SUPPLEMENTARY DATA CONTENT

Supplement to: 'Multi-national observational study to assess quality of life and treatment preferences in patients with Crohn's perianal fistulas'

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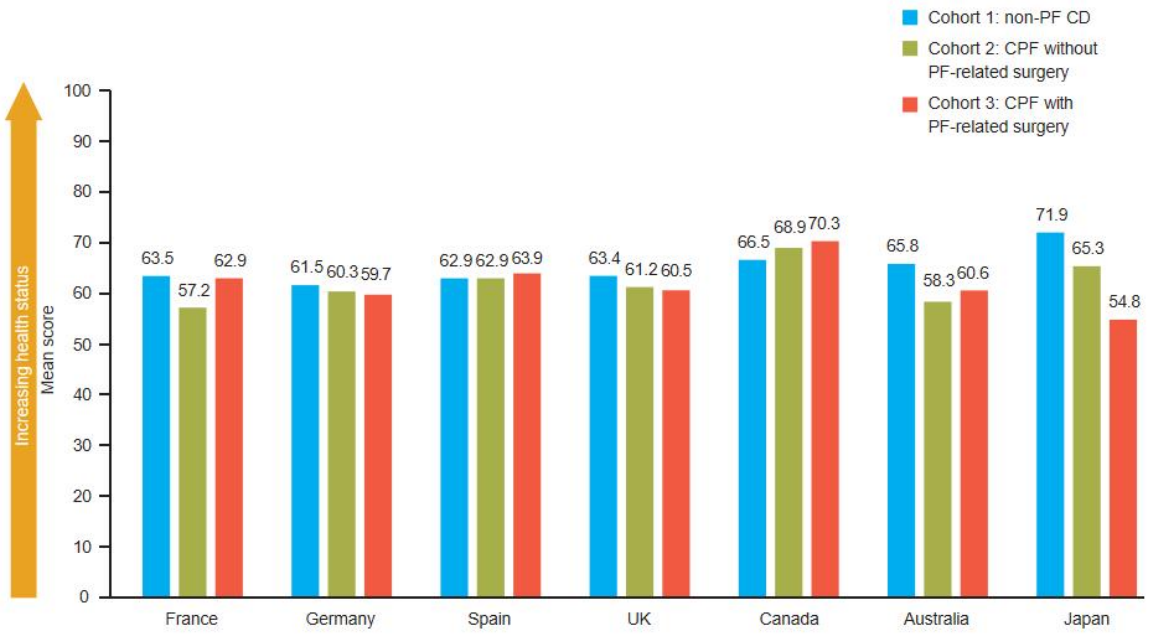

Supplementary Figure 1 EQ-5D visual analog scale scorest. Scoring key for EQ-5D visual analog scale (range 0-100): higher scores indicate better HRQoL. Populations for each country for cohorts 1, 2, and 3, respectively: France, n = 100, n = 32, and n = 18; Germany, n = 100, n = 17, and n = 33; Spain, n = 100, n = 36, and n = 14; UK, n = 100, n = 33, and n = 17; Canada, n = 100, n = 24, and n = 26; Australia, n = 60, n = 12, and n = 17; Japan, n = 60, n = 20, and n = 10. CD: Crohn's disease; CPF: Crohn's perianal fistulas.

Supplementary Table 1 Additional baseline demographics

	Cohort 1 **All non-PF CD** **(*n* = 620)**	**Cohort 2** **CPF no surgery** **(*n* = 174)**	**Cohort 3** **CPF with surgery** **(*n* = 135)**	**Cohorts 2 + 3** **All CPF** **(*n* = 309)**
Employment status, *n* (%)				
Homemaker	32 (5)[a]	9 (5)[a]	6 (4)[a]	15 (5)[a]
Student	4 (1)[a]	1 (1)[a]	2 (1)[a]	3 (1)[a]
Retired	45 (7)[b-d]	3 (2)[e]	0 (0)[e]	3 (1)[e]
Other	8 (1)[d]	0 (0)[a]	0 (0)[a]	0 (0)[e]
Disabled	28 (5)[a]	5 (3)[a]	3 (2)[a]	8 (3)[a]
Unemployed	64 (10)[d]	12 (7)[a]	6 (4)[a]	18 (6)[e]
Full-time	348 (56)[b,c]	125 (72)[e]	99 (73)[e]	224 (72)[a]
Part-time	91 (15)[a]	19 (11)[a]	19 (14)[a]	38 (12)[a]
Marital status, *n* (%)				
Single	105 (17)[a]	22 (13)[a]	19 (14)[a]	41 (13)[a]
Married or domestic partnership	458 (74)[d]	142 (82)[a]	111 (82)[a]	253 (82)[e]
Widowed	10 (2)[d]	0 (0)[a]	0 (0)[a]	0 (0)[e]
Divorced	40 (6)[d]	7 (4)[a]	2 (1)[a]	9 (3)[e]
Separated	7 (1)[a]	3 (2)[a]	3 (2)[a]	6 (2)[a]

P values are shown where there is a statistically significant difference between specified cohorts. Bonferroni adjustment was applied when comparing more than 2 groups at $P < 0.05$. [a]No statistically significant difference versus any other cohort; [b]$P < 0.05$ *vs* cohort 2; [c]$P < 0.05$ *vs* cohort 3; [d]$P < 0.05$ *vs* cohort 2 + 3 combined; [e]$P < 0.05$ *vs* cohort 1. From each country, except Australia and Japan, $n = 100$ and $n = 50$ patients were recruited to cohort 1 and cohorts 2 + 3 combined, respectively. From Australia, 60 and 29 patients were recruited, and from Japan, 60 and 30 patients were recruited to cohorts 1 and 2 + 3 combined, respectively. CD: Crohn's disease; CPF: Crohn's perianal fistulas; PF: Perianal fistulas.

Supplementary Table 2 Multivariable analysis of SIBDQ scores to control for potential confounders

	Estimate	**SE**	**t value**	**Pr(>|t|)**
Intercept	4.261	0.119	35.834	$P < 0.001$
Patient with CPF (*vs* patient without CPF)	−0.174	0.063	−2.761	$P = 0.006$
Patient is male (*vs* female)	0.223	0.060	3.734	$P < 0.001$
Time since CD diagnosis (in years)	0.013	0.003	4.084	$P < 0.001$
Patient is part of a patient association (*vs* is not part of a patient association)	−0.433	0.059	−7.032	$P < 0.001$
Patient is aged 40 years or younger (*vs* is aged more than 40 years)	−0.202	0.062	−3.284	$P = 0.001$
Experienced a CD flare-up (*vs* did not experience a flare-up)	−0.558	0.058	−9.574	$P < 0.001$
Patient is not obese (*vs* obese)	0.251	0.082	3.071	$P = 0.002$

Adjusted R squared: 0.222. The dependent variable here is the SIBDQ score (range 1-7; 1 = poor health-related quality of life, 7 = optimum health-related quality of life). CD: Crohn's disease; CPF: Crohn's perianal fistulas; SE: Standard error; SIBDQ: Short Inflammatory Bowel Disease Questionnaire.

Supplementary Table 3 Multivariable analysis of RFIS scores to control for potential confounders

	Estimate	**SE**	**t value**	**Pr(>|t|)**
Intercept	9.573	1.241	7.717	$P < 0.001$
Patient with CPF (*vs* patient without CPF)	0.984	0.368	2.671	$P = 0.008$
Experienced a CD flare-up (*vs* did not experience a flare-up)	1.855	0.354	5.246	$P < 0.001$
Patient is not diagnosed with COPD (*vs* is diagnosed with COPD)	−2.117	0.870	−2.434	$P = 0.015$
Patient is part of a patient association (*vs* is not part of a patient association)	1.493	0.359	4.156	$P < 0.001$
Non-obese patients (*vs* obese patients)	−1.447	0.452	−3.198	$P = 0.001$
Patients married (*vs* patients not married)	0.785	0.395	1.990	$P = 0.047$

Adjusted R squared: 0.187. The dependent variable here is the RFIS score (range 0-20; < 4 = no FI or very mild, 4-6 = mild, 7-12 = moderate, ≥ 13 = severe). CD: Crohn's disease; COPD: Chronic obstructive pulmonary disease; CPF: Crohn's perianal fistulas; FI, Fecal incontinence; RFIS: Revised Faecal Incontinence Scale; SE: Standard error.

Supplementary Table 4 CD complication experience

	Cohort 1 **All non-PF CD** **(*n* = 620)**	**Cohort 2** **CPF no surgery** **(*n* = 174)**	**Cohort 3** **CPF with surgery** **(*n* = 135)**	**Cohorts 2 + 3** **All CPF** **(*n* = 309)**
CD complication experience in the past 12 months, *n* (%)				
Fatigue, *n* (%)	585 (94)[a,b]	172 (99)[c]	132 (98)[d]	304 (98)[c]
Mode of reported frequency	More than once per day[d]	Once a week[d]	Once per day[d]	Once a week[d]
Severity of ≥ 6	228 (39)[d]	65 (38)[d]	62 (47)[d]	127 (42)[d]
Abdominal pain and cramping, *n* (%)	575 (93)[b]	168 (97)[d]	129 (96)[d]	297 (96)[c]
Mode of reported frequency	Once a week[d]	Once a week[d]	Once a week[d]	Once a week[d]
Severity of ≥ 6	193 (34)[d]	60 (36)[d]	54 (42)[d]	114 (38)[d]
GI pain, *n* (%)	573 (92)[b]	166 (95)[d]	131 (97)[d]	297 (96)[c]
Mode of reported frequency	Twice a week[d]	Twice a week[d]	Once every other day[d]	Twice a week[d]
Severity of ≥ 6	190 (33)[b]	64 (39)[d]	55 (42)[d]	119 (40)[c]
Pain/difficulty with bowel movement, *n* (%)	534 (86)[a,b,e]	168 (97)[c]	132 (98)[c]	300 (97)[c]

Mode of reported frequency	Once a week[d]	Once every other day[d]	Twice a week[d]	Once a week/every other day[d]
Severity of ≥ 6	142 (27)[b,e]	54 (32)[d]	53 (40)[c]	107 (36)[c]
Pain when sitting, *n* (%)	504 (81)[a,b,e]	162 (93)[c,e]	134 (99)[a,c]	296 (96)[c]
Mode of reported frequency	Once a week[d]	Once a month[d]	Once every other day[d]	Once every other day[d]
Severity of ≥ 6	122 (24)[b,e]	44 (27)[e]	57 (43)[a,c]	101 (34)[c]

P values are shown where there is a statistically significant difference between specified cohorts. Bonferroni adjustment was applied when comparing more than 2 groups at $P < 0.05$. [a]$P < 0.05$ *vs* cohort 2; [b]$P < 0.05$ *vs* cohort 2 + 3 combined; [c]$P < 0.05$ *vs* cohort 1; [d]No statistically significant difference versus any other cohort; [e]$P < 0.05$ *vs* cohort 3. CD: Crohn's disease; CPF: Crohn's perianal fistulas; GI: Gastrointestinal; PF: Perianal fistulas.

Supplementary Table 5 Complications after PF-related surgery

Most frequent complications after surgery or seton placement, *n* (%)	**CPF patients with PF-related surgical care cohort 3 (*n* = 135)**
Fever/infection	44 (33)
Worsening of pain and swelling around the anus	43 (32)
Worsening of bloody or foul-smelling drainage (pus) from an opening around the anus	42 (31)
Worsening of pain/difficulty with bowel movements	39 (29)
Worsening of frequency of anal abscesses	39 (29)
Patients experiencing 1 postoperative complication	19 (14)
Patients experiencing 2-3 postoperative complications	64 (47)
Patients experiencing more than 3 postoperative complications	34 (25)
Patients experiencing 1 or more postoperative complications	117 (87)
Patients experiencing no postoperative complications	18 (13)

Complications for CPF patients after surgery or seton placement provided as options in the survey include: worsening of dyspareunia, worsening of frequency of anal abscesses, worsening of pain and swelling around the anus, worsening of bloody or foul-smelling drainage (pus) from an opening around the anus, worsening of irritation of the skin around the anus from drainage, worsening of pain/difficulty with bowel movements, fever/infection, worsening of fecaluria, worsening of

pneumaturia, worsening of anorectal stricture, fistulas in the upper part of the sphincter complex, and multiple fistulas/external openings. CPF: Crohn's perianal fistulas; PF: Perianal fistulas.

Supplementary Table 6 Overall impact of CD/CPF on life

	Cohort 1 **All non-PF CD** **(*n* = 620)**	**Cohort 2** **CPF no surgery** **(*n* = 174)**	**Cohort 3** **CPF with surg** **(*n* = 135)**
CD/CPF overall interference with life (on a scale of 1-9), mean (SD)	5.0 (2.0)[a-c]	6.0 (1.7)[d]	6.0 (1.7)[d]
CD/CPF overall interference with life during a flare-up (on a scale of 1-9), mean (SD)	6.7 (1.6)[e]	7.0 (1.5)[e]	6.8 (1.4)[e]

On a scale of 1-9, a higher number indicates a more significant interference with life. *P* values are shown where there is a statistically significant difference between specified cohorts. Bonferroni adjustment was applied when comparing more 2 groups at $P < 0.05$. [a]$P < 0.05$ *vs* cohort 2; [b]$P < 0.05$ *vs* cohort 3; [c]$P < 0.05$ *vs* cohort 2 + 3 combined; [d]$P < 0.05$ *vs* cohort 1; [e]No statistically significant difference versus any other cohort. CD: Crohn's disease; CPF: Crohn's perianal fistulas; PF: Perianal fistulas; SD: Standard deviation.

Supplementary Table 7 Impact of CD attributes

	Cohort 1 **All non-PF CD** **(*n* = 620)**	**Cohort 2** **CPF no surgery** **(*n* = 174)**	**Cohort 3** **CPF with surgery** **(*n* = 135)**
Impact of CD attribute on HRQoL (on a scale of 1-9), mean (SD)			
Diarrhea	5.7 (2.1)[a]	6.2 (1.8)[b]	5.9 (2.1)[b]
Fistulas in the upper sphincter complex	NA	5.6 (2.0)[b]	5.7 (2.0)[b]
Fatigue	5.2 (2.3)[a,d,e]	6.1 (2.0)[c]	5.8 (2.2)[c]
Abdominal pain and cramping	5.1 (2.3)[a,d,e]	5.7 (2.0)[c]	5.8 (2.0)[c]
Anorectal stricture	4.7 (2.2)[a,d,e]	5.8 (1.9)[c]	6.0 (2.0)[c]
Perianal abscess	4.6 (2.3)[a,d,e]	5.6 (2.0)[c]	5.9 (1.9)[c]
Pain/difficulty with bowel movement	4.7 (2.3)[a,d,e]	5.7 (2.0)[c]	5.9 (2.0)[c]
Constipation	4.7 (2.2)[a,d,e]	5.4 (2.1)[c,e]	5.9 (2.0)[c,d]
Inflammation of joints/arthritis	4.6 (2.3)[a,d,e]	5.3 (2.2)[c]	5.7(2.4)[c]
Dyspareunia	4.4 (2.2)[a,d,e]	5.5 (2.2)[c]	5.7 (2.3)[c]

On a scale of 1-9, a higher number indicates a more negative impact on quality of life. *P* values are shown where there is a statistically significant difference between specified cohorts. Bonferroni adjustment was applied when comparing more than 2 groups at $P < 0.05$. [a]$P < 0.05$ *vs* cohort 2 + 3 combined; [b]No statistically significant difference versus any other cohorts; [c]$P < 0.05$ *vs* cohort 1; [d]$P < 0.05$ *vs* cohort 2; [e]$P < 0.05$ *vs* cohort 3. Additional disease attributes provided as options in the survey included: pain or drainage near or around the anus, bloody or foul-smelling drainage (pus), reduced appetite and weight loss, pneumaturia, irritation of the skin around the anus, blood in stool, fecal incontinence, fecaluria, purulent rectal discharge, bleeding, inflammation of skin and eyes, mouth sores, and fever. Disease attributes are shown in descending order of impact on quality of life. CD: Crohn's

disease; CPF: Crohn's perianal fistulas; HRQoL: Health-related quality of life; NA: Not applicable; PF: Perianal fistulas.