# Figures

**Figure 1: Smoking status at and following the time of Ulcerative Colitis diagnosis.**



**UC** – Ulcerative Colitis

**QOF** – UK Quality Outcomes and Framework introduced to GPs in 2004

**IBD** – Inflammatory Bowel Disease

**Figure 2: KM curves showing probability of oral CS exposure in patients with Ulcerative Colitis given smoking status at diagnosis**



Log rank test for trend: p=0.53

**CS -** corticosteroid **UC** – Ulcerative Colitis

**Figure 3: KM curves showing probability of colectomy in patients with Ulcerative Colitis by smoking status at diagnosis**

Log rank test for trend: p=0.24



Log rank test for trend: p=0.24

**UC** – Ulcerative Colitis

**Never-Smoker** – UC patients who were non-smokers at the time of UC diagnosis with no previous Read codes indicating they were ex-smokers

**Smoker** – UC patients who were smokers at diagnosis

**Ex-Smoker** – UC patients who were non-smokers at the time of UC diagnosis with Read codes indicating previous smoking

# Tables

**Table 1: baseline characteristics of cohort**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Never-Smoker at UC diagnosis****(n=2,698)** | **Ex-Smoker at UC diagnosis****(n=3,178)** | **Smoker at UC diagnosis****(n=878)** | **p-value** |
| **Sex** % male | 46.2 | 57.7 | 53.3 | **<0.001** |
| **Age at diagnosis**a **(%)** A1 A2 A3 | 1.737.860.5 | 0.120.879.2 | 042.957.1 | **<0.001** |
| **BMI category at diagnosis**b **(%)** Underweight Normal Overweight Obese | 3.543.835.517.2 | 1.234.044.220.7 | 4.244.836.214.7 | **<0.001** |
| **Social deprivation**c **(%)** IMD 1 IMD 2 IMD 3 IMD 4 IMD 5 | 26.525.117.719.111.6 | 25.824.919.517.911.8 | 18.923.819.820.617.0 | **0.006** |
| **Comorbidities (%)** IBSd Depressione | 13.66.3 | 13.19.3 | 16.411.4 | **0.038****<0.001** |

a - Age at diagnosis categories as per Montreal classification (A1 <17 years, A2 17-40, A3 >40 years)

b - BMI (Body Mass index) - calculated as the closest BMI recording within one year of UC diagnosis. Data available for 88% of patients

c - IMD (Index of Multiple Deprivation). Data available for 58% of patients.

d - IBS (Irritable Bowel Syndrome) - co-diagnosis considered as any patient with a defined Read code for IBS in records

e - Premorbid depression considered if patient had any Read code for depressive illness in CPRD record before UC diagnosis

**Table 2: Simple and multiple regression analysis for risk of corticosteroid dependency\* in patients with Ulcerative Colitis**

|  |  |  |
| --- | --- | --- |
|  | **simple logistic regression****n=6714** | **multiple logistic regression****n=3,558** |
| **OR** | **95% CI** | **p value** | **OR** | **95% CI** | **p value** |
| **Smoking status at diagnosis** Never-Smoker Smoker Ex-Smoker | 10.750.89 | -0.60-0.930.78-1.02 | -**0.009**0.10 | 10.850.90 | -0.61-1.180.73-1.11 | -0.340.32 |
| **Sex** (ref to female) | 1.15 | 1.01-1.31 | **0.033** | 1.51 | 1.24-1.85 | **<0.001** |
| **Age at IBDdiagnosis**a A1 A2 A3 | 3.40 10.77 | 2.12-5.47-0.67-0.88 | **<0.001-<0.001** | 2.9110.99 | 1.06-7.98-0.97-1.23 | **0.038**-0.14 |
| **Era of IBD diagnosis**bEra 1 Era 2 Era 3 Era 4 Era 5 Era 6 | 11.060.950.960.870.84 | -0.87-1.290.78-1.170.78-1.200.69-1.090.62-1.14 | -0.570.630.740.230.26 | 10.910.830.880.980.79 | -0.68-1.220.61-1.110.63-1.210.70-1.370.47-1.34 | -0.530.210.430.910.39 |
| **BMI category**c Underweight Normal Overweight Obese | 1.3910.820.85 | 0.95-2.04-0.71-0.960.70-1.03 | 0.80-**0.014**0.09 | 1.6410.840.92 | 0.96-2.81-0.67-1.040.70-1.22 | 0.07-0.110.57 |
| **Social deprivation**d IMD lower | 0.96 | 0.79-1.17 | 0.68 | 0.97 | 0.79-1.19 | 0.79 |
| **Co-morbidities**e IBS Depression | 0.960.83 | 0.79-1.160.64-1.07 | 0.650.15 | 1.160.98 | 0.89-1.520.67-1.43 | **0.28**0.91 |
| **Oral 5-ASAf** | 6.95 | 5.47-8.83 | **<0.001** | 6.04 | 4.34-8.40 | **<0.001** |

Multiple regression includes all covariates of simple regression. Significant odds ratios shown in bold.

**OR** – Odds Ratio **CI** - Confidence Interval **IBD** - Inflammatory Bowel Disease **BMI** - Body Mass Index **IMD** - index of multiple deprivation **IBS** - irritable bowel syndrome **5-ASA** - 5-aminosalicylates

a- Age categories as per Montreal classification (A1 <17 years, A2 17-40, A3 >40 years)

b - Era 1: 2005-06, Era 2: 2007-08, Era 3: 2009-10, Era 4: 2011-12, Era 5: 2013-14, Era 6: 2015-04/2016

c – calculated as the closest recorded BMI to date of IBD diagnosis, one year either side of IBD diagnosis, data available for 88% of patients

d – IMD upper includes IMD categories 1 and 2 (versus IMD category 3,4 and 5), data available for 58% of patients

e – IBS co-diagnosis defined as any patient with a Read code for IBS before or after IBD diagnosis. Depression defined as any patient with a Read code for depression before IBD diagnosis

f – exposure of oral 5-ASA defined as any patients with at least one or more prescription for oral 5-ASA after IBD diagnosis

\* steroid dependency calculated as any patient with a repeat steroid prescription within 3 months of the end of a previous steroid prescription or patients with steroid prescriptions for greater than 3 consecutive months

**Table 3: Simple and multiple Cox regression analysis for risk of thiopurine use in patients with Ulcerative Colitis**

|  |  |  |
| --- | --- | --- |
|  | **simple Cox regression****n=6664** | **multiple Cox regression****n=3545** |
| **HR** | **95% CI** | **p value** | **HR** | **95% CI** | **p value** |
| **Smoking status at diagnosis** Never-Smoker Ex-Smoker Smoker | 10.920.90 | -0.80-1.050.60-0.93 | -0.22**0.009** | 11.030.92 | -0.84-1.270.67-1.25 | -0.760.60 |
| **Sex** (ref to female) | 1.16 | 1.02-1.32 | **0.023** | 1.41 | 1.16-1.72 | **0.001** |
| **Age at IBD diagnosis**a A1 A2 A3 | 2.4010.49 | 1.48-3.90-0.43-0.56 | **<0.001****-****<0.001** | 0.9610.54 | 0.30-3.07-0.44-0.66 | 0.95-**>0.001** |
| **Era of IBD diagnosis**b Era 1 Era 2 Era 3 Era 4 Era 5 Era 6 | 11.121.171.431.331.34 | -0.91-1.390.95-1.451.15-1.781.06-1.681.01-1.79 | -0.280.14**0.001****0.014****0.044** | 10.900.951.141.111.22 | -0.67-1.220.70-1.290.83-1.560.79-1.550.77-1.94 | -0.500.750.430.550.39 |
| **BMI category**c Underweight Normal Overweight Obese | 1.5110.800.82 | 1.04-2.18-0.69-0.930.68-0.99 | **0.031**-**0.005****0.046** | 1.0610.850.91 | 0.60-1.87-0.68-1.060.69-1.20 | 0.85-0.150.50 |
| **Social deprivation**d IMD lower | 1.14 | 0.95-1.38 | 0.15 | 1.23 | 1.02-1.51 | **0.035** |
| **Co-morbidities**e IBS Depression | 0.800.70 | 0.65-0.970.54-0.92 | **0.024****0.010** | 0.760.82 | 0.56-1.020.56-1.22 | 0.0660.34 |
| **IBD medication**f Oral 5-ASA | 13.96 | 10.13-19.23 | **<0.001** | 9.84 | 6.16-15.72 | **<0.001** |
| **Early CSg** | 2.81 | 2.46-3.20 | **<0.001** | 1.91 | 1.57-2.33 | **<0.001** |

Multiple regression includes all covariates of simple regression. Significant hazard ratios shown in bold.

**HR** – Hazard Ratio **CI** - Confidence Interval **IBD** - Inflammatory Bowel Disease **BMI** - Body Mass Index **IMD** - index of multiple deprivation **IBS** - irritable bowel syndrome **5-ASA** - 5-aminosalicylates **CS** - Corticosteroid

a – Age categories as per Montreal classification (A1 <17 years, A2 17-40, A3 >40 years)

b – Era 1: 2005-06, Era 2: 2007-08, Era 3: 2009-10, Era 4: 2011-12, Era 5: 2013-14, Era 6: 2015-04/2016

c – calculated as the closest recorded BMI to date of IBD diagnosis, one year either side of IBD diagnosis

d – IMD lower includes IMD categories 4 and 5 (versus IMD category 1, 2 and 3), data available for 58% of patients

e – IBS co-diagnosis defined as any patient with a Read code for IBS before or after IBD diagnosis. Depression defined as any patient with a Read code for depression before IBD diagnosis

f – exposure of oral 5-ASA defined as any patients with at least one or more prescription for oral 5-ASA after IBD diagnosis

g – corticosteroid prescription within 30 days of diagnosis with UC

**Table 4: Simple and multiple Cox regression analysis for risk of first hospitalization in patients with Ulcerative Colitis**

|  |  |  |
| --- | --- | --- |
|  | **simple Cox regression** **n=3633** | **multiple Cox regression****n=3327** |
| **HR** | **95% CI** | **p value** | **HR** | **95% CI** | **p value** |
| **Smoking status at diagnosis**Never-Smoker Ex-Smoker Smoker | 10.820.91 | -0.70-0.970.71-1.17 | -**0.017**0.46 | 10.870.92 | -0.73-1.030.70-1.20 | -0.110.54 |
| **Sex**  (ref to female) | 0.91 | 0.78-1.06 | 0.23 | 1.01 | 0.86-1.19 | 0.90 |
| **Age at IBD diagnosis**aA1 A2 A3 | 2.3610.72 | 1.12-5.02-0.61-0.84 | **>0.001-0.025** | 1.2610.85 | 0.31-5.14-0.71-1.02 | 0.74-0.086 |
| **Era of IBD diagnosis**b Era 1 Era 2 Era 3 Era 4 Era 5 Era 6 | 11.131.121.171.371.44 | -0.90-1.420.88-1.430.89-1.521.04-1.810.99-2.11 | -0.300.360.26**0.026**0.058 | 11.171.181.181.331.75 | -0.9-1.500.91-1.530.89-1.580.98-1.801.17-2.61 | -0.200.200.250.066**0.006** |
| **BMI category**c Underweight Normal Overweight Obese | 1.2910.841.01 | 0.77-2.17-0.70-1.100.81-1.25 | 0.34-0.0520.95 | 1.1110.861.03 | 0.66-1.88-0.72-1.040.82-1.29 | 0.70-0.120.79 |
| **Social deprivation**d IMD lower | 1.38 | 1.18-1.62 | **>0.001** | 1.41 | 1.19-1.66 | **<0.001** |
| **Co-morbidities**e IBS Depression | 1.011.23 | 0.81-1.250.94-1.61 | 0.950.13 | 0.981.24 | 0.78-1.230.94-1.65 | 0.870.13 |
| **IBD medication**fOral 5-ASA  | 1.96 | 1.64-2.35 | **0.006** | 1.94 | 1.59-2.38 | **<0.001** |
| **Early CS**g | 1.26 | 1.09-1.47 | **0.003** | 1.01 | 0.87-1.19 | 0.95 |

Multiple regression includes all covariates of simple regression. Significant hazard ratios shown in bold.

**HR** – Hazard Ratio **CI** - Confidence Interval **IBD** - Inflammatory Bowel Disease **BMI** - Body Mass Index **IMD** - index of multiple deprivation **IBS** - irritable bowel syndrome **5-ASA** - 5-aminosalicylates  **TP** – Thiopurine **CS** - Corticosteroid

a – Age categories as per Montreal classification (A1 <17 years, A2 17-40, A3 >40 years)

b – Era 1: 2005-06, Era 2: 2007-08, Era 3: 2009-10, Era 4: 2011-12, Era 5: 2013-14, Era 6: 2015-04/2016

c – calculated as the closest recorded BMI to date of IBD diagnosis, one year either side of IBD diagnosis, data available for 88% of patients

d – IMD lower includes IMD categories 4 and 5 (versus IMD category 1, 2 and 3), data available for 58% of patients

e – IBS co-diagnosis defined as any patient with a Read code for IBS before or after IBD diagnosis. Depression defined as any patient with a Read code for depression before or after IBD diagnosis

f – exposure of oral 5-ASA defined as any patients with at least one or more prescription for oral 5-ASA after IBD diagnosis

g – corticosteroid prescription within 30 days of diagnosis with UC

**Table 5: Simple and multiple Cox regression analysis for risk of colectomy in patients with Ulcerative Colitis**

|  |  |  |
| --- | --- | --- |
|  | **simple Cox regression****n=4069** | **multiple Cox regression****n=3483** |
| **HR** | **95% CI** | **p value** | **HR** | **95% CI** | **p value** |
| **Smoking status at diagnosis**Never-Smoker Ex-Smoker Smoker | 11.120.76 | -0.91-1.370.53-1.07 | -0.290.12 | 11.060.89 | -0.80-1.410.56-1.40 | -0.700.60 |
| **Sex**  (ref to female) | 1.12 | 0.92-1.36 | 0.25 | 1.35 | 1.03-1.77 | **0.031** |
| **Age at IBD diagnosis**aA1 A2 A3 | 2.1810.82 | 0.96-4.94-0.67-1.01 | 0.061**-**0.062 | 3.8410.94 | 1.18-12.50-0.69-1.27 | **0.026-**0.68 |
| **Era of IBD diagnosis**b Era 1 Era 2 Era 3 Era 4 Era 5 Era 6 | 11.060.910.960.890.80 | -0.80-1.400.67-1.230.70-1.340.60-1.230.48-1.32 | -0.710.550.850.410.37 | 11.080.961.110.950.63 | -0.74-1.580.64-1.450.72-1.740.57-1.560.27-1.50 | -0.690.840.630.830.30 |
| **BMI category**c Underweight Normal Overweight Obese | 0.5010.770.75 | 0.20-1.21-0.61-0.960.56-1.00 | 0.12-**0.022**0.053 | 0.5310.700.68 | 0.17-1.67-0.52-0.940.46-0.99 | 0.28-**0.0180.049** |
| **Social deprivation**d IMD lower | 1.02 | 0.78-1.33 | 0.90 | 1.04 | 0.79-1.38 | 0.76 |
| **Co-morbidities**e IBS Depression | 0.870.99 | 0.65-1.160.70-1.42 | 0.350.99 | 0.571.45 | 0.37-0.900.92-2.30 | **0.016**0.11 |
| **IBD medication**fOral 5-ASA | 1.36 | 1.09-1.69 | **0.006** | 1.18 | 0.87-1.62 | 0.29 |
| **Early CS**g | 1.39 | 1.14-1.68 | **0.001** | 1.25 | 0.94-1.66 | 0.12 |

Multiple regression includes all covariates of simple regression. Significant hazard ratios shown in bold.

**HR** – Hazard Ratio **CI** - Confidence Interval **IBD** - Inflammatory Bowel Disease **BMI** - Body Mass Index **IMD** - index of multiple deprivation **IBS** - irritable bowel syndrome **5-ASA** - 5-aminosalicylates **CS** - Corticosteroid

a – Age categories as per Montreal classification (A1 <17 years, A2 17-40, A3 >40 years)

b – Era 1: 2005-06, Era 2: 2007-08, Era 3: 2009-10, Era 4: 2011-12, Era 5: 2013-14, Era 6: 2015-04/2016

c – calculated as the closest recorded BMI to date of IBD diagnosis, one year either side of IBD diagnosis, data available for 88% of patients

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e – IBS co-diagnosis defined as any patient with a Read code for IBS before or after IBD diagnosis. Depression defined as any patient with a Read code for depression before or after IBD diagnosis

f – exposure of oral 5-ASA defined as any patients with at least one or more prescription for oral 5-ASA after IBD diagnosis

g – corticosteroid prescription within 30 days of diagnosis with UC