

SUPPLEMENTARY TABLE S1: CHARACTERISTICS OF THE FULL STUDY COHORT ACCORDING TO DIABETIC STATUS AND EXPOSURE TO METFORMIN

Characteristic		Any Metformin Exposure in Year Prior to Diagnosis			P -value
		Non-diabetic (n=3501)	Diabetic Unexposed (n=108)	Diabetic Exposed (n=207)	
Patient Details					
Age – Median (IQR)	Years	75 (69, 80)	76 (71, 79)	74 (71, 80)	0.74
Comorbidity – Median (IQR)	Number of drug classes	8 (5, 13)	14 (10, 20)	15 (11, 19)	<0.001
Gender – (%)	Male	1879 (53.7)	67 (62.0)	127 (61.4)	0.03
Smoking status – (%)	Current	559 (16.0)	10 (9.3)	17 (8.2)	0.05
	Former	1540 (44.0)	49 (45.4)	100 (48.3)	
	Never	724 (20.7)	26 (24.1)	49 (23.7)	
	Unspecified	678 (19.4)	23 (21.3)	41 (19.8)	
Socioeconomic status – (%)	Least deprived	499 (14.3)	10 (9.3)	21 (10.1)	0.44
	.	391 (11.2)	13 (12.0)	26 (12.6)	
	.	473 (13.5)	18 (16.7)	26 (12.6)	
	.	617 (17.6)	19 (17.6)	28 (13.5)	
	Most deprived	1264 (36.1)	40 (37.0)	89 (43.0)	
	Unspecified	257 (7.3)	8 (7.4)	17 (8.2)	
Tumour Details					
TNM Stage – (%)	I	666 (19.0)	23 (21.3)	36 (17.4)	0.49
	II	1505 (43.0)	38 (35.2)	86 (41.6)	
	III	1330 (38.0)	47 (43.5)	85 (41.1)	
Grade – differentiation (%)	Well/moderate	2682 (76.6)	75 (69.4)	159 (76.3)	0.55
	Poorly differentiated	419 (12.0)	17 (15.7)	24 (11.6)	
	Unspecified	400 (11.4)	16 (14.8)	25 (12.1)	
Site – (%)	Colon (v rectum)	2232 (63.8)	81 (75.0)	147 (71.0)	0.01
Morphology – (%)	Adenocarcinoma	2996 (85.6)	93 (86.1)	179 (86.5)	0.93
	Other	505 (14.4)	15 (13.9)	28 (13.5)	
Treatment ^a – (%)	Surgery	3337 (95.3)	104 (96.3)	192 (92.8)	0.21
	Chemotherapy	1103 (31.5)	22 (20.4)	59 (28.5)	0.03
	Radiation	555 (15.9)	9 (8.3)	33 (15.9)	0.11
Year of Diagnosis – (%)	2001	475 (13.6)	15 (13.9)	20 (9.7)	0.49
	2002	496 (14.2)	18 (16.7)	25 (12.1)	
	2003	608 (17.4)	19 (17.6)	37 (17.9)	
	2004	639 (18.3)	12 (11.1)	38 (18.4)	
	2005	678 (19.4)	21 (19.4)	42 (20.3)	
	2006	605 (17.3)	23 (21.3)	45 (21.7)	
Drug exposures ^b – (%)					
Sulfonylurea		-	78 (72.2)	108 (52.2)	<0.001
Insulin		-	30 (27.8)	18 (8.7)	<0.001
Other ADDs		-	9 (8.3)	31 (15.0)	0.09
Aspirin		1199 (34.3)	65 (60.2)	144 (69.6)	<0.001
Metformin Exposure Details					

Dosing Intensity – median (IQR) ^c	-	-	0.92	(0.55, 1.0)
Mean daily dose – median (IQR) ^d mg/day	-	-	1148	(682, 4318)
Exposure to metformin following diagnosis - (%)	100	(2.9)	20	(18.5)
			178	(86.0)

- a) Refers to treatment received in year post diagnosis.
- b) Exposures in year prior to diagnosis.
- c) Exposure intensity calculated as number of days with supply available in year prior to diagnosis, divided by 365.
- d) Mean daily dose calculated as cumulative dose in year prior to diagnosis, divided by 365.

IQR: Interquartile range