

SUPPLEMENTARY TABLE S3: UNIVARIATE AND MULTIVARIATE HAZARD RATIOS FOR METFORMIN EXPOSURE AND MORTALITY; DIABETIC SUBGROUP, ALL STAGES COLORECTAL CANCER.

Exposure Information			Colorectal cancer-specific survival			Overall survival		
Main analysis ^a	N (N=444)	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	159	416	72 (173)	(Ref)	(Ref)	123 (296)	(Ref)	(Ref)
Any Metformin	285	918	111 (133)	0.72 (0.54-0.97)	0.84 (0.60-1.18)	194 (211)	0.74 (0.59-0.93)	0.87 (0.68-1.13)
Stratified Analyses								
Dosing intensity^a								
Any Metformin (Low)	144	445	59 (133)	0.78 (0.55-1.10)	0.93 (0.64-1.36)	107 (240)	0.83 (0.64-1.08)	0.99 (0.75-1.31)
Any Metformin (High)	141	473	52 (110)	0.66 (0.47-0.95)	0.75 (0.50-1.13)	87 (184)	0.65 (0.50-0.86)	0.75 (0.55-1.02)
Co-prescription^b								
Metformin + Co-Rx ADDs	178	547	71 (155)	0.76 (0.55-1.05)	0.88 (0.63-1.24)	125 (273)	0.79 (0.61-1.01)	0.91 (0.70-1.18)
Metformin exclusively	107	371	40 (108)	0.66 (0.45-0.98)	0.86 (0.58-1.28)	69 (186)	0.67 (0.50-0.90)	0.78 (0.58-1.06)
Dosing intensity & Co-prescription^b								
Metformin (Low) + Co-Rx ADDs	93	290	35 (121)	0.71 (0.48-1.07)	0.84 (0.55-1.26)	68 (235)	0.81 (0.60-1.09)	0.93 (0.69-1.26)
Metformin (High) + Co-Rx ADDs	85	258	36 (140)	0.81 (0.54-1.20)	0.94 (0.62-1.43)	57 (221)	0.76 (0.56-1.05)	0.88 (0.63-1.21)
Metformin (Low) exclusively	51	156	24 (154)	0.90 (0.57-1.43)	1.26 (0.78-2.02)	39 (250)	0.87 (0.61-1.24)	1.09 (0.75-1.59)
Metformin (High) exclusively	56	215	16 (74)	0.48 (0.28-0.82)	0.58 (0.33-1.01)	30 (139)	0.51 (0.35-0.77)	0.56 (0.37-0.85)

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).

b) Adjusted for age, tumour stage, tumour grade, year of diagnosis, comorbidity score, aspirin use. 'Co-Rx' ADDs include sulfonylureas, insulin and/or other ADDs.

c) Rate calculated as deaths per 1000 person-years