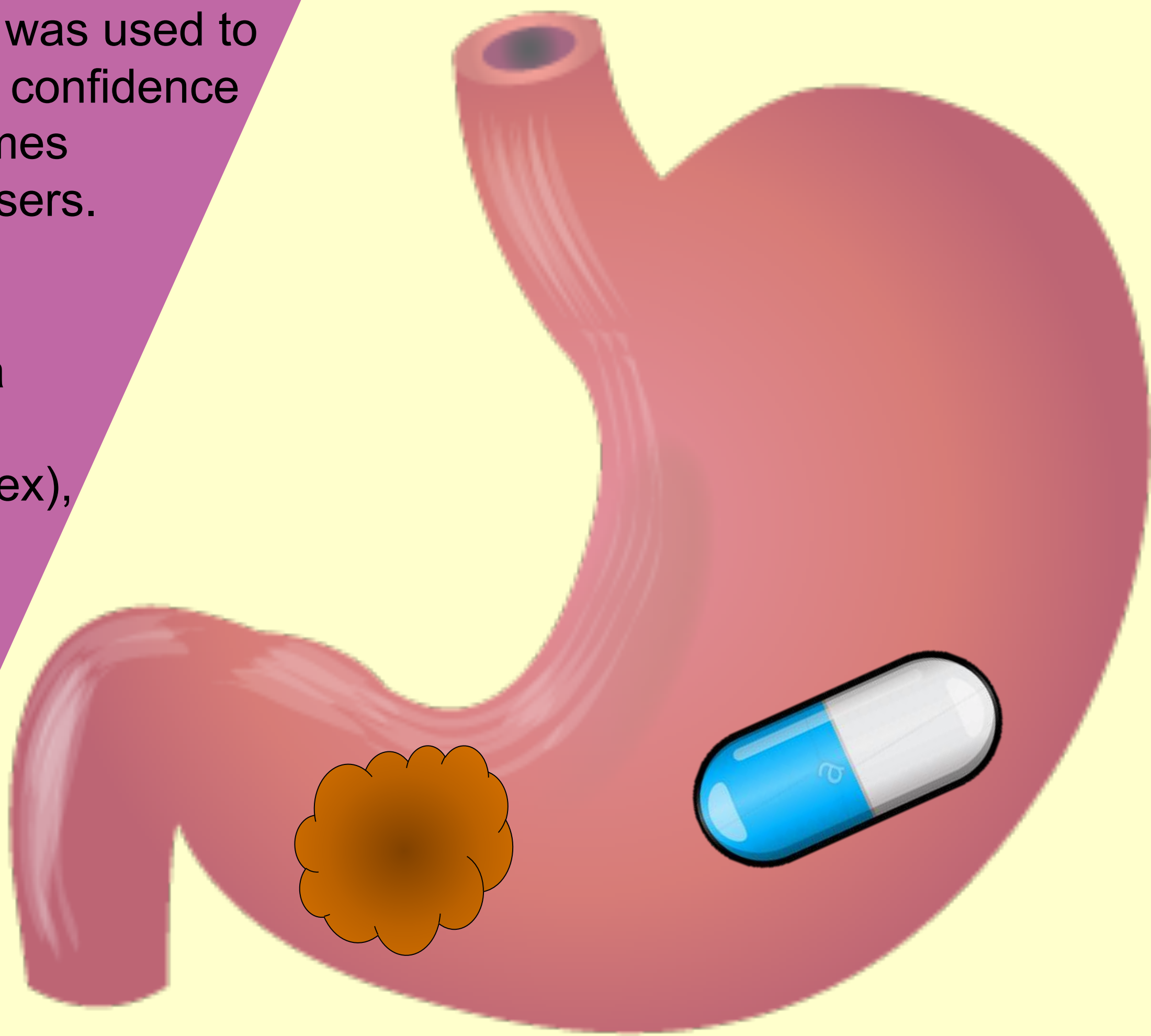


Figure 1. Kaplan–Meier survival curves by metformin use

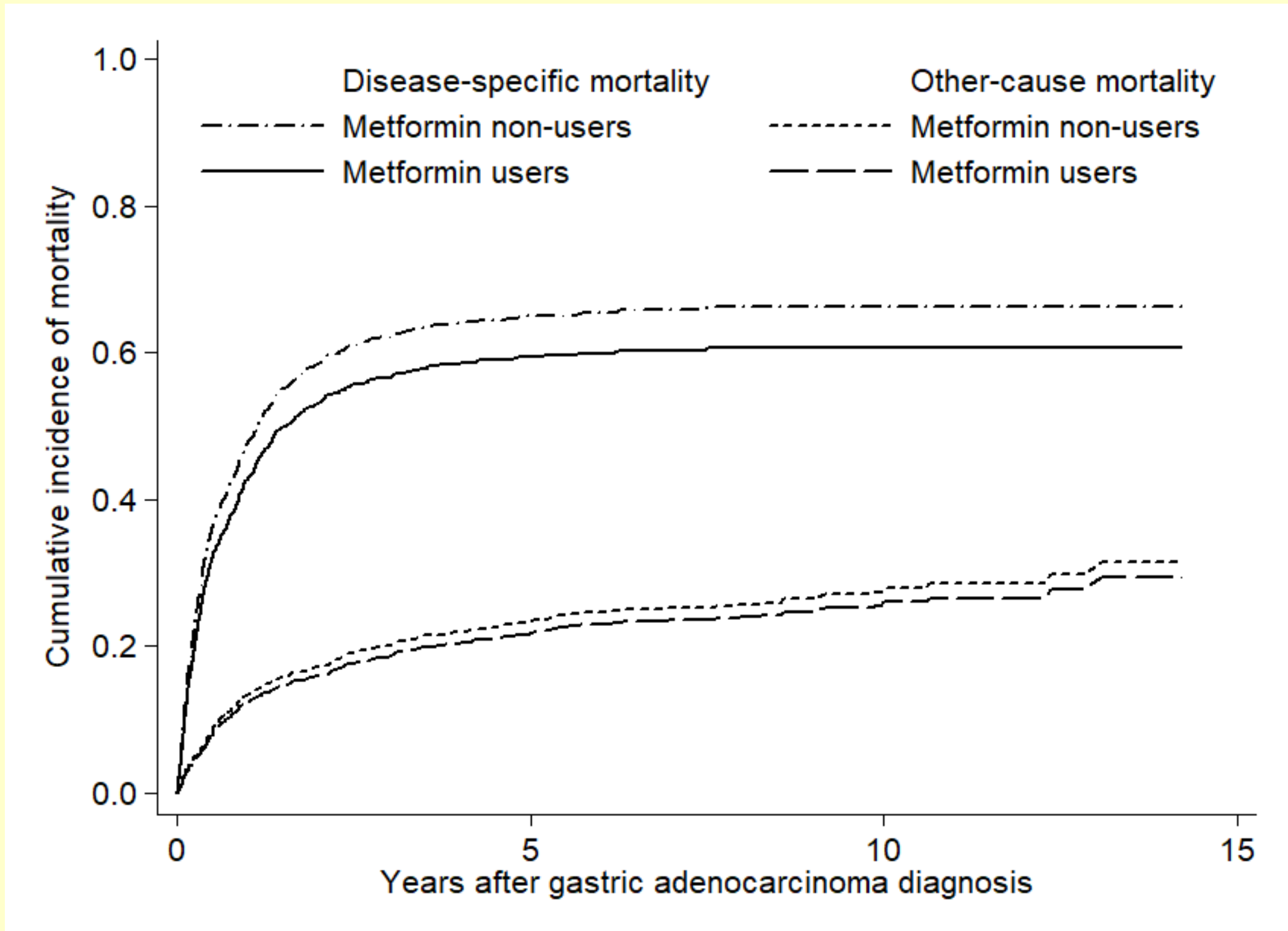


Figure 2. Cumulative disease-specific and other-cause mortality by metformin use

	Disease-specific mortality Adjusted HR (95% CI)	All-cause mortality Adjusted HR (95% CI)
All patients		
Metformin vs. no metformin	0.79 (0.67 - 0.93)	0.78 (0.68 - 0.90)
Male patients		
Metformin vs. no metformin	0.85 (0.69 - 1.03)	0.84 (0.71 - 0.99)
Female patients		
Metformin vs. no metformin	0.66 (0.49 - 0.89)	0.84 (0.48 - 0.81)
Tumour stage Tis-II		
Metformin vs. no metformin	0.87 (0.57 - 1.31)	0.89 (0.64 - 1.23)
Tumour stage III-IV		
Metformin vs. no metformin	0.71 (0.58 - 0.88)	0.71 (0.59 - 0.85)
Charlson Comorbidity Index 0		
Metformin vs. no metformin	0.71 (0.57 - 0.89)	0.70 (0.58 to 0.85)
Charlson Comorbidity Index 1		
Metformin vs. no metformin	0.91 (0.66 - 1.27)	0.90 (0.68 - 1.19)
Charlson Comorbidity Index ≥2		
Metformin vs. no metformin	0.85 (0.59 - 1.22)	0.81 (0.59 - 1.11)

- The analyses were also conducted with stratification by age (above or below the median), anatomical tumour sub-location (non-cardia or cardia), and gastrectomy (yes or no), and the risk estimates were similar to those of the main results.
- No dose –response association was found between metformin use and risk of mortality

Conclusions:

- Pre-diagnosis use of metformin improves the prognosis in gastric adenocarcinoma among diabetes patients.
- Such associations are stronger among patients of female sex, more advanced tumour stage, and less comorbidity.



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