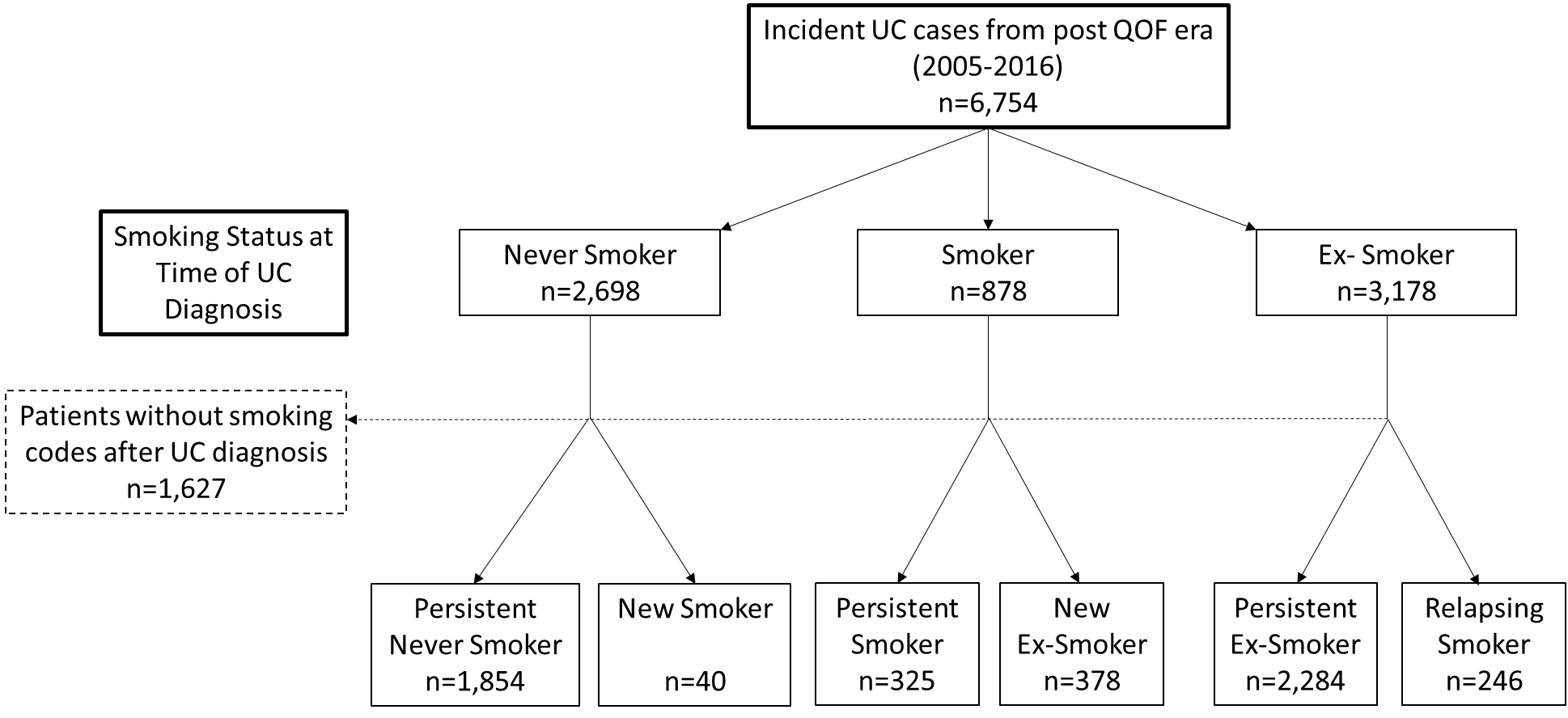
# Figures

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

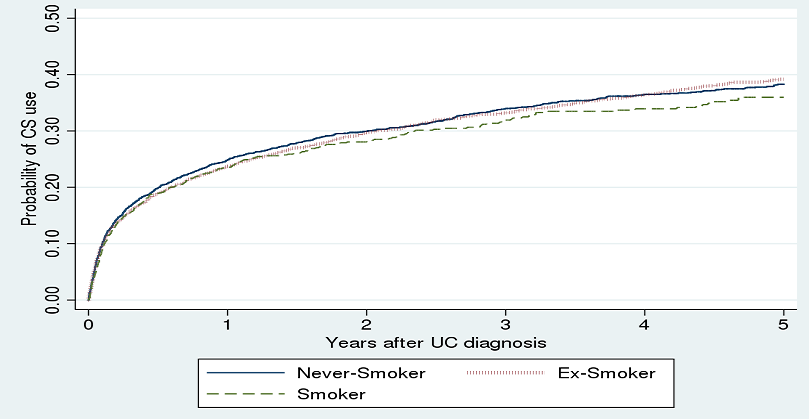


**UC** – Ulcerative Colitis

**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**

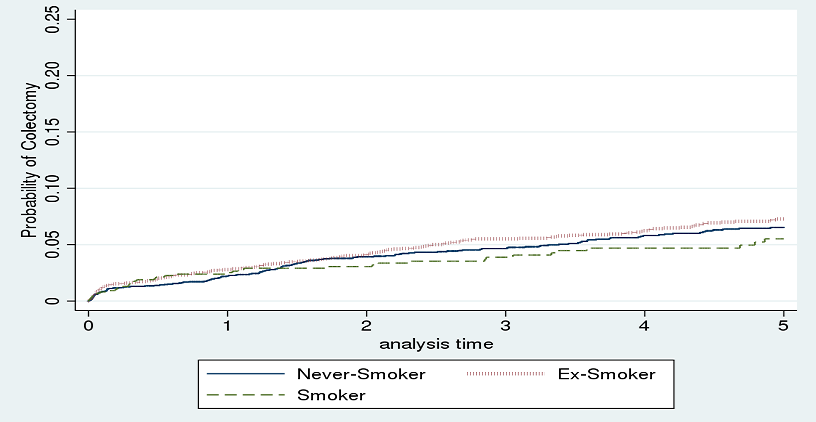


Log rank test for trend: p=0.53

**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 | 1.7  37.8  60.5 | 0.1  20.8  79.2 | 0  42.9  57.1 | **<0.001** |
| **BMI category at diagnosis**b **(%)**  Underweight  Normal  Overweight  Obese | 3.5  43.8  35.5  17.2 | 1.2  34.0  44.2  20.7 | 4.2  44.8  36.2  14.7 | **<0.001** |
| **Social deprivation**c **(%)**  IMD 1  IMD 2  IMD 3  IMD 4  IMD 5 | 26.5  25.1  17.7  19.1  11.6 | 25.8  24.9  19.5  17.9  11.8 | 18.9  23.8  19.8  20.6  17.0 | **0.006** |
| **Comorbidities (%)**  IBSd  Depressione | 13.6  6.3 | 13.1  9.3 | 16.4  11.4 | **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 | 1 0.75 0.89 | - 0.60-0.93 0.78-1.02 | - **0.009** 0.10 | 1 0.85 0.90 | - 0.61-1.18 0.73-1.11 | - 0.34 0.32 |
| **Sex**  (ref to female) | 1.15 | 1.01-1.31 | **0.033** | 1.51 | 1.24-1.85 | **<0.001** |
| **Age at IBD diagnosis**a A1  A2  A3 | 3.40  1 0.77 | 2.12-5.47 - 0.67-0.88 | **<0.001 - <0.001** | 2.91 1 0.99 | 1.06-7.98 - 0.97-1.23 | **0.038** - 0.14 |
| **Era of IBD diagnosis**b Era 1  Era 2  Era 3  Era 4  Era 5  Era 6 | 1 1.06 0.95 0.96 0.87 0.84 | - 0.87-1.29 0.78-1.17 0.78-1.20 0.69-1.09 0.62-1.14 | - 0.57 0.63 0.74 0.23 0.26 | 1 0.91 0.83 0.88 0.98  0.79 | - 0.68-1.22 0.61-1.11 0.63-1.21 0.70-1.37 0.47-1.34 | - 0.53 0.21 0.43 0.91 0.39 |
| **BMI category**c  Underweight  Normal  Overweight  Obese | 1.39 1 0.82 0.85 | 0.95-2.04 - 0.71-0.96 0.70-1.03 | 0.80 - **0.014** 0.09 | 1.64 1 0.84 0.92 | 0.96-2.81 - 0.67-1.04 0.70-1.22 | 0.07 - 0.11 0.57 |
| **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 | 0.96 0.83 | 0.79-1.16 0.64-1.07 | 0.65 0.15 | 1.16 0.98 | 0.89-1.52 0.67-1.43 | **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 | 1  0.92  0.90 | -  0.80-1.05  0.60-0.93 | -  0.22 **0.009** | 1 1.03  0.92 | -  0.84-1.27  0.67-1.25 | -  0.76  0.60 |
| **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 | 2.40  1  0.49 | 1.48-3.90  -  0.43-0.56 | **<0.001**  **-**  **<0.001** | 0.96  1  0.54 | 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 | 1  1.12  1.17  1.43  1.33 1.34 | -  0.91-1.39  0.95-1.45  1.15-1.78  1.06-1.68  1.01-1.79 | -  0.28  0.14  **0.001**  **0.014**  **0.044** | 1  0.90  0.95  1.14  1.11  1.22 | -  0.67-1.22  0.70-1.29  0.83-1.56  0.79-1.55  0.77-1.94 | -  0.50  0.75  0.43  0.55  0.39 |
| **BMI category**c  Underweight  Normal  Overweight  Obese | 1.51  1  0.80  0.82 | 1.04-2.18  -  0.69-0.93  0.68-0.99 | **0.031**  -  **0.005**  **0.046** | 1.06  1  0.85  0.91 | 0.60-1.87  -  0.68-1.06  0.69-1.20 | 0.85  -  0.15  0.50 |
| **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 | 0.80  0.70 | 0.65-0.97  0.54-0.92 | **0.024**  **0.010** | 0.76  0.82 | 0.56-1.02  0.56-1.22 | 0.066  0.34 |
| **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 | 1 0.82 0.91 | - 0.70-0.97 0.71-1.17 | - **0.017** 0.46 | 1 0.87 0.92 | - 0.73-1.03 0.70-1.20 | - 0.11 0.54 |
| **Sex**  (ref to female) | 0.91 | 0.78-1.06 | 0.23 | 1.01 | 0.86-1.19 | 0.90 |
| **Age at IBD diagnosis**a A1  A2  A3 | 2.36 1 0.72 | 1.12-5.02 - 0.61-0.84 | **>0.001 - 0.025** | 1.26 1 0.85 | 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 | 1 1.13 1.12 1.17 1.37  1.44 | - 0.90-1.42  0.88-1.43  0.89-1.52  1.04-1.81  0.99-2.11 | - 0.30  0.36  0.26  **0.026**  0.058 | 1 1.17  1.18 1.18 1.33 1.75 | - 0.9-1.50  0.91-1.53  0.89-1.58  0.98-1.80  1.17-2.61 | - 0.20 0.20  0.25  0.066  **0.006** |
| **BMI category**c  Underweight  Normal  Overweight  Obese | 1.29 1 0.84 1.01 | 0.77-2.17 - 0.70-1.10 0.81-1.25 | 0.34  -  0.052  0.95 | 1.11 1 0.86 1.03 | 0.66-1.88 - 0.72-1.04 0.82-1.29 | 0.70 -0.12 0.79 |
| **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 | 1.01 1.23 | 0.81-1.25 0.94-1.61 | 0.95 0.13 | 0.98 1.24 | 0.78-1.23 0.94-1.65 | 0.87 0.13 |
| **IBD medication**f  Oral 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 | 1 1.12 0.76 | - 0.91-1.37 0.53-1.07 | - 0.29 0.12 | 1 1.06 0.89 | - 0.80-1.41 0.56-1.40 | - 0.70 0.60 |
| **Sex**  (ref to female) | 1.12 | 0.92-1.36 | 0.25 | 1.35 | 1.03-1.77 | **0.031** |
| **Age at IBD diagnosis**a A1  A2  A3 | 2.18 1 0.82 | 0.96-4.94 - 0.67-1.01 | 0.061 **-** 0.062 | 3.84 1 0.94 | 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 | 1 1.06 0.91 0.96 0.89  0.80 | - 0.80-1.40  0.67-1.23  0.70-1.34  0.60-1.23  0.48-1.32 | - 0.71  0.55  0.85  0.41  0.37 | 1 1.08  0.96 1.11 0.95 0.63 | - 0.74-1.58 0.64-1.45 0.72-1.74 0.57-1.56 0.27-1.50 | - 0.69 0.84  0.63  0.83  0.30 |
| **BMI category**c  Underweight  Normal  Overweight  Obese | 0.50 1 0.77 0.75 | 0.20-1.21 - 0.61-0.96 0.56-1.00 | 0.12 - **0.022**  0.053 | 0.53 1 0.70 0.68 | 0.17-1.67 - 0.52-0.94 0.46-0.99 | 0.28 - **0.018 0.049** |
| **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 | 0.87 0.99 | 0.65-1.16 0.70-1.42 | 0.35 0.99 | 0.57 1.45 | 0.37-0.90 0.92-2.30 | **0.016** 0.11 |
| **IBD medication**f  Oral 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

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