Supplementary Materials

Chronic Inflammatory Conditions

- Crohn's Disease (CD): **ICD-9**=555.0-555.2, 555.9; **ICD-10**=K50.0, K50.1, K50.8, K50.9

- Ulcerative Colitis (UC): **ICD-9**=556.0-556.6, 556.8, 556.9; **ICD-10**=K51.0-K51.5, K51.8, K51.9

- Psoriasis (Ps)/Psoriatic Arthritis (PsA): **ICD-9**=696.0-696.5, 696.8; **ICD-10**=L40.0-L40.4, L40.8

- Rheumatoid Arthritis (RA): **ICD-9**=714.0-714.2, 714.30-714.33, 714.4; **ICD-10**=M05.0-M05.9

- Ankylosing Spondylitis (AS)/Spondyloarthritis (SpA): **ICD-9**=720.20-720.2, 720.8, 720.9; **ICD-10**=M45.0-M45.9

- Hidradenitis Suppurativa (HS): **ICD-9**=705.83; **ICD-10**=L73.2

- Uveitis (UV): **ICD-9**=364.00-364.05; **ICD-10**=H20.00-H20.05, H20.1

Comorbidities

- Hypertension (HTN): **ICD-9** = 401.0, 401.1, 401.9, 403.00, 403.01, 403.10, 403.11, 403.90, 403.91; **ICD-10** = I10, I11.0, I11.9, I12.0, I12.9

- Hyperlipidemia (HLD): **ICD-9** = 272.4; **ICD-10** = E78.0-E78.5

- Diabetes Mellitus: **ICD-9** = 250.0-250.9; **ICD-10** = E10 (Type 1, 84 sub-codes), E11 (Type II, 84 sub-codes)

- Congestive Heart Failure (CHF): **ICD-9** = 428.0, 428.1, 428.20-428.23, 428.30-428.33, 428.40-428.43, 428.9; **ICD-10** = I50.1-I50.4, I50.8, I50.9

- Coronary Artery Disease (CAD): **ICD-9** = 410.0-410.9 (all .00-.02 only), 411.0, 411.1, 411.81, 411.89, 412, 414.00-414.07, 414.10-414.12, 414.19,414.2-414.4, 414.8, 414.9; **ICD-10** = I20-I25

- Chronic Kidney Disease (CKD): **ICD-9** = 585.1-585.1, 585.9; **ICD-10** = N18.1-N18.6, N18.9

- Chronic Obstructive Pulmonary Disease (COPD): **ICD-9** = 491-494; **ICD-10** = J41-J44, J47

- HIV/AIDS: **ICD-9** = 042; **ICD-10** = B20

- *Lynch Syndrome: **ICD-9** = 758.5 (Other conditions due to autosomal abnormalities); **ICD-10** = Z15.02 (ovary), Z15.04 (endometrium), Z15.09 (genetic susceptibility to other malignant neoplasm)

- *Gardner Syndrome: **ICD-9** = 758.5 (Other conditions due to autosomal abnormalities); **ICD-10** = Z15.09(genetic susceptibility to other malignant neoplasm)

- *Li-Fraumeni Syndrome: **ICD-9** = 758.5 (Other conditions due to autosomal abnormalities); **ICD-10** = Z15.01 (breast), Z15.09 (genetic susceptibility to other malignant neoplasm)

- HPV: **ICD-9** = 078.10-078.12, 078.19, 079.4; **ICD-10** = B07.0, B07.8, B07.9

- EBV: **ICD-9** = 075; **ICD-10** = B27.90-B27.92, B27.99

- Hepatitis B (HBV): **ICD-9** = 070.20-070.23, 070.30-070.33; **ICD-10** = B16.0-B16.2, B16.9, B18.0, B18.1, B19.10, B19.11

- Hepatitis C (HCV): **ICD-9** = 070.41, 070.44, 070.51, 070.54, 070.70, 070.71; **ICD-10** = B17.10, B17.11, B18.2, B19.20, B19.21

- H. pylori: **ICD-9** = 041.86; **ICD-10** = B96.81

*comorbidity can only be identified by generic genetic abnormality ICD-9/10 code

Supplementary Methods 2: Urologic Malignancy ICD-9 and ICD-10 Codes.

ICD-9 Codes:

- Prostate: 185

- Testis: 186

- Bladder: 188

- Kidney: 189

- Corresponding in situ neoplasms: 230-234

ICD-10 Codes:

- Prostate: C61

- Testis: C62

- Kidney: C64-C65

- Bladder: C66-C67

- Corresponding in situ neoplasms: D00-D09

Supplementary Methods 3: Prostate Cancer Screening Variables

- Number of encounters for prostate cancer screening: ICD-10 Z12.5

- Initial PSA value

- Number of PSA tests: CPT 84152

- Number of transrectal diagnostic ultrasounds: CPT 76872/76942

- Number of prostate MRI: CPT 72197

- Number of prostate biopsies: CPT 55700/55706

- Abnormal digital rectal examination: ICD-9 796.4

- Prostate induration: ICD-9 600.10/600.11

Supplementary Table 1: System Wide Demographics of Diagnosed Prostate Cancer Patients

	TNF-I Unexposed (n=490)	TNF-I Exposed (n=53)	P-value
Age	61 (54, 69)	61 (55, 67)	>0.9
Follow up time (months)			
Overall	87 (38, 144)	101 (56, 168)	<0.001
Post-exposure	-	46 (21, 78)	
Race			0.8
Black	58 (12%)	7 (13%)	
White	421 (86%)	46 (87%)	
Other	11 (2.2%)	0 (0%)	
Smoking			0.059
Current	40 (8.2%)	2 (3.8%)	
Former	214 (44%)	16 (30%)	
Never	236 (48%)	35 (66%)	
TNF-I			<0.001
Adalimumab	0 (0%)	26 (49%)	
Infliximab	0 (0%)	10 (19%)	
Etanercept	0 (0%)	14 (26%)	
Certolizumab	0 (0%)	2 (3.8%)	
Golimumab	0 (0%)	1 (1.9%)	
PSA at diagnosis			
Median (IQR)	5.98 (4.26, 8.60)	5.00 (3.80, 7.93)	0.2
<4	69 (14%)	12 (23%)	0.3
4-10	225 (46%)	25 (47%)	
>10	69 (14%)	6 (11%)	
Unknown	127 (26%)	10 (19%)	
Grade Group on Biopsy			0.6

1	165 (34%)	22 (42%)	
2	100 (20%)	10 (19%)	
3	70 (14%)	5 (9%)	
4	33 (7%)	4 (8%)	
5	29 (6%)	5 (9%)	
Unknown	93 (19%)	7 (13%)	
# of positive cores			0.5
1	76 (16%)	14 (26%)	
2-6	194 (40%)	20 (38%)	
7-10	37 (8%)	5 (9%)	
>10	20 (4%)	2 (4%)	
Unknown	163 (32%)	12 (23%)	
Adverse Pathology			
EPE	48 (10%)	12 (23%)	0.4
SVI	15 (3%)	2 (4%)	>0.9
LVI	10 (2%)	4 (8%)	0.3
N1	7 (1%)	3 (6%)	0.4
M1	37 (8%)	4 (8%)	>0.9

*p < 0.05 considered statistically significant

Supplementary Table 2: System Wide Demographics of Diagnosed Renal Cell Carcinoma

Patients

	TNF-I Unexposed (n=142)	TNF-I Exposed (n=30)	P-value
Age	56 (49, 65)	58 (50, 64)	0.8
Gender			0.6
Female	74 (52%)	14 (47%)	
Male	68 (48%)	16 (53%)	
Follow up (months)			
Overall	87 (38, 144)	101 (56, 168)	<0.001*
Post-exposure	-	46 (21, 78)	
Race			0.7
Black	23 (16%)	5 (17%)	
White	117 (82%)	24 (80%)	
Other	2 (2%)	1 (3%)	
Smoking Status			0.3
Current	21 (15%)	7 (23%)	
Former	55 (39%)	8 (27%)	
Never	66 (46%)	15 (50%)	
Clinical Stage at Dx			0.5
T1	96 (68%)	22 (73%)	
T2	7 (5%)	0 (0%)	
T3	7 (5%)	3 (10%)	
T4	4 (3%)	0 (0%)	
N1/M1	5 (4%)	0 (0%)	
Unknown	23 (24%)	5 (17%)	
Surgical Approach			0.065
PNx	59 (42%)	17 (57%)	

RNX	63 (44%)	8 (26%)	
None	20 (14%)	5 (17%)	
Histologic Subtype			0.3
Chromophobe	5 (4%)	2 (7%)	
Clear cell	92 (65%)	22 (73%)	
Papillary	18 (13%)	1 (3%)	
Variant	7 (5%)	0 (0%)	
Unknown	20 (14%)	5 (17%)	
Recurrence	14 (10%)	1 (3%)	0.5
Mortality	23 (24%)	0 (0%)	0.015*
Average Year of Diagnosis	2012	2014	

*$p < 0.05$ considered statistically significant

Supplementary Table 3: System Wide Demographics of Diagnosed Urothelial Cell Carcinoma Patients

	TNF-I Unexposed (n=162)	TNF-I Exposed (n=16)	P-value
Age	65 (57, 73)	65 (56, 68)	0.6
Gender			0.2
Female	59 (36%)	3 (19%)	
Male	103 (64%)	13 (81%)	
Follow up time (months)			
Overall	87 (38, 144)	101 (56, 168)	<0.001*
Post-exposure	-	46 (21, 78)	
Race			>0.9
Black	13 (8%)	1 (6%)	
White	142 (88%)	15 (94%)	
Other	7 (4%)	0 (0%)	
Smoking Status			0.7
Current	23 (14%)	1 (6%)	
Former	83 (51%)	8 (50%)	
Never	56 (35%)	7 (44%)	
Location			0.2
Lower Tract	127 (78%)	15 (94%)	
Upper Tract	35 (22%)	1 (6%)	
Clinical Stage at Dx			0.4
≤T1	108 (67%)	14 (87%)	
≥T2	35 (21%)	2 (13%)	
Unknown	19 (12%)	0 (0%)	
Grade at Dx			>0.9
Low	57 (35%)	6 (38%)	

High	84 (52%)	9 (56%)	
Unknown	21 (13%)	1 (6%)	
Number of Tumors			0.4
1	94 (58%)	10 (62%)	
2+	35 (22%)	6 (38%)	
Unknown	33 (20%)	0 (0%)	
Histologic Subtype			>0.9
Urothelial	140 (87%)	15 (94%)	
Variant	10 (6%)	1 (6%)	
Unknown	12 (7%)	0	
LN+	17 (10%)	0 (0%)	0.063
Metastasis	20 (12%)	0 (0%)	0.2
Mortality	45 (28%)	2 (13%)	0.2

*p < 0.05 considered statistically significant

Supplementary Table 4: Propensity Score-Adjusted Risk of Urologic Cancers for Adalimumab

		Relative Risk (RR)	95% CI	p-value
Prostate				
	Number of Elevated PSA's	0.898	(0.772, 1.045)	0.163
	Number of Prostate MRI's	0.649	(0.529, 0.795)	<0.001*
	Number of PNB	1.730	(0.083, 35.87)	0.723
	Elevated PSA at Diagnosis	0.961	(0.853, 1.083)	0.516
	Clinical Stage	0.445	(0.325, 0.61)	<0.001*
	Biopsy Grade Group 1 vs. 2+	1.158	(1.039, 1.292)	0.008*
	Biopsy Grade Group 2- vs. 3+	0.669	(0.529, 0.845)	0.001*
	Prostatectomy TNM Stage	0.472	(0.294, 0.756)	0.002*
	Prostatectomy Grade Group 1 vs. 2+	0.925	(0.803, 1.067)	0.286
Bladder				
	Number of Locations 1 vs. 2+	1.791	(1.156, 2.773)	0.009*
	Grade at Diagnosis	1.489	(1.202, 1.844)	<0.001*
	Radical Cystectomy	0.001	(0, Inf)	0.989
Kidney				
	Clinical Stage 2 or Greater	0.991	(0.626, 1.57)	0.970
	Clinical Stage 3 or Greater	1.424	(0.838, 2.418)	0.191
	Pathologic Stage 2 or Greater	0.877	(0.56, 1.375)	0.568
	Pathologic Stage 3 or Greater	0.877	(0.56, 1.375)	0.568
	Partial Nephrectomy	1.451	(1.14, 1.846)	0.002*
	Radical Nephrectomy	0.403	(0.277, 0.586)	<0.001*

*p < 0.05 considered statistically significant

Supplementary Table 5: Propensity Score-Adjusted Risk of Urologic Cancers for Infliximab

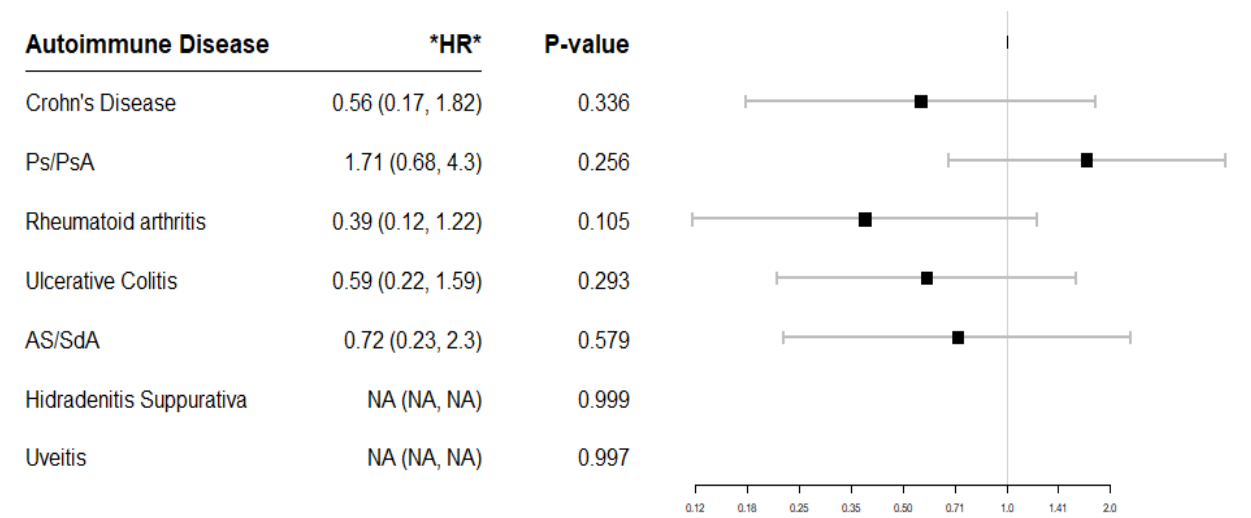|		Relative Risk (RR)	95% CI	p-value
Prostate				
	Number of Elevated PSA's	1.804	(1.579, 2.062)	<0.001*
	Number of Prostate MRI's	1.831	(1.602, 2.094)	<0.001*
	Elevated PSA at Diagnosis	0.759	(0.664, 0.868)	<0.001*
	Clinical Stage	2.219	(1.837, 2.679)	<0.001*
	Biopsy Grade Group 1 vs. 2+	0.699	(0.607, 0.805)	<0.001*
	Prostatectomy TNM Stage	2.182	(1.69, 2.818)	<0.001*
	Prostatectomy Grade Group 1 vs. 2+	0.632	(0.552, 0.724)	<0.001*
Bladder				
	Higher Pathologic Stage at Diagnosis	0.852	(0.437, 1.663)	0.639
	Radical Cystectomy	0.788	(0.414, 1.5)	0.468
Kidney				
	Clinical Stage 2 or Greater	1.314	(0.754, 2.291)	0.335
	Clinical Stage 3 or Greater	1.873	(1.008, 3.478)	0.047*
	Pathologic Stage 2 or Greater	1.163	(0.674, 2.008)	0.588
	Pathologic Stage 3 or Greater	1.163	(0.674, 2.008)	0.588

*p < 0.05 considered statistically significant

Supplementary Table 6: Propensity Score-Adjusted Risk of Urologic Cancers for Etanercept

		Relative Risk (RR)	95% CI	p-value
Prostate				
	Number of Elevated PSA's	1.080	(0.94, 1.242)	0.278
	Number of Prostate MRI's	0.693	(0.565, 0.85)	<0.001*
	Elevated PSA at Diagnosis	0.516	(0.428, 0.623)	<0.001*
	Clinical Stage	0.473	(0.337, 0.664)	<0.001*
	Biopsy Grade Group 1 vs. 2+	0.877	(0.771, 0.998)	0.046*
	Biopsy Grade Group 2- vs. 3+	1.531	(1.288, 1.82)	<0.001*
	Prostatectomy Grade Group 1 vs. 2+	1.178	(1.072, 1.294)	<0.001*
Bladder				
	Number of Tumors	0.001	(0, Inf)	0.991
	Grade at Diagnosis	1.213	(0.97, 1.516)	0.090
	Radical Cystectomy	0.001	(0, Inf)	0.991
Kidney				
	Pathologic Stage 2 or Greater	0.903	(0.239, 3.421)	0.881
	Radical Nephrectomy	0.254	(0.063, 1.026)	0.054

*p < 0.05 considered statistically significant

Supplementary Figure 1: Forest Plot of Odds Ratio of Prostate Cancer for Each Autoimmune

Disease Type

Autoimmune Disease	*HR*	P-value
Crohn's Disease	0.56 (0.17, 1.82)	0.336
Ps/PsA	1.71 (0.68, 4.3)	0.256
Rheumatoid arthritis	0.39 (0.12, 1.22)	0.105
Ulcerative Colitis	0.59 (0.22, 1.59)	0.293
AS/SdA	0.72 (0.23, 2.3)	0.579
Hidradenitis Suppurativa	NA (NA, NA)	0.999
Uveitis	NA (NA, NA)	0.997

Supplementary Figure 2: Multivariable regression of PCa diagnosis risk controlled for number of

screening PSA's (Sensitivity Analysis)

Cancer Type	HR*	P-value
Prostate	0.5 (0.27, 0.91)	0.023