Appendix Table 8. Genotype Screening Studies in Various Populations*

Study, Year (Reference)	Population	C282Y:C282Y Frequency	TS† (Initial Test Unless Stated)	SF†	Iron Overload	Diabetes	Elevated Liver Enzyme Levels	Hepatic Fibrosis or Cirrhosis	Quality
Health clinics									
Beutler et al., 2002a (32); Beutler et al., 2002b (48), Beutler et al., 2000 (49), Waalen et al., 2002 (50)	KP San Diego *n* = 41 038 Mean age, 57 y Non-Hispanic white persons: 77% 140 C282YY homozygotes from KP San Diego screening study	152 of 41 038 3.7/1000	>0.50: men, 75%; women, 40% Elevated overall: 57% After exclusion of frequent blood donors: 76% men, 41% women	>250 μg/L: men, 76% >200 μg/L: women, 54% Elevated overall: 65% After exclusion of frequent blood donors: men; 77%; women, 56%	NR 102 eligible (not previously treated) 54 completed treatment 13 of 54 (24%) had > 5 g iron removed	C282YY: 5.6% Non-C282YY: 8.4%	AST level > 40 U/L C282YY: 8.2% Non-C282YY: 3.8%	NR	Good—excellent controls. Excluded previously identified C282Y homozygotes in determining prevalence of genotype and disease expression.
Deugnier et al., 2002 (51)	Brittany, France *n* = 9396 35.8% men (deliberately weighted to include younger men)	54 of 9396 5.7/1000	>0.55: men, 80% >0.50: women, 41% Elevated overall: 48%	>280 μg/L: men, 70% >130 μg/L: women, 33% Elevated overall: 40%	NR	Men C282YY: 0% Non-C282YY: 0.8% Women C282YY: 2.3% Non-C282YY: 0.9%	Men ALT level > 70 U/L C282YY: 10% Non-C282YY: 5% Women ALT level > 35 U/L C282YY: 5% Non-C282YY: 5%	Fair—not strictly population-based because overselected. Inclusion of younger men could minimize disease expression.	
Population screening									
Olynyk et al., 1999 (52)	Busselton, Australia *n* = 3011, randomly selected 50% men Predominately white persons Age, 20–79 y	16 of 3011 5.3/1000 4 of 16 previously diagnosed 12 new C282YY (5.3/1000)	>0.45: 93.8% 2nd measurement > 0.45: 93.8%	>300 μg/L: 50% >300 μg/L in untreated persons: 58.3%	Liver biopsy: 7 of 12 (58%) HII > 1.9: 4 of 7 (57.1%) of those having biopsy 33% of C282YY homozygotes HIC> 20 μmol/g dry: 100% of those biopsied (7/7) 58% C282YY	NR	NR	Fibrosis: 29% of persons having biopsy (2 of 7) Cirrhosis: 14% of persons having biopsy (1 of 7) (also had history of alcohol intake >60 g/d) No controls	Good—considered confounders for liver disease. Excluded previously identified C282Y homozygotes.
Voter rolls									
Burt et al., 1998 (53)	*n* = 1064 voters in New Zealand 39.8% men Mean age: 50 y	5 of 1064 4.7/1000	> 0.55: 100%	Second measurement: >300 μg/L: men, 100% >160 μg/L: women, 50% Elevated overall: 60%	Liver biopsy: 60% HII > 1.9: 3 of 3 (100%) selected C282YY homozygotes 3 of 5 (60%) all C282YY homozygotes	NR	NR	NR	Fair—did not exclude previously identified C282Y homozygotes, so estimates of screening prevalence are less accurate. Did not consider confounders for liver disease.
Employment screening									
Distante et al., 1999 (54)	*n* = 505 hospital employees in Oslo, Norway 79% women Mean age: 38 y	2 of 505 4/1000	>0.50: 100%	>200 μg/L: 100%	TP in 50%: 5.2 g of iron removed 1 of 1 with IO by TP HIC: 47 μmol/g Biopsy: 0 of 1 IO: 50% selected C282YY homozygotes Total IO: 100%	NR	NR	NR	Good
McDonnell et al., 1999 (55)	*n* = 1450 HMO employees in Springfield, Missouri 83% women 98% white Mean age: 41 y	6 of 1450 4.1/1000	>0.50: women, 2 >0.60: men, 2 Elevated overall: 67% of C282YY homozygotes	>95th percentile for age and sex: 50% of C282YY homozygotes	HII = 2.2: 1 of 1 by biopsy 1 of 2 by TP 2 of 3 (67%) of selected C282YY homozygotes 2 of 6 (33%) of all C282YY homozygotes	NR	NR	Fibrosis: 0 of 1 (0%)	Fair/good—some inconsistencies between data reported in text and figures/tables. Did not consider confounders for liver disease.

Appendix Table 8—**Continued**

Study, Year (Reference)	Population	C282Y:C282Y Frequency	TS† (Initial Test Unless Stated)	SF†	Iron Overload	Diabetes	Elevated Liver Enzyme Levels	Hepatic Fibrosis or Cirrhosis	Quality
Delatycki et al., 2005 (56)	*n* = 11 307 workplace employees in Australia 47% men 63% northern European	51 of 11 307 4 previously diagnosed 4.5/1000 47 new C282YY homozygotes	Criteria for elevation not given; 65% had "elevated" values	NR	6 recommended for testing; 4 had biopsy	NR	NR	Fibrosis: 2 of 4 had biopsy 50% of selected C282YY homozygotes 4.3% (2 of 47) of all C282YY homozygotes	Fair—did not exclude previously identified C282Y homozygotes, so estimates of screening prevalence are less accurate. Did not consider confounders for liver disease. Unclear criteria for iron overload.
Family studies									
Barton et al., 1999 (57)	*n* = 150 relatives of 61 probands in Alabama 52% women 100% white Mean age: 46 y 1 patient < 18 y was C282YY homozygote	25/149 161/1000	> 0.50: women, 2 > 0.60: men, 2 Overall: 87.5%	> 300 μg/L (men) > 200 μg/L (women) Elevated overall: 96%	NR	16%	NR	2/25 (8%)	Fair—unable to determine how many tested family members were spouses.
Powell et al., 2006 (58)	401 C282YY first-degree relatives of 259 probands with proven C282YY-associated HC 50% female Mean age: Men, 38 y; Women, 44 y	ND	Men: Mean, 72% (range, 12%–100%) Women: Mean, 64% (range, 7%–100%)	Men: Median, 700 μg/L Women: Median, 300 μg/L	Hepatic stain ≥ 3+: Men Selected C282YY homozygotes: 82 of 111 (74%) All C282YY homozygotes: 82 of 200 (41%) Women Selected C282YY homozygotes: 46 of 74 (62%) All C282YY homozygotes: 46 of 201 (23%)	Men: 4 of 200 (2%) Women: 7 of 201 (3%)	Men: 24% Women: 7%	Fibrosis or cirrhosis: Men Selected C282YY homozygotes: 32 of 111 (29%) All C282YY homozygotes: 32 of 200 (16%) Women Selected C282YY homozygotes: 5 of 74 (7%) All C282YY homozygotes: 5 of 201 (2%)	Fair—large sample with reasonably well-specified diagnostic and case criteria. Sample clearly was selected, but no information provided to judge how selective. May fairly represent family screening-detected, but no information given on number tested or whether some were omitted. Did not represent "asymptomatic" general population screening because all persons who underwent genotyping had some initial elevation in serum iron levels. Very selective group for treatment responsiveness; all those with alcohol intake were omitted.

* ALT = alanine aminotransferase; AST = aspartate aminotransferase; C282YY = C282Y/C282Y; HIC = hepatic iron content; HII = hepatic iron index; HMO = health maintenance organization; IO = iron overload; KP = Kaiser Permanente; ND = not determined; NR = not recorded; SF = serum ferritin; TP = therapeutic phlebotomy.
† In homozygotes.