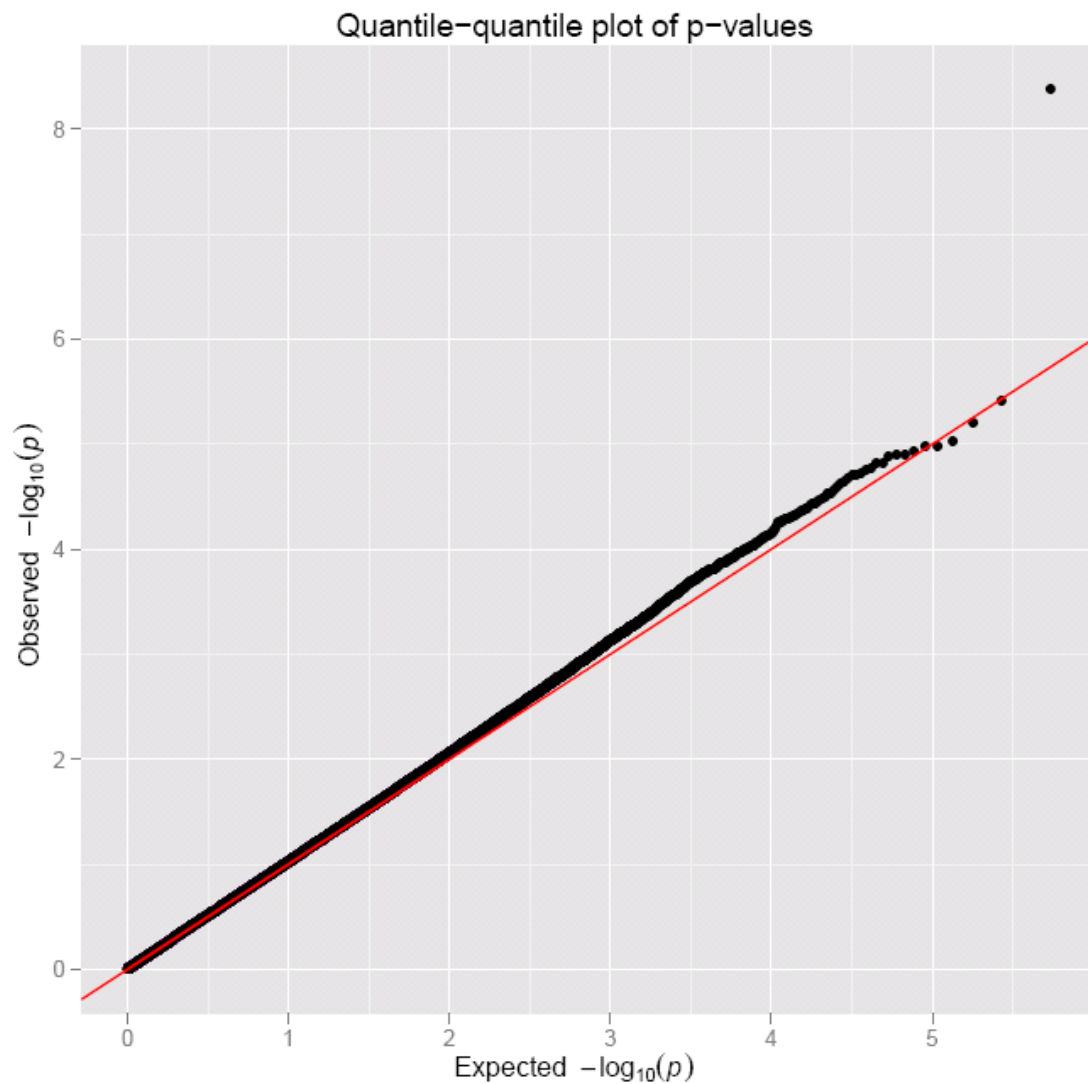


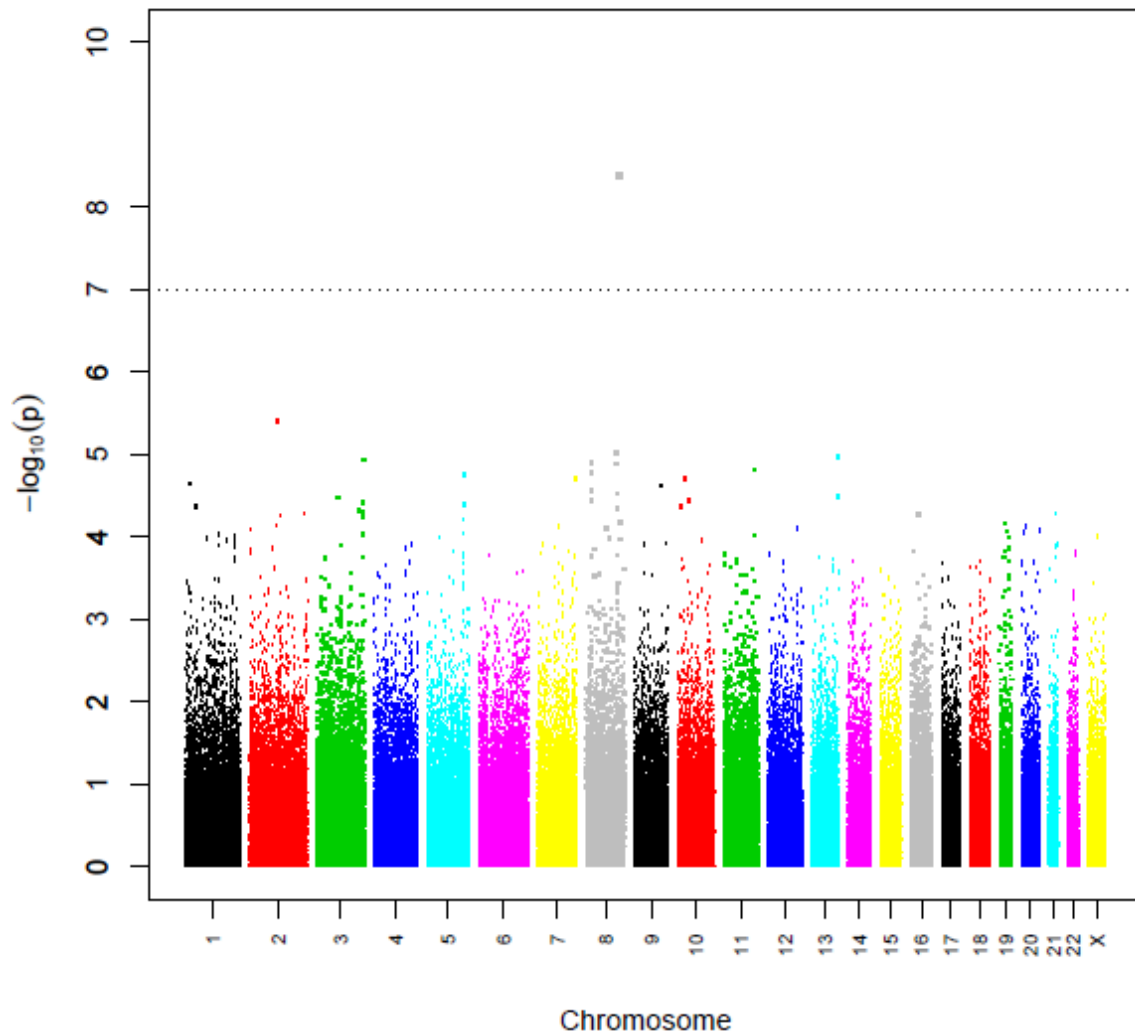
## SUPPLEMENTARY INFORMATION

**A multi-stage genome-wide association study of bladder cancer identifies multiple susceptibility loci** Rothman N, et al.

**Supplementary Figure 1. Quantile-quantile plot of  $P$  values for the combined case-control and cohort studies in the NCI bladder cancer GWAS.** Observed  $P$  values are compared with the expected uniform distribution



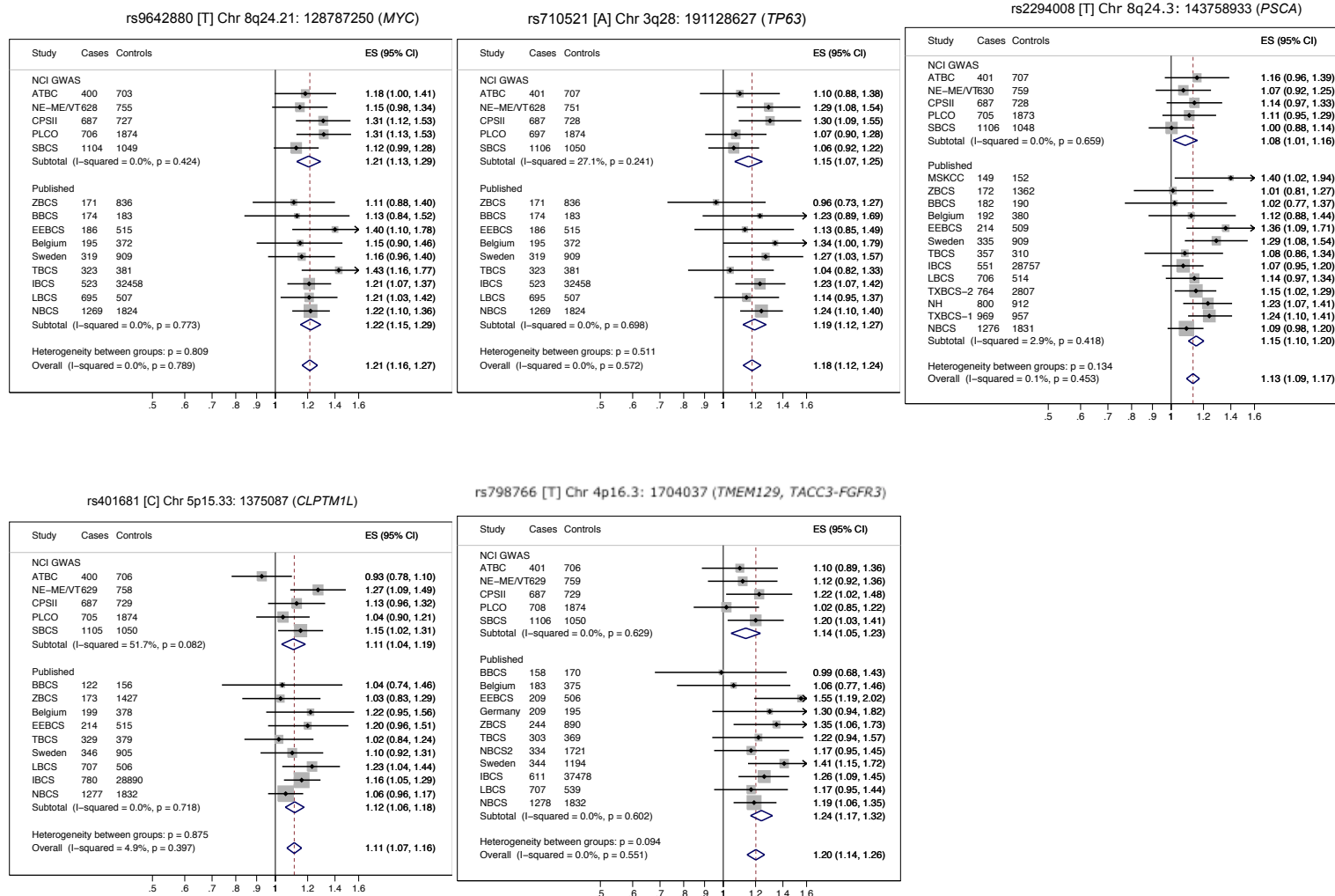
**Supplementary Figure 2. Manhattan plots of the  $P$  values in the stage I bladder cancer GWAS.** Association with bladder cancer was assessed using unconditional logistic regression adjusted for study, age, sex, smoking status and DNA source. The x axis represents chromosomal location and the y axis shows  $P$  values on a logarithmic scale.



### Supplementary Figure 3. Forest plot of previously reported genetic variants associated with urinary bladder cancer risk below genome-wide significance.

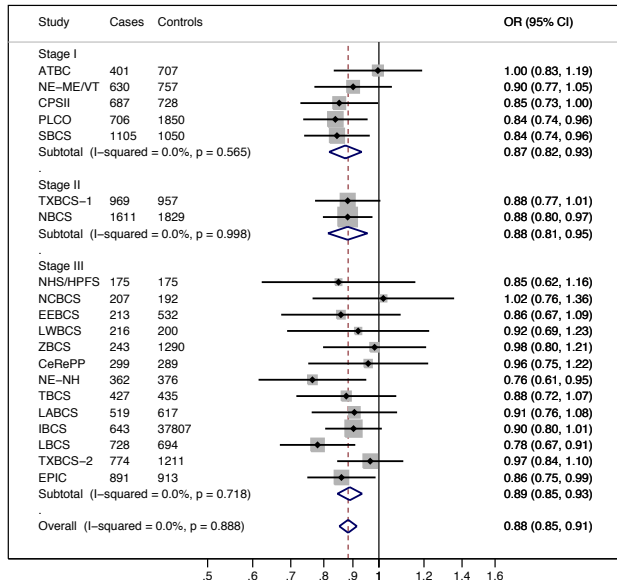
Squares represent the estimated odds ratio (OR) for each study, within each of the three replication phases. Lines indicate the 95% confidence interval (CI).

Diamonds represent the summary OR estimates and confidence intervals for the subgroups indicated. Study names corresponding to the acronyms shown in the plots and statistical methods are detailed in the Online Methods and Supplementary Table 1.

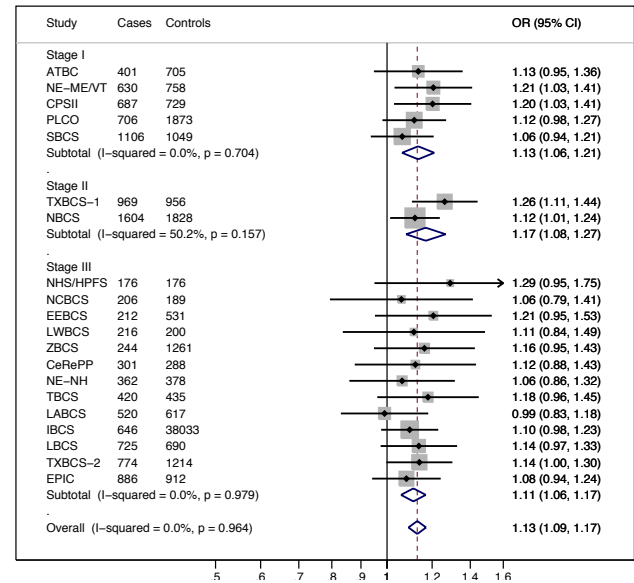


**Supplementary Figure 4. Forest plots of 4 SNPs genotyped in stages I, II and III.** Squares represent the estimated per-allele odds ratio (OR) for each study, within each of the 3 stages. Lines indicate the 95% confidence interval (CI). Diamonds represent the summary OR estimates and confidence intervals for the subgroups indicated. Study names corresponding to the acronyms shown in the plots and statistical methods are detailed in the **Online Methods** and **Supplementary Table 1**.

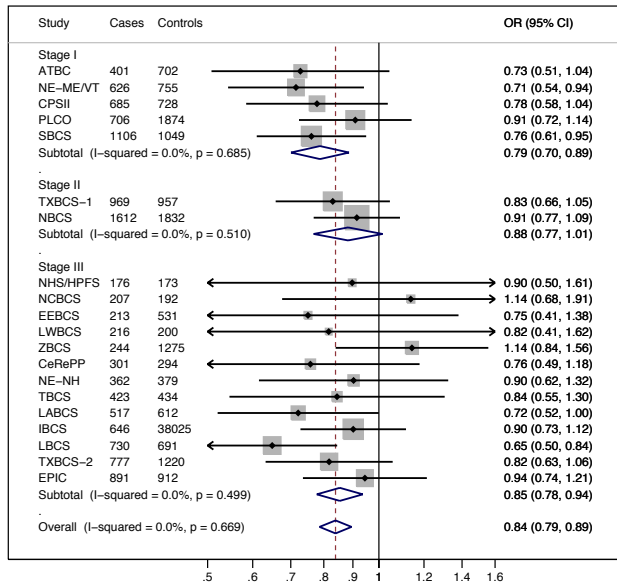
rs1014971 [C] Chr 22q13.1: 37662569 (*CBX6*, *APOBEC3A*)



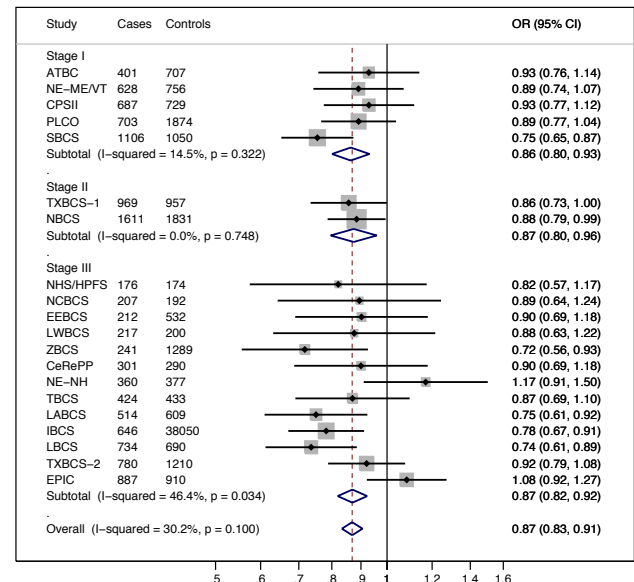
rs8102137 [C] Chr 19q12: 34988693 (*CCNE1*)



rs11892031 [C] Chr 2q37.1: 234230022 (*UGT1A* family)

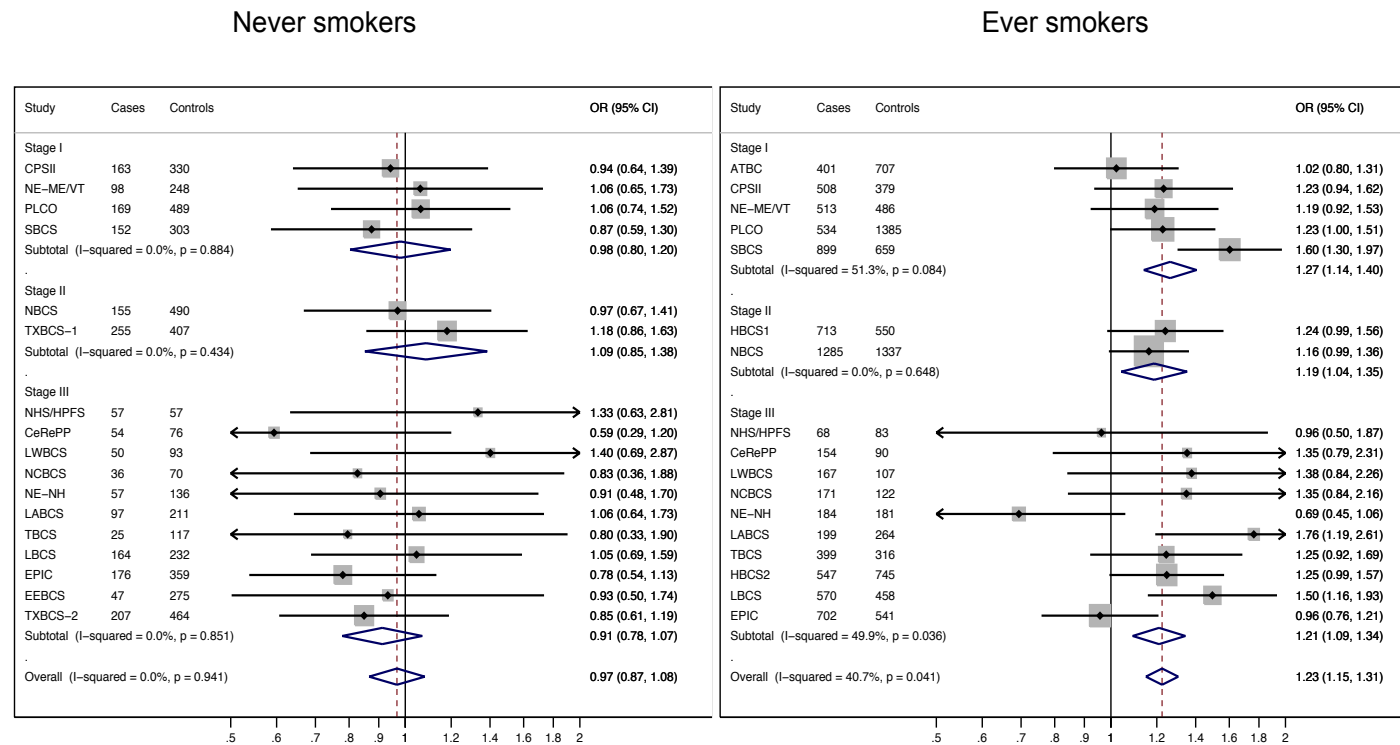


rs1495741 [G] Chr 8p22: 18317161 (*NAT2*)

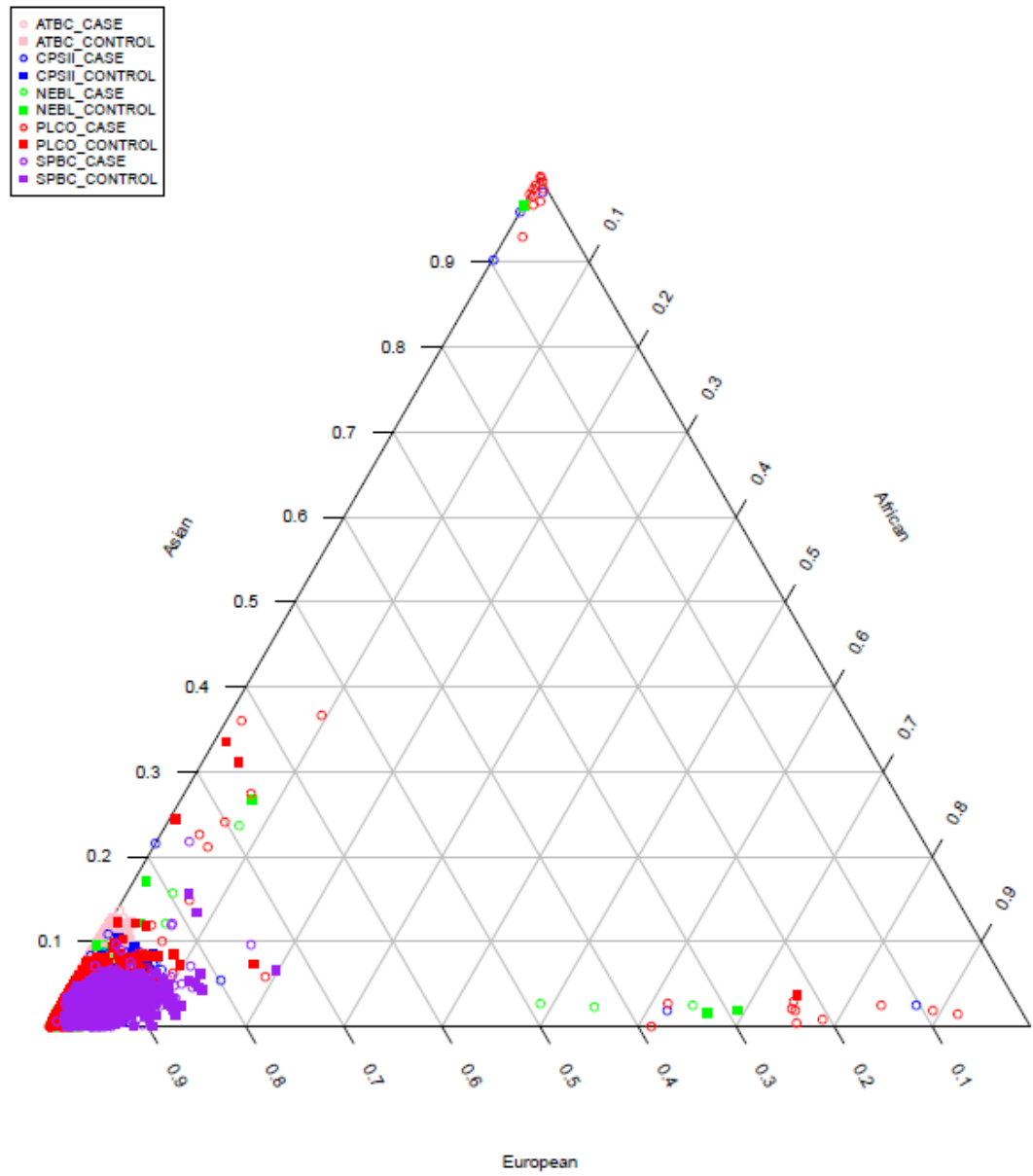


**Supplementary Figure 5. Forest plot of rs1495741 GG (*NAT2* slow acetylator<sup>26</sup>) compared to AG/AA (*NAT2* intermediate/rapid acetylators<sup>26</sup>) by cigarette smoking status.**

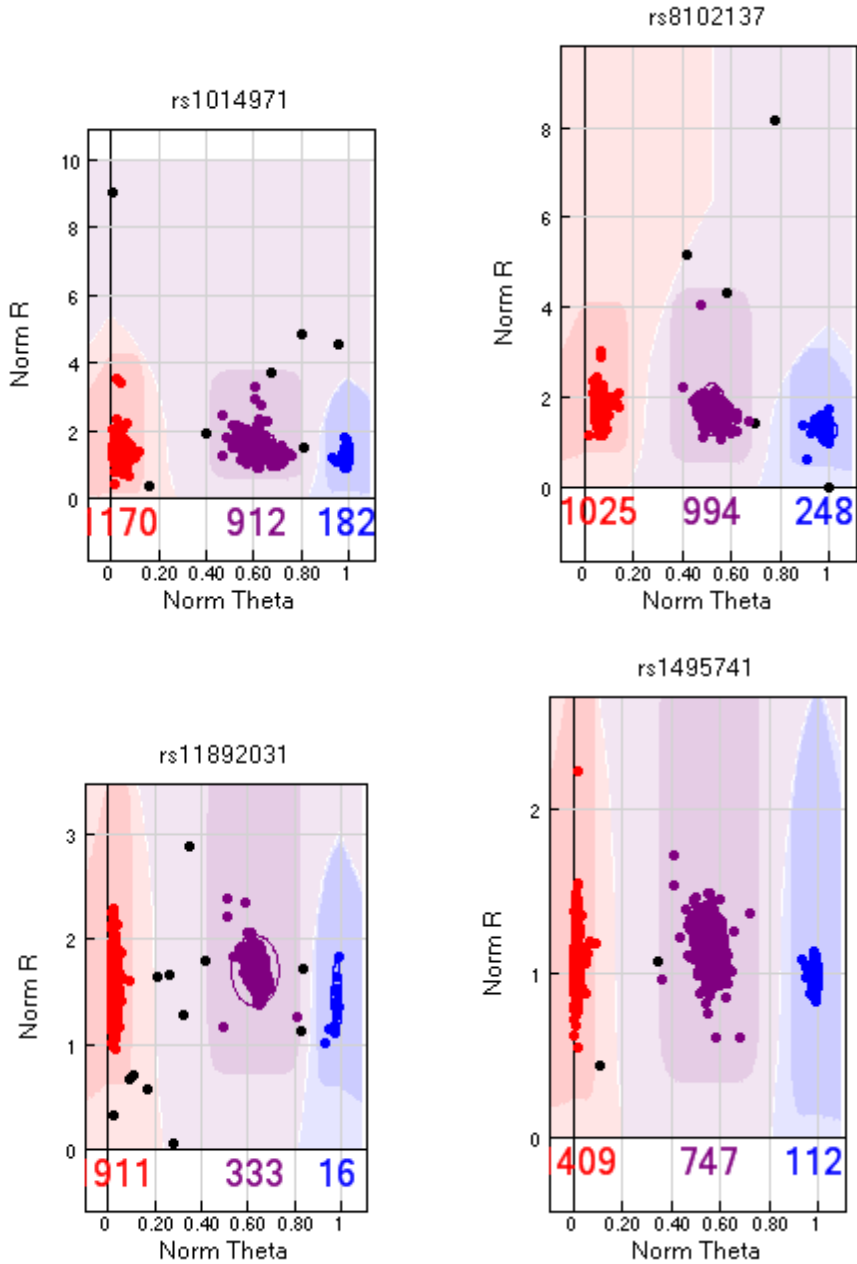
Squares represent the estimated odds ratio (OR) for each study, within each of the 3 stages. Lines indicate the 95% confidence interval (CI). Diamonds represent the summary OR estimates and confidence intervals for the subgroups indicated. Summary estimates are slightly different from those in Table 3 because of use of different methods (see Online Methods). Study names corresponding to the acronyms shown in the plots and statistical methods are detailed in the Online Methods and Supplementary Table 1.



**Supplementary Figure 6. Plot of admixture defined by analysis with STRUCTURE.**  
See Online Methods.



Supplementary Figure 7 Illumina genotype clustering for the 4 SNPs from Table 2.



**Supplementary Table 1. Characteristics of studies in multi-stage GWAS of urinary bladder cancer. Studies are sorted by number of cases within GWAS stages**

Stage	Study	Cases N	Controls N	Design, location	Source of cases	Source of controls	Cases			Controls			Genotyping platform
							Diagnosis age, mean (range)	Male, %	Smoking status Never, % Former, % Current %	Age, mean (range)	Male, %	Smoking status Never, % Former, % Current %	
I	Spanish Bladder Cancer Study (SBCS)	1106	1050	Hospital-based Case-control, Spain	Incident cases from 18 hospitals in five different areas in Spain diagnosed from 1998 to 2001, aged 21-80 years, with a blood or buccal cell sample.	Patients from case hospitals, individually matched to the cases on age at diagnosis/interview (within 5 year categories), gender, and hospital/region	66 (22-81)	88%	14% 41% 45%	65 (20-81)	88%	29% 37% 26%	Illumina Human1M-Duo
I	Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO)	708	1874	Prospective cohort, USA	All cases reported from 1993 to 2008 (includes N pre-enrollment cases)	Cohort members free of bladder cancer.,	67 (35-86)	81%	24% 60% 16%	64 (54-74)	81%	26% 44% 30%	Illumina Human 610-Quad
I	The American Cancer Society Cancer Prevention Study II Nutrition Cohort (CPS II)	687	730	Prospective cohort, USA	All cases verified by medical record, cancer registry, or National Death Index, diagnosed from 1992 to 2004 who donated a blood (1998-2001) or buccal sample (2000-2001)	Cohort members free of bladder cancer,	71 (54-87)	80%	24% 63% 12%	69 (52-89)	68%	45% 48% 4%	Illumina Human 610-Quad
I	New England Bladder Cancer Study (NEBCS-ME, VT)	630	759	Population-based case-control, USA (ME, VT)	Incident cases from cancer registries in Maine (ME) and Vermont (VT) diagnosed from 2001 to 2004, aged 30 to 79 years, with a buccal cell sample	Selected randomly from Department of Motor Vehicle records in each state (ages 30 to 64 yrs), and beneficiary records of the Centers for Medicare and Medicaid Services (ages 65 to 79 yrs.). Frequency matched to cases by state, gender and age of diagnosis /age at control selection.	65 (32-79)	79%	16% 52% 32%	64 (30-79)	76%	33% 49% 15%	Illumina Human 610-Quad



I	Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC)	401	707	Prospective cohort, Finland	All cases reported from 1985 to 2006, who donated a whole blood sample for DNA extraction in 1992.	Cohort members (all male and Caucasian) free of bladder cancer,	70 (52-88)	100%	0% 0% 100%	70 (60-82)	100%	0% 0% 100%	Illumina Human 610-Quad
IIa	Texas GWAS - (Texas Bladder Cancer Study 1 (TXBCS 1))	969	957	Hospital based, case control, US (TX)	Incident bladder cancer cases recruited from the University of Texas M.D. Anderson Cancer Center and Baylor College of Medicine between 1999 and 2007	Healthy individuals with no prior history of cancer (except non-melanoma skin cancer) recruited from Kelsey Seybold	65 (18-98)	81%	26% 50% 23%	65 (18-98)	81%	34% 50% 16%	Illumina Human 610
IIb	Nijmegen Bladder Cancer Study (NBCS)*	1,612 (1274 +338)	1,832	Population-based case-control, The Netherlands	All Caucasian cases diagnosed between 1995 and 2006 in one of 8 hospitals in the catchment area of the Comprehensive Cancer Center East and still alive at 1 August 2007.	Age and sex-stratified random sample of the Caucasian population of the municipality of Nijmegen, frequency age-matched to the cases. No history of cancer at the time of recruitment.	62 (25-93)	82%	10% 58% 22%	61 (27-79)	49%	27% 52% 21%	Illumina Human CNV370-duo
III	European Prospective Investigation Into Cancer and Nutrition Study (EPIC)	899	921	Prospective cohort, France, Italy, Spain, Greece, Germany, Sweden, Norway	All cases reported from 1992 to 2006.	Cohort members free of bladder cancer, matched to cases on sex, center, age, date of blood draw, alive at the time the case was diagnosed	58 (23-76)	73%	20% 36% 44%	58 (23-76)		30% 35% 35%	TaqMan
III	Texas Validation - (Texas Bladder Cancer Study 2 (TXBCS 2))	783	1229	Hospital based, case control, US (TX)	including incident bladder cancer cases from M.D. Anderson's ongoing case-control study and also included additional cases excluded from the tissue bank	Healthy individuals with no prior history of cancer (except non-melanoma skin cancer)	66 (18-98)		28% 53% 19%	65 (18-98)	80%	34% 51% 15%	Taqman
III	Leeds Bladder Cancer Study (LBCS)	756	782	Hospital-based case-control, UK	Cases from the County of West Yorkshire UK, diagnosed from 2002 to 2008	Population-based control series (n=242) plus hospital controls (n=540) from County of West Yorkshire UK	73 (39-99)	71%	23% 52% 25%	70 (18-96)	68%	34% 53% 14%	TaqMan
III	Iceland (IBCS)	646	38,064	Population-based case-control, Iceland	All prevalent cases available in 2001 and incident cases since 2001	Individuals from ongoing genome-wide association studies at deCODE	68 (26-94)	77%	Unknown	54 (20-105)	41%	Unknown	Illumina 370K

III	Los Angeles Bladder Cancer Study (LABCS)	540	643	Case-control	Incident cases from Los Angeles County Cancer Surveillance Program diagnosed from 1987 to April 1996, non-Asians aged 25 to 64 years, who donated a blood sample in 1992-96	Identified by a standard procedure defining a sequence of houses on specified neighborhood blocks.	54 (23-65)	79%	19% 39% 42%	54 (20-68)	80%	35% 43% 18%	TaqMan
III	Torino Bladder Cancer (TBCS)	427	435	Hospital-based Case-control, Torino, Italy	Cases from Torino, diagnosed from 1994 to 2007	Torino metropolitan area	57 (42-74)	100%	6% 48% 46%	57 (40-74)	100%	27% 46% 27%	TaqMan
III	New England Bladder Cancer Study (NEBCS-NH)	367	385	Population-based case-control, NH, USA	Incident cases from cancer registries in Maine (ME) and Vermont (VT) diagnosed from 2001 to 2004, aged 30 to 79 years, with a buccal cell sample	Selected randomly from Department of Motor Vehicle records in each state (ages 30 to 64 yrs), and beneficiary records of the Centers for Medicare and Medicaid Services (ages 65 to 79 yrs.). Frequency matched to cases by state, gender and age of diagnosis /age at control selection.	65 (31-79)	75%	16% 53% 31%	65 (30-79)	72%	36% 48% 14%	TaqMan
III	The CeRePP French bladder case-control (CeRePP )	301	300	Case-control, Paris, France	Cases from Academic centers from the University of Paris	Controls free of bladder cancer, matched to cases on race, sex and age	64 (30-91)	80%	26% 47% 27%	64 (27-92)	80%	46% 39% 15%	TaqMan
III	Zaragoza Bladder Cancer Study (ZBCS)	245	1,305	Hospital-based case-control, Zaragoza, Spain	Cases diagnosed at the University Hospital in Zaragoza from 2007 to 2009	Individuals attending the University Hospital in Zaragoza for diseases other than cancer between 2001 and 2007	66 (27-94)	87%	Unknown	51 (12-87)	50%	Unknown	TaqMan
III	Lutherstadt Wittenberg Bladder Cancer Study (LWBCS)	217	200	Hospital-based case-control, Germany	Cases from one hospital in Lutherstadt Wittenberg, enrolled from 1995 to 1999, first diagnosis from 1974 - 1999	Controls from one hospital in Lutherstadt Wittenberg enrolled from 2000 to 2005	67 (20-93)	86%	23% 48 % 29%	67 (29-91)	86%	47% 44% 10%	TaqMan
III	Eastern European Bladder Cancer Study (EEBCS)	214	533	Hospital-based case-control, Hungary, Romania and Slovakia	Cases diagnosed from 2002 to 2004	Hospital based controls recruited from 2002 to 2004 in Hungary, Romania and Slovakia	65 (36-90)	83%	23% 50% 28%	60 (28-83)	51%	52% 28% 20%	TaqMan
III	North Carolina Bladder Cancer Study (NCBCS)	207	198	Hospital-based Case-control, NC, USA	Cases from 1989 to 1992 at Duke and UNC	Frequency matched controls from 1989 to 1992 at Duke and UNC	61 (27-85)	77%	17% 58% 25%	63 (29-84)	81%	33% 47% 11%	TaqMan

III	Health Professionals Follow up Study (HPFS)	128	273	Prospective cohort, USA	All cases reported from 1986 to 2000, who donated a blood sample in 1993-1995.	Cohort members free of bladder cancer, matched to cases on race, age, date of blood draw, alive at the time the case was diagnosed, smoking status (never/former/current)	68 (48-86)	100%	31% 50% 19%	69 (49-86)	100%	33% 53% 14%	TaqMan
III	Nurse's Health Study (NHS)	71	218	Prospective cohort, USA	All cases reported from 1976 to 2000, who donated a blood sample in 1989-1990.	Cohort members free of bladder cancer, matched to cases on race, age, date of blood draw, alive at the time the case was diagnosed, smoking status (current/not current)	60 (37-79)	0%	28% 25% 46%	60 (37-79)	0%	31% 39% 30%	TaqManH

**Supplementary Table 2. Association of previously reported and novel SNPs with the risk for urinary bladder cancer, stratified by tumor grade and risk of progression (low risk (Ta and G1/2) and high risk (T1-T4 or G3/4)).** Results from polytomous logistic regression analyses adjusted by study. Grade analyses include SBCS, NEBCS-ME,VT, CPS II, ATBC, PLCO, NHS, LABCS and NEBCS-NH (the three later studies are included for novel SNPs only). Analyses by risk of progression include a subset of studies with information on both grade and stage, i.e. SBCS, NEBCS-ME,VT, CPSII, NEBCS-NH, LABCS (the two later studies are included for novel SNPs only).

Marker <sup>a</sup> , allele <sup>b</sup> , chr <sup>c</sup> , and gene <sup>d</sup>	Case-control status	N	Case-control			Case- only	
			OR	95% CI	P	P	
<b>Analyses by tumor grade (SBCS, NEBCS, CPSII, ATBC, PLCO, LABCS, NHS)</b>							
rs9642880 [T]	Controls	5,109					
Chr 8q24.21:	G1 cases	825	1.20	1.08	1.34	7.5E-04	
128787250	G2 cases	855	1.22	1.10	1.36	2.1E-04	
<i>MYC</i>	G3/4 cases	1,081	1.06	0.96	1.17	2.2E-01	0.031
rs710521 [A]	Controls	5,111					
Chr 3q28:	G1 cases	825	1.18	1.04	1.33	1.1E-02	
191128627	G2 cases	855	1.17	1.03	1.32	1.3E-02	
<i>TP63</i>	G3/4 cases	1,077	1.14	1.02	1.27	1.9E-02	0.689
rs2294008 [T]	Controls	5,116					
Chr 8q24.3:	G1 cases	826	1.08	0.97	1.21	1.5E-01	
143758933	G2 cases	855	1.08	0.98	1.21	1.3E-01	
<i>PSCA</i>	G3/4 cases	1,082	1.11	1.00	1.22	4.2E-02	0.812
rs401681 [C]	Controls	5,118					
Chr 5p15.33:	G1 cases	826	1.22	1.09	1.36	3.2E-04	
1375087	G2 cases	855	1.10	0.99	1.23	7.1E-02	
<i>CLPTM1L</i>	G3/4 cases	1,081	1.06	0.96	1.17	2.3E-01	0.047
rs798766 [T]	Controls	5,119					
Chr 4p16.3:	G1 cases	827	1.27	1.11	1.44	3.0E-04	

1704037	G2 cases	856	1.21	1.07	1.37	2.8E-03	
<i>TMEM129</i>	G3/4 cases	1,082	0.96	0.85	1.09	5.3E-01	0.00034
<i>TACC3-FGFR3</i>							
<i>GSTM1</i> del	Controls	3,568					
Chr 1p13.3	G1 cases	798	1.31	1.15	1.48	2.9E-05	
	G2 cases	833	1.55	1.36	1.76	2.8E-11	
	G3/4 cases	1,044	1.40	1.25	1.57	8.5E-09	0.537
rs1014971 [C]	Controls	6,145					
Chr 22q13.1:	G1 cases	1,153	0.87	0.79	0.96	5.2E-03	
<i>CBX6, APOBEC3A</i>	G2 cases	1,175	0.91	0.83	1.00	5.5E-02	
	G3/4 cases	1,336	0.82	0.75	0.90	4.0E-05	0.360
rs8102137 [C]	Controls	6,170					
Chr 19q12:	G1 cases	1,156	1.07	0.97	1.18	1.6E-01	
<i>CCNE1</i>	G2 cases	1,172	1.02	0.92	1.12	7.1E-01	
	G3/4 cases	1,338	1.23	1.13	1.35	4.6E-06	0.016
rs11892031 [C]	Controls	6,161					
Chr 2q37.1:	G1 cases	1,151	0.90	0.80	1.00	5.7E-02	
<i>UGT1A</i> cluster	G2 cases	1,168	0.86	0.77	0.97	9.9E-03	
	G3/4 cases	1,335	0.85	0.76	0.95	3.2E-03	0.523
rs1495741 [G]	Controls	6,157					
Chr 8p22:	G1 cases	1,154	0.75	0.62	0.90	1.6E-03	
<i>NAT2</i>	G2 cases	1,169	0.83	0.70	0.99	3.7E-02	
	G3/4 cases	1,334	0.72	0.60	0.85	1.6E-04	0.576
<b>Analyses by tumors with low risk and high risk of progression (SBCS, NEBCS, CPSII, LABCS)</b>							
rs9642880 [T]	Controls	2532					
Chr 8q24.21:	Low risk	1145	1.25	1.13	1.38	8.6E-06	
128787250	High risk	889	1.07	0.96	1.19	2.4E-01	0.008

*MYC*

rs710521 [A]	Controls	2530						
Chr 3q28:	Low risk	1146	1.21	1.08	1.36	1.0E-03		
191128627	High risk	889	1.15	1.02	1.31	2.3E-02	0.459	
<i>TP63</i>								
rs2294008 [T]	Controls	2536						
Chr 8q24.3:	Low risk	1147	1.05	0.95	1.16	3.2E-01		
143758933	High risk	890	1.12	1.01	1.25	3.9E-02	0.370	
<i>PSCA</i>								
rs401681 [C]	Controls	2538						
Chr 5p15.33:	Low risk	1146	1.23	1.11	1.36	7.5E-05		
1375087	High risk	890	1.09	0.98	1.22	1.1E-01	0.084	
<i>CLPTM1L</i>								
rs798766 [T]	Controls	2539						
Chr 4p16.3:	Low risk	1147	1.28	1.14	1.45	4.8E-05		
1704037	High risk	890	1.08	0.94	1.23	2.7E-01	0.019	
<i>TMEM129</i>								
<i>TACC3-FGFR3</i>								
<i>GSTM1 del</i>	Controls	2263						
Chr 1p13.3	Low risk	1122	1.42	1.26	1.59	4.3E-09		
	High risk	866	1.47	1.29	1.68	4.1E-09	0.647	
rs1014971 [C]	Controls	3529						
Chr 22q13.1:	Low risk	1652	0.91	0.84	1.00	4.5E-02		
<i>CBX6, APOBEC3A</i>	High risk	1181	0.81	0.73	0.90	6.6E-05	0.038	
rs8102137 [C]	Controls	3532						
Chr 19q12:	Low risk	1652	1.04	0.95	1.13	4.1E-01		

<i>CCNE1</i>	High risk	1183	1.15	1.04	1.27	5.4E-03	0.080
rs11892031 [C]	Controls	3524					
Chr 2q37.1:	Low risk	1647	0.78	0.67	0.92	2.8E-03	
<i>UGT1A cluster</i>	High risk	1181	0.74	0.62	0.89	1.6E-03	0.584
rs1495741 [G]	Controls	3522					
Chr 8p22:	Low risk	1644	0.86	0.78	0.95	4.1E-03	
<i>NAT2</i>	High risk	1181	0.84	0.74	0.94	2.5E-03	0.664

**Supplementary Table 3. Association of SNPs on Chromosomes 22q13.1, 19q12, 2q37.1 and 8p22 with the risk for urinary bladder cancer, under different genetic models and after adjustment for covariates.** Results from meta-analyses of genotype frequencies generated in 21 case-control and cohort studies.

rsnumber	Chr	Location	Gene	Cases	Controls	MAF <sup>f</sup>	Allelic OR (95%CI) <sup>g</sup>			P value <sup>h</sup>	Het <sup>i</sup> OR (95%CI)			P value	Hom <sup>i</sup> OR (95%CI)			P value	Dominant OR (95%CI)			P value	Recessive OR (95%CI)			P value	Adjusted* OR (95%CI)			P value
rs1014971 [C]	22q13.1	37662569	<i>CBX6, APOBEC3A</i>	11,806	52,609	0.38	0.88	0.85	0.91	8.4E-12	0.89	0.85	0.94	1.1E-05	0.77	0.71	0.83	1.5E-10	0.87	0.82	0.91	4.4E-09	0.82	0.76	0.88	1.9E-07	0.89	0.85	0.92	4.4E-10
rs8102137 [C]	19q12	34988693	<i>CCNE1</i>	11,791	52,822	0.33	1.13	1.09	1.17	1.7E-11	1.16	1.10	1.22	7.5E-09	1.25	1.15	1.35	5.8E-08	1.18	1.12	1.24	2.8E-11	1.15	1.07	1.24	1.6E-04	1.13	1.09	1.17	3.1E-10
rs11892031 [C]	2q37.1	234230022	<i>UGT1A</i>	11,808	52,835	0.08	0.84	0.79	0.89	1.0E-07	0.83	0.78	0.89	1.9E-07	0.78	0.57	1.08	1.4E-01	0.83	0.77	0.89	7.7E-08	0.81	0.58	1.11	1.9E-01	0.85	0.79	0.91	2.6E-06
rs1495741 [G]	8p22	18317161	<i>NAT2</i>	11,804	52,860	0.24	0.87	0.83	0.91	4.2E-11	0.86	0.81	0.90	5.3E-09	0.78	0.69	0.88	5.6E-05	0.85	0.81	0.89	8.1E-11	0.83	0.73	0.93	1.5E-03	0.87	0.83	0.91	1.9E-09



**Supplementary Table 4. Association of SNPs on chromosomes 22q13.1, 19q12, 2q37.1, and 8p22 with the risk for urinary bladder cancer, stratified by smoking status.** Results from logistic regression of genotype frequencies generated in 21 case-control and cohort studies, adjusted by study.

Smoking status	Cases			Controls			OR	95% CI		Pvalue
	Hom1	Het	Hom2	Hom1	Het	Hom2				
Previous SNPs										
rs9642880										
Never smoker	144	297	143	416	683	269	1.27	1.11	1.47	7.9E-04
Former smoker	433	789	370	610	948	365	1.21	1.10	1.33	1.2E-04
Current smoker	308	642	311	476	838	372	1.17	1.05	1.30	4.7E-03
Interaction former vs never							0.95	0.80	1.13	5.5E-01
Interaction current vs never							0.92	0.77	1.09	3.3E-01
rs710521										
Never smoker	34	210	333	106	510	753	1.16	0.99	1.36	6.7E-02
Former smoker	88	599	907	152	743	1025	1.17	1.04	1.30	6.3E-03
Current smoker	65	406	789	93	596	1001	1.13	0.99	1.28	6.3E-02
Interaction former vs never							1.00	0.83	1.22	9.7E-01
Interaction current vs never							0.97	0.79	1.19	7.8E-01
rs2294008										
Never smoker	165	283	135	404	662	304	1.07	0.93	1.23	3.3E-01
Former smoker	416	834	346	555	957	412	1.08	0.98	1.19	1.2E-01
Current smoker	285	698	279	455	870	365	1.12	1.01	1.26	3.6E-02
Interaction former vs never							1.01	0.85	1.19	9.2E-01
Interaction current vs never							1.05	0.88	1.25	5.9E-01
rs401681										
Never smoker	109	291	183	271	667	433	1.01	0.88	1.16	9.0E-01
Former smoker	272	764	559	386	970	571	1.17	1.06	1.29	1.9E-03
Current smoker	260	616	384	385	786	517	1.03	0.93	1.15	5.3E-01
Interaction former vs never							1.16	0.97	1.37	9.5E-02
Interaction current vs never							1.02	0.86	1.22	7.9E-01
rs798766										
Never smoker	359	201	24	899	418	54	1.17	0.98	1.39	8.1E-02
Former smoker	998	520	79	1240	604	83	1.09	0.97	1.22	1.7E-01
Current smoker	764	445	53	1073	549	67	1.13	0.99	1.28	7.7E-02
Interaction former vs never							0.93	0.76	1.15	5.0E-01
Interaction current vs never							0.97	0.78	1.20	7.5E-01
GSTM1 Del										
	Present	Null		Present	Null					
Never smoker	210	346		519	510		1.71	1.38	2.12	6.9E-07
Former smoker	564	961		622	653		1.62	1.39	1.89	4.7E-10
Current smoker	545	688		576	563		1.19	1.00	1.40	4.5E-02
Interaction former							0.95	0.73	1.23	6.9E-01
Interaction current							0.69	0.53	0.91	8.1E-03
Novel SNPs										
rs1014971										
Never smoker	884	868	213	1831	1981	540	0.91	0.84	0.99	2.5E-02

Former smoker	2354	2313	526	2381	2620	756	0.85	0.81	0.90	3.9E-08
Current smoker	1360	1300	323	1212	1348	347	0.92	0.85	1.00	3.9E-02
Interaction former vs never							0.93	0.85	1.03	1.8E-01
Interaction current vs never							1.01	0.90	1.13	8.7E-01
<b>rs8102137</b>										
Never smoker	800	931	234	2029	1837	492	1.15	1.06	1.25	5.2E-04
Former smoker	2108	2433	640	2603	2579	584	1.17	1.10	1.24	1.5E-07
Current smoker	1237	1375	363	1295	1290	320	1.11	1.03	1.21	6.7E-03
Interaction former vs never							1.01	0.92	1.12	8.0E-01
Interaction current vs never							0.97	0.87	1.08	5.7E-01
<b>rs11892031</b>										
Never smoker	1695	262	10	3663	674	123	0.69	0.61	0.79	1.3E-07
Former smoker	4509	669	24	4883	856	42	0.83	0.75	0.92	5.2E-04
Current smoker	2528	353	18	2438	415	22	0.81	0.71	0.94	4.4E-03
Interaction former vs never							1.20	1.01	1.43	3.3E-02
Interaction current vs never							1.17	0.96	1.43	1.1E-01
<b>rs1495741</b>										
Never smoker	1194	679	89	2675	1458	224	1.01	0.92	1.11	8.1E-01
Former smoker	3334	1643	219	3455	2045	260	0.87	0.81	0.93	4.3E-05
Current smoker	1938	928	117	1720	1038	149	0.82	0.75	0.90	1.6E-05
Interaction former vs never							0.86	0.77	0.96	9.8E-03
Interaction current vs never							0.81	0.71	0.92	1.4E-03

## **Supplementary Note**

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