Web Appendix 1: SUPPLEMENTARY METHODS

Shanghai study (present case-control study)

Haplotyping of the *ABO* SNPs rs8176746 and rs8176719 is shown in Table 1 in the paper. Two SNPs allow nine possible genotypes, of which six identify the common alleles of the four ABO blood group phenotypes. Only the one compound heterozygote genotype rs8176746 AC × rs8176719 GD ("D" = deletion) requires phase determination. The haplotypes AG and CD identify the common *B* and *O* alleles, respectively. The reverse haplotypes AD and CG correspond to alleles *O24*, *O41* or *O42*, and common *A* (*A101*), respectively (1). Four studies of *O* alleles in Chinese Han populations have not found any of these *O* alleles in more than 700 individuals (2-5), nor have they been seen in four studies totaling more than 1,300 Japanese or Korean individuals (6-9). In our data, of 1,415 individuals with unambiguous haplotypes (i.e., all except compound heterozygotes), aside from the common *ABO* allele types, we observed one case and one control with rs8176746 AA × rs8176719 GD genotype, giving haplotypes AG and AD, corresponding to alleles *B* and *O24*, *O41* or *O42*, respectively. We conclude that these *O* alleles are rare in the Han Chinese population and thus that essentially all of the compound heterozygote genotype individuals carry haplotypes AG and CD and therefore common alleles *B* and *O*.

Meta-analysis—Shanghai and Heidelberg Studies

Four studies involved participants in Shanghai, China (Wang et al. (10) was carried out in Guangzhou, in southern China, and Gong et al. (11) in Beijing). The study by Zhou and Li (12) recruited pancreatic cancer patients diagnosed in three Shanghai military-affiliated hospitals,

Changhai Hospital, Eastern Hepatobiliary Surgery Hospital, and Changzheng Hospital, from 6/1/1993-5/31/2001. Participants were resident in eastern China (Jiangsu, Zhejiang, Fujian, Jiangxi, Anhui and Shandong) and non-eastern China, not solely in Shanghai. Ben et al. (13) recruited patients diagnosed in Changhai Hospital from 1/1/2000-8/31/2009, and in the tertiary care Jiao Tong University Ruijin Hospital, from 1/1/2000-8/31/2008. Some overlap of cases may have occurred in these two studies, though the numbers are likely small. The PanScan study (14) involved 12 cohorts, one of which was carried out in urban Shanghai. This cohort recruited 140,000 Shanghai residents in 1996-2000 and followed them for about 8 years. There may be some case overlap with the two previous studies, though the Shanghai cohort comprises only a small fraction of the total PanScan cohort, thus the overlap is probably minor. Finally, the present study recruited pancreatic cancer patients resident in Shanghai diagnosed in the city's 37 major hospitals from 12/1/2006-1/31/2011. Some overlap with Ben et al. (13) is possible, as with the Shanghai cohort study subjects included in Wolpin et al. (14), though because the Shanghai cohort includes less than 2% of the general older population of Shanghai permanent residents, the overlap is again likely to be small. Given that all of the study overlaps are probably minimal, we have included all four studies in the meta-analysis.

Two studies involved substantially the same pancreatic cancer patients from the University of Heidelberg. Rizzato et al. (15) included surgical patients diagnosed from 1996-2009, and examined ABO genotype only through GWAS genotyping of rs505922 which distinguishes non-O from O blood group. Rahbari et al. (16) included surgical patients diagnosed from 2001-2008 but obtained ABO blood group information from existing medical records. Rizzato et al. (15) was limited to subjects with existing DNA samples and thus included fewer cases than Rahbari et al. (16). We have therefore chosen to include the Heidelberg

subjects only from the Rahbari et al. (16) study. Also included in the analysis of Rizzato et al. (15) were cases from Liverpool, England, and comparable English controls. Those subjects have been included in our meta-analysis.

REFERENCES FOR SUPPLEMENTARY METHODS

1. Patnaik SK, Helmberg W, Blumenfeld OO. BGMUT: NCBI dbRBC database of allelic variations of genes encoding antigens of blood group systems. Nucleic Acids Res 2012;40(1):D1023-D1029.
2. Roubinet F, Despiau S, Calafell F, et al. Evolution of the O alleles of the human ABO blood group gene. Transfusion 2004;44(5):707-715.
3 Yang BC, Zeng JQ, Yu Q, et al. Molecular polymorphism of O alleles in the Chinese Han population. Ann Clin Lab Sci 2007;37(1):71-74.
4. Yip SP. Single-tube multiplex PCR-SSCP analysis distinguishes 7 common ABO alleles and readily identifies new alleles. Blood 2000;95(4):1487-1492.
5. Zhu F, Tao S, Xu X, et al. Distribution of ABO blood group allele and identification of three novel alleles in the Chinese Han population. Vox Sang 2010;98(4):554-559.
6. Fukumori Y, Ohnoki S, Shibata H, et al. Suballeles of the ABO blood group system in a Japanese population. Hum Hered 1996;46(2):85-91.
7. Kang SH, Fukumori Y, Ohnoki S, et al. Distribution of ABO genotypes and allele frequencies in a Korean population. Jpn J Hum Genet 1997;42(2):331-335.
8. Kobayashi K, Iwasaki M, Anan K, et al. An analysis of polymorphism for the ABO blood group genes in a Japanese population based on polymerase chain reaction. Anthropol Sci

1999;107(2):109-121.

9. Ogasawara K, Yabe R, Uchikawa M, et al. Molecular genetic analysis of variant phenotypes of the ABO blood group system. Blood 1996;88(7):2732-2737.
10. Wang D-S, Chen D-L, Ren C, et al. ABO blood group, hepatitis B viral infection and risk of pancreatic cancer. Int J Cancer 2012;131:461-468.
11. Gong Y, Yang Y-S, Zhang X-M, et al. ABO blood type, diabetes and risk of gastrointestinal cancer in northern China. World J Gastroenterol 2012;18(6):563-569.
12. Zhou G-Z, Li Z-S. Clinical epidemiological research on pancreatic cancer: an analysis of 1027 cases. World Chin J Digestol 2005;13(1):55-60.
13. Ben Q, Wang K, Yuan Y, et al. Pancreatic cancer incidence and outcome in relation to ABO blood groups among Han Chinese patients: a case-control study. Int J Cancer 2011;128(5):1179-1186.
14. Wolpin BM, Kraft P, Gross M, et al. Pancreatic cancer risk and ABO blood group alleles: results from the pancreatic cancer cohort consortium. Cancer Res 2010;70(3):1015-1023.
15. Rizzato C, Campa D, Giese N, et al. Pancreatic cancer susceptibility loci and their role in survival. PLoS ONE 2011;6(11):e27921.
16. Rahbari NN, Bork U, Hinz U, et al. AB0 blood group and prognosis in patients with pancreatic cancer. BMC Cancer 2012;12:319. doi:10.1186/1471-2407-12-319.

Web Table 1. Characteristics of Case Patients With Pancreatic Cancer and Normal Population Control Subjects in Urban Shanghai, 2006-2011. Values are Numbers (%) of Participants Unless Indicated Otherwise.

Characteristic	All Cases (n=890)	All Controls (n=1067)	*P* value	Successfully Genotyped Cases (n=846)	Successfully Genotyped Controls (n=971)	*P* value
Age, years, mean (SD)	64.9 (9.6)	65.1 (9.9)	0.40	64.8 (9.7)	65.1 (10.0)	0.53
Gender						
Male	517 (58.1)	605 (56.7)	0.54	492 (58.2)	557 (57.4)	0.73
Female	373 (41.9)	462 (43.3)		354 (41.8)	414 (42.6)	
Education						
Primary school or lower	171 (19.2)	208 (19.5)		162 (19.1)	183 (18.8)	
Middle school	525 (59.0)	651 (61.0)	0.45	500 (59.1)	595 (61.3)	0.57
College or higher	194 (21.8)	208 (19.5)		184 (21.8)	193 (19.9)	
Regular alcohol use						
No	493 (55.4)	555 (52.0)	0.14	468 (55.3)	499 (51.4)	0.094
Yes	397 (44.6)	512 (48.0)		378 (44.7)	472 (48.6)	
Tobacco use						
Never	493 (55.4)	626 (58.7)		467 (55.2)	563 (58.0)	
Former	123 (13.8)	144 (13.5)	0.30	118 (13.9)	134 (13.8)	0.43
Current	274 (30.8)	297 (27.8)		261 (30.9)	274 (28.2)	

Web Table 2. Characteristics of Studies Included in Meta-analysis of ABO Blood Group and Risk of Pancreatic Cancer.

Reference[a]	Location	CagA Endemic[b]	O Cases	Non-O Cases	O Controls	Non-O Controls	Relative Weight (%)[c]	ABO Determination	Cancer Diagnosis	Type of Controls
Walther et al. 1956 (5)	London, UK	No	4	9	1,070	1,255	0.41	Seroagglutination[d]	Histopathologic	Local volunteer blood donors
Aird et al. 1960 (28)	11 UK centers	No	272	348	29,907	32,893	7.05	Seroagglutination[d]	Not Applicable	Local volunteer blood donors
Moniwa 1960 (29)	Sendai, Japan	Yes	20	45	6,769	14,430	1.76	Seroagglutination[d]	Surgical/Radiologic	Middle-school students
Macafee 1964 (19)	Belfast, UK	No	56	63	5,522	5,805	3.17	Seroagglutination[d]	Laparotomy/Autopsy	Belfast volunteer blood donors
Rai et al. 1972 (30)	Patiala, India	Yes	3	3	1,409	2,866	0.23	Seroagglutination	Histopathologic	Random population sample
Newell et al. 1974 (18) (blacks)	New Orleans, US	Yes	47	67	1,809	1,954	2.85	Seroagglutination[d]	Histopathologic/clinical	Friends/relatives of general hospital patients
Newell et al. 1974 (18) (whites)	New Orleans, US	No	13	10	585	647	0.80	Seroagglutination[d]	Histopathologic/clinical	Friends/relatives of general hospital patients
Mikhailichenko 1976 (31)	Donetsk, Ukraine	No	130	445	955	1,816	5.78	Seroagglutination[d]	Histopathologic	Paid local volunteer blood donors
Annese et al. 1990 (32)	Rome, Italy	No	79	145	3,519	3,801	4.41	Seroagglutination[d]	Histopathologic	Local volunteer blood donors
Vioque and Walker 1991 (33)	US, Scotland, Israel, West Germany, New Zealand, Canada	No	32	56	104	119	2.12	Seroagglutination[d]	Histopathologic/clinical	Hospital patients with non ABO-related diseases, matched on age, sex, race, hospital
Guleria et al. 2005 (34)	Punjab, India	Yes	2	6	48	112	0.22	Seroagglutination[d]	Histopathologic	Volunteer blood donors
Zhou and Li 2005 (25)	Shanghai Military Hospitals, China	Yes	215	476	354	845	5.94	Seroagglutination[d]	Hospital records	Non-cancer outpatients frequency matched on gender, dates of birth and hospital visit, region of residence, marriage status
Greer et al. 2010 (35)	Pittsburgh, US	No	88	186	311,795	397,047	4.84	Seroagglutination	Histopathologic/clinical	Local volunteer blood donors over 30 years of age
Iodice et al. 2010 (11,12)	Milan, Italy	No	26	64	7,099	8,156	2.25	Seroagglutination[d]	Histopathologic	All non-pancreatic cancers, adjusted

										to the "AVIS" distribution of Italian ABO blood groups
Low et al. 2010 (36)	Tokyo and Osaka, Japan	Yes	266	725	1,574	3,635	7.22	rs505922	Histopathologic/clinical	Club and staff volunteers, plus biobank subjects with various non-cancer, non-diabetes diseases
Risch et al. 2010 (9)	Connecticut, US	No	147	214	315	375	4.71	Seroagglutination	Histopathologic/clinical	Population, frequency matched on age, gender
Wolpin et al. 2010 (27)	Mixed US, Europe, Shanghai	No	511	1,023	657	926	8.11	rs505922, rs8176746	Not stated	Non-cancer cohort members matched on age, gender, race/ethnicity, etc.
Ben et al. 2011 (26)	Shanghai Military and other Hospitals, China	Yes	409	1,022	479	970	6.98	Seroagglutination[d]	Histopathologic	Non-cancer acute-care patients with traumatic, eye, surgical, and other admissions, non-tobacco and non-alcohol related, matched on age, sex
Nakao et al. 2011 (7)	Nagoya, Japan	Yes	38	147	428	1,037	4.40	rs8176719, rs8176746	Histopathologic/clinical	Non-cancer hospital outpatients
Rizzato et al. 2011 (15)[e]	Liverpool, England	No	38	71	60	76	1.77	rs505922	Surgical resection	EPIC Study non-cancer England cohort members
Engin et al. 2012 (37)	Zonguldak, Turkey	Yes	39	93	111	239	2.43	Seroagglutination[d]	Histopathologic/clinical	Non-cancer hospital outpatients
Gong et al. 2012 (24)	PLA Hospital, Beijing, China	Yes	183	479	232	513	4.44	Seroagglutination	Histopathologic/clinical	Non-cancer hospital outpatients
Rahbari et al. 2012 (38)[e]	Heidelberg, Germany	No	196	431	4,972	8,072	6.69	Seroagglutination[d]	Surgical resection	Surgery patients without pancreatic cancer
Wang et al. 2012 (23)	Guangzhou, China	Yes	228	399	300	411	5.50	Seroagglutination	Histopathologic	Hospital non-cancer patients with gallbladder polyps, polycystic kidney, breast fibroadenoma, uterine fibroids, etc., matched on age, gender
Risch et al. (this study)	Shanghai, China	Yes	221	625	308	663	5.91	rs8176719,	Histopathologic	Population, frequency matched on

	rs8176746	age, gender

[a] Reference numbers are for the publications as listed in the References section of the paper.

[b] Populations with high frequency of colonization by CagA-positive *Helicobacter pylori* strains. See text for additional details.

[c] Random effects meta-analysis relative weight for studies comparing non-O to O blood groups.

[d] Presumed seroagglutination, though not mentioned in original article.

[e] The report by Rizzato et al. (15) included cases from both Liverpool and Heidelberg, genotyped only for rs505922. The study by Rahbari et al. (38) involved a larger group of the Heidelberg cases having major overlap with the German cases in Rizzato et al. (15), but included full ABO blood group determination. See text and Web Appendix 1 for additional details.

Web Table 3. Odds-Ratio Changes With Individual Studies Removed, Studies Included in Meta-analysis of ABO Blood Group and Risk of Pancreatic Cancer.

Analysis	A OR	A 95% CI	B OR	B 95% CI	AB OR	AB 95% CI	Non-O OR	Non-O 95% CI
Complete Analysis, All Studies	**1.400**	**1.282, 1.528**	**1.191**	**1.050, 1.351**	**1.288**	**1.098, 1.510**	**1.309**	**1.211, 1.414**
Minimum	1.360		1.157		1.243		1.286	
Min. Δ% from complete analysis	-2.87%		-2.87%		-3.51%		-1.74%	
Maximum	1.426		1.245		1.338		1.337	
Max. Δ% from complete analysis	1.88%		4.49%		3.92%		2.14%	
Complete Analysis, non-Endemic	**1.424**	**1.240, 1.635**	**1.379**	**1.160, 1.640**	**1.515**	**1.241, 1.849**	**1.407**	**1.261, 1.569**
Minimum	1.357		1.324		1.455		1.370	
Min. Δ% from complete analysis	-4.69%		-4.01%		-3.98%		-2.63%	
Maximum	1.476		1.457		1.607		1.463	
Max. Δ% from complete analysis	3.62%		5.66%		6.06%		4.03%	
Complete Analysis, Endemic	**1.361**	**1.237, 1.498**	**1.047**	**0.918, 1.195**	**1.125**	**0.916, 1.382**	**1.199**	**1.106, 1.301**
Minimum	1.320		1.016		1.035		1.177	
Min. Δ% from complete analysis	-3.02%		-2.99%		-8.01%		-1.85%	
Maximum	1.417		1.117		1.177		1.245	
Max. Δ% from complete analysis	4.13%		6.68%		4.64%		3.84%	

Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval; Δ, change in value.

Web Table 4. HW *P* Values and ABO Phenotype Frequencies by Ethnicity, Studies Included in Meta-analysis of ABO Blood Group and Risk of Pancreatic Cancer.

Reference[a]	Location	Cases HW *P* value	Controls HW *P* value	CagA En-demic[b]	Comparison Population	Cases				Controls			
						A %	B %	AB %	O %	A %	B %	AB %	O %
Walther et al. 1956 (5)	London, UK	0.560	0.543	No	White-European	61.5%	0.0%	7.7%	30.8%	44.0%	6.8%	3.1%	46.0%
Aird et al. 1960 (28)	11 UK centers	0.718	0.679	No	White-European	46.0%	7.6%	2.6%	43.9%	40.5%	8.9%	3.0%	47.6%
Moniwa 1960 (29)	Sendai, Japan	0.914	0.304	Yes	Japan	44.6%	16.9%	7.7%	30.8%	36.7%	22.8%	8.6%	31.9%
Macafee 1964 (19)	Belfast, UK	NA[c]	NA[c]	No	White-European	30.3%	22.7%	0.0%	47.1%	37.0%	14.2%	0.0%	48.8%
Rai et al. 1972 (30)	Patiala, India	0.773	0.476	Yes	India	16.7%	33.3%	0.0%	50.0%	21.8%	37.3%	7.9%	33.0%
Newell et al. 1974 (blacks) (18)	New Orleans, US	0.657	0.942	Yes	Black-American	30.7%	23.7%	4.4%	41.2%	25.0%	22.2%	4.7%	48.1%
Newell et al. 1974 (whites) (18)	New Orleans, US	0.279	0.459	No	White-European	34.8%	0.0%	8.7%	56.5%	40.0%	8.6%	3.9%	47.5%
Mikhailichenko 1976 (31)	Donetsk, Ukraine	0.765	0.362	No	White-European	50.3%	16.7%	10.4%	22.6%	36.4%	20.0%	9.1%	34.5%
Annese et al. 1990 (32)	Rome, Italy	0.586	0.840	No	White-European	41.1%	18.3%	5.4%	35.3%	36.9%	11.4%	3.6%	48.1%
Vioque and Walker 1991 (33)	US, Scotland, Israel, West Germany, New Zealand, Canada	0.856	0.554	No	White-European	52.3%	8.0%	3.4%	36.4%	44.4%	5.4%	3.6%	46.6%
Guleria et al. 2005 (34)	Punjab, India	0.588	0.816	Yes	India	25.0%	50.0%	0.0%	25.0%	13.8%	47.5%	8.8%	30.0%
Zhou and Li 2005 (25)	Shanghai Military Hospitals, China	0.589	0.613	Yes	China	33.7%	24.3%	10.9%	31.1%	28.9%	30.3%	11.3%	29.5%
Greer et al. 2010 (35)	Pittsburgh, US	0.766	0.009	No	White-European	47.8%	13.9%	6.2%	32.1%	39.1%	12.3%	4.6%	44.0%
Iodice et al. 2010 (11,12)	Milan, Italy	0.557	0.505	No	White-European	52.2%	14.4%	4.4%	28.9%	41.6%	8.9%	3.0%	46.5%
Risch et al. 2010 (9)	Connecticut, US	0.556	0.428	No	White-European	41.0%	11.9%	6.4%	40.7%	40.0%	11.7%	2.6%	45.7%
Wolpin et al. 2010 (27)	Mixed US, Europe, Shanghai	0.592	0.502	No	White-European	45.6%	14.7%	6.3%	33.3%	40.6%	12.3%	5.6%	41.5%
Ben et al. 2011 (26)	Shanghai Military and other Hospitals, China	0.841	0.834	Yes	China	35.4%	25.1%	10.9%	28.6%	29.5%	28.2%	9.3%	33.1%
Nakao et al. 2011 (7)	Nagoya, Japan	0.732	0.819	Yes	Japan	45.9%	21.6%	11.9%	20.5%	39.0%	22.1%	9.6%	29.2%
Wang et al. 2012 (23)	Guangzhou, China	0.286	0.372	Yes	China	32.1%	26.5%	5.1%	36.4%	25.6%	24.2%	8.0%	42.2%
Risch et al. (this study)	Shanghai, China	0.654	0.411	Yes	China	37.7%	25.5%	10.6%	26.1%	28.5%	28.4%	11.3%	31.7%
Rahbari et al. (38)	Heidelberg, Germany	0.453	0.780	No	White-European	52.3%	11.6%	4.8%	31.3%	44.6%	12.1%	5.2%	38.1%
Engin et al. 2012 (37)	Zonguldak, Turkey	0.518	0.509	Yes	Turkey	51.5%	14.4%	4.5%	29.5%	37.1%	20.0%	11.1%	31.7%

Gong et al. 2012 (24)	PLA Hospital, Beijing, China	0.942	0.871	Yes	China	27.9%	33.4%	11.0%	27.6%	32.3%	27.1%	9.4%	31.1%
					Totals:								
					White-European	46.6%	13.4%	5.8%	34.2%	39.3%	12.0%	4.4%	44.3%
					China	33.9%	26.5%	10.0%	29.5%	29.0%	28.0%	10.0%	33.0%
					Japan	45.6%	20.4%	10.8%	23.2%	36.9%	22.7%	8.6%	31.8%
					India	21.4%	42.9%	0.0%	35.7%	21.6%	37.6%	8.0%	32.9%
					Turkey	51.5%	14.4%	4.5%	29.5%	37.1%	20.0%	11.1%	31.7%
					Black-American	30.7%	23.7%	4.4%	41.2%	25.0%	22.2%	4.7%	48.1%
					Bloodbook (62) Frequencies:								
					White-European					40%	11%	4%	45%
					China					27%	32%	13%	29%
					Japan					38%	22%	10%	30%
					India					22%	33%	7%	37%
					Turkey					34%	18%	6%	43%
					Black-American					27%	20%	4%	49%

Abbreviations: CagA, cytoxin-associated gene A of *Helicobacter pylori*; HW, Hardy-Weinberg; NA, not applicable.
[a] Reference numbers are for the publications as listed in the References section of the paper.
[b] CagA-positive *H. pylori* endemic populations discussed in text.
[c] Small numbers of AB subjects combined into B group, invalidating HW calculation.