

The risk of subsequent surgery following bowel resection for Crohn's disease in a national cohort of 19,207 patients

King, Dominic; Coupland, Benjamin ; Dosanjh, Amandeep; Cole, Andrew; Ward, Stephen; Reulen, Raoul; Adderley, Nicola; Patel, Prashant; Trudgill, Nigel

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Supplementary Appendices

Appendix 1

Surgical Code List

OPCS-4 (Office of Population Censuses and Surveys Classification of Interventions and Procedures 4th revision)

ICD-10 (International Classification of Diseases version 10)

Crohn's Disease	Ulcerative Colitis	Index Surgery	Further Surgery	Index surgery at risk of elective staged procedures
ICD-10	ICD-10	OPCS-4	OPCS-4	OPCS-4
K50	K51	H04 - Total excision of colon and rectum	G74 - Creation of artificial opening into ileum	H151 - Loop colostomy
		H05 - Total excision of colon	G75 - Attention to artificial opening into ileum	H152 - End colostomy
		H06 - Extended excision of right hemicolon	G60 - Artificial opening into jejunum	H158 - Other specified other exteriorisation of colon
		H07 - Other excision of right hemicolon	G63 - Other open operations on jejunum	H159 - Unspecified other exteriorisation of colon
		H08 - Excision of transverse colon	G67 - Other operations on jejunum	H328 - Other specified exteriorisation of colon
		H09 - Excision of left hemicolon	G785 - Exclusion of segment of ileum	H329 - Unspecified exteriorisation of colon
		G613 - Bypass of jejunum, anastomosis of jejunum-colon	G714 - Bypass ileum anastomosis ileum-trans colon	G741 - Creation of continent ileostomy
		H11 - Other excision of colon	H14 - Exteriorisation of caecum	G742 - Creation of temporary ileostomy
		H19 - Other open operations on colon	H15 - Other exteriorisation of colon	G743 - Creation of defunctioning ileostomy
		H29 - Subtotal excision of colon	H32 - Exteriorisation of colon	H064 - Extended right hemicolectomy & ileostomy
		H30 - Other operations on colon	H162 - Caecotomy	H074 - Right hemicolectomy and ileostomy HFQ
		H33 - Excision of rectum	H163 - Colotomy	H084 - Transverse colectomy and ileostomy HFQ
		G715 - Bypass ileum anastomosis ileum-colon	H04 - Total excision of colon and rectum	H094 - Left hemicolectomy and ileostomy HFQ
		G713 - Bypass of jejunum, anastomosis of jejunum-caecum	H05 - Total excision of colon	H104 - Sigmoid colectomy and ileostomy HFQ
		G714 - Bypass ileum, anastomosis ileum-transverse colon	H06 - Extended excision of right hemicolon	H114 - Colectomy and ileostomy NEC
		H10 - Excision of sigmoid colon	H07 - Other excision of right hemicolon	H335 - Rectosigmoidectomy & closure of rectal stump & exteriorisation of bowel
		G724 - Anastomosis of ileum to rectum	H08 - Excision of transverse colon	
		G721 - Anastomosis of ileum to caecum	H09 - Excision of left hemicolon	
		G722 - Anastomosis ileum-transverse colon	H10 - Excision of sigmoid colon	
		G723 - Anastomosis of ileum to colon NEC	H11 - Other excision of colon	
		G694 - Ileectomy & anastomosis ileum-colon	H19 - Other open operations on colon	
		G782 - Strictureplasty of ileum	H29 - Subtotal excision of colon	
		G58 - Excision of jejunum	H30 - Other operations on colon	
		G69 - Excision of ileum	H33 - Excision of rectum	
		G73 - Attention to connection of ileum	G613 - Bypass jejunum anastomosis jejunum-colon	
		G71 - Bypass of ileum	G713 - Bypass ileum anastomosis ileum-caecum	
		G61 - Bypass of jejunum	G721 - Anastomosis of ileum to caecum	
			G722 - Anastomosis ileum-transverse colon	
			G725 - Anastomosis ileum-anus, pouch creation	
			G724 - Anastomosis of ileum to rectum	
			G715 - Bypass ileum anastomosis of ileum to colon NEC	
			G723 - Anastomosis of ileum to colon NEC	
			G734 - Resection of ileocolic anastomosis	
			G694 - Ileectomy & anastomosis ileum to colon	
			G782 - Strictureplasty of ileum	
			G58 - Excision of jejunum	
	G69 - Excision of ileum			
	G73 - Attention to connection of ileum			
	G71 - Bypass of ileum			
	G61 - Bypass of jejunum			
	H661 - Excision of ileoanal pouch			
	H662 - Revision of ileoanal pouch			
	H668 - Other therapeutic operations on ileoanal pouch			
	H669 - Unspecified operations on ileoanal pouch			
	G733 - Resection of ileostomy			

Appendix 2

Perianal surgery codes (including operations undertaken to aid perianal disease healing where no resectional code was recorded)

OPCS-4 Code	Description
H551	Laying open of low anal fistula
H552	Laying open of high anal fistula
H553	Laying open of anal fistula NEC
H554	Insertion of seton into high anal fistula and partial laying open of track HFQ
H555	Fistulography of anal fistula
H557	Repair of anal fistula using plug
H558	Other specified other operations on perianal region
H559	Unspecified other operations on perianal region
H564	Excision of anal fissure
H581	Drainage of ischiorectal abscess
H582	Drainage of perianal abscess
H583	Drainage of perirectal abscess

Appendix 3

Extraintestinal Manifestations of Inflammatory Bowel Disease (EIM) Categories – codes

Ophthalmologic EIMs		Hepatobiliary EIMs		Dermatologic EIMs		Musculoskeletal EIMs	
ICD-10		ICD-10		ICD-10		ICD-10	
Code	Description	Code	Description	Code	Description	Code	Description
H150	Scleritis	K830	Cholangitis	K12	Stomatitis and related lesions	M091	Juvenile arthritis in Crohn's disease
H151	Episcleritis			L40	Psoriasis	M45	Ankylosing spondylitis
H20	Iridocyclitis			L52	Erythema nodosum	M461	Sacroiliitis, not elsewhere classified
				L88	Pyoderma gangrenosum		
				L982	Febrile neutrophilic dermatosis [Sweet]		

Appendix 4

Comparison of inclusion and exclusion characteristics

		All patients			Patients with ≥ 5 years follow-up		
		Included N (%)	Excluded N (%)	p- value	Included N (%)	Excluded N (%)	p-value
Sex	Male	8677 (45)	3656 (48)	<0.001	5971 (45)	2753 (48)	<0.001
	Female	10530 (55)	3955 (52)		7397 (55)	2979 (52)	
Total		19207	7611		13368	5732	
Age quintile	18-25	4344 (23)	591 (9)	<0.001	2678 (22)	411 (9)	<0.001
	26-34	3536 (18)	778 (12)		2775 (20)	650 (14)	
	35-44	3738 (19)	1254 (20)		2706 (19)	958 (20)	
	45-57	3793 (20)	1462 (23)		2606 (20)	1074 (22)	
	58+	3796 (20)	2322 (36)		2603 (20)	1707 (36)	
Total		19207	6407		13368	4800	
Deprivation quintile	1 (Most deprived)	4127 (21)	1490 (20)	0.093	2826 (21)	1147 (21)	0.214
	2	4127 (21)	1520 (21)		2879 (22)	1123 (20)	
	3	3958 (21)	1510 (21)		2770 (21)	1126 (20)	
	4	3650 (19)	1433 (20)		2522 (19)	1096 (20)	
	5 (Least deprived)	3345 (17)	1343 (18)		2371 (18)	1012 (20)	
Total		19207	7296		13368	5504	
Charlson comorbidity category	0	15620 (81)	5896 (77)	<0.001	11009 (82)	4538 (79)	<0.001
	1-4	2465 (13)	1071 (14)		1615 (12)	749 (13)	
	5+	1122 (6)	646 (8)		744 (6)	446 (8)	
Total		19207	7613		13368	5733	
Ethnicity	White	16903 (88)	6701 (88)	0.448	11850 (89)	5081 (89)	0.603
	Asian	562 (3)	247 (3)		350 (3)	167 (3)	
	Other minority ethnicities	609 (3)	238 (3)		410 (3)	176 (3)	
	Unknown	1133 (6)	427 (6)		758 (6)	309 (5)	
Total		19207	7613		13368	5733	

Appendix 5

Index surgery and further surgery by age decile

Index Surgery Age	(N)	Further Surgery Age	(N)
18-29	5807	18-29	759
30-39	3949	30-39	753
40-49	3576	40-49	674
50-59	2536	50-59	476
60-69	1960	60-69	297
70+	1379	70+	182
Total	19207	Total	3141

Appendix 6

All further surgery demographics table including within 30-days and those thought to be an elective staged procedure.

Demographics		Patients with ≥ 5 years follow-up (%)	All further CD surgery within 5 years (%)
Sex	Male	5971 (44.7)	1159 (19.4)
	Female	7397 (55.3)	1355 (18.3)
Age quintile	18-25	2678 (20.0)	517 (19.3)
	26-34	2775 (20.8)	550 (19.8)
	35-44	2706 (20.2)	539 (19.9)
	45-57	2606 (19.5)	489 (18.8)
	58+	2603 (19.5)	419 (16.1)
Provider volume of index surgery	Low	1731 (12.9)	298 (17.2)
	Medium	4071 (30.5)	723 (17.8)
	High	7566 (56.6)	1493 (19.7)
Ethnicity	White	11850 (88.6)	2236 (18.9)
	Asian	350 (2.6)	81 (23.1)
	Other minority ethnicities	410 (3.1)	83 (20.2)
	Unknown	758 (5.7)	114 (15.0)
Deprivation quintile	1 (Most Deprived)	2826 (21.1)	560 (19.8)
	2	2879 (21.5)	565 (19.6)
	3	2770 (20.7)	529 (19.1)
	4	2522 (18.9)	447 (17.7)
	5 (Least Deprived)	2371 (17.7)	413 (17.4)
Index surgery admission method	Emergency	5879 (44.0)	1333 (22.7)
	Elective	7385 (55.2)	1159 (15.7)
	Unknown	104 (0.8)	22 (21.2)
Year of index surgery	2007	1816 (13.6)	341 (18.8)
	2008	1848 (13.8)	364 (19.7)
	2009	1886 (14.1)	369 (19.6)
	2010	1901 (14.2)	359 (18.9)
	2011	1962 (14.7)	341 (17.4)
	2012	2004 (15.0)	395 (19.7)
	2013	1951 (14.6)	345 (17.7)
Charlson comorbidity score	0	11009 (82.4)	2034 (18.5)
	1-4	1615 (12.1)	316 (25.8)
	5+	744 (5.6)	164 (26.0)
Prior perianal surgery		1148 (8.6)	296 (25.8)
Presence of extraintestinal manifestations		622 (4.7)	162 (26.0)

Index surgery performed laparoscopically	3051 (22.8)	442 (14.5)
Total	13368 (69.8)	2514 (18.8)

Appendix 7

Sensitivity analysis: Multivariable logistic regression of factors associated with all further surgery within 5 years of index Crohn's disease surgery

Demographic		Odds Ratio	[95% Conf. Interval]		p-value
Sex	Male	reference			
	Female	0.99	0.91	1.09	0.879
Age quintile	18-25	reference			
	25-34	1.05	0.91	1.20	0.507
	35-44	1.05	0.92	1.21	0.450
	45-57	0.98	0.85	1.13	0.824
	58+	0.73	0.63	0.86	<0.001
Provider volume of index surgery	Low	reference			
	Medium	1.04	0.89	1.21	0.634
	High	1.19	1.03	1.36	0.016
Ethnicity	White	reference			
	Asian	1.18	0.91	1.53	0.201
	Non-White	1.05	0.82	1.35	0.677
	Unknown	0.75	0.61	0.93	0.008
Deprivation quintile	1 (Most Deprived)	reference			
	2	1.00	0.88	1.15	0.949
	3	1.00	0.88	1.15	0.983
	4	0.92	0.80	1.06	0.255
	5 (Least Deprived)	0.91	0.79	1.05	0.215
Index surgery admission method	Emergency	reference			
	Non-Emergency	0.66	0.61	0.73	<0.001
Charlson comorbidity score	0	reference			
	1-4	1.11	0.97	1.27	0.132
	5+	1.30	1.07	1.57	0.009
Year of index surgery	2007	reference			
	2008	1.05	0.89	1.23	0.601
	2009	1.04	0.88	1.22	0.684
	2010	0.99	0.83	1.17	0.873
	2011	0.90	0.76	1.06	0.206
	2012	1.05	0.89	1.24	0.527
	2013	0.93	0.79	1.10	0.411
Prior perianal surgery		1.51	1.31	1.74	<0.001
Presence of extraintestinal manifestations		1.53	1.27	1.85	<0.001
Index surgery performed laparoscopically		0.76	0.67	0.85	<0.001

Appendix 8

Crohn's colitis sub-cohort demographic table

Demographic		Patients (%)	Further surgery (%)	Patients with ≥5 year follow-up (%)	Further surgery within 5 years (%)
Sex	Male	992 (42.6)	229 (23.0)	691 (42.6)	138 (20.0)
	Female	1337 (57.4)	278 (20.7)	932 (57.4)	164 (17.6)
Age quintile	18-26	513 (22.0)	122 (23.8)	360 (22.2)	66 (18.3)
	27-35	428 (18.4)	100 (23.4)	292 (18.0)	56 (19.2)
	36-46	486 (20.9)	116 (23.9)	337 (20.8)	73 (21.7)
	47-59	459 (19.7)	96 (20.9)	325 (20.0)	58 (17.8)
	60+	443 (19.0)	73 (16.5)	309 (19.0)	49 (15.9)
Median (IQR) Age		41 (28-54)	38 (27-51)	41 (28-54)	39 (28-53)
Provider volume of index surgery	Low (1-10)	322 (13.8)	58 (18.0)	250 (15.4)	34 (13.6)
	Medium (11-17)	686 (29.5)	155 (22.6)	469 (28.9)	72 (15.4)
	High (18+)	1321 (56.7)	294 (22.3)	904 (55.7)	196 (21.7)
Ethnicity	White	2047 (87.9)	449 (21.9)	1437 (88.5)	271 (18.9)
	Asian	79 (3.4)	19 (24.1)	46 (2.8)	11 (23.9)
	Other minority ethnicities	74 (3.2)	16 (21.6)	49 (3.0)	8 (16.3)
	Unknown	129 (5.5)	23 (17.8)	91 (5.6)	12 (13.2)
Deprivation quintile	1 (Most Deprived)	499 (21.4)	106 (21.2)	361 (22.2)	71 (19.7)
	2	484 (20.8)	109 (22.5)	333 (20.5)	67 (20.1)
	3	478 (20.5)	106 (22.2)	322 (19.8)	54 (16.8)
	4	448 (19.2)	108 (24.1)	309 (19.0)	62 (20.2)
	5 (Least Deprived)	420 (18.0)	78 (18.6)	298 (18.4)	48 (16.1)
Index surgery admission method	Emergency	1058 (45.4)	259 (24.5)	759 (46.8)	155 (20.4)
	Elective	1257 (54.0)	241* (*)	852 (52.5)	140* (*)
	Unknown	14 (0.6)	*	12 (0.7)	*
Year of index surgery	2007	204 (8.8)	55 (27.0)	204 (12.6)	37 (18.1)
	2008	231 (9.9)	74 (32.0)	231 (14.2)	51 (22.1)
	2009	225 (9.7)	45 (20.0)	225 (13.9)	35 (15.6)
	2010	228 (9.8)	54 (23.7)	228 (14.0)	40 (17.5)
	2011	236 (10.1)	56 (23.7)	236 (14.5)	45 (19.1)
	2012	240 (10.3)	51 (21.3)	240 (14.8)	47 (19.6)
	2013	259 (11.1)	52 (20.1)	259 (16.0)	47 (18.1)

	2014	222 (9.5)	51 (23.0)	-	-
	2015	244 (10.5)	36 (14.8)	-	-
	2016	240 (10.3)	33 (13.8)	-	-
Charlson	0	1862 (79.9)	418 (22.4)	1314 (18.0)	252 (19.2)
comorbidity	1-4	314 (13.5)	71 (22.6)	208 (12.8)	40 (19.2)
score	5+	153 (6.6)	18 (11.8)	101 (6.2)	10 (9.9)
Perianal surgery up to index surgery		309 (13.3)	90 (29.1)	201 (12.4)	54 (26.9)
Median (IQR) time to further surgery			783 (428-		686 (394-1130)
	(days)		1451)		
Extraintestinal manifestations		173 (7.4)	53 (30.6)	94 (5.8)	24 (25.5)
Index surgery performed laparoscopically		585 (25.1)	119 (20.3)	336 (20.7)	58 (17.3)
Totals		2329	507 (21.8)	1623	302 (18.6)

** ≤ 5 subjects: data not shown to ensure subject anonymity*

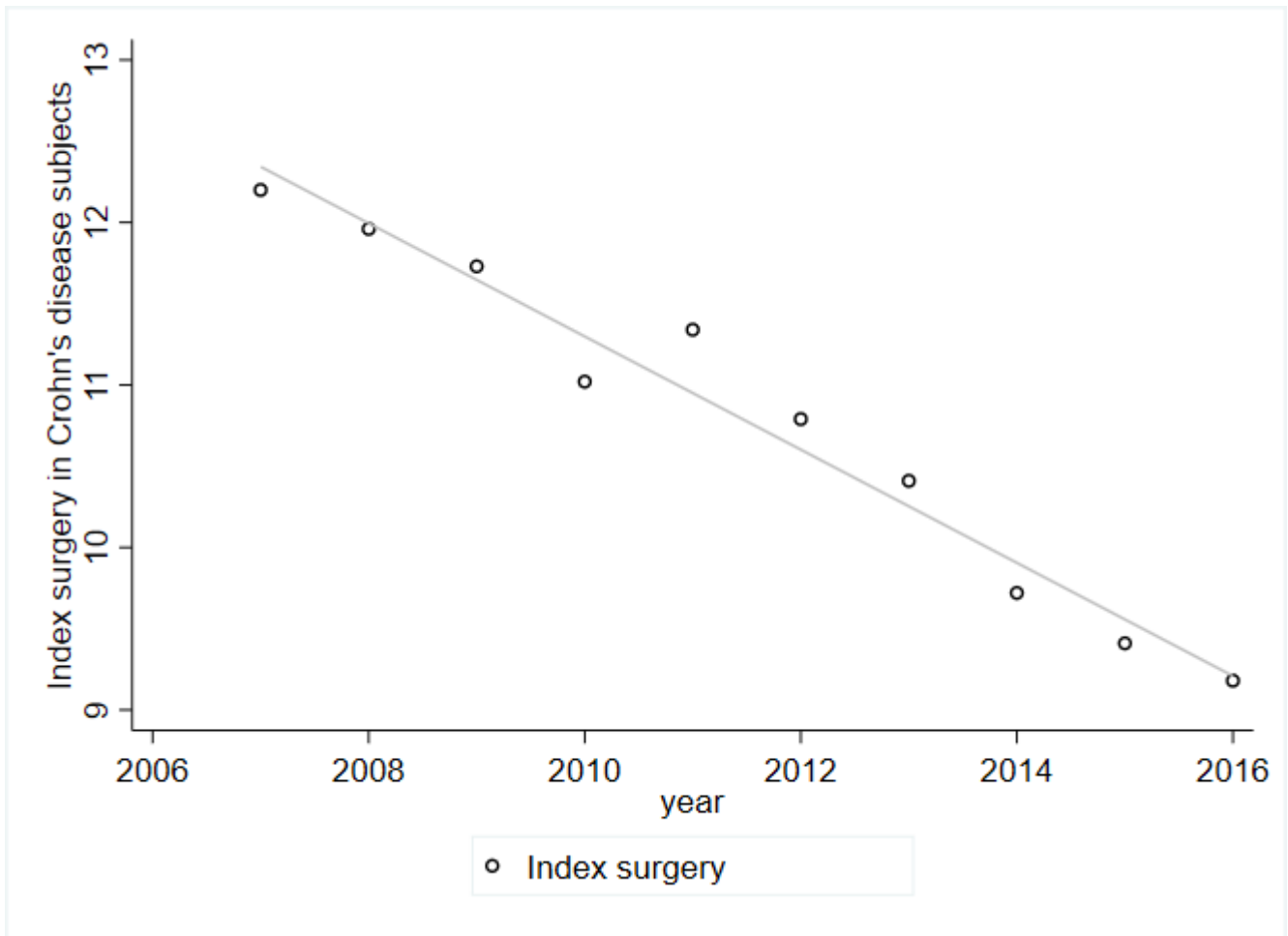
Appendix 9

Multivariable logistic regression of factors associated with further surgery within 5 years in the Crohn's colitis sub-cohort

Factors		Odds ratio	[95% Conf. Interval]		P-value
Sex	Male	reference			
	Female	0.86	0.67	1.12	0.268
Age quintile	18-26	reference			
	27-35	1.06	0.71	1.58	0.788
	36-46	1.25	0.86	1.83	0.242
	47-59	1.03	0.69	1.54	0.872
	60+	0.99	0.64	1.53	0.970
Provider volume of index surgery	Low (1-81)	reference			
	Medium (82-143)	1.15	0.74	1.81	0.533
	High (144+)	1.70	1.13	2.54	0.010
Ethnicity	White	reference			
	Asian	1.30	0.64	2.65	0.467
	Other minority ethnicities	0.85	0.39	1.88	0.695
	Unknown	0.64	0.34	1.20	0.165
Index of multiple deprivation (quintiles)	1 (Most deprived)	reference			
	2	1.00	0.68	1.46	0.997
	3	0.86	0.57	1.28	0.445
	4	0.99	0.67	1.46	0.947
	5 (Least deprived)	0.76	0.50	1.14	0.188
Index surgery admission	Emergency	reference			
	Non-Emergency	0.75	0.57	0.98	0.033
Charlson comorbidity Score	0	reference			
	1-4	0.96	0.65	1.40	0.815
	5+	0.47	0.23	0.95	0.035
Year of index surgery	2007	reference			
	2008	1.24	0.77	2.02	0.378
	2009	0.88	0.52	1.48	0.624
	2010	0.93	0.56	1.54	0.780
	2011	1.07	0.65	1.76	0.781
	2012	1.13	0.69	1.84	0.629
	2013	0.98	0.60	1.60	0.933
Prior perianal surgery		1.65	1.16	2.34	0.005
Presence of extraintestinal manifestations		1.53	0.93	2.52	0.095

Index surgery performed laparoscopically	0.99	0.70	1.39	0.950
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Appendix 10.



Graph showing fall in index resectional surgery per 1,000 subjects with Crohn's disease (CD) by year of study in England.

Appendix 11. Table of infliximab use before and after index surgery and in those who went on to have further surgery

	Index Surgery Year	All Surgery		
		Infliximab Patients	Total Patients	Percentage
1 Year Before Index Surgery	2007	101	1816	5.6%
	2008	148	1848	8.0%
	2009	163	1886	8.6%
	2010	206	1901	10.8%
	2011	228	1962	11.6%
	2012	242	2004	12.1%
	2013	265	1951	13.6%
	2014	310	1902	16.3%
	2015	293	1964	14.9%
	2016	375	1973	19.0%
	Total	2331	19207	12.1%
1 Year After Index Surgery	2007	52	1816	2.9%
	2008	53	1848	2.9%
	2009	70	1886	3.7%
	2010	74	1901	3.9%
	2011	78	1962	4.0%
	2012	97	2004	4.8%
	2013	114	1951	5.8%
	2014	119	1902	6.3%
	2015	128	1964	6.5%
	2016	147	1973	7.5%
	Total	932	19207	4.9%
Both of the Above	2007	11	1816	0.6%
	2008	21	1848	1.1%
	2009	19	1886	1.0%
	2010	37	1901	1.9%
	2011	37	1962	1.9%
	2012	39	2004	1.9%
	2013	54	1951	2.8%
	2014	68	1902	3.6%
	2015	75	1964	3.8%
	2016	77	1973	3.9%
	Total	438	19207	2.3%
Further Surgery		573	3141	18.2%

Appendix 11. Table of index surgery coded as laparoscopic over the study period

Year	Index Surgery	Laparoscopic Surgery	Percentage
2007	1816	208	11.5%
2008	1848	322	17.4%
2009	1886	392	20.8%
2010	1901	452	23.8%
2011	1962	525	26.8%
2012	2004	532	26.5%
2013	1951	620	31.8%
2014	1902	604	31.8%
2015	1964	706	35.9%
2016	1973	737	37.4%