# **Supplemental Online Content**

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This supplemental material has been provided by the authors to give readers additional information about their work.

#### eTable 1. List of Bowel Disorders and Related Procedures

### 1. List of bowel disorder diagnosis codes (ICD codes)

ICD9		ICD10	
558.1	Gastroenteritis and colitis due to radiation	K52.0	Gastroenteritis and colitis due to radiation
560.1	Paralytic ileus	K56.0	Paralytic ileus
560.1	Paralytic ileus	K56.7	Ileus, unspecified
565.1	Anal fistula	K60.3	Anal fistula
565.1	Anal fistula	K60.4	Rectal fistula
565.1	Anal fistula	K60.5	Anorectal fistula
569.2	Stenosis of rectum and anus	K62.4	Stenosis of anus and rectum
569.3	Hemorrhage of rectum and anus	K62.5	Hemorrhage of anus and rectum
569.41	Ulcer of anus and rectum	K62.6	Ulcer of anus and rectum
569.42	Anal or rectal pain	K62.89	Other specified diseases of anus and rectum
569.49	Other specified disorders of rectum and anus	K62.89	Other specified diseases of anus and rectum
578.1	Blood in stool	K92.1	Melena
578.9	Hemorrhage of gastrointestinal tract, unspecified	K92.2	Gastrointestinal hemorrhage, unspecified
787.6	Incontinence of feces		
787.6	Full incontinence of feces	R15.9	Full incontinence of feces
787.61	Incomplete defecation	R15.0	Incomplete defecation
787.62	Fecal smearing	R15.1	Fecal smearing
787.63	Fecal urgency	R15.2	Fecal urgency

## 2. List of procedure codes related to bowel disorders (CPT codes)

code	description
45110	Proctectomy; complete, combined abdominoperineal, with colostomy
45111	Proctectomy; partial resection of rectum, transabdominal approach
45112	Proctectomy, combined abdominoperineal, pull-through procedure (eg, colo-anal anastomosis)
	Proctectomy, partial, with rectal mucosectomy, ileoanal anastomosis, creation of ileal reservoir (S or J), with or without
45113	loop ileostomy
45114	Proctectomy, partial, with anastomosis; abdominal and transsacral approach
45116	Proctectomy, partial, with anastomosis; transsacral approach only (Kraske type)
	Proctectomy, combined abdominoperineal pull-through procedure (eg, colo-anal anastomosis), with creation of colonic
45119	reservoir (eg, J-pouch), with diverting enterostomy when performed
45123	Proctectomy, partial, without anastomosis, perineal approach
45150	Division of stricture of rectum
45303	Proctosigmoidoscopy, rigid; with dilation (eg, balloon, guide wire, bougie)
	Proctosigmoidoscopy, rigid; with control of bleeding (eg, injection, bipolar cautery, unipolar cautery, laser, heater probe,
45317	stapler, plasma coagulator)
45327	Proctosigmoidoscopy, rigid; with transendoscopic stent placement (includes predilation)
45334	Sigmoidoscopy, flexible; with control of bleeding, any method
45340	Sigmoidoscopy, flexible; with transendoscopic balloon dilation
45382	Colonoscopy, flexible; with control of bleeding, any method
45386	Colonoscopy, flexible; with transendoscopic balloon dilation
45387	Colonoscopy, flexible, proximal to splenic flexure; with transendoscopic stent placement (includes predilation)
45395	Laparoscopy, surgical; proctectomy, complete, combined abdominoperineal, with colostomy
	Laparoscopy, surgical; proctectomy, combined abdominoperineal pull-through procedure (eg, colo-anal anastomosis),
45397	with creation of colonic reservoir (eg, J-pouch), with diverting enterostomy, when performed
45500	Proctoplasty; for stenosis
45562	Exploration, repair, and presacral drainage for rectal injury;
45563	Exploration, repair, and presacral drainage for rectal injury; with colostomy
45800	Closure of rectovesical fistula;
45805	Closure of rectovesical fistula; with colostomy
45820	Closure of rectourethral fistula;

45825	Closure of rectourethral fistula; with colostomy
45905	Dilation of anal sphincter (separate procedure) under anesthesia other than local
45910	Dilation of rectal stricture (separate procedure) under anesthesia other than local
46270	Surgical treatment of anal fistula (fistulectomy/fistulotomy); subcutaneous
46275	Surgical treatment of anal fistula (fistulectomy/fistulotomy); intersphincteric
	Surgical treatment of anal fistula (fistulectomy/fistulotomy); transsphincteric, suprasphincteric, extrasphincteric or multiple,
46280	including placement of seton, when performed
46285	Surgical treatment of anal fistula (fistulectomy/fistulotomy); second stage
46604	Anoscopy; with dilation (eg, balloon, guide wire, bougie)
	Anoscopy; with control of bleeding (eg, injection, bipolar cautery, unipolar cautery, laser, heater probe, stapler, plasma
46614	coagulator)
46700	Anoplasty, plastic operation for stricture; adult
	Physician or other qualified health care professional attendance and supervision of hyperbaric oxygen therapy, per
99183	session
44188	Aparoscopic colostomy
44320	Open colostomy
44340	Revision of colostomy; simple (release of superficial scar) (separate procedure)
44345	Revision of colostomy; complicated (reconstruction in-depth) (separate procedure)
44346	Revision of colostomy; with repair of paracolostomy hernia (separate procedure)
44620	Closure of enterostomy, large or small intestine Closure of colostomy
44625	Closure of enterostomy, large or small intestine; with resection and anastomosis other than colorectal
	Closure of enterostomy, large or small intestine; with resection and colorectal anastomosis (eg, closure of Hartmann type
44626	procedure)
90911	Biofeedback training, perineal muscles, anorectal or urethral sphincter, including EMG and/or manometry
	Biofeedback training, perineal muscles, anorectal or urethral sphincter, including EMG and/or manometry, when
90912	performed; initial 15 minutes of one-on-one physician or other qualified health care professional contact with the patient
	Biofeedback training, perineal muscles, anorectal or urethral sphincter, including EMG and/or manometry, when
90913	performed; initial 15 minutes of one-on-one physician or other qualified health care professional contact with the patient

## 3. List of procedure codes related to bowel disorders (ICD codes)

ICD9		ICD10	
48.5	Abdominoperineal resection of the rectum, not otherwise specified	0D1N0Z4	Bypass Sigmoid Colon to Cutaneous, Open Approach
48.5	Abdominoperineal resection of the rectum, not otherwise specified	0DTP0ZZ	Resection of Rectum, Open Approach
48.5	Abdominoperineal resection of the rectum, not otherwise specified	0DTP4ZZ	Resection of Rectum, Percutaneous Endoscopic Approach
48.5	Abdominoperineal resection of the rectum, not otherwise specified	0DTP7ZZ	Resection of Rectum, Via Natural or Artificial Opening
48.5	Abdominoperineal resection of the rectum, not otherwise specified	0DTP8ZZ	Resection of Rectum, Via Natural or Artificial Opening Endoscopic
48.51	Laparoscopic abdominoperineal resection of the rectum	0D1N0Z4	Bypass Sigmoid Colon to Cutaneous, Open Approach
48.51	Laparoscopic abdominoperineal resection of the rectum	0DTP4ZZ	Resection of Rectum, Percutaneous Endoscopic Approach
48.52	Open abdominoperineal resection of the rectum	0D1N0Z4	Bypass Sigmoid Colon to Cutaneous, Open Approach
48.52	Open abdominoperineal resection of the rectum	0DTP0ZZ	Resection of Rectum, Open Approach
48.59	Other abdominoperineal resection of the rectum	0D1N0Z4	Bypass Sigmoid Colon to Cutaneous, Open Approach
48.59	Other abdominoperineal resection of the rectum	0DTP7ZZ	Resection of Rectum, Via Natural or Artificial Opening
48.59	Other abdominoperineal resection of the rectum	0DTP8ZZ	Resection of Rectum, Via Natural or Artificial Opening Endoscopic
48.91	Incision of rectal stricture	0DNP0ZZ	Release Rectum, Open Approach
48.91	Incision of rectal stricture	0DNP3ZZ	Release Rectum, Percutaneous Approach
48.91	Incision of rectal stricture	0DNP4ZZ	Release Rectum, Percutaneous Endoscopic Approach
48.91	Incision of rectal stricture	0DNP7ZZ	Release Rectum, Via Natural or Artificial Opening
48.91	Incision of rectal stricture	0DNP8ZZ	Release Rectum, Via Natural or Artificial Opening Endoscopic
48.93	Repair of perirectal fistula	0DQP0ZZ	Repair Rectum, Open Approach
48.93	Repair of perirectal fistula	0DQP3ZZ	Repair Rectum, Percutaneous Approach

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		1	
48.93	Repair of perirectal fistula	0DQP4ZZ	Repair Rectum, Percutaneous Endoscopic Approach
48.93	Repair of perirectal fistula	0DQP7ZZ	Repair Rectum, Via Natural or Artificial Opening
48.93	Repair of perirectal fistula	0DQP8ZZ	Repair Rectum, Via Natural or Artificial Opening Endoscopic
49.1	Unknown	Unknown	Unknown
49.11	Anal fistulotomy	0H89XZZ	Division of Perineum Skin, External Approach
49.12	Anal fistulectomy	0DBQ0ZZ	Excision of Anus, Open Approach
49.12	Anal fistulectomy	0DBQ3ZZ	Excision of Anus, Percutaneous Approach
49.12	Anal fistulectomy	0DBQ4ZZ	Excision of Anus, Percutaneous Endoscopic Approach
49.72	Anal cerclage	0DVQ0CZ	Restriction of Anus with Extraluminal Device, Open Approach
49.72	Anal cerclage	0DVQ0DZ	Restriction of Anus with Intraluminal Device, Open Approach
49.72	Anal cerclage	0DVQ0ZZ	Restriction of Anus, Open Approach
49.72	Anal cerclage	0DVQ3CZ	Restriction of Anus with Extraluminal Device, Percutaneous Approach
49.72	Anal cerclage	0DVQ3DZ	Restriction of Anus with Intraluminal Device, Percutaneous Approach
49.72	Anal cerclage	0DVQ3ZZ	Restriction of Anus, Percutaneous Approach
49.72	Anal cerclage	0DVQ4CZ	Restriction of Anus with Extraluminal Device, Percutaneous Endoscopic Approach
49.72	Anal cerclage	0DVQ4DZ	Restriction of Anus with Intraluminal Device, Percutaneous Endoscopic Approach
49.72	Anal cerclage	0DVQ4ZZ	Restriction of Anus, Percutaneous Endoscopic Approach
49.72	Anal cerclage	0DVQ7DZ	Restriction of Anus with Intraluminal Device, Via Natural or Artificial Opening
49.72	Anal cerclage	0DVQ7ZZ	Restriction of Anus, Via Natural or Artificial Opening
49.72	Anal cerclage	0DVQ8DZ	Restriction of Anus with Intraluminal Device, Via Natural or Artificial Opening Endoscopic
49.72	Anal cerclage	0DVQ8ZZ	Restriction of Anus, Via Natural or Artificial Opening Endoscopic
49.72	Anal cerclage	0DVQXCZ	Restriction of Anus with Extraluminal Device, External Approach
49.72	Anal cerclage	0DVQXDZ	Restriction of Anus with Intraluminal Device, External Approach

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		1	
49.72	Anal cerclage	0DVQXZZ	Restriction of Anus, External Approach
49.73	Closure of anal fistula	0DQQ0ZZ	Repair Anus, Open Approach
49.73	Closure of anal fistula	0DQQ3ZZ	Repair Anus, Percutaneous Approach
49.73	Closure of anal fistula	0DQQ4ZZ	Repair Anus, Percutaneous Endoscopic Approach
49.73	Closure of anal fistula	0DQQ7ZZ	Repair Anus, Via Natural or Artificial Opening
49.73	Closure of anal fistula	0DQQ8ZZ	Repair Anus, Via Natural or Artificial Opening Endoscopic
49.73	Closure of anal fistula	0DQQXZZ	Repair Anus, External Approach
57.83	Repair of fistula involving bladder and intestine	0DQ80ZZ	Repair Small Intestine, Open Approach
57.83	Repair of fistula involving bladder and intestine	0DQ83ZZ	Repair Small Intestine, Percutaneous Approach
57.83	Repair of fistula involving bladder and intestine	0DQ84ZZ	Repair Small Intestine, Percutaneous Endoscopic Approach
57.83	Repair of fistula involving bladder and intestine	0DQ87ZZ	Repair Small Intestine, Via Natural or Artificial Opening
57.83	Repair of fistula involving bladder and intestine	0DQ88ZZ	Repair Small Intestine, Via Natural or Artificial Opening Endoscopic
57.83	Repair of fistula involving bladder and intestine	0DQB0ZZ	Repair Ileum, Open Approach
57.83	Repair of fistula involving bladder and intestine	0DQB3ZZ	Repair Ileum, Percutaneous Approach
57.83	Repair of fistula involving bladder and intestine	0DQB4ZZ	Repair Ileum, Percutaneous Endoscopic Approach
57.83	Repair of fistula involving bladder and intestine	0DQB7ZZ	Repair Ileum, Via Natural or Artificial Opening
57.83	Repair of fistula involving bladder and intestine	0DQB8ZZ	Repair Ileum, Via Natural or Artificial Opening Endoscopic
57.83	Repair of fistula involving bladder and intestine	0DQE0ZZ	Repair Large Intestine, Open Approach
57.83	Repair of fistula involving bladder and intestine	0DQE3ZZ	Repair Large Intestine, Percutaneous Approach
57.83	Repair of fistula involving bladder and intestine	0DQE4ZZ	Repair Large Intestine, Percutaneous Endoscopic Approach
57.83	Repair of fistula involving bladder and intestine	0DQE7ZZ	Repair Large Intestine, Via Natural or Artificial Opening
57.83	Repair of fistula involving bladder and intestine	0DQE8ZZ	Repair Large Intestine, Via Natural or Artificial Opening Endoscopic
57.83	Repair of fistula involving bladder and intestine	0DQN0ZZ	Repair Sigmoid Colon, Open Approach
57.83	Repair of fistula involving bladder and intestine	0DQN3ZZ	Repair Sigmoid Colon, Percutaneous Approach
57.83	Repair of fistula involving bladder and intestine	0DQN4ZZ	Repair Sigmoid Colon, Percutaneous Endoscopic Approach
57.83	Repair of fistula involving bladder and intestine	0DQN7ZZ	Repair Sigmoid Colon, Via Natural or Artificial Opening

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57.83	Repair of fistula involving bladder and intestine	0DQN8ZZ	Repair Sigmoid Colon, Via Natural or Artificial Opening Endoscopic
57.83	Repair of fistula involving bladder and intestine	0DQP0ZZ	Repair Rectum, Open Approach
57.83	Repair of fistula involving bladder and intestine	0DQP3ZZ	Repair Rectum, Percutaneous Approach
57.83	Repair of fistula involving bladder and intestine	0DQP4ZZ	Repair Rectum, Percutaneous Endoscopic Approach
57.83	Repair of fistula involving bladder and intestine	0DQP7ZZ	Repair Rectum, Via Natural or Artificial Opening
57.83	Repair of fistula involving bladder and intestine	0DQP8ZZ	Repair Rectum, Via Natural or Artificial Opening Endoscopic
57.83	Repair of fistula involving bladder and intestine	0TQB0ZZ	Repair Bladder, Open Approach
57.83	Repair of fistula involving bladder and intestine	0TQB3ZZ	Repair Bladder, Percutaneous Approach
57.83	Repair of fistula involving bladder and intestine	0TQB4ZZ	Repair Bladder, Percutaneous Endoscopic Approach
57.83	Repair of fistula involving bladder and intestine	0TQB7ZZ	Repair Bladder, Via Natural or Artificial Opening
57.83	Repair of fistula involving bladder and intestine	0TQB8ZZ	Repair Bladder, Via Natural or Artificial Opening Endoscopic
57.83	Repair of fistula involving bladder and intestine	0TQD0ZZ	Repair Urethra, Open Approach
57.83	Repair of fistula involving bladder and intestine	0TQD3ZZ	Repair Urethra, Percutaneous Approach
57.83	Repair of fistula involving bladder and intestine	0TQD4ZZ	Repair Urethra, Percutaneous Endoscopic Approach
57.83	Repair of fistula involving bladder and intestine	0TQD7ZZ	Repair Urethra, Via Natural or Artificial Opening
57.83	Repair of fistula involving bladder and intestine	0TQD8ZZ	Repair Urethra, Via Natural or Artificial Opening Endoscopic
93.95	Hyperbaric oxygenation	5A05121	Extracorporeal Hyperbaric Oxygenation, Intermittent
93.95	Hyperbaric oxygenation	5A05221	Extracorporeal Hyperbaric Oxygenation, Continuous
96.22	Dilation of rectum	0D7P7ZZ	Dilation of Rectum, Via Natural or Artificial Opening
96.22	Dilation of rectum	0D7P8ZZ	Dilation of Rectum, Via Natural or Artificial Opening Endoscopic
96.23	Dilation of anal sphincter	0D7Q7ZZ	Dilation of Anus, Via Natural or Artificial Opening
96.23	Dilation of anal sphincter	0D7Q8ZZ	Dilation of Anus, Via Natural or Artificial Opening Endoscopic

ICD-9/10-CM, International Classification of Diseases, 9<sup>th</sup>/10<sup>th</sup> Edition, Clinical Modification;

eTable 2. Cumulative Incidence of Gastrointestinal Problems and Procedures at 4 Years Post Radiation Therapy Compared to the General Population

	Cumulative Incidence (%)			PHS vs General		No PHS vs General			PHS vs No PHS			
	General population	PHS	No PHS	HR	CI	<i>P</i> Value	HR	CI	<i>P</i> Value	HR	CI	<i>P</i> Value
GI problems (Diagnosis OR Procedure)	10.31%	12.41%	17.07%	1.00	(0.96, 1.05)	0.822	1.35	(1.32, 1.37)	<0.001	0.75	(0.72, 0.77)	<0.001
Severe GI problems (Procedure)	0.73%	1.08%	1.99%	1.11	(0.96, 1.29)	0.153	1.92	(1.79, 2.06)	<0.001	0.58	(0.51, 0.66)	<0.001

Radiotherapy patients (PHS (n=25,211) and No PHS (n=245,289)) were compared with an age-matched general population who were not diagnosed with prostate cancer nor did undergo radiotherapy (n=85,821) who has the similar average age as PHS/no PHS group. Data for the general population are from Medicare 5% and MarketScan, and the proportion of people from each dataset correspond to the ratio found in PHS/no PHS datasets. Cumulative rates are based on Cox proportional hazards regression, controlling for baseline bowel diagnosis and secondary cancer diagnosis.

PHS, polyethylene glycol-based hydrogel spacer; CI, confidence interval; HR, hazard ratio

eTable 3. Adjusted 4-year Cumulative Incidence of Bowel Disorders and Related Procedures After Radiation Therapy, by NPI procedure volume quartile

	NPI p	rocedure	volume q				
Cumulative incidence	Lowest	Lower	Higher	Highest	HR1 (CI)	HR2 (CI)	HR3 (CI)
Adjusted* (n=63,802)							
Bowel disorders (Diagnosis OR Procedure)	18.70%	15.02%	15.01%	11.57%	0.89 (0.84, 0.94)	0.92 (0.87, 0.97)	0.79 (0.74, 0.83)
Procedures related to bowel disorders (Diagnosis AND Procedure)	1.62%	1.48%	1.48%	1.22%	0.98 (0.84, 1.14)	1.08 (0.92, 1.25)	0.86 (0.73, 1.02)

HR1: comparison between lowest and lower, HR2: comparison between lowest and higher, HR3: comparison between lowest and highest

CI, confidence interval; HR, hazard ratio

eTable 4. Adjusted 4-year Cumulative Incidence of Bowel Disorders and Related Procedures After Radiation Therapy, without Premier Data

	PHS (Cumulative Incidence)	No PHS (Cumulative Incidence)	HR	95% CI	<i>P</i> Value
Adjusted Cumulative Incidence* (n=236,002)					
Bowel disorders (Diagnosis OR Procedure)	13.28%	17.91%	0.75	(0.72, 0.78)	<0.001
Procedures related to bowel disorders (Diagnosis AND Procedure)	1.01%	1.85%	0.54	(0.47, 0.63)	<0.001

PHS, polyethylene glycol-based hydrogel spacer

eTable 5. Race Distribution within Patients from the Medicare or Premier Datasets by Use of a Polyethylene Glycol-Based Hydrogel Spacer

	No PHS	PHS	P Value	Standardized mean difference
Black	28,317 (12.6%)	2,228 (9.3%)		
White	181,943 (80.6%)	19,740 (82.7%)	<0.001	0.015
Other	15,385 (6.8%)	1,905 (8.0%)		

<sup>\*</sup>Other race includes all other races than Black and White.

eTable 6. Adjusted 4-year Cumulative Incidence of Bowel Disorders and Related Procedures After Radiation Therapy adjusted for Race, without MarketScan Data

	PHS (Cumulative Incidence)	No PHS (Cumulative Incidence)	HR	95% CI	<i>P</i> Value
Cumulative incidence					
Age					
Bowel disorders (Diagnosis OR Procedure)					
Age below 65	11.05%	7.69%	0.83	(0.72, 0.94)	0.005
Age 65-69	14.88%	9.75%	0.78	(0.72, 0.84)	<0.001
Age 70-74	17.56%	11.99%	0.73	(0.67, 0.78)	<0.001
Age 75-79	18.43%	12.99%	0.72	(0.68, 0.76)	<0.001
Age 80 and above	19.52%	17.60%	0.77	(0.68, 0.87)	<0.001
Procedures related to bowel disorders (Diagnosis AND Procedure)				1	
Age below 65	1.12%	0.01%	0.77	(0.50, 1.16)	0.211
Age 65-69	1.43%	0.11%	0.52	(0.39, 0.70)	<0.001
Age 70-74	2.08%	-	0.51	(0.39, 0.65)	<0.001
Age 75-79	2.05%	-	0.48	(0.39, 0.58)	<0.001
Age 80 and above	1.19%	0.15%	0.69	(0.47, 1.00)	0.053
Race				1	
Bowel disorders (Diagnosis OR Procedure)					
White	16.84%	12.48%	0.74	(0.70, 0.77)	<0.001
Black	16.41%	9.59%	0.72	(0.62, 0.82)	<0.001
Other race	13.98%	8.92%	0.84	(0.72, 0.99)	0.034
Procedures related to bowel disorders (Diagnosis AND Procedure)					
White	1.74%	0.99%	0.52	(0.44, 0.60)	<0.001
Black	1.45%	0.00%	0.41	(0.23, 0.73)	0.003
Other race	1.42%	0.00%	0.71	(0.43, 1.16)	0.17

PHS, polyethylene glycol-based hydrogel spacer

eTable 7. Baseline Characteristics for Percentage PHS

% PHS	No./total No. (%)	P value	Standardized mean difference
SBRT only	2743/11 553 (23.7)		
IMRT only	12 755/155 755 (8.2)		
Proton only	723/2535 (28.5)	<.001	NA
Brachytherapy only	1211/13 943 (8.7)		
3D CRT only	114/26 975 (0.4)		
Combination	7621/51 743 (14.7)		

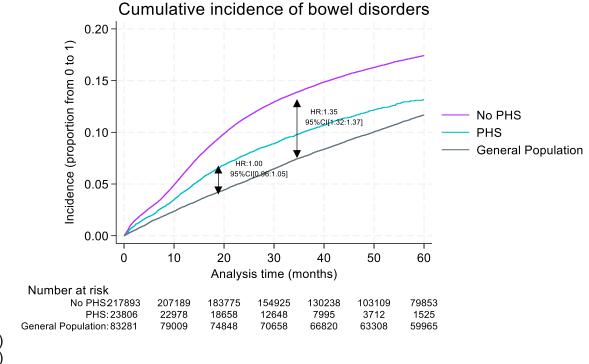
3D CRT, 3-dimensional conformal radiation therapy; IMRT, intensity modulated radiotherapy; NA, not applicable; PHS, polyethylene glycol-based hydrogel spacer; SBRT, stereotactic body radiation therapy.

eTable 8. Number of Bowel Diagnosis Codes at 4 Years

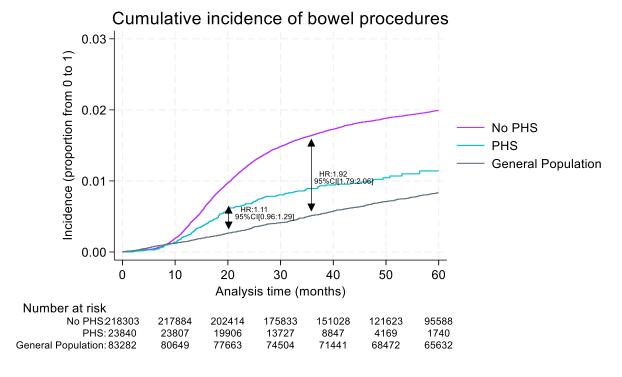
			P
	PHS	No PHS	Value
Number of bowel diagnosis codes, mean (SD)	0.13 (0.46)	0.22 (0.62)	<0.001
Number of bowel diagnosis codes			
among those with at least one diagnosis code,			
mean (SD)	1.37 (0.72)	1.50 (0.82)	<0.001

SD, standard deviation; PHS, polyethylene glycol-based hydrogel spacer

eFigure 1. Comparison of Cumulative Incidence of Bowel Disorders (A) and Related Procedures (B) with General Population







Note: Analysis time is months since the radiotherapy among No PHS / PHS patients. Analysis time among the agematched general population is months from the time they reached the average age of prostate cancer patients.

eFigure 2. Hazard Ratio of Bowel Disorders and Related Procedures for PHS vs. No PHS, Stratified by Type of Radiation Therapy

