

SUPPLEMENTARY TABLE S2: UNIVARIATE AND MULTIVARIATE HAZARD RATIOS FOR METFORMIN EXPOSURE AND MORTALITY; DIABETIC SUBGROUP, STAGES I-III COLORECTAL CANCER.

Exposure Information			Colorectal cancer-specific survival (Definition 2) ^d			Colorectal cancer-specific survival (Definition 3) ^e		
Main analysis ^a	N (N=315)	Person -years	Deaths (Crude Rate) ^c	Univariate HR (95% CI)	Adjusted HR (95% CI)	Deaths (Crude Rate) ^c	Univariate HR (95% CI)	Adjusted HR (95% CI)
No Metformin	108	361	36 (100)	(Ref)	(Ref)	47 (130)	(Ref)	(Ref)
Any Metformin	207	833	62 (74)	0.75 (0.50-1.13)	0.63 (0.38-1.03)	77 (92)	0.72 (0.50-1.03)	0.59 (0.38-0.92)
Stratified Analyses								
Dosing intensity^a								
Any Metformin (Low)	103	406	33 (81)	0.81 (0.51-1.31)	0.63 (0.36-1.10)	44 (108)	0.83 (0.55-1.25)	0.67 (0.41-1.09)
Any Metformin (High)	104	427	29 (68)	0.69 (0.42-1.13)	0.63 (0.35-1.11)	33 (77)	0.61 (0.39-0.95)	0.52 (0.31-0.87)
Co-prescription^b								
Metformin + Co-Rx ADDs	125	483	37 (77)	0.77 (0.48-1.21)	0.73 (0.45-1.18)	45 (93)	0.72 (0.48-1.08)	0.66 (0.43-1.01)
Metformin exclusively	82	350	25 (71)	0.73 (0.44-1.22)	0.65 (0.38-1.11)	32 (91)	0.72 (0.46-1.13)	0.61 (0.38-0.98)
Dosing intensity & Co-prescription^b								
Metformin (Low) + Co-Rx ADDs	65	259	18 (70)	0.70 (0.40-1.24)	0.61 (0.34-1.12)	24 (93)	0.71 (0.44-1.16)	0.61 (0.36-1.04)
Metformin (High) + Co-Rx ADDs	60	223	19 (85)	0.84 (0.48-1.46)	0.86 (1.53-0.60)	21 (94)	0.72 (0.43-1.21)	0.70 (0.41-1.20)
Metformin (Low) exclusively	38	146	15 (103)	1.01 (0.55-1.84)	0.83 (0.43-1.60)	20 (137)	1.04 (0.62-1.76)	0.88 (0.50-1.56)
Metformin (High) exclusively	44	204	10 (49)	0.52 (0.26-1.05)	0.49 (0.23-1.02)	12 (59)	0.48 (0.25-0.90)	0.40 (0.20-0.78)

a) Adjusted for age, tumour stage, tumour grade, year of diagnosis, comorbidity score, aspirin use, exposure to non-metformin ADDs (sulfonylureas yes/no, insulin yes/no, other ADDs yes/no), socioeconomic status, radiation therapy.

- b)** Adjusted for age, tumour stage, tumour grade, year of diagnosis, comorbidity score, aspirin use, socioeconomic status, radiation therapy. 'Co-Rx' ADDs include sulfonylureas, insulin and/or other ADDs.
- c)** Rate calculated as deaths per 1000 person-years
- d)** Includes deaths where CRC was identified as a secondary/contributory cause of death.
- e)** Includes deaths due to malignant neoplasms of other/ill-defined digestive organs (C26), ill-defined cancer sites (C76.1, C80), secondary cancer sites (C77-79), cancers of uncertain or unknown behaviour (D48.6, D48.9) and unspecified causes of death.